Institutionen för klinisk forskning och utbildning, Södersjukhuset, Karolinska Institutet

Drug-related problems: nurses role and responsibility

AKADEMISK AVHANDLING
Som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentligen försvaras I Södersjukhusets aula,

Fredagen den 28 maj 2010, kl 9.00

Av
Monica Bergqvist
Leg. Sjuksköterska

Huvudhandledare
Med.dr. Johanna Ulfvarson
Institutionen för neurobiologi
vårdvetenskap och samhälle,
Karolinska Institutet

Bihandledare
Docent Eva Andersén Karlsson
Institutionen för klinisk forskning
och utbildning, Södersjukhuset,
Karolinska Institutet

Fakultetsopponent:
Professor Karin Kjellgren
Göteborgs universitet,
Institutionen för vårdvetenskap
och hälsa

Betygsnämnd:
Professor Gun Nordström
Karlstads Universitet, Fakulteten
för samhälls- och livsvetenskaper
Avdelningen för omvårdnad

Docent Georgios Panagiotidis
Karolinska Institutet Institutionen
för laboratoriemedicin

Docent Olle Broström
Institutionen för klinisk forskning
och utbildning, Södersjukhuset,
Karolinska Institutet

From **Department of Clinical Science and Education, Södersjukhuset,**
Karolinska Institutet, Stockholm, Sweden

DRUG-RELATED PROBLEMS:
NURSES ROLE AND RESPONSIBILITY

Monica Bergqvist

Stockholm 2010

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ISBN 978-91-7409-850-1

ABSTRACT

Drug-related problems (DRPs) are common and can cause serious adverse effects, even death. The elderly are an exposed group having a higher prevalence of DRPs.
As nurses are involved in all steps of the medication process they are particularly well positioned to detect, prevent and alert for DRPs. Nurses are usually situated in the frontline when medication errors occur and are thus exposed to being responsible for such. The aims of this thesis was to evaluate if nurses can improve the quality of drug therapy, and to investigate what types of medication error most frequently reported and which factors most frequently preceded an error.

Study 1 was designed to determine whether medication reviews made by a clinical pharmacologist and a nurse could affect rates of re-hospitalisation and/or death in hospitalized patients. DRPs detected and judged to be of clinical relevance resulted in written advice to the physician in charge of the patient. In 150 patients, 299 DRPs were found which resulted in 106 advice´s to the physicians. After 6 months re-admission and death was measured and compared with patients in a control group receiving usual care, and there was no statistically significant difference in the two groups.

In ***Study II*** 15 nurses conducted structured, nurse-led medication reviews after a 1-day education in clinical pharmacology. The nurses identified 59 clinically relevant DRPs in 80 patients, not detected by the usual care. Out of these, 37 DRPs resulted in an intervention such as dose reduction or withdrawal of one or more drugs.

Study III was designed to determine whether medication reviews made by nurses could improve the quality of the drug therapy of elderly hospitalized patients. In 250 patient, 86 clinically significant DRPs were found not detected by the usual care. After 3 months re-admission and inappropriate drug use were measured and compared with patients in a control group receiving usual care, and there was no statistically significant difference in the two groups.

In ***studyIV*** a content analysis was used to develop a tentative classification model of medication errors and contributing factors. The findings showed a high level of complexity with system and human factors interacting.

In ***study V*** 585 errors made by nurses were analyzed. Inexperienced nurses and male nurses were reported for a higher number of medication errors than their number in Sweden would lead one to expect. “Lack of knowledge” was a contributing factor more often associated with inexperienced nurses. “Practice beyond scope of practice” was more often associated with male nurses.

Conclusion, DRPs are common. By using nurse-led medication review DRPs not detected by the usual care could be found. Medication errors made by nurses are a result of interrelated human and system factors. Experienced nurses can be a valuable resource for improving the quality of drug-treatment and for ensuring patient safety.

Populärvetenskaplig sammanfattning

Läkemedel räddar och förlänger liv samt lindrar lidande, men läkemedelsbehandling innebär också en risk för läkemedelsrelaterade problem (LRP). LRP är olika problem relaterade till läkemedelsbehandling, allt ifrån att inte kunna svälja den förskrivna tabletten till allvarliga läkemedelsbiverkningar. Äldre personer är känsligare för läkemedel och använder ofta fler läkemedel än yngre och drabbas därmed lättare. Upp till 30 % av alla sjukhusinläggningar av äldre personer är relaterade till läkemedel. En läkemedelsgenomgång är en systematisk genomgång för att optimera patientens läkemedelsbehandling och utförs ofta i samarbete med klinisk farmakolog eller apotekare. Sjuksköterskor är involverade i alla delar av läkemedelshanteringen, har farmakologisk kunskap och arbetar nära patienten under dygnets alla timmar. Sjuksköterskornas helhetsbild talar för deras lämplighet att upptäcka och förebygga LRP. En del LRP utgörs av läkemedelsfel som uppstår av många olika faktorer såväl organisatoriska som mänskliga. Sjuksköterskan är ofta den som utgör den sista barriären innan ett läkemedelsfel når fram till patienten.

Syftet med denna avhandling var att ta reda på om sjuksköterskor kan förbättra kvalitén på patienters läkemedelsbehandling. Vidare var syftet att ta reda på vilken typ av läkemedelsfel som oftast rapporteras till Socialstyrelsen samt dess bidragande orsaker.

Delstudie I genomfördes av en klinisk farmakolog och en sjuksköterska för att studera vilken betydelse läkemedelsgenomgångar, hade på återinläggning och död av patienter på en internmedicinsk klinik. De kliniskt relevanta LRP som hittades resulterade i ett skriftligt råd till den ansvarige läkaren om att förändra patientens läkemedels behandling. Hos 150 patienter hittads 299 LRP som den vanliga vården inte hade upptäckt. Detta resulterade i 106 skriftliga råd.

I ***delstudie II*** utförde sjuksköterskor, efter att först genomgått en 1-dagsutbildning i klinisk farmakologi, självständigt strukturerade läkemedelsgenomgångar. Sjuksköterskorna kunde identifiera 59 kliniskt relevanta LRP hos 80 patienter som den ordinarie vården inte upptäckt. Av dessa resulterade 37 i en förändring av patientens läkemedelsbehandling.

I ***delstudie III*** undersöktes om läkemedelsgenomgångar utförda av sjuksköterskor kunde förbättra kvalitén på äldre patienters läkemedelsbehandling. Alla sjuksköterskor på en internmedicinsk avdelning genomgick en heldags utbildning i klinisk farmakologi och genomförde därefter självständigt läkemedelsgenomgångar på inneliggande patienter. Hos 250 patienter hittads 86 LRP som den vanliga vården inte hade upptäckt.

I ***delstudie IV*** utvecklades en preliminär klassificering av läkemedelfel och dess bidragande orsaker där sjuksköterskor varit ansvariga. Resultatet visade att omständigheterna kring sjuksköterskors läkemedelsfel är komplexa där systemfaktorer och mänskliga faktorer påverkar varandra.

I ***delstudie V*** analyserades 585 läkemedelsfel där en sjuksköterska varit ansvarig. Oerfarna sjuksköterskor och manliga sjuksköterskor var anmälda för läkemedelsfel i högre utsträckning än erfarna och kvinnliga sjuksköterskor och var ansvariga för olika typer av fel. ”Bristande kunskap” var en bidragande orsak som oftare associerades med oerfarna sjuksköterskor. Att ”agera utanför sina befogenheter” var vanligare bland manliga sjuksköterskor.

Slutsatse*r*. LRP är vanligt. En intervention utförd av en klinisk farmakolog och sjuksköterskor ledde inte till någon minskning av återinläggning eller död. Genom att använda en sjuksköterskeledd läkemedelsgenomgång kunde flera LRP identifieras som den vanliga vården inte upptäckt. Omständigheterna kring sjuksköterskors läkemedelsfel är komplexa där systemfaktorer och mänskliga faktorer påverkar varandra. Sjuksköterskors erfarenhet har betydelse för patientens säkerhet och sjuksköterskors insatser är en värdefull resurs för att förbättra kvalitet och säkerhet i patienters läkemedelsbehandling.

LIST OF PAPERS

I Mannheimer B, Ulfvarson J, Eklöf S, **Bergqvist M,** Andersén Karlsson E, Pettersson H, von Bahr C. **Drug-related problems and pharmacotherapeutic advisory intervention at a medicine clinic**. *Eur J Clin Pharmacol*. 2006;62(12):1075-81.

II. **Bergqvist M**, Ulfvarson J, Andersén Karlsson E, von Bahr C. **A nurse-led intervention for identification of drug-related problems** *Eur J Clin Pharmacol.* 2008;64(5):451-6

III. **Bergqvist M**, Ulfvarson J, Andersén Karlsson E. **Nurse-led medication reviews and the quality of drug treatment of elderly hospitalized patients.** *Eur J Clin Pharmacol.* 2009;65(11):1089-96.

IV. **Bergqvist M**, Andersén Karlsson E, Sparring Björkstén K, Ulfvarson J **Medication errors by nurses in Sweden -classification and contributing factors.** *Submitted* 091125

V. **Bergqvist M,** Andersén Karlsson E, Sparring Björkstén K, Modigh C, Benson L, Ulfvarson J. **Medication errors made by nurses - a result of interrelated human and system factors.** *Manuscript*

CONTENTS

LIST OF ABBREVIATIONS

ADR	Adverse Drug Reaction "A response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function." (WHO 1972)
AE	Adverse Event “Any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with this treatment”(Delamothe 1992)
CCC	Calculation of creatinine clearance
CDSS	Computerised Decision Support Systems
DIA	Drug-interaction assessment
DDI	Drug-drug interaction. The administration of one drug can alter the action of another (Rang 2003)
DRP	Drug-related problem “An event or circumstance involving drug therapy that actually or potentially interferes with desired health outcome.” (ASHP 1993b)
GFR	Glomerular filtration rate
IDU	Inappropriate drug use. Drugs with an unfavourable risk/benefit ratio when safer or equally effective alternatives are available (Beers 1997)
NBHW	National Board of Health and Welfare
NSAID	Non-steroidal anti-inflammatory drug
SYM	Symptoms assessment form

1 BACKGROUND

1.1 Introduction

What is the concept of nursing? In 1970, Virginia Henderson stated that the concept of nursing is: *"a service that helps human beings with their essential daily activities when they lack the strength, knowledge or will to carry them out unaided, and in working towards the development of a healthy independency. Further, it is: to help the patient to carry out the therapeutic plan, and acting as a member of the multidisciplinary healthcare team. The concept is limited only by the imagination and the competence of the nurse who interprets it"* (Henderson 1978). In 2003 the Royal College of Nursing (RCN 2003) added to Mrs Henderson's definition a dimension of clinical judgement: *"The use of clinical judgement in the provision of care, to enable people to improve, maintain, or recover health, to cope with health problems, and to achieve the best possible quality of life, whatever their disease or disability, until death".*

1.2 Drug-related problems

Drugs are important to prevent and to treat diseases, to ameliorate a symptom, or for diagnostic purposes, and to induce anaesthesia. Medication saves lives, extends lives, palliates suffering and symptoms. Today, nearly 10,000 drugs are available for prescribing worldwide (Leape *et al.* 1995) and about 6,000 different drugs are used in Sweden (the Medical Products Agency-Sweden). In Sweden, 6.2 million individuals received at least one dispensed drug during 12 months in 2006, thus a prevalence of 67.4% (Hovstadius *et al.* 2009). In an ideal world every patient gets proper investigation and is diagnosed correctly, and the drugs are used as intended and in an optimal way, the treatment and monitoring are optimal on the basis of evidence and reliable experience and into line with the individual patient's needs. Furthermore, in the ideal world all health-care personnel managing drugs are well aware of the risk of causing a patient harm and therefore conduct all steps in the medication process most carefully to avoid medication errors. The organizations have clear and safe guidelines and methods to avoid medication errors and to promote a perfect drug treatment. But, we do not live in this ideal world. Whenever a patient is treated with one drug or more, drug-related problems (DRPs) may occur. The definition of DRP are wide and could be all sorts of

problems ranging from the patient not being able to open the can lid to an adverse drug reaction (ADR) or a lethal medication error (Table 1).

Table 1 Drug-related problems

No indication	No current diagnosis or symptom indicating the use of the drug
Non-compliance	The patient does not use the drug the way it is prescribed
Under- or over-dose	Insufficient dosage on basis of available evidence and patient's status.
Practical difficulties	E.g. impossible for the patient to swallow the pill or the patient has no money to bye the prescribed drugs.
Adverse drug reaction	E.g. bleedings due to anticoagulantia or constipation due to analgesics.
Drug-drug interaction	E.g. risk of intestinal bleeding due to a combination of antithrombotic agents and NSAIDs or risk of nil effect of antibiotics due to a DDI between ciprofloxacin and iron compounds and calcium compounds.
Medication error	"Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient, or consumer. Such events may be related to professional practice, health-care products, procedures and systems including prescribing, order communication, product labelling, packaging, nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use" (NCC MERP)

DRPs may occur in all steps of the medication process from prescribing to monitoring (Figure 1). Prescribing errors may occur in either the decision making phase or in the actual writing, or choosing from a data-list, phase. Decision making errors are e.g. drug or dose not in concordance with available evidence, or not on the basis of the patient's age, other drugs taken or individual needs. When writing the prescription there could be an order- writ error, due to poor handwriting, illegibility or not accepted abbreviations or to a decimal error. When dispensing the drug from the pharmacy the majority of errors are due to similar sounding and looking names or misreading of the prescription resulting in the wrong drug, dose or strength dispensed (Page & McKinney 2007).When preparing the drug there could be a mix-up of drug names or strength, or the wrong solution, or the wrong quantity of solution could be used. When administering the drug, there could be a mix-up of patient or the drug could be administered at the wrong time or by the wrong route, or the wrong rate could be used. The final step in the medication process is monitoring of the treatment. A poorly monitored drug-treatment could also result in a DRP. Everybody involved in the treatment process is responsible for their part of the process.

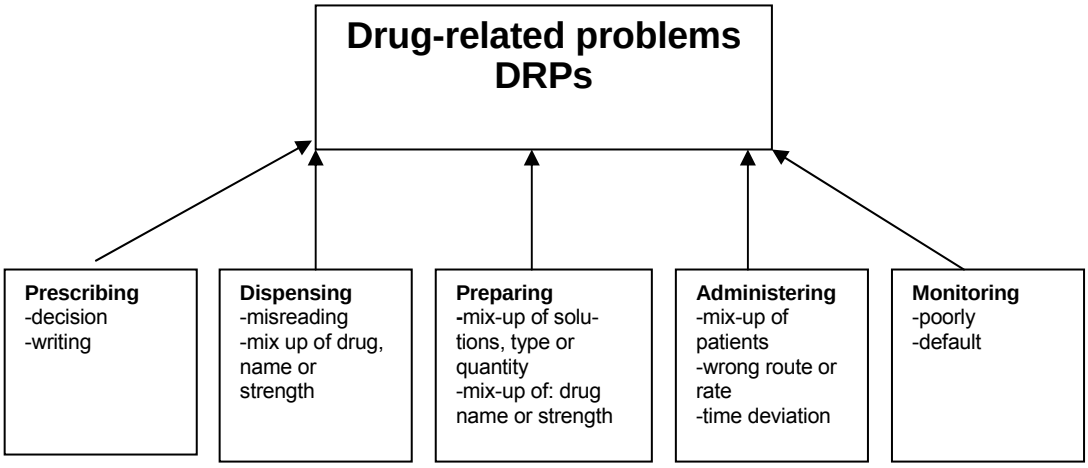

Figure.1 *The medication process and DRP*

1.3 The prevalence of DRPs

DRPs are common and can cause serious adverse effects and even death. Suspected fatal drug reactions account for approximately 3% of all deaths in the Swedish population (Wester *et al.* 2008). Fatal adverse drug reactions are estimated to be the seventh most common cause of death in Sweden (Jönsson 2007). At in-patient clinics, the incidence of ADEs ranges between 0.7 and 6.5%. Up to 57% of these are considered preventable (Thomas *et al.* 2000, von Laue *et al.*, 2003 Brennan *et al.* 2004) The proportion of patients admitted to hospital due to DRPs or when DRPs have been a contributing factor for admission, varies from 0.7% to 30 % depending on the definition of the DRPs and the patient group studied. There is a substantially higher proportion of drug-related hospitalization among elderly patients, and up to 88% of the DRPs have been judged being avoidable (Einarson 1993, Beijer & de Blaey 2002, Mjorndal *et al.* 2002, Brennan *et al.* 2004, Dormann *et al.* 2004, Pirmohamed *et al.* 2004, Kongkaew *et al* 2008, Paul *et al.* 2008).

1.4 Drug treatment of elderly

Elderly patients are prescribed a substantially higher number of drugs than young patients, and the number of drugs is increasing (Socialstyrelsen 1999, Veehof *et al.* 2000, Linjakumpu *et al.* 2002, Socialstyrelsen 2002, Kragh 2004, Socialstyrelsen 2005, Socialstyrelsen 2009).The use of drugs, polypharmacy and potential DDIs have increased during the 10-year period 1992-2002 among the elderly (Haider *et al.* 2007). In 2008 the NBHB scrutinized the drug-use among the oldest people in home-health-care. Mean age was 91 years and mean number of daily used drugs was 8.2. The largest number of drugs used by a single patient was 29 which was an expansion from 2005 when the number was 22. Furthermore, the NBHB found the use of inappropriate drugs to be high and had increased since the measurement in 2005 (Socialstyrelsen 2009). Older patients more often show a complex clinical picture with polypathology and thus use many different drugs (Fulton & Allen 2005, Jorgensen *et al.* 2001). Polypharmacy, multiple drug use, increases the risk of drug-drug interactions (DDIs) and other DRPs (Beer 1997, Veehof *et al.* 2000, Routledge *et al.* 2004, Klarin *et al.* 2005, Passarelli *et al.* 2005, Gallagher *et al.* 2007, Johnell *et al.* 2007, Zopf *et al.* 2008) Inappropriate drug use (IDU) in elderly is drug-use on no clear evidence-based indication or drugs that carry a substantially higher risk of adverse side-effects

in the elderly compared to young people (Beers 1997, O'Mahony & Gallagher 2008). Recently published studies state that prescription of inappropriate medication to elderly people is highly prevalent, ranging from 12 to 40% in community-dwelling elderly and nursing home residents, respectively (Klarin *et al.* 2005, Bergman *et al.* 2007, Gallagher *et al.* 2007, Fick *et al*. 2008). A Swedish study where the quality of the drug therapy of elderly nursing home residents was evaluated, showed that over 70% of the residents used one or more inappropriate drugs or drug combinations (Bergman *et al.* 2007). Other Swedish population-based studies among people 75 years and older have shown that IDU is common, (Johnell *et al.* 2007) with a prevalence of 19% (Klarin *et al.* 2005). IDU is an important reason for unplanned admittance to hospital of elderly people (Beijer & de Blaey 2002, Mjörndal *et al*. 2002, Klarin *et al.* 2005, Blix *et al* 2006, Yee et al. 2005, Royal *et al.* 2006,) Furthermore, there are pharmacokinetic and pharmacodynamic changes in the elderly leading to greater and more long lasting effects due to extended duration and accumulation. Elderly are more sensitive to drugs. The same plasma concentration of a drug can cause different effects in young and old patients. The main reason for age-related effects on the drug action is that the drug elimination is less efficient in elderly people, i.e. drugs often produce greater and more long-lasting effects (Range *et al* 2003). Many commonly prescribed drugs are excreted renally and a considerable number of elderly patients with decreased renal function are being prescribed drugs that should be dose adjusted, used with caution, or avoided (Klarin *et al.* 2005, Blix *et al.* 2006, Hellden *et al.* 2009, Pena Porta *et al.* 2007).Glomerular filtration rate (GFR) starts to decline from the age of 20 and will have fallen by about 50% at 75 years of age. The elimination rate is impaired as a result of age-related changes in the renal structure. The proportion of the body that is fat increases with age leading to an increased distribution volume of lipid soluble drugs. One consequence of this is the increased half-life of benzodiazepines with advancing age. This may result in drug accumulation and adverse drug reactions (Rang *et al.* 2003). Hypotensive drugs cause postural hypotension more commonly in elderly than in young patients due to, among other things, increased sensitivity to drugs and the decreased elasticity of the blood vessels. Medication is also the most common reversible cause for confusion in the elderly, (Alagiakrishnan & Wiens 2004) and falls and fractures in the elderly are an important complication associated with all types of drugs (Fonad *et al.* 2009). Additionally, elderly´s increased disability and dependency on assistance may result in difficulty to adhere to the drug regime.

1.5 Interventions to prevent DRPs

There are methods aimed to prevent DRPs, such as medication reviews. Medication review is defined as: 'a structured, critical examination of a patient's medicines with the objective of reaching an agreement with the patient about treatment, optimising the impact of medicines, minimising the number of DRPs and reducing waste' (DoH 2002). In UK national guidelines were issued in 2001 for performing medication reviews once a year in elderly patients consuming more than four different drugs daily. Australia uses similar guidelines. In Sweden no guidelines are established for how and how often medication reviews should be performed. Regular monitoring of prescribed drugs is presumed to be part of the prescriber´s responsibility in the same way as all recommended treatments are monitored (SFS 1998:531, SBU 2009). Furthermore, no established model for how performing medication reviews exists. The intervention can be done in various ways depending on knowledge, priorities and economics within the specific unit. The General Medical Services Contract (GMS) in UK stated that medication reviews may be carried out by general practitioners, pharmacists or nurses The most common way however, is that a medication review is led by a clinical pharmacologist or a pharmacist. Quite many studies have been published on pharmacists´ medication reviews (Gillespie *et al.* 2009, Krska *et al.* 2001, Royal *et al.* 2006, Zermansky *et al.* 2001), whereas documentation on nurse-led intervention studies aimed at preventing DRPs is scarce. An intervention study performed by ward-based pharmacists among older patients showed a 16% reduction of all visits to the hospital and a 47% reduction of visits to the emergency department, and drug-related re-admissions were reduced by 80% (Gillespie *et al.* 2009). An intervention study from Hong Kong has also shown reduced mortality after interventions by pharmacists. In this study, patients prescribed five or more drugs and being non-compliant with their drug regime were randomized to either a telephone counselling group or a control group. The patients in the telephone group received a 10-15 minutes telephone call from a pharmacist at the midpoint between clinic visits throughout the study period. The pharmacist asked about the patient's treatment regimen; clarified any misconceptions; explained the nature of any side-effects; reminded the patient of his/her next clinic appointment; reinforced the importance of compliance with the treatment and gave relevant aspects on self-care. The patients in the control group received no telephone intervention (Wu *et al.* 2006). Also, an intervention by a team with a nurse and a pharmacist has shown a 25% reduction in unplanned re-admissions to hospital (Stewart

et al. 1998). However, others have failed to show any effect on mortality, morbidity, consumption of health-care or quality of life (Krska *et al.* 2001, Nazareth *et al.* 2001, Ulfvarson *et al.* 2003, Zermansky *et al.* 2001 Midlov *et al.* 2005, Holland 2008, SBU 2009). The Homer study, based on medication reviews undertaken in patients' homes was even associated with a significantly higher rate of admission to hospital (Holland *et al.* 2005). This shows the complexity of the problem and the need for new approaches to reduce DRPs. As mentioned intervention studies on nurse-led interventions are few. However, there are some studies have shown that specialist nurses can reduce re-admission to hospital of patients with heart failure (Blue *et al.* 2001, Bruggink-Andre de la Porte *et al.* 2006). and others have shown that patients participating in a nurse-initiated intervention for medication review had better knowledge of their medication and were able to manage it in a better way after the nurse-led intervention. (Griffiths *et al.* 2004, Hansford *et al.* 2009). Medication administration is a traditional daily task for the registered nurse in almost all clinical settings. Registered nurses spend up to 40% of their time administering drugs (Armitage & Knapman 2003) and are involved in all steps of the medication process (Figure 1). Nurses contribute by making observations of the patient´s clincal condition in relation to changes in the patient´s drug treatment. Furthermore, nurses prescribe drugs, perform ordinations, calculate doses, prepare solutions, administer the medication to the patient and monitor the effects and side-effects of the drug treatment.

1.6 Medication error

"*C'est pire qu'un crime; c'est une faute (It is worse than a crime; it is an error).*"
(Charles Maurice de Talleyrand-Périgord 1754 – 1838)

One part of the DRPs is medication errors. Medication errors can be defined in many ways and there is no universally agreed definition of the concept. In the current literature an amount of definitions can be found (Table 2).

Table 2 Definitions of medication errors

Medication error	References
"Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient, or consumer. Such events may be related to professional practice, healthcare products, procedures and systems including prescribing, order communication, product labelling, packaging, nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use".	(NCC MERP)
"The administration of a drug not in accordance with the recommended guidelines on the manufacturer's product package insert. The error could involve dose, rate, route of administration, formulation, the drug itself, or the patient."	(Barker & Mc 1962)
"Errors in drug ordering, transcribing, dispensing, administering, or monitoring."	(Kaushal *et al.* 2001)
"The administration of the wrong medication, drug, diagnostic agent, chemical or treatment requiring the use of such agents, to the wrong patient or at the wrong time or failure to administer such agents at the specified time or in the manner prescribed or normally considered as accepted practice."	(ASHP 1982, ASHP 1993a)
"Any serious injury or death caused by a health care professional, physician hospital staff member of any type of medicine related mistake is a medication error. Mishaps that occur during prescribing, transcribing, dispensing, administering, adherence, or monitoring a drug."	(VA Center for Medication Safety)

"Episodes of drug misadventure that should be preventable through effective systems controls involving pharmacists, physicians and other prescribers, nurses, risk management personnel, legal counsel, administrators, patients and others in the organizational setting, as well as regulatory agencies and the pharmaceutical industry".	(ASHP 1993a)
"Any error in the medication process, whether there are adverse consequences or not."	(Barker *et al.* 2002)
"A dose administered differently than as ordered on the patient's medication record."	(Barker *et al.* 2002)
"A failure in the treatment process that leads to, or has the potential to lead to, harm to the patient."	(Kohn 1999, Ferner & Aronson 2006)
"A dose administered to the patient that deviates from the physician´s orders, such as an omission, wrong dosage, or unauthorized drug."	(Barker *et al*. 1982)

In 1999 The Quality of Health Care in America Committee of the Institute of Medicine (IOM) reported that up to 7,000 persons die due to medication errors each year (Kohn 1999) although the precise frequency of medication errors are not known. The estimated frequency is highly variable due to the method of detection, the definition of the concept, and the type of setting that is studied, and any comparison of error rates is only accurate when the definitions are at least similar. To detect and to measure medication errors four methods are mostly used; spontaneous reporting studies, screening of medication orders and patient medical charts, observational studies, and qualitative studies, where health-care personnel are interviewed of their experience about medication errors. The result differs depending on the definition and the method. In observational studies in hospital and nursing facilities 19% of the doses (605/3216) were found to be erroneous (Barker *et al.* 2002) In Sweden, the National Board of Health and Welfare (NBHW) scrutinized 1,967 patient medical charts and found 169 patients (8,6%) with treatment-caused injuries. If these results are extrapolated to all episodes of care in hospital during one year they correspond to approximately 105,000 treatment-caused injuries, of which 27% are drug-related (Socialstyrelsen 2008)

1.7 Theoretical framework

Traditionally, error theories have used a person-centred approach. Sigmund Freud argued in the beginning of the 20th century that maybe mistakes are determined by unconscious intentions. He illustrate this with a case where a doctor accidentally gives his own uncle (an uncle who had been a "stand-in" for father) the wrong drug. Freud explained the mistake as the doctor´s unconscious hostility towards his uncle (father) (Freud 1901). There has also traditionally been a focus on "the error-prone nurse" and a culture of blaming the individual. If the "bad" nurses were removed everything would be all right. (Reason 2000, Leape & Berwick 2005, Collins *et al.* 2009) Fortunately, today, the concept that bad systems, not bad people, lead to the majority of errors is well accepted. Health-care professionals are mostly aware of the fact that it is the complex interplay of circumstances in the clinical setting rather than an individual's carelessness that contributes to the occurrence of an error (Leape 1997, Dickey *et al.* 2003, Runciman *et al.* 2003). The link between employee stress in health-care settings and the quality of the patient care and safety is well known. The focus of blame has changed from the 'blame-the-pilot culture" to a non-punitive and a ''blame-free culture''(Reason 1997). Medication errors rarely have one single explanation. There is often a complex interaction between an amount of factors, such as human behaviour, technological aspects of the system, socio-cultural factors, and a range of organizational and procedural weaknesses (DoH 2000). The Organizational accident model by James Reason is a model which has had a great influence during the past decades. The organizational accident model is explained as: latent conditions within the system sets the stage, and the active human error is a consequence of weaknesses in the system (Eagle *et al.* 1992, Reason 2008). Several factors are contributing at many levels of the system. These factors open up a row of opportunities in which the hazards are allowed to pass unchecked, and finally may harm the patient. The model is known as 'the Swiss cheese model' and is adopted as the model of investigation by many industries. The model has shifted the end-points of accident investigations from a 'pilot error' explanation to organizational explanations. In an ideal world the defensive layers would be intact. In reality they are more like Swiss cheese: full of holes. The Swiss Cheese Model can also be used to illustrate coping resources (Figure 2). When all defences and barriers have been penetrated, it is still possible for the person or the persons at the sharp end to recover the situation before it affects the patient (Reason 2008). The last link before a medication error affects the patient is often a nurse. The nurse can recover

the situation by a successful compensation and initially this coping resource is intact but, nurse's vigilance can diminish by the accumulated stress associated with minor events such as distractions or communication problems. Minor events are inevitable. Isolated they have little impact, but multiplied they are strongly related to negative outcomes. A person can only foresee and prepare for a limited number of scenarios. A series of minor events, for example interruptions or the absence of guidelines, sets a sequence of incidents in motion, and the organizational defences are slowly destructed. The capability to compensate is resource-limited and affected by the total number of minor events met (figure 2.) (Reason 2008).

Figure 2 *Nurse's resources to recover errors are gnawed away by the accumulation of minor events* (Adapted from Reason 2008, page 190).

However, fanatical implementation of this theoretical framework may led to an illusion of management responsibility for all errors. The 'blame-the-pilot' culture must not swing to a 'no blame' culture. Personal qualities matter of course. To think otherwise is to fall prey to learned helplessness blaming the system for everything. The Swiss cheese model may lead to an illusion that the roots of all errors derive from the organisation's management. The Swiss cheese model makes it tempting to draw a line back

from an outcome to a set of ‘latent conditions’ that are widely separated in both time and place from the errors themselves. When looking back at an error you might find contributing factors that in fact are not there. The harder you look the more latent conditions you will find. This will overestimate what we knew or could have known before an error occurred. Without wanting to return to the dark ages of “the blame culture” when the individual nurse was the company scapegoat for all medication errors, there is a balance to be redressed in accounting for the role of active errors. As David Pruce argued in a session on professional regulation and pharmacist: “We should be aiming at a fair-blame culture” (Pruce 2007). All health-care personnel have a professional medical responsibility which involves working in the concept of science and reliable experience, and providing competent and careful health-care (SFS 1998:531). The individual must take her/his responsibility for the actions made and also do the right thing when something goes wrong.

Contributing factors

Errors do not occur “out of the blue”, different errors derive from different situations with variable contributing factors. Medication errors rarely have one single explanation. There is a complex interaction between a varied set of elements including human behaviour, technological aspects of the system, socio-cultural factors and a range of organizational and procedural weaknesses´ (DoH 2000). Various studies have classified medication errors in order to develop taxonomies and identify characteristics of medication errors and contributing factors. According to current literature, the factors contributing to medication errors can be viewed in two ways: system approach (latent errors) and person approach. The premise in the system approach is that humans are fallible and errors are to be expected. Latent errors are built into the system and thus present long before the actual error occurs (Reason, 2000). Sometimes the latent conditions are known and sometimes they are unknown until an error occurs. The reason why the weaknesses are not eliminated could be other priorities, costs, or the fact that no one could identify the weakness as a weakness until an error occurred. The person approach focuses on the unsafe acts of people. At the sharp end the human individual finally makes the active error (Kohn 1999, Reason 2000, McBride-Henry & Foureur 2007). Although all health care providers are prone to committing medication errors, it is the nurses who are placed at the frontline (Benner *et al.* 2002). The risk of RNs making medication errors is imminent. Also nurses are often the last link in the

patient´s safety net to protect him against medication errors.(McBride-Henry & Foureur 2006).

1.8 Error reporting

The health-care system is a high-risk organisation, but in contrast to other high-risk organisations the catastrophy strikes only one person at a time. Therefore data must be assembled from different settings to highlight the risks and the shortages in order to identify possible patterns in the errors and contributing factors. Similar situations provoke similar types of error. One of the main purposes of an error reporting system is to identify these recurrences, learn from them and make an effort to prevent errors from happening over and over again (Reason 2008, Ödegård 2006).World-wide there are different reporting systems for medication errors. In the USA two national medication error databases are often referred to the Medication Error Reporting Program (MER) and MED MARX The databases are voluntary programmes for use by clinicians and are anonymous reporting systems using standard definitions and structured data collection approaches, based on voluntary reporting. (Beyea *et al.* 2004). The information from these databases has contributed to knowledge of the nature of medication errors.

1.9 The Lex Maria

In Sweden, all health-care providers are required to report adverse events of significance and if a patient is put at risk of getting seriously injured as caused by a treatment in the health-care system. The regulation is called Lex Maria (SOSFS 2005:28) and is administered by the NBHW The inquiries can lead to criticism of an individual healt-care professional as well as to a demand for changes of routines. The regulation has a history that goes back to 1936 and begins at Maria hospital in Stockholm: *A summer night in August 1936 two young men arrived at the hospital. Karl Eriksson had hurt his thumb and Stig Tärnholm had cut his finger. They were both given local anaesthetics before their wounds were sewn and were then sent home. After just a few hours Eriksson returned with substantial vomiting and a swollen thumb. He was readmitted to the hospital for observation. The very next day a Mrs Elsa Berglund was admitted to the hospital for removing a very disfiguring wart on her chin. She was administered local anaesthetics before the wart was successfully removed. A few hours later Mrs Berglund returned to the hospital and was readmitted due to vomiting and an enormously*

swollen face. The physician in charge, who had seen Eriksson earlier and now Mrs Berglund started to "smell a rat". He told his colleague about his suspicion that something must have gone wrong with the treatment in the hospital. He also found out that another patient admitted to another ward had been very ill after having local anaesthetic. Later that afternoon also Stig Tärnholm with the finger cut, was readmitted to the hospital due to similar symptoms. During a period of 3 days, all four patients died due to mercurial poisoning and five staff members were prosecuted. But way was there mercurial in the anaesthetics? Well, at this ward disinfections and medications were kept in the same cupboard but on different shelves. The disinfections contained mercurial. The Medical board had issued guidelines according to which disinfections and medications were to be kept in separate cupboards but the director of the department had not followed the guideline. Probably this is what happened; first, the pharmacy had not marked the bottles in a correct way. The labels marked poison were missing on the disinfection bottles. Second, a nurse student had placed the bottles in the cupboard on the wrong shelves. And third, a nurse picked a bottle with no poison label from the shelf where the local anaesthetics usually were placed but without controlling if it was the correct bottle. All prosecuted personnel were absolved thus, it was impossible to determine how the mix-up had happened. When the event was known, the authorities acted quite fast. The governor general established a llist of necessary actions to be taken. In January the following year a notification came saying that the physician in charge should without delay report to the police and the medical board if a patient when treated by the health-care system suffered an injury or illness of severe art. This notification was called Lex Maria (Wennergren 2005,translated from Swedish by M. B.). Even if more than 70 years have gone by since these tragic deaths, the basic idea remains, and is as current today as it was back then.

Health-care providers from all over Sweden send in more than 1500 reports as per the Lex Maria each year. In 2008, 1,618 events were reported 30% of these were related to drugs. Since 2004 the reports have increased by approximately 63% from 1,016 reports in 2004 to 1,618 reports in 2008 (Socialstyrelsen). The increasing number of reports does not mean that the Swedish health care has deteriorated it could rather be the other way around: many reports indicate a qualified, safe culture (Chiang *et al.* 2010, Wakefield *et al.* 1996, Wakefield *et al.* 1999). Another explanation of the increased number of reports is that since 2006 health-care providers are obliged to ensure that all suicides occurring while under the care of a health professional, or four months after contact with the health-care system shall be reported (Ödegård 2006). During recent years also other local reporting systems have been introduced and frequently used. It is well known that both voluntary and mandatory reporting systems of medication errors suffer

from severe underreporting due either to lack of appreciation that an error has occurred, the error is not considered serious enough to report, or there is a reluctance to report (McBride-Henry 2006, Antonow *et al.* 2000, Chiang *et al.* 2010, Mayo & Duncan 2004, Wakefield *et al.* 1996, Wakefield *et al.* 1999). Nurses who feel the pressure of a punitive environment may underreport their medication errors. An American study by Antonow et al. found that administration errors were more likely to be reported by registered nurses if they had actually reached the patient, whereas 'ordering' errors were less likely to be reported since the error never affected the patient (Antonow *et al.* 2000).

1.10 Nurses´ working experience

Some nurse-characteristics may be predictive for specific error types, e.g. the clinically inexperienced nurse may be affectable by other system factors than are experienced nurse. The nurse´s clinical experience may be an important factor for what kind of unsafe action the nurse takes before an error occurs (Chang & Mark 2009). In addition, as nurses gain experience, they are more able to interpret a situation and to identify and intercept medication errors before they affect the patient. Studies linking nurses´ clinical experience and medication errors are inconclusive. Some have shown that inexperienced nurses are correlated to increased risk for medication errors (Blegen *et al.* 2001, McGillis Hall *et al.* 2004, Prot *et al.* 2005, Seki & Yamazaki 2006, Tang *et al.* 2007, Davis *et al.* 2009), while others have found no such relationship (Blegen *et al.* 2001, Mayo & Duncan 2004, Wilkins & Shields 2008). Studies in office workers have indicated that experienced workers more often make rule-based errors, while novice make more knowledge-based errors (Zapf 1992).

1.11 Nurses gender

Other characteristics such as gender may also be of importance when discussing how we are affected by weaknesses of the system and clinical performance. A Canadian study exploring unsafe patient care events by nursing students reported that male nursing students were responsible for a higher number of unsafe events than their number in the sample would lead one to expect (Gregory *et al.* 2009). It is known that males are more prone to risk-taking in various contexts (Ayanian & Epstrin 1997, Byrnes *et al.* 1999, Zuckerman & Kuhlman 2000) Also, males tend to score higher

confidence bias than females when tested in cognitive tasks and overconfidence may increase the likelihood for errors in the medical area. The term overconfidence bias is used as a measure of a person's overestimation of the accuracy of a choice he/she has made, i.e. people with high confidence bias trust their own judgement to be correct to a higher extent (Arkes 1981, Griffin *et al.* 1990).

1.12 Summary of the background

- DRPs are common
- The elderly have an increased risk of being admitted to hospital due to ADRs.
- Nurses are involved in all of the steps of the medication process and are thus in a perfect position to contribute to the work of improving the quality of elderly patients´ drug treatment.
- There are methods aimed at the prevention of DRPs, such as medication reviews but no guidelines are used for how and how often medication reviews should be performed, and the effects of medication reviews are contradictory.
- Medication errors are common
- Medication errors occur in a complex interplay between circumstances in the clinical setting and human behaviour.
- The risk of nurses making medication errors is imminent but on the other hand nurses are placed in the frontline, and ere able to intercept an error before it affects the patient.

2 AIMS OF THE THESIS

The overall aim of this thesis was to develop and test a model for nurses to prevent and solve DRPs and to contribute with knowledge on how medication errors arise and what factors antecede medication errors made by nurses.

Specific aims were:

Study I

To describe the scenario of DRPs and elucidate whether a pharmacotherapeutic advisory intervention affects the incidence of re-hospitalisation and/or death.

Study II

To investigate whether nurses can identify DRPs in in-patients by using a new, structured, nurse-led medication review model and to assess the feasibility and effectiveness of this model.

Study III

To evaluate if nurses, after specific training in clinical pharmacology, can improve the quality of the drug therapy in elderly hospitalized patients.

Study IV

To describe the medication error phenomenon from the nurse's perspective and to develop a tentative classification of medication errors and contributing factors for future analyses of co-variations.

Study V

To describe the characteristics of medication errors reported to the NBHW and to elucidate what error types are reported most frequently and which contributing factors most frequently preceded an error. A second aim was to investigate how the nurse´s working experience and gender were related to the frequency and type of error and to the contributing factors.

3 METHODS

Different study designs have been used to investigated the fesability of nurses´ interventions to prevent and solve DRPs and to determine the nature of nurses´ medication errors (Table 3).

Table 3 An overwiew of study subjects included and methods used

PAPER	STUDY PERIOD (YEAR)	INCLUDED STUDY SUBJECTS	DATA SOURCES	NUMBER OF STUDY SUBJECTS	STUDY DESIGN	METHOD
I	2003-2004	Patients from the division of internalmedicine Södersjukhuset	Patient-interviews Medical chart Hospital Episode Statistics	300	Randomized controlled intervention study	Descriptive statistics and chi-square t- test
II	2005	Nurses from Södersjukhuset and one geriat-ric ward outside	Nurses reports Medical chart	15	Descriptive intervention study	Descriptive statistics.
III	2006	Patients from the division of internalmedicine Södersjukhuset	Medical chart Hospital Episode Statistics	460	Intervention study with historical controls	Descriptive statistics and chi-square t- test
IV	2005	Various healt-care settings in Sweden	the NBHW	33	Descriptive qualitative study	Content analysis
V	1996-2006	Various healt-care settings in Sweden	the NBHW	585	Qualitative, and quanti-tative cross-sectional study	Content analysis, descriptive statistics, chi-square t- test Fisher's exact test, logistic regression

3.1 The education (paper II and III)

An education was designed by the research team and included basic clinical pharmacology including pharmacodynamics, pharmacokinetics and instructions on drug–drug interactions (DDIs). Physiological changes with increased age, elderly and drugs, as well as diagnosis of side effects, were also addressed. The education lasted for 1-day and was given to the nurses participating in studies II and III. The nurses were also

given instruments to assess symptoms, measure renal function and screen for potential DDIs.

3.2 Instruments (papers I, II and III)

Symptoms Assessment Form (SYM)

This form has been tested and further developed in previous studies (Ulfvarson *et al.* 2003) and contains frequent symptoms caused by common drugs. The form contains the following 21 symptoms: dizziness, headache, fatigue, insomnia, anxiety, sweating, swollen feet, muscular pain, joint pain, cough, stomach pain, nausea, diarrhoea, constipation, appetite loss, weight loss, sensitivity to coldness, dry mouth, eye problems, sadness and itch. The symptoms were assessed on a Likert scale 0–4, showing the patient's own opinion of how much inconvenience these symptoms caused.

Calculation of Creatinine Clearance (CCC)

Creatinine clearance was estimated using the Cockroft and Gault formula (Cockcroft & Gault 1976) for identifying patients at possible risk of adverse drug reactions due to impaired kidney excretion

Drug-Interaction Assessment (DIA)

Drug interactions were identified by a computer programme specially designed to signal for drug-drug interactions (Sjöqvist 2003) where interactions were categorized according to clinical significance.

3.3 Data sources

The Hospital Episode Statistics

The Hospital Episode Statistics is a statistical programme called Business Objects and was used to find data on hospital admissions, discharge and death. Data from all admitted patient charts are automatically transferred to the Hospital Episode Statistics programme.

The National Board of Health and Welfare, the Lex Maria

All Swedish health-care providers are required to report adverse events of significance and if a patient is put at risk of getting seriously injured as caused by a treatment in the health-care system. The regulation is called Lex Maria (SOSFS 2005:28) and is

administered by the NBHW. The inquiries can lead to a criticism of an individual healt-care professional as well as to a demand for changes of routines. The Lex Maria data include data on the patient's characteristics, the nurse's characteristics and the nurse's statement of the error, and in some cases statements by other persons involved e.g. colleague or patient. The case files also include the NBHW´s total assessment of the error made.

3.4 Procedure

Study I was a prospective, randomized, controlled advisory intervention study including 300 patients from four wards. Patients taking two drugs or more were included. In the intervention group, medication reviews were done by a nurse evaluating if the patient had any symptoms which might have been caused by a drug. The nurse estimated the patient's renal function by calculating creatinine clearance and identified possible drug interactions by using a special web application. Thereafter a clinical pharmacologist scrutinized the patient´s medical record for DRPs together with the nurse. DRPs judged to be clinically relevant resulted in written advice to the physician in charge of the patient. The control group received ordinary care.

In study number II, fifteen nurses from 10 wards received a 1-day education in clinical pharmacology. Patients taking 3 drugs or more were included. Medication reviews like the ones in study number I were done by the nurses. If any DRPs were found, the nurses intervened by informing or educating the patients, or by alerting the physician in charge on the DRPs in order to achieve a correct change of the patients´ drug treatment.

In study number III, all nurses at an internal medicine ward received a 1-day education in clinical pharmacology. All patients admitted to the ward aged 65 or more were included. Patients at the same ward admitted before the intervention were considered as controls. Outcome variables were re-hospitalization 3 months from discharge, drug-related re-admissions, the proportion of inappropriate drug use (IDU), and DRPs found by the nurses.

In study number IV a content analysis was used to develop a tentative classification of nurses´ medication errors and to identify contributing factors. All medication errors reported to NBHW -Lex Maria from 2005 were a nurse was responsible, were inves-

tigated (n = 33). Specific data on error characteristics were extracted. Error characteristics included type and a description of the error and possible contributing factors. To answer the questions “What sort of medication error is this” and “What factors were contributing to the error”, a procedure of deductive content analysis of narrative data was followed (Graneheim & Lundman 2004). The coding came from the written statements by the nurses and by other persons involved in the error and the composed assessment of the error by the NBHW.

Study number V was a retrospective, descriptive, qualitative, and quantitative cross-sectional analysis of all (n = 585) reports on medication errors made by nurses from January 1, 1996, to December, 31, 2006 submitted to the NBHB- the Lex Maria.

3.5 Statistical methods

Descriptive statistics

Descriptive statistics were used to summarize the samples in studies I, II, III, and IV. Means, minimum, and maximum were estimated for the continuous variables. For the categorical variables, percent and number were estimated.

Chi-square tests

For comparisons of intervention- and control group, Chi-square tests were used in studies I and III. And V.

Content analysis

In studies number IV and V, content analysis was conducted to categorize the error types, individual factors, and system factors contributing to the error. First, the text was read several times to obtain a sense of the whole incident. Second, the relevant text that answered the research questions was extracted. Third, the text was divided into meaning units that were condensed and labelled in categories. During the process, reflections and discussions between the authors resulted in agreement. Categories were linked with recent literature to discover new perspectives from the file cases and to compare and contrast categories and relationships. Finally, the reported errors were grouped into six categories. Similarly, the contributing factors were divided into two sub-groups: “system factors” and “individual factors”. In the results section, representative stories and quotations from the case files were selected to describe each

category. The statements were written by the nurses and other persons involved shortly after the error was made. The statements have been translated from Swedish with the intention to keep the true meaning and emotion (Graneheim & Lundman 2004).

Fisher´s exact test

Fisher´s exact test was used in study number V. If the assumptions for the chi-square test, no more than 20% of the expected counts less than 5 and no expected counts less than 1, were fulfilled, Fishers exact test was used to test for statistic significant differences between nurses with < 2 years working experience in the sample versus the total number of active nurses with < 2 years working experience in Sweden and male nurses in the sample versus totally numbers of male active nurses in Sweden.

Logistic regression

To measure the relationship between the dependent variables (nurse´s experience and nurse´s gender) and the independent variables (error types and contributing factors) and to compute relative risk, logistic regression analyses were performed. The analysis were conducted in three steps. First the potential predictors were identified by using univariate logistic regression with categorical working experience or gender as the dependent variable. Twenty-three simple logistic regression models were performed for each of the 23 independent variables (9 error types, 6 individual factors and 8 system factors). Thereafter, a multiple model was estimated including the variables that showed having an effect in the simple model (*P-value* < 0.10). The final model consisted of predictors with P-value < 0.05 in the multiple model.

4 RESULTS

4.1 Study I

In 150 patients in the intervention group, a total of 299 DRPs were found in 71% (*n*=106) of the patients. The DRPs are listed in Table 4. Thirty-five per cent (*n*=106) of the DRPs were judged to be of such importance that written advice was given to the physician. The types of advice given are presented in Table 5. Out of these, 63% were accepted by the physician. After 6 months, the proportion of re-hospitalizations and/or deaths were measured. In the intervention group 49% (73/150) were either re-admitted to hospital or had died compared to 46% (69/150) in the control group. The difference was not significant.

Table 4. Frequency of DRPs and the corresponding number of letters of advice given regarding the 150 patients in the intervention group

DRP	***N*=299**	**ADVICE GIVEN (*N*=106)**
Potential interactions	150	24
Adverse drug reactions	93	45
Inappropriate drug	15	14
No clear indication	11	7
Inappropriate duplication	8	5
Drug dose too high	7	6
Drug not taken	5	2
Wrong drug taken	4	0
Therapy failure	3	2
Patient dissatisfied with therapy	2	0
Drug dose too low	1	1

Table 5. Classification of the 106 letters of advice regarding the 150 patients in the intervention group

TYPE OF ADVICE GIVEN	*N*=106
Provide information	36
Withdraw drug	33
Reduce dose	20
Change drug	13
Change time of administration	2
Measure concentration of drug in plasma	1
Report adverse drug reaction	1

4.2 Study II

Fifteen nurses fulfilled their participation and were able to identify 59 clinically relevant DRPs in 80 patients, not detected by the usual care (Table 6). Seven nurses worked in a medicine clinic, six in a surgical, one in an orthopaedic, and one nurse worked in a geriatric clinic. Nurses' characteristics are presented in Table 7. The nurses enrolled from 1 to 16 patients each (mean six). Out of the detected DRPs 63% (*n*=37) resulted in an intervention. The types of intervention are presented in Table 8. The nurses had tools to help them identify DRPs. Of these the Symptoms assessment form (SYM) most frequently contributed to identifying a DRP (*n*=32). The Drug-Interaction Assessment (DIA) contributed to the detection of 22 potential DRPs and calculation of creatinine clearance (CCC) contributed to the detection of 7 DRPs.

Table 6 Frequency DRPs detected by nurses

DRP	*N=59* (%)
Adverse drug reactions	32 (54)
Potential interactions	13 (22)
Inappropriate drug	12 (20)
No clear indication	1 (2)
Other	1 (2)

Table 7 Nurses' baseline characteristics

VARIABLE	*N=15*	MEAN (RANGE)
Female	14	
Male	1	
Age <25 25–30 31–40 >40 Missing	 2 4 5 2 2	
Working experience (years) 1–5 6–10 >15 Missing	 10 2 1 2	
Enrolled patients		6 (1–16)
Detected drug-related problems		4 (0–17)

Table 8 Intervention classification

TYPE OF INTERVENTION	*N=37* (%)
Information to the patient	14 (38)
Drug withdrawal	10 (27)
Dose reduction	4 (11)
Concentration of drug measured in plasma	4 (11)
Blood pressure or serum electrolytes measurement	3 (8
Dose increase	1 (3)
Changed time of administration	1 (3)

4.3 Study III

Of 460 patients (250 in the intervention group and 210 in the control group) 38 and 36%, respectively, had at least one re-admission to hospital (*P-value* = 0.86), and 24% of the patients died. There was no statistical difference in the number of drug-related re-admissions between the groups, 14/16, respectively, (*P-value* = 0.40). There was no significant difference in the use of inappropriate drugs between the groups, 18 and 17% (43/37), respectively (*P-value* = 0.90). Some of the patients used more than one

inappropriate drug or drug combination. The overall prevalence of IDU was 102 (60 /42). Anticholinergics accounted for 40% (*n*=24/17) of the inappropriate drugs used, long-acting benzodiazepines for 17% (*n*=9/8), three or more psychotropic drugs for 32% (*n*=22/11), and potentially serious drug-drug interactions (grade D) counted for 11% (*n*=5/6) of the inappropriate drugs or drug combination used. The most common potentially serious drug-drug interaction found was a combination of potassium supplement and potassium-sparing diuretic. The nurses found 86 clinically significant DRPs not detected by the usual care and a substantial part of the detected DRPs were revealed with assistance of the SYM. The detected DRPs are presented in Table 9. The nurses revealed patients at risk of adverse drug reactions (ADRs) due to a combination of decreased renal function and too high a dosage of drugs, or inappropriate drugs for the patient's age. The nurses also found potential DDIs (types C and D), such as risk of intestinal bleeding due to a combination of antitrombotic agents and NSAIDs. Furthermore, 23 ADRs were detected by the nurses. The ADRs are listed in Table 10.

Table 9 Drug-related problems detected by nurses

DRP	***N* = 86 (%)**
Risk of ADR	34 (40)
Potential DDI	25 (29)
ADR	23 (27)
Other	3 (3)
No clear indication	1 (1)

Table 10 Adverse drug reactions detected by the nurses

SYMPTOM	***N=23***	**DRUG INVOLVED**
Dry mouth	4	Diuretics
Nausea	4	Analgesics, antibiotics
Constipation	3	Analgesics, iron compounds
Confusion	3	Analgesics, antipsychotic agents
Muscle pain	2	Lipid-modifying agents
Restless legs	1	Hypnotics
Dizziness	1	Hypnotics
Hangover	1	Hypnotics
Diarrhoea	1	Antibiotics
Hypotension	1	Angiotensin-converting enzyme (ACE) inhibitor
Nightmare	1	Betablockers
Itch	1	Anastrozole

4.4 Studies IV and V

Study number IV is a pilot study including 33 medication errors made by nurses reported as per the Lex Maria. The errors and contributing factors are described from the nurse's perspective and classified. In study number V a total of 585 reported errors were analyzed. The error types and contributing factors were further developed and categorized. The errors were categorized into 9 categories, the individual contributing factors into 6 categories, and the system contributing factors were categorized into 8 categories which are presented in table 11-13. The most common identified error was "wrong dose" 41% (*n* = 241) and the most common individual factor preceding the error was "negligence, forgetfulness or lack of attentiveness" 68% (*n* = 399) and the system factor most commonly identified was "role overload" 36% (*n* =212).

Table 11. Types of errors

ERROR TYPES AND DESCRIPTIVE EXAMPLES	***585 CASES*** (%)
Wrong dose *A newborn baby was treated with vancomycin. The diluting was supposed to be done in two steps. Accidentally step two was never done and the child was administered too much of the drug.*	241 (41)
Wrong drug due to mix-up of drugs *A subcutaneous venous port was to be flushed with Heparin, but Insulin was administered instead due to a mix-up of the bottles.*	96 (16)
Wrong patient due to mix-up of patients *One patient at a nursing home with the same first name as another resident accidentally got the wrong drugs.*	76 (13)
Omission (ordered drug not given) *A patient treated with vitamin B_{12} injections every three months did not get any injections for more than 6 months because the nurse had not made any note in the work schedule.*	69 (12)
Unauthorized drug *The nurse treated a patient's dyspnoea with terbutaline not ordered by the physician in charge, without contacting the physician.*	57 (10)
Wrong route (e.g. oral solution given IV) *A nurse administered an oral solution in the patient's central venous catheter.*	35 (6)
Wrong judgement of the patient's need of treatment *Despite a very low level of blood glucose the nurse gave the patient his ordinary insulin dose*	16 (3)
Wrong management and storage of the drug *A nurse administered a drug to a patient that she had picked from a box of discarded drugs*	11 (2)
Allergy-related error *The nurse gave alimemazine to a patient from the list of "general directives" without noticing that the patient, according to his medical record, was allergic to the drug.*	9 (2)
Total	610*

* More than one error could be noted in each case

Table 12. Individual factors contributing to the errors

INDIVIDUAL FACTORS	***585 CASES*** (%)
Negligence, forgetfulness or lack of attentiveness	399 (68)
Failure to follow proper protocol	147 (25)
Lack of adequate knowledge	76 (13)
Practice beyond scope of practice.A nurse administers a drug or a dose not ordered or authorized by a health-care professional with authorization for prescribing drugs.	68 (12)
Communication faulty- nurse	62 (10)
Disease or drug abuse	20 (3)
Total	772*

* More than one individual factor could be noted in each case

Table 13. System factors contributing to the errors

SYSTEM FACTORS	***585 CASES*** (%)
Role overload A condition in which there is insufficient time in which to carry out all of the expected role functions.	212 (36)
Unclear communication or order	177 (30)
Lack of adequate access to guidelines or unclear organizational routines	176 (30)
Inappropriate location of medication or look-alike medication	79 (14)
Interruption or distraction when preparing or administering medications	47 (8)
Inadequate physical environment (e.g. insufficient lights) **or pharmaceutical or technique related issues**	31 (5)
Pressure from patient/ patient's family or staff members to satisfy the patient's immediate need.	28 (5)
Emergency situation	7 (1)
Total	757*

* More than one system factor could be noted in each case.

Inexperienced nurses and male nurses were responsible for a higher number of errors than their number in Sweden would lead one to expect. To measure what error types, individual factors and system factors are associated with inexperienced nurses and male nurses, logistic regressions were performed with the dependent variable "years of working experience" or gender. Table 14 and 15 shows the results of the multiple logistic regression analysis. There were two types of error with higher odds that an inexperienced nurse would be responsible for: mix-up of the patients and use of the wrong route of administration. There were also two individual factors contributing to an error with higher odds to be found among the inexperienced nurses: "negligence" or "lack of knowledge". If "practice beyond scope of practice" was found as a contributing individual factor, the odds for the responsible nurse being male was more than

three times higher than the odds that the responsible nurse would be female (*P-value* = 0.002 OR = 3.999). It was also more likely that the responsible nurse was male if a contributing factor was "disease or drug abuse" (*P-value* = < 0.019 OR = 3.256).

Table 14. Variables associated with working experience in the logistic regression analysis.

Final multiple model

INDEPENDENT VARIABLES	***P- VALUE***	**OR**
Error types		
Wrong patient due to mix up of patients	0.004	3.056
Wrong route	0.009	3.847
Individual factors		
Negligence, forgetfulness or lack of attentiveness	0.025	2.884
Lack of adequate knowledge	0.001	4.038

OR = odds ratio
The reference category is: ≥ 2 years of working experience

Table15. Variables associated with nurse's gender in the logistic regression analysis.

Final multiple model

INDEPENDENT VARIABLES	***P-VALUE***	**OR**
Individual factors		
Practice beyond scope of practice	0.002	3.999
Disease or drug abuse	0.019	3.256

OR = odds ratio
The reference category is: female

The majority of the medication errors did not involve treatment, intervention or changes of the patient's status. Most of the errors (82%) did not cause the patient any harm. The outcome for the patient was not related to the nurse's working experience or gender.

5 DISCUSSION

In 1859 Florence Nightingale said about drug treatment: "*Now, instead of giving medicine, of which you cannot possibly know the exact and proper application, nor all its consequences, would it not be better if you were to persuade and help your poorer neighbours to remove the dung-hill from before the door, to put in a window which opens, or an Arnott's ventilator, or to cleanse and lime-wash the cottages? Of these things the benefits are sure. The benefits of the inexperienced administration of medicines are by no means so sure."* (Nightingale 1859). This might be something to consider also today. Drugs may not be the one and only solution to every health problem, especially not among the elderly where you cannot be sure the treatment actually will benefit the patient.

5.1 Methodological considerations

Studies I and III were designed as randomized controlled intervention studies with the end-points re-hospitalization, death, and IDU. Many of the DRPs found were causing ADRs that are known to severely affect the patient´s quality of life but are not life-threatening or a cause for re-hospitalization. Also, some drugs routinely considered to be inappropriate may be appropriate for the individual patient within the clinical context (Bain & Weschules 2007). Therefore these "harsh" end-points may not relate to the intervention delivered. In study number III a reasonable reduction of re-admissions would have been 5 percentage units, i.e. approximately half of the expected drug-related hospital admissions (10%–30% of the hospitalizations of elderly is known to be drug-related (Beijer & de Blaey 2002, Einarson 1993, Kongkaew *et al.* 2008, Mjorndal *et al.* 2002, Paul *et al.* 2008). To test this difference statistically with an alpha of 0.05 and a beta of 80%, the study would have required at least 9,336 patients in each group. Such a study was not possible for us to do in our clinical setting. Although we had no power for the primary outcome, we wanted the outcome to be re-admission because of its indisputable value as indicator for health. Since it was impossible for us to obtain power for our primary outcome, we chose to calculate power for our secondary outcome, IDU at discharge. IDU is a more subtle, flexible but disputable indicator for health.

The 3-month cut-off point in study III was selected to capture the majority of re-admitted patients. Study number I had shown that almost 40% of all patients admitted to an internal medicine ward are re-admitted within 6 months after discharge, and that 17% die.

In studies IV and V the method content analysis was used. The essential idea in content analysis is that lots of words in a text are classified into fewer categories. It is a method of analysing written, verbal or visual communication messages (Weber 1990, Krippendorf 2004). The method can be used with either qualitative or quantitative data, in an inductive or a deductive way (Elo & Kyngas 2008). The inductive way refers to the latent content "how" and the deductive way refers to the manifest content "what" (Baxter 1991). The inductive approach is generally used when there is limited knowledge of the phenomenon. The aim of the deductive approach is to expand the knowledge of already existing research and to create categories based on earlier research (Elo & Kyngas 2008). The specific type of content analysis approach chosen varies with the problem being studied. In studies number IV and V we used a deductive taxonomic analysis because the error phenomenon is earlier described in the literature, and our studies further sorted error types and contributing factors into more general category types (Baxter 1991). The coding came from the written statements by the nurses and by other persons involved in the error and by NBHW´s composed assessment of the error. During the process, reflections and discussions between the authors resulted in an agreement. There are various opinions on the appropriateness of seeking agreement as realities are subjective and dependent on interpretations among the researchers (Sandelowski 1993, Graneheim & Lundman 2004). Another way to achieve credibility in how well categories cover data is to illustrate the text with representative quotations from the interviews or transcribed text. In study number IV, this is illustrated by stories and quotations from the nurses involved. There are discussions if content analysis is a separate method or just a tool used in the qualitative analysis (Graneheim & Lundman 2004).

5.2 Limitations and strengths

Study number I was an advisory intervention study with an intervention group and a control group. There was a possibility of contamination of information between the groups that could result in a smaller difference in terms of measured morbidity and

mortality. However, the 106 letters of advice given concerned drugs from many different ATC groups and were given to 41 physicians. Hence, the number of advice given to each physician was small. Moreover, the advice given was very diversified, which indicates that the learning effect was likely to be low.

In study II the low response rate of nurses´ participation may be a weakness of the study. The fact that 42 nurses were interested in participating but only 15 actually went through with the study may be due to the nurses´ high work load. Some nurses could not participate because they were not given permission by their head nurse.

Although the nurses in studies II and III only got a 1-day education, they were able to identify several DRPs that the usual care had not detected. This indicates that even a short instruction and training can give positive results. If the nurses had got a longer training, the results might have been better still.

The material in study V is unique. It consists of all reported errors made by nurses during an 11-year period. The reports are compiled by the NBHB, which is a Swedish authority. The nurses responsible for the reported errors worked in various settings, the material thus gives a broad picture of medication errors and contributing factors. Even so, reported errors contain only the tip of the iceberg of medication errors. Therefore, caution should be applied when interpreting the results as indicative of all medication errors.

5.3 Study I

In study I we studied how a clinical pharmacologist together with a nurse were able to detect DRPs. With written letters of advice sent to the physicians in charge they intervened for changes of the patient's drug treatment. We found 299 DRPs leading to 106 letters of advice. However, in a 6-month follow-up, no difference was found between the groups when counting the number of re-hospitalisations and/or deaths. Previous studies of interventions aiming at reducing DRPs are inconsistent. Pharmacist-led interventions aiming at reducing DRPs are quite common but without consistent evidence of their value for reducing re-admissions (Holland 2005, Royal *et al.* 2006, SBU 2009, Holland *et al.* 2008). One of the studies even showed a higher rate of hospital admissions after intervention by a pharmacist, which shows the complexity of the

problem (Holland *et al*. 2005). A Dutch study indicated that a combined intervention by a clinician and a cardiovascular nurse substantially reduced hospitalization for worsening heart failure and/or all-cause mortality (Bruggink-Andre de la Porte *et al.* 2006).

A "formal" problem does not always imply that there is an essential pharmaco-therapeutic problem in a specific patient at a certain time. Some drugs routinely considered to be inappropriate may be appropriate for the individual patient within the clinical context. The difference between observed drug-related problems and advice given may reflect this issue in our study. Two hundred and ninety-nine DRPs were counted, 106 of which were estimated to have enough clinical importance, and a letter of advice was therefore passed on to the physician in charge of the patient. An even smaller proportion of the advice given was accepted by the physicians (63%).

5.4 Study II

Study number II was conducted to find out if nurses, by using a new structured nurse-led medication review, were able to identify DRPs in in-patients. Previous studies describing nurse-led interventions for identification and prevention of DRPs are uncommon (SBU 2009). A meta-analysis from 2006 showed no evidence for the effectiveness of nurse-led interventions aiming at reducing re-admission to hospital and drug-related morbidity (Royal *et al.* 2006). In contrast, Blue et al.(Blue *et al.* 2001) were able to demonstrate that nurses could improve the outcome of patients with heart failure admitted to hospital. Compared with the usual care, the patients in the intervention group had fewer re-admissions and spent fewer days in hospital because of heart failure. Griffiths *et al* showed that patients were able to manage their medication in a better way after their intervention Griffiths *et al.* 2004). In our study, 15 participating nurses were able to identify 59 clinically relevant DRPs in 80 patients, not detected by the usual care. Out of these 63% (n = 37) resulted in an intervention such as: information to the patient, dose reduction or withdrawal of one or more drugs. The new feature of this method was the structure whereby the nurse had a leading role. Three measurements undertaken were: completion of a Symptoms assessment form (SYM) containing questions on symptoms caused by common drugs, measurement of the patient's renal function, and determination of possible drug-drug interactions (DDIs). The nurses each enrolled from one to 16

patients (mean six). This vast difference could depend on available time, access to patients matching the inclusion criteria, the nurse's commitment to the task, the climate and acceptance in the participating ward for this kind of nursing activity, or a combination of all. Nurses' working experience is also a possible contributing factor. The majority of the nurses had a working experience of 1 to 5 years. This relatively short working experience may have contributed to the low rate of included patients. Nurses with extended experience may have been able to include more patients and even to detect more DRPs. However, nurses in the study with the longest working experience (6–15 years) seemed to enrol even fewer patients (mean three) than all nurses (mean six). In another study in which nurses successfully reported suspected ADRs they had in mean 14 years of working experience.(Backstrom *et al.* 2007). This nurse-led medication review model was well accepted by the nurses and the physicians.

5.5 Study III

In paper III we wanted to evaluate if nurses could improve the quality of the drug therapy and reduce re-admission of elderly patients. The nurses in this study found 86 clinically significant DRPs not detected by the usual care. Although there was no decrease of re-admissions after the intervention, we could show that many DRPs not detected by the usual care easily could be detected by nurses. In concordance with other studies, our study described the proportion of inappropriate drugs used in the elderly as high (Bergman *et al.* 2007, Fick *et al.* 2008, Johnell *et al.* 2007, Klarin *et al.* 2005, Passarelli *et al.* 2005). In our study population 17% took one or more inappropriate drug or drug combinations. There may be a risk of overestimating the use of inappropriate drugs when using computer-based decision support systems (CDSS). A medication review must always include a clinical judgement by a physician with knowledge of the patient's current health and social status. A substantial part of the DRPs found by the nurses were of a kind that could not have been detected with a CDSS. To be able to find these DRPs, a symptoms assessment made by a nurse was needed.

5.6 Renal function

To avoid IDU in the elderly, an accurate assessment of the renal function is extremely important (Corsonello *et al.* 2005, Fields *et al.* 2008). Although serum creatinine is the most common laboratory test used for identifying renal insufficiency, it fails to detect such in many patients, particularly elderly women (Akbari *et al.* 2004, Corsonello *et al.* 2005, Fields *et al.* 2008, Swedko *et al.* 2003). In our studies I, II, and III a substantial part of the patients had some degree of renal insufficiency, and the prevalence of "hidden renal insufficiency" (serum creatinine levels within the normal range but reduced estimated GFR) was high. Many of the patients were taking medication that is mainly excreted by the kidney or is potentially nephrotoxic. In study number II, 38 patients with normal serum creatinine were found to have reduced renal function when using the Cockcroft-Gault formula to quantify renal function instead of only using serum creatinine levels. Most likely, these patients´ reduced renal function was undetected by the usual care. Thus, a major portion of the DRPs found by the nurses were patients at risk of getting ADRs due to insufficient renal function. "Hidden renal insufficiency" increases the risk of getting too high drug doses. Medication safety can potentially be improved through a more comprehensive assessment of the renal function. Calculation of an estimated creatinine clearance is easily and quickly done and could be part of a routine assessment by nurses to identify patients at risk of having DRPs (Fields *et al.* 2008). Other routines are already implemented in many clinical areas to identify at-risk patients, e.g. calculation of body mass index (BMI) to identify patients at risk of malnutrition, and calculation of risk of pressure ulcers by using the modified Norton scale.

5.7 Study I, II and III - summary

DRPs are common in hospitalized patients. Medication reviews performed by a clinical pharmacologist do not necessarily reduce drug-related morbidity or mortality. Nurses are able to identify a high number of DRPs not detected by the usual care. Furthermore, the nurses´ detection of the DRPs lead to interventions and changes of the patient drug treatment, which indicates the clinical relevance of the detected DRPs. Others studies evaluating medication reviews done by nurses and general practitioners (GPs) have demonstrated that after training, both GPs and nurses are able to identify relevant pharmaceutical care issues (Hansford *et al.* 2009, Krska 2005). Certainly, reviews done

by different professionals will differ in dimension and results as GPs, pharmacists and nurses have different educational and working experiences (Krska 2005, Krska *et al.* 2006, Hansford *et al.* 2009,). Also, when pharmacists conduct medication reviews they are leased and paid to do this particular task within the care unit for an established period of time and can stay focused on this specific task. When nurses or GPs conduct medication reviews they often perform them during their working-day where the ordinary tasks waiting to be performed. This issue is seen in studies which investigate the feasibility and acceptability of training of nurses and GPs for medication reviews. In such studies, lack of time was an important barrier for performing medication reviews.(Krska *et al.* 2005,Krska *et al.* 2006, Hansford *et al.* 2009). A speculation: if nurses were provided with the right conditions time and training to perform medication reviews they might be the most appropriate professionals for the task. Nurses have good knowledge of illnesses and symptoms. Nurses are working near the patient 24 hours a day and have the comprehensive view of the patient's health status. In general nurses also have good knowledge of the patient's history and entire drug use. Our studies show that nurses are an excellent resource for detecting DRPs in hospitalized patients.

5.8 Study IV and V

"It is easy to say why things went wrong- I have spent a lifetime doing it" (Reason 2008).

The findings in studies IV and V showed a high level of complexity in the medication errors and the contributing factors. In almost all errors more than one contributing factor could be identified. Although a nurse was held responsible for all of the errors described in the studies there were also factors contributing at a system level. The nurses´ stories revealed that the circumstances preceding an error are complex with various contributing factors included, which is illustrated in cases 1-3. Organizational routines and culture do not always support safe practice, and suboptimal working conditions create stress that increase the nurses´ risk of committing errors (Rassin *et al.* 2005, Wilkins & Shields 2008) The main finding in study number V was that the frequency, types and antecedents of the errors differ between experienced and in-experienced nurses and between male and female nurses. Furthermore, the study showed that " wrong dose" was the main type of error accounting for more than 40% of total errors. These findings are consistent with previous studies which have found

"wrong dose" to be a common medication error (Tissot *et al.* 2003, Tang *et al.* 2007, Pham *et al.* 2008, Sheu *et al.* 2009) Our results show that 15% of the nurses who were responsible for the occurrence of a medication error had less than two years of experience of nursing. This indicates a higher number of inexperienced nurses being reported than their number in Sweden would lead one to expect. Other studies linking nurses´ clinical experience and medication errors are inconclusive. Some have shown a correlation between inexperienced nurses and increased risk of medication errors (Blegen *et al.* 2001, McGillis Hall *et al.* 2004, Prot *et al.* 2005, Seki & Yamazaki 2006, Tang *et al.* 2007) while others have found no such relationship (Blegen *et al.* 2001, Mayo & Duncan 2004, Wilkins & Shields 2008). Some suggest that health-care units with more experienced nurses have a lower medication error rate than health-care units with less experienced nurses (Blegen *et al.* 2001, McGillis Hall *et al.* 2004, Prot *et al.* 2005, Sheu *et al.* 2009, Smith & Crawford 2003, Tang *et al.* 2007). Newly graduated nurses need guidance and supervision when starting out to work in their nursing profession. It is impossible for nursing students to learn all they must know to practise in a qualified and safe way in the 3-year education; moreover science is never static and there are always new knowledge and new skills to be acquired and new therapeutic approaches to learn (Henderson 1978). Our results show that inexperienced and experienced nurses are responsible for different types of medication errors and that there are different factors contributing to the errors. Likewise, Chang et al showed that nurses experience had a statistically significant relationship with nonsevere medication errors only and nursing units with more experienced nurses reported more nonsevere medication errors. (Chang & Mark 2009). To have good knowledge of the drugs that the nurse administers on a daily basis may seem essential but is not always the case (King 2004, Ndosi & Newell 2009). In our study number V, lack of knowledge was identified as a contributing factor in 13% of the cases. It could be lack of knowledge of the drug, the technique of preparation and administration, or the patient's condition. Other studies indicate lack of knowledge as a major contributing factor for errors (Leape *et al.* 1995, O'Shea 1999, Armitage & Knapman 2003, Taxis & Barber 2003, Tissot *et al.* 2003, Prot *et al.* 2005, Santell & Cousins 2005Krahenbuhl-Melcher *et al.* 2007, Ndosi & Newell 2009). Inexperienced nurses were more prone to make a medication error due to "lack of adequate knowledge" and to administer drugs the wrong way while experienced nurses showed a tendency to "practice beyond scope of practice" more often. Inexperienced nurses were affected to a higher extent by absence of guidelines and by unclear organizational routines than experienced nurses. These

results are in accordance with studies of office workers which have shown experienced workers´ tendency to make rule-based errors while inexperienced workers´ commit more knowledge-based errors (Zapf 1992). One possible explanation of our results is that nurses with extended experience have seen a large number of errors and near-misses and may know more about when and where errors occur and what is needed to prevent them. A possible explanation of the differences in the type of errors that inexperienced and experienced nurses make is that as nurses gain experience they do not have to strictly follow the rule-book but can act out of their own knowledge and experience. Furthermore, the organizational policies, routines and guidelines do not always accommodate the complexity of nursing, and nurses sometimes have to solve problems outside the guidelines (Chang & Mark 2009). Experienced nurses are able to detect nuances in various situations and to interpret the situation in its context, and they are accomplished to predict what is to be expected in a given situation.

Our results show that male nurses in Sweden are more often reported for medication errors than female nurses. The literature on gender differences in nurses´ medication error rate is missing, and no other reports have been found on the gender differences in error frequency. Moreover, our results show that male nurses tend to solve problems by acting on their own initiative to a higher extent than female nurses, who tend to rely on authorities and follow regulations. There are several possible explanations of these findings. First, the male nurse may make a decision to administer a drug to a patient in an emergency situation relying on his experience and job-specific know-how. Although the choice of drug in itself may be correct, it still leads to a medical error because the drug was administered without prescription by a qualified staff member. The reason for male individuals valuing their skills higher and relying more on their own ability seems very complex and probably derives from a web of factors ranging from societal imprint on the male infant to expectations of gender-stereotype traits and role-stressors. It is known that males are more prone to risk-taking in various contexts (Ayanian & Epstein 1997, Byrnes 1999, Zuckerman & Kuhlman 2000). Men have scored significantly higher when measured for gambling risk and risky driving than females. When tested on decision-making and risk-taking related to major health issues, men were more likely than women to state risk-prone attitudes (Ayanian & Epstein 1997).On the other hand, it is possible that the male nurse does not at all consider his action as risk-taking, as he trusts his experience and ability to such an extent that he is certain of making the right decision. To generalize, a conclusion can be that men are more confident in their

know-how and may act on their own in a decision-making situation to a higher extent than women simply because women are less confident and prefer to seek help from superiors before deciding what action to take. Other studies have shown that over-confidence may increase the likelihood of errors (Arkes 1981, Griffin *et al.* 1990). Finally, male nurses are still a minority in Sweden which may lead men to compensate and excel in their job as they experience both external and internal pressures. This could cause male nurses to "act out of role" more frequently than female nurses. Also male nurses may be more carefully observed for possible mistakes by their colleagues.

Case 1 Practice beyond scope of practice

Sten is a nursing home resident. He has cancer and severe pain. He is now receiving palliative care. He is prescribed Dexofen (dextropropoxyphene) 100 mg four times a day, paracetamol 500 mg four times a day and Morphine 10 mg "when needed". It is a Saturday morning and Pia, the responsible nurse, is talking to Sten The drug treatment does not have enough effect. Sten is not successfully pain relieved. He wants to have Morphine more often. Pia suggests he takes Morphine four times a day instead of Dexofen. Sten thinks that is a good suggestion. Pia withholds Dexofen and writes Morphine 10 mg. X 4 in the medical chart She prepares his dosette according to the new regime for the weekend. She also writes laxantia two times a day in the patient's medical chart. The laxantia she ordered is a general ordination at the nursing home and can thus, be administered" when needed". Pia reported to the nurse working the evening shift and told her to test the new drug regime over the weekend and to inform the physician on Monday and get the regime properly confirmed.

Comments: Pia had recently taken a course in pain treatment and she probably made a correct judgement. The dose was probably correct and the change was of benefit to the patient. Despite this Pia is reported to the NBHB due to "practice beyond scope of practice". Although the choice of drug in itself may be correct, it still leads to a medical error because the drug was administered without prescription by qualified personnel. The nurse makes a concession due to a fallible organization with an unclear distribution of responsibility.

Case 2 “Reality surpasses fiction”.

This event took place at a nursing home. It's early night and the registered nurse – Anna- is administering the evening and night medication to the residents. Anna had earlier spoken to the physician and they had decided to withdraw one patient´s Baclofen (a centrally acting skeletal muscle relaxant). So Anna is busy with taking out all the Baclofen pills from the patient's dosette when she is interrupted by the nurse assistant. The nurse assistant is worried about a patient whose foot is swollen and red. Anna interrupts her doings and follows the nurse assistant to the patient to examine his foot. She puts the cup with all the ablated Baclofen, on the chest in the Axel´s room. Anna examines Axel's foot and decides to call for a doctor. When she leaves the room she forgets the cup with medication on the chest. Axel has dementia and as Anna and the nurse assistant leave the room he takes all the pills. When the nurse assistant a few minutes later discovered what had happened. Axel had managed to take 20 pills.

Case 3 The need to solve other problems while administering drugs

It is a busy morning at the department of medicine. A nurse asks a colleague- Sara to help her out with an infusion of Impugan (diuretic). Sara had a lot to do herself but gave priority to the infusion and starts preparing it in the medication room. She takes sodium, write a label with the name of the patient, the name, strength and dose of the diuretic. The patient's chart is lying on the bench. She starts getting syringes and injection needles when she is interrupted by one of "her own" patients, Mr Bergman, standing in the doorway. He is in pain and wants to have his Morphine. Sara tells him she has to finish what she is doing and will then immediately prepare his injection. Mr Bergman stays in the doorway talking to the nurse describing the pain and its location. Sara hurries finishing the preparation of the diuretic sticks the label on the infusion, makes a last control of the patient chart and connects it to the patient. After that she gives Mr Bergman his injection of Morphine. Half an hour later the assisting nurse alerts the nurse that the patient with the diuretic infusion is acting "weird", he talks "sputter". Sara rushes to the patient and realizes that she has prepared the infusion with 250 mg. Morphine instead of 250 mg. Impugan. In the medication room Impugan and Morphine are placed right next to each other and the nurse had Morphine in her head while preparing Impugan. The patient received antidote and did not get any permanent injuries.

5.9 Error reporting systems

According to the literature variability in medication errors and contributing factors is largely due to the methods by which medication errors are detected and measured, which renders the results from different studies difficult to compare (Krahenbuhl-Melcher *et al.* 2007). Previous studies on predictors of medication errors have often focused on observation and minor medication errors (Han *et al.* 2005, Prot *et al.* 2005, Seki & Yamazaki 2006). Other researchers have focused on what factors nurses

imagine to be predictive of medication errors or what errors they remember having made during their career (Smith & Crawford 2003, Mayo & Duncan 2004, Fry & Dacey 2007, Tang *et al.* 2007, Wilkins & Shields 2008, Davis *et al.* 2009, Sheu *et al.* 2009). The limitations of such studies are that the errors are either minor or have not yet happened. Furthermore, there may be a re-call bias as well as the participants telling the investigators what they want to know. The medication errors and contributing factors the nurses can imagine they can also be extra vigilant of, and so the error does not occur. In summary, there could be a difference between imagined error scenarios and real errors, and also there might be a difference in minor errors and errors of significance (Chang & Mark 2009) Subjects from studies number IV and V are medication errors of significance that have actually happened and have been judged to put the patient at risk of getting seriously injured.

5.10 The interaction between human and system factors

"No man is an island entire of itself; every man is a piece of the continent, a part of the main" (John Donne 1572-1631)

To try to discriminate between medication errors where the error is a result of individual factors such as incompetence or neglect, and those which occurred as a result of system factors such as pressure of work, is not easy. There is not one factor causing an error but a result of interrelated human and system factors. Several recurrent contributing factors are involved in medication errors. So, what are system factors and what are individual factors? Negligence, forgetfulness or lack of attentiveness are common contributing factors for medication errors. You could make it easy and argue that this a typically individual factor for which the system cannot be responsible. But on the other hand in our study as well as others the results show that lack of attentiveness or forgetfulness often derive from interruptions and the need to solve other problems while administering drugs (Biron *et al.* 2009) case 3 indeed illustrates this. Likewise, practice beyond scope of practice may at first sight appear to be an individual choice by the nurse to diverge from guidelines having no roots in the system. But, as health-care organizations and systems are not perfect, nurses are sometimes forced to find alternative solutions outside the guidelines for the benefit of the patient. Furthermore, nurses are often held accountable for ensuring that they keep their knowledge and skills up-to-date throughout their working lives to ensure that they deliver lawful, safe and

effective practice (Ndosi & Newell 2009). We cannot blame lack of knowledge only on the individual nurse. Health-care managers ought to take a greater responsibility for the continuous education of nurses´. Lack of knowledge of drug administration amongst health-care professionals is also a system failure (Leape 1997, Page 2007).

5.11 Measures to be taken

There are errors waiting to happen, and we must provide a safe thinking to stop them. We cannot easily change the human cognition, but we can create contexts in which errors are less likely to happen and, when they do occur, increase the likelihood of detection and correction of such (Reason 2008). The best people can make the worst errors and errors will occur, even in the best organizations, therefore we need to have "both braces and belt" (multiple barriers and safeguards) in the organization. Despite a world-wide focus on improving patient safety, the last decades the progress is slow. We must understand that the current approaches for preventing medication errors are inadequate. Also, we must improve the error-reporting systems, avoid punishment, and focus on identifying performance improving opportunities, and understand and enhance human performance within the medication process (Crane 2000). The concept of latent errors or system failures is important. These system errors are "built in" and are present long before the active failure (human error) occurs. Discovering and correcting latent failures may have a greater effect on reducing errors than does focusing attention on errors when they occur (Kohn 1999). We need to create a change of behaviour and develop the culture of patient safety. If a nurse knows something puts a patient at risk, it´s her/his responsibility to react and to not accept a procedure because it has always been done that way. Nurses should not be expected to prepare or administer medication in a distracting environment. It might seem impossible for nurses to avoid this, because of the nature of the nurse's work and the clinical settings. Nurses are often hurried, distracted, and interrupted during critical steps in the medication process. Nurses frequently perform more than one task at a time within this complex environment, and drugs are often prepared and administered in stressful situations. Nurses must be constantly prepared to interrupt their work due to priority changes. A multitude of physicians, patients, students, visitors, and co-workers are often seen interrupting nurses at inopportune times. Simply because they are standing still in front of the automated medication dispensing machine or medication cart, they fall prey to being interrupted. This is a culture and organizational issue that leads to decreased patient

safety. Innovative methods that reduce distractions and promote focus are needed. Safety begins with strong leadership and management principles. (Armitage & Knapman 2003, Balas *et al.* 2004, Bates *et al.* 1995, Biron *et al.* 2009, Pape *et al.* 2005). Only nurses and nurse leaders can change this situation by not accepting distraction during medication preparing and administration. Nurse leaders need to change the culture and the facilitate for nurses to perform drug preparation and administration in a safe way.

When analysing the errors in our studies number IV and V, one is struck by the unbelievably peculiar circumstances in some cases. If it had not really happened you would think that it never could. "Reality surpasses fiction". Some errors cannot be predicted and nurses cannot be vigilant of such. Cases 2 illustrate this very well. Like Tage Danielsson said in his famous probability monologue from 1979. *"Sannolikt betyder något som är likt sanningen. Men lika sant som sanning är det inte. En sannolikhetskalkyl blir ju väldigt olika före och efter. Före en händelse är det ytterst osannolikt att det skulle kunna hända, men så fort det har hänt så rakar ju sannolikheten plötsligt upp till 100% så att det blir nästan sant att det har hänt, men bara nästan sant."* (Danielsson 1979)

5.12 The nurse's role and responsibility in drug treatment

What is the nurses´ role today in medication management and what role is desirable? Older literature consists of repeated publications of procedures and techniques specifically directed at nurses to prevent them from making errors. Included are procedures as the "Golden rules", "Five rights" and the "The three times check" addressing the nurse's behaviour and not considering factors in the environment and the current situation (Anderson & Webster 2001, Gibson 2001) The essence is that if the "Five rights" are followed errors will not occur. However, safe and high quality administration is more complex, not just a technical process. In the drug administering process, nurses must of course use their critical thinking and clinical judgement (Eisenhauer *et al.* 2007, Page & Mc Kinney 2007). Safe administration of medication involves administering the correct drug to the right patient as well as ability to monitor its effectiveness by having knowledge of the pharmacological actions and possible side-effects of the drug and of the patient's current clinical status.

It is important for nurses to take control of developing and thereby ensuring the quality of the medication process, instead of taking advice from other disciplines who do not understand the complexity of the nurse's profession (McBride-Henry & Foureur 2005, Gibson 2001). As frontline providers of care, nurses are in a key position to intercept a medical error before it affects a patient (Henneman et al. 2006, Page & McKinney 2006). Nurses work near the patient 24 hours a day and supervises the patient's daily life; when sleeping, eating, going to the toilet etcetera and have a comprehensive view of the patient´s health status. In general nurses also have good knowledge of the patient's history and entire drug use. Nurses are thus in a perfect position to monitor the effect of a drug and to identify and alert for possible DRPs. Nurses are able to prevent an inappropriate drug administration by checking on a patient's status or laboratory data. Nurses can detect an adverse effect, and anticipate an adverse reaction related to the patient's pathophysiology, e.g., drug toxicity because of renal dysfunction (Eisenhauer *et al.* 2007). Nurses are involved in all steps of the medication process (Figure.1). Although the prescribing step in most cases is the physician´s responsibility, nurses are often the first to notify the physician of the need for medication or dose changes. Nurses are responsible for preparing the prescribed drug and dose. Nurses are responsible for informing and educating the patient, and the patient's family. Nurses are responsible for administering the drug in an for the patient, optimal way. Finally, nurses together with the physician, are responsible for monitoring the reaction on the drug treatment. This was already known in 1859 as Florence Nightingale said: *"In diseases which have their origin in the feeble or irregular action of some function, it is quite an accident if the doctor who sees the case only once a day, and generally at the same time, can form any but a negative idea of its real condition. In the middle of the day, when such a patient has been refreshed by light and air, by his tea, his brandy, by hot bottles to his feet, by being washed and by clean linen, you can scarcely believe that he is the same person as lay with a rapid fluttering pulse, with puffed eye-lids, with short breath, cold limbs, and unsteady hands, this morning. Now what is a nurse to do in such a case? Not cry, "Lord, bless you, sir, why you'd have thought he were a dying all night.". What he wants is not your opinion, but your facts. In all diseases it is important, but in diseases which do not run a distinct and fixed course, it is not only important, it is essential that the facts the nurse alone can observe, should be accurately observed, and accurately reported to the doctor"* (Nightingale 1859).

6 CONCLUSIONS

- *Paper I* Although DRPs are common our study suggests that medication reviews performed by a clinical pharmacologist do not necessarily reduce drug-related morbidity or mortality. It is of importance to clarify if and in what way drug-related problems are preventable.
- *Paper II* By using a structured nurse-led medication review, nurses can independently identify DRPs not detected by the usual care and contribute to providing safer and more effective drug treatment.
- *Paper III* A structured nurse-led medication review showed no effect on re-hospitalization or IDU. But, nurses were able to detect a high proportion of clinically relevant DRPs not detected by the usual care, thereby improving the quality of the drug treatment of elderly hospitalized patients. By using a symptoms assessment form, nurses can find DRPs that computer-based decision support systems (CDSS) and the usual care oversees.
- *Paper IV* The study highlights that medication errors made by nurses is a result of interrelated human and system factors. Several recurrent contributing factors are involved in medication errors made by nurses.
- *Paper V* Inexperienced nurses and male nurses are responsible for a higher proportion of reported medication errors than experienced nurses, and female nurses are. Also, the error type and the contributing factors are dissimilar within the groups. Inexperienced nurses more often make knowledge-based errors. Male nurses more often practice beyond scope of practice. Because of shortcomings within the system nurses sometimes are forced to make role-based errors.

- In summary my thesis generates new knowledge of how nurses can contribute to a safe drug treatment of high quality. Nurses play an important role in ensuring patient safety. To be able to function in this role, nurses need to know how errors occur and what factors contribute. This study can contribute to better understanding of the nature of medication errors made by nurses.

7 ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to all of you who have helped me complete this thesis. Without you it would never have happened. I would especially like to thank:

Johanna Ulfvarson, my supervisor, for introducing me into the world of science, for always having faith in me and "kicking" me to the limit of my capacity. You have given me laughter, knowledge and self-confidence. Believe me, without you I would have given up a long long time ago.

Eva Andersén Karlsson, my supervisor, for always giving me support, good ides and wise points of views.

Christer von Bahr, for sharing your unlimited knowledge in pharmacology with me and for making it understandable and so interesting.

Margareta Carlström, for always being there with coffee and knowledge to transform my Swenglish into excellent British English.

Karin Sparring Björkstén, for good collaboration and valuable assistance with the writing.

Caroline Modigh, for good collaboration, nice lunches and for your innovative feminist Initiatives.

Lina Benson, for good collaboration and for so patiently guiding me through the jungle called statistics.

Carina Ursing, my research mentor, for supportive talk, discussions and for kind interest in my work.

Anita Stålsäter at KI/SÖS, for all help with stubborn papers and other tiresome procedures during my postgraduate student journey.

Sari Ponzer and Göran Elinder, Prefects at KI/SÖS, for support and for providing good research conditions for me.

Sara Eklöf, for valuable cooperation in my studies and for being such a good friend and listener. You brought order into my bizarre thoughts and confused discussions.

Emmy Bergqvist, for rapid and correct data collection.

All participating nurses and patients at Södersjukhuset for your time and for making the studies possible.

Elisabeth Pantzar, my boss, for never holding me back and for always giving me the presupposition to do what I needed to do.

My colleagues, friends and room-mates: Buster Mannheimer, Pi Caust,

Marie-Louise Ovesjö, Sara Eklöf and Sten Ronge, for being great room-mates and sharing your knowledge in different fields with me. You have given me great support, valuable assistance, and many laughter both on and off work.

My colleagues and friends at department 26, for participating in my studies and for your great interest in my work, and not least for taking me out for beers now and then.

My mother, for always being there for me and my family and for always believing in me.

My father, it is sad you are not here. I know you would have been proud of me.

My kids Emmy, Micke, Thomas and Rebecca, for reminding me of other important things in life such as ice hockey, figure skating, job interviews, shopping clothes, drinking tea and watching "non-quality shows" on TV. I love you!

Anders, my husband, my love and my best friend, for being there. Hold on, soon it will be just you and me and two bikes.

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