eMedication

– improving medication management using information technology
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eMedication – improving medication management using information technology.
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Abstract


Medication is an essential part of health care and enables the prevention and treatment of many conditions. However, medication errors and drug-related problems (DRP) are frequent and cause suffering for patients and substantial costs for society. eMedication, defined as information technology (IT) in the medication management process, has the potential to increase quality, efficiency and safety but can also cause new problems and risks.

In this thesis, we have studied the employment of IT in different steps of the medication management process with a focus on the user’s perspective. Sweden is one of the leading countries when it comes to ePrescribing, i.e. prescriptions transferred and stored electronically. We found that ePrescribing is well accepted and appreciated by pharmacists (Study I) and patients (Study II), but that there was a need for improvement in several aspects. When the pharmacy market in Sweden was re-regulated, four new dispensing systems were developed and implemented. Soon after the implementation, we found weaknesses related to reliability, functionality, and usability, which could affect patient safety (Study III). In the last decade, several county councils in Sweden have implemented shared medication lists within the respective region. We found that physicians perceived that a regionally shared medication list generally was more complete but often not accurate (Study IV). Electronic expert support (EES) is a decision support system which analyses patients’ electronically-stored prescriptions in order to detect potential DRP, i.e. drug–drug interactions, therapy duplication, high dose, and inappropriate drugs for geriatric or pediatric patients. We found that EES detected potential DRP in most patients with multi-dose drug dispensing in Sweden (Study V), and that the majority of alerts were regarded as clinically relevant (Study VI).

For an improved eMedication, we need a holistic approach that combines technology, users, and organization in implementation and evaluation. The thesis suggests a need for improved sharing of information and support for decision making, coordination, and education, as well as clarification of responsibilities among involved actors in order to employ appropriate IT. We suggest collaborative strategic work and that the relevant authorities establish guidelines and requirements for IT in the medication management process.

Keywords: eMedication, eHealth, medication, ePrescribing, electronic prescribing, information technology, drug-related problems, clinical decision support system, health care, pharmacy, patient
To my family
LIST OF PAPERS

I. Swedish pharmacists value ePrescribing: a survey of a nationwide implementation.
   Hammar T, Nyström S, Petersson G, Rydberg T, Åstrand B.

II. Patients satisfied with e-prescribing in Sweden: a survey of a nationwide implementation.
   Hammar T, Nyström S, Petersson G, Åstrand B, Rydberg T.

III. Implementation of information systems at pharmacies – a case study from the re-regulated pharmacy market in Sweden.
    Hammar T, Hanson E, Ohlson M, Petersson G.
    *Research in Social and Administrative Pharmacy*. Published online: 11 August 2014

IV. Implementation of a shared medication list - physicians’ views on availability, accuracy and confidentiality.
    Hammar T, Ekedahl A, Petersson G.
    *International Journal of Clinical Pharmacy*. Published online: 6 September 2014.

   Hammar T, Hovstådus B, Lidström B, Petersson G, Eiermann B.
   *International Journal of Clinical Pharmacy*. Published online: 29 June 2014.

VI. Physicians’ views on electronic expert support system: perceived benefits and clinical relevance of the alerts.
    Hammar T, Lidström B, Petersson G, Gustavsson Y, Eiermann B.
    *Manuscript.*

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POPULÄRVETENSKAPLIG SAMMANFATTNING

eMedicinering

– IT-stöd i läkemedelsprocessen

Läkemedel förbättrar och förlänger livet för många och utgör en väsentlig del av dagens hälso- och sjukvård men om läkemedel tas i fel dos eller kombineras felaktigt med varandra kan behandlingen leda till en försämrad livskvalitet, sjukhusinläggningar och dödsfall. En del av dessa problem skulle kunna förebyggas med rätt information till rätt person vid rätt tidpunkt och i rätt form. Informationsteknik i läkemedelsprocessen har potentialen att öka kvalitet, effektivitet och säkerhet genom att göra information tillgänglig och användbar men kan också innehålla problem och risker. Det är dock en stor utmaning att i läkemedelsprocessen föra in effektiva och användbara IT-system som stödjer och inte stör personalen inom sjukvård och på apotek, skyddar den känsliga informationen för obehöriga och dessutom fungerar tillsammans med andra system. Dagens IT-stöd i läkemedelsprocessen är otillräckliga. Till exempel saknar läkare, farmaceuter och patienter ofta tillgång på fullständig och korrekt information om en patients aktuella läkemedel; det händer att fel läkemedel blir utskrivet eller expedierat på apotek; och bristande eller långsamma system skapar frustration hos användarna. Dessutom är det flera delar av läkemedelsprocessen som fortfarande är pappersbaserade. Därför är det viktigt att utvärdera IT-system i läkemedelsprocessen.

Vi har studerat IT i olika delar av läkemedelsprocessen, före eller efter införandet, framför allt utifrån användarnas perspektiv. Sverige har lång erfarenhet och tillhör de ledande länderna i världen när det gäller eRecept, det vill säga recept som skickas och lagras elektroniskt. I två studier fann vi att eRecept är väl accepterat och uppskattat av farmaceuter (Studie I) och patienter (Studie II), men att det finns behov av förbättringar. När apoteksmarknaden omreglerades 2009 infördes fyra nya receptexpeditionssystem på apotek. Vi fann att det efter införandet uppstod problem med användbarhet, tillförlitlighet och funktionalitet som kan ha inneburit en risk för patientsäkerheten (Studie III). I Sverige har man inom flera sjukvårdsregioner infört gemensamma elektroniska läkemedelslistor. I en av studierna kunde vi visa att detta har inneburit en ökad tillgänglighet av information, men att en gemensam lista inte alltid blir mer korrekt och kan innebära en ökad risk att känslig information nås av obehöriga (Studie IV).
I två av studierna undersökt beslutsstödssystemet elektroniskt expertstöd (EES):s potential som stöd för läkare att upptäcka läkemedelsrelaterade problem till exempel om en patient har två olika läkemedel som inte passar ihop, eller ett läkemedel som kanske är olämpligt för en äldre person. Studierna visade att EES gav signaler för potentiella problem hos de flesta patienter med dosdispenserade läkemedel i Sverige (Studie V), och läkarna ansåg att majoriteten av signalerna är kliniskt relevanta och att några av signalerna kan leda till förändringar i läkemedelsbehandlingen (Studie VI).

ABBREVIATIONS

ADE – adverse drug event
ADR – adverse drug reaction
CDSS – clinical decision support system
CPOE – computerized prescriber order entry
DRP – drug-related problems
EES – electronic expert support
EHR – electronic health record
IT – information technology
MDDD – multi-dose drug dispensing
NEF – national ePrescription format
OTC – over-the-counter
PIP – potentially inappropriate prescription
SIL – Swedish information database for medications
INTRODUCTION

Medication is an essential part of health care and the appropriate treatment with drugs enables the cure and prevention of many conditions [1]. However, drug-related problems (DRP) are frequent and cause suffering for patients, and substantial costs for society [2-4]. Some of these problems could be prevented with the right information to the right person at the right time and in the right form [5, 6]. There are many expectations and hopes that the employment of information technology (IT) and eHealth will solve many health care problems and improve health [7-9]. The EU has launched a number of calls within Horizon 2020 to promote eHealth [10]. In Sweden, there is a national strategy for eHealth and medication, respectively [11, 12]. In the different steps of the medication management process, IT has the potential to increase efficiency and safety by making information accessible and useful, but IT can also cause new problems and risks [9, 13-16]. It is a major challenge to implement appropriate IT that supports, not interferes with, professionals in healthcare and pharmacies, protects sensitive information from unauthorized access, and is interoperable with other existing systems [7, 17, 18]. Therefore, evaluation of IT in the medication management process is important [14, 19].

Medication

The word medication can describe both an act and an item. In this thesis, medication is used to describe the act of treatment with or utilization of drugs in medicine, while the words medications and drugs are used interchangeably to describe the substance used in the treatment. Prescribing of drugs is the most frequent and cost-effective medical intervention performed by physicians and can prevent or cure many diseases, and increase quality of life [20, 21]. Drugs are used in all age groups but the use is related to morbidity, age, gender, and socioeconomic factors [22-24]. Prescription drugs represent the vast majority of all drugs being used, but drugs are also administered in hospitals, and sold as over-the-counter (OTC) drugs, dietary supplements, or complementary and alternative medicine [25, 26]. Rational use of medications can be described as physicians prescribing appropriate drugs to the patients according to the patients´ clinical needs, in doses that meet individual requirements, for an adequate period of time, and at the lowest cost to patients and communities [27]. The use of drugs and the proportion of people prescribed multiple drugs simultaneously have increased, increasing the risk of DRP [24, 28-30].
The medication management process

Medication management is a complex process requiring communication and information sharing among many actors, across different settings [1, 3, 21]. This complexity can lead to medication errors that may result in DRP. The medication management process includes assessing and making decisions on medication, prescribing, order communication, dispensing, administering and use, monitoring and evaluation of treatment (Figure 1) [16, 31]. In outpatient health care, the medication management process differs from that within hospitals since prescribed medications are primarily dispensed at community pharmacies [32]. In hospitals, medications are often dispensed and administered by nurses from a local medical supply. If living at home, the patient or a relative is responsible for medications being administered according to the prescription, or if living in a nursing home, the patient’s medications are being handled by nurses or other health care personnel [33]. Monitoring and follow-up are important parts of medication, but sometimes insufficient [1].

![Diagram](image)

Figure 1. The steps in the medication management process in primary and secondary care. In primary care, prescribed medications are primarily dispensed at community pharmacies and administered either at home or at a nursing home. In secondary care, medications are often dispensed and administered by nurses from a local medical supply.

Drug-related problems and medication errors

DRP are events or circumstances that involves a patient’s drug treatment that actually, or potentially, interferes with the achievement of an optimal outcome and may occur in any of the steps in the medication management process [2, 34]. DRP are frequent and cause suffering for patients and substantial costs for society [35-38]. DRP are a common reason for hospital care and can even be fatal [4, 34, 36, 38-40]. A large portion of DRP can be prevented [41-43]. There are a number of terms and concepts related to DRP, and partly overlapping, as well as a variety of definitions for each term (Table 1) [2, 21]. DRP, the term primarily used in this thesis, include adverse drug reactions (ADR), adverse drug events (ADE), medication errors, and potentially inappropriate prescriptions (PIP), as well as other circumstances such as therapy failure, underuse of drug,
overuse of drug, contraindication, drug-drug- interaction, drug duplication, unmet need for additional treatment, uncertainty about the aim of the drug, or other practical problems among other things [2, 34]. Medication errors are failures in the medication management process and may cause harm, but far from all errors lead to patient harm [2, 6, 21]. In contrast, ADEs relate to actual harm and may be caused by errors but often there is no error involved. Medication errors in health care can be caused by human factors, e.g. memory lapses, action slips, knowledge and rule based mistakes or violations [44]. These actions can in turn be caused by social or organizational factors, e.g. insufficient training and experience, poor communication, lack of information, heavy workload, local working culture, or inadequate procedures.

<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
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<tbody>
<tr>
<td>Drug-related problem (DRP)</td>
<td>A circumstance that involves a patient’s drug treatment that actually, or potentially, interferes with the achievement of an optimal outcome [2].</td>
</tr>
<tr>
<td>Medication error</td>
<td>Any error in the process of prescribing, dispensing or administering a drug, whether there are adverse consequences or not [2].</td>
</tr>
<tr>
<td>Adverse drug reaction (ADR)</td>
<td>Any response to a drug which is noxious and unintended and which occurs at doses normally used in humans for prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function [2, 4].</td>
</tr>
<tr>
<td>Adverse drug event (ADE)</td>
<td>An injury related to the use of a drug [2, 4].</td>
</tr>
<tr>
<td>Potentially inappropriate prescription (PIP)</td>
<td>Prescriptions in which risks outweigh benefits, especially used when assessing medication for older people [45].</td>
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Medication amongst older people and other frail patient groups

Increasing proportion of older people in the population and, in parallel, an increased lack of personnel and resources are anticipated [1]. Drug treatment in the elderly is especially challenging due to an increased prevalence of multi-morbidity, and changes in physiology, pharmacokinetics, and pharmacodynamics [1, 46]. In addition, many older people may have difficulties handling their medication due to cognitive impairment. Medication in children is also challenging due to large variations in weight and metabolism in combination with lack of knowledge and documentation concerning efficacy and safety of many medications [47].

Multi-dose drug dispensing (MDDD) is a service in which patients receive their medication machine-packed into unit dose bags for each time of administration [48-51]. Patients with MDDD are often old, have several diseases and many different medications. MDDD has been suggested to reduce medication errors, increase drug adherence, and decrease waste of unused drugs [51, 52]. However, a high prevalence of potential DRP, a lower quality of drug treatment than for other patients, an increased number of drugs after a patient’s transition to MDDD, and fewer changes in drug treatment have been found among patients with MDDD [29, 48-50, 53].
**Actors and information in the medication management process**

There are several actors in the medication management process: patients, physicians, pharmacists, nurses, other health care professionals, relatives and carers, as well as health care providers, non-governmental organizations, and authorities (Figure 2) [16, 17]. From a legal point of view, physicians are responsible for the prescribed medication being appropriate in relation to the patient’s entire medication [54]. However, physicians have various opinions concerning their responsibility for performing medication reconciliation, providing an accurate medication list, or reviewing whether the treatment is appropriate [55-58]. Pharmacists are primarily involved in medication management during the dispensing of medications where they often are the last health care provider the patient encounters before using (or not using) a medication. At community pharmacies, pharmacists are responsible for safe dispensing of prescription drugs, and examine prescriptions before dispensing. Pharmacists’ modification of prescription errors has been shown to be of clinical value [59-63]. Clinical pharmacists are increasingly included in the health care team, and their interventions has been shown to be of clinical value [64].

![Figure 2. Actors' exchange of information in the medication management process: e.g. patients' current medication, patient specific parameters, reimbursement and generic substitution, knowledge and instructions regarding medication, as well as regulation, guidelines, and recommendations. Information exchange can be oral, paper based, or electronic.](image-url)
One of the key components to achieving appropriate drug treatment is the access to the needed information for the involved actors [5, 6, 65]. It has been estimated that half of the medication errors are associated with the insufficient information on the patient and/or drug [5]. Information exchange between different actors can be oral, paper based, or electronic. Physicians making decisions on treatment need patient specific information, current medication list, and other patient specific information, e.g. age, weight, allergies, co-morbidities, medical history, and other factors that may affect the pharmacokinetics of the drug such as renal and hepatic function [66]. In addition, drug specific information, e.g. dosage information for certain age groups, indications and contraindications, information about drug-drug interactions, and related guidelines are necessary to provide optimal care. Pharmacists also need information on reimbursement and generic substitution. Patients, or relatives/carers, need information on which drugs to use and how to use them. Health care organizations, authorities, and non-governmental organizations request information for monitoring but also provide information in form of e.g. regulation, guidelines, and recommendations. Information and knowledge need to be continuously updated [5, 7-9, 14, 17]. Information overload can result in new knowledge not being adopted into clinical practice [67]. Thus, information has to be presented and made accessible in a usable form.

Patient adherence to drug treatment is vital to reach the desired outcome. However, non-adherence to treatment is common for various reasons such as ADR, lack of motivation or knowledge [1, 68]. Patients can be more or less involved in decisions and handling of their medication, and are at times assisted by relatives [69]. Patients are generally becoming increasingly engaged in their health care and this development is supported by the growth of IT in society, e.g. a majority of Internet users search for health information on the Internet [70-73]. The importance of patient centered care, empowering patients, and involving them in the medication management process is becoming more and more prioritized. Informed and motivated patients are more likely to continue using health care services, value and maintain relationships with health care providers, comply with treatment, and take an active role in their own health care [74, 75].

**Strategies for improving medication appropriateness**

The transition between different health care providers and settings is a known risk for DRP and medication errors [1, 76]. An increased number of prescribers or dispensing pharmacies can also increase the risk of DRP [1]. Consequently, medication reconciliation has been endorsed as a method of improving the accuracy of the medication list. Medication reconciliation is the process of obtaining a complete and accurate list of all the medications an individual is taking from different sources, and communicating that list to all the patient’s health care encounters, and is recognized as a method for preventing medication errors [46, 57, 77-79]. However, this process is seldom straightforward and can often be time consuming depending on the accuracy and availability of information sources.
To monitor the quality of prescribing, different measurements and indicators can be used. Since inappropriate prescribing for older people has become an important public health issue, there are different approaches in measuring and detecting inappropriate prescribing, and measuring quality of prescribing [46, 80, 81].

Many DRP can be avoided by different strategies such as evaluation of therapy, education of professionals or patients, medication review, or other actions performed by clinical pharmacists joining the health care team [1, 3, 41, 43, 46, 82]. To increase safety and prevent errors, health care systems and processes should be designed to make it harder for people to do something wrong and easier for them to do it right [5]. Since the medication management process is complex and many actors are involved, there is a need for facilitating the information handling in order to make it simpler and safer, reducing human errors, and if possible automatize some parts. Here, there are many expectations associated with the opportunities to take advantage of modern IT in the medication management process.

**eMedication - IT in the medication process**

For an appropriate, safe, and efficient medication, there is a need for tools that can support professionals in handling the information and making it available to the actors involved. eHealth has received increasing attention in the past decade defined by the European Commission as:

*eHealth is the use of IT in health products, services and processes combined with organizational change in healthcare systems and new skills, in order to improve health of citizens, efficiency and productivity in healthcare delivery, and the economic and social value of health. eHealth covers the interaction between patients and health-service providers, institution-to-institution transmission of data, or peer-to-peer communication between patients and/or health professionals.*

eMedication, in this thesis defined as IT in the medication management process, has been suggested to reduce cost, improve efficiency, medication appropriateness, and safety by for example increasing legibility, standardization, and availability of information, as well as reducing the need for manual re-entering of information and providing automated checks for potential DRP [5, 7-9, 14, 16, 17, 83]. However, in contrast to the large expectations and investments, the effects of IT in health care and the medication management process are inconsistent, partly unidentified, and not always expected, and IT has even created new problems [7, 13, 15, 84, 85].

During the last decades, the prescribing of medications and handling of information in the medication management process have gone through a major transition from paper to electronic based [86, 87]. The adaptation of the traditional process to the electronic era offers new opportunities as well as challenges for the involved actors. Worldwide, there is a large variation in the degree to which IT is implemented in the medication management process, some variation that can be explained in differences in the model of health care delivery and insurance [88, 89]. Sweden has been one of the leading countries in the implementation of ePrescribing and electronic documentation in health care, with the world’s first ePrescription being transmitted
in Sweden [32, 90]. However, IT has become widely used in health care in many other countries in the past decade [89, 91-93].

In the eMedication process, IT is used in several steps, e.g. ordering and prescribing in health care, electronic transfer and storing of prescriptions, processing and dispensing of prescriptions at pharmacies, accessing information on a patient’s current prescriptions, and support for decision making and detection of potential DRP. Terminology and description of the main IT involved in the thesis is found in Table 2 below.

Table 2. Involvement of IT in the different steps of the medication management process.

<table>
<thead>
<tr>
<th>IT system</th>
<th>Description</th>
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<tbody>
<tr>
<td>Electronic prescribing (ePrescribing)</td>
<td>Electronic entering and transmission of prescriptions. Alternative terminology: electronic prescribing, e-prescribing, eRx. (Note that ePrescribing in the literature sometimes refers to stand-alone technology for entering and reviewing, but not transmitting ePrescriptions [32]).</td>
</tr>
<tr>
<td>Electronic health record (EHR)</td>
<td>A record of electronic health information about an individual patient or population. Alternative terminology: The terms EHR, EPR (electronic patient record) and EMR (electronic medical record) are often used interchangeably, although differences between them can be defined.</td>
</tr>
<tr>
<td>Computerized prescriber order entry (CPOE)</td>
<td>Information systems that enable providers to prescribe medications. Alternative terminology: Computerized physician order entry, medical order entry systems.</td>
</tr>
<tr>
<td>Dispensing system</td>
<td>The information system used at pharmacies for processing and dispensing prescriptions. Alternative terminology: eDispensing, pharmacy computer system, pharmacy information system, pharmacy computer software.</td>
</tr>
<tr>
<td>Clinical decision support systems (CDSS)</td>
<td>Computer-based information systems used to integrate clinical and patient information and provide support for decision-making in patient care. Alternative terminology: Computerized clinical decision support systems, decision support.</td>
</tr>
</tbody>
</table>

**ePrescribing**

ePrescribing is a broad term used to describe a variety of IT systems to support the prescribing process [32, 88]. Some make a distinction between first and second generation of ePrescribing. The first generation of ePrescribing, implemented for example in the US, was stand-alone technology for electronic entering and reviewing of prescriptions, but where prescriptions were printed and handed to the patient. The second generation of ePrescribing includes the electronic transmission of prescriptions from the prescriber to the pharmacy, either to a specific pharmacy (push model) or to a centralized repository (pull model) [32]. In this thesis, ePrescribing refers primarily to the Swedish ePrescribing model including electronic entering and transmission of a prescription from the prescriber to the pharmacy as well as electronic storing and handling of prescriptions, i.e. second generation of ePrescribing with the pull model for electronic transmission (Figure 3).
A prescription, no matter the route of transfer, functions to communicate decisions on drug therapy from the physician to the pharmacist dispensing the medication and should be unambiguous, correct, and complete [90]. The handwritten prescription has a number of well recognized weaknesses, including risk of misinterpretation of poorly written prescriptions, unidirectional communication, and risk of falsification or patient losing the prescription [94, 95]. ePrescribing has been proposed as an important tool to improve quality, safety, efficiency, and cost-effectiveness in prescribing and dispensing processes [88, 90, 96]. Although some of the proposed strengths with ePrescribing have been confirmed, weaknesses with paper prescriptions are not necessarily solved, and ePrescribing may even create new errors [87, 97, 98]. The electronic handling of prescriptions in health care and at pharmacies enables the use of computerized tools to assist physicians and pharmacists in decision making and dispensing [6, 31].

In Sweden, ePrescribing has been used for more than three decades and has been the primary way of prescribing in the last decade with more than 90% of prescriptions being electronic today [90]. In addition, since 2005, it has been possible for patients to store their valid prescriptions electronically in the national prescription repository [90, 94]. At the pharmacy, patients can choose to store their prescriptions electronically, or to have their prescriptions in paper form. Patients can have their medication from electronically stored prescriptions dispensed at any pharmacy with the presentation of valid identification, and prescriptions can also be accessed via the Internet, by means of secure digital authentication. To increase the quality of ePrescriptions and thereby patient safety, as well as facilitate future development of related services, a National ePrescription Format (NEF) has been implemented. After a nationwide implementation in June 2009, NEF has introduced more formal requirements with automated quality checks of all ePrescriptions, improving interoperability and decreasing errors [99].

**Electronic health record (EHR)**

An electronic health record (EHR) is used for documentation and information sharing in health care, often also for support of clinical care and decision making, as well as patient administration functions. The information system enabling electronic prescribing and order entry is often referred to as computerized prescriber order entry (CPOE) system. In this thesis, EHR will be used to describe the information system used for documentation as well as prescribing because the prescribing module in Sweden is a part of the EHR. EHRs are almost completely implemented in all Swedish health care units in primary and secondary care [100, 101]. Each county council makes its own procurement of an EHR system. In the last decade, Sweden has moved towards using region-wide EHR systems, i.e. EHR shared between care providers within the region. Currently, the six most common EHRs have a market share of 95%. In addition to the EHR, a large number of other electronic information systems are used to support the needs of health care providers.
Figure 3. Electronic handling of prescriptions in primary care in Sweden. Prescribers can prescribe a medication via a prescribing module in the EHR system. The prescription is transferred to the national prescription repository, where it can be stored for several iterations through the entire period of its validity. Prescribers can cancel their own prescriptions if their EHR system supports this function, but they cannot view the patient’s prescriptions stored in the prescription repository. Prescribing for patients with MDDD is managed in a separate system usually not linked to the EHR. From the prescription repository, the medication can be dispensed at any Swedish pharmacy. Pharmacists can, upon request, view and dispense patients’ prescriptions via their dispensing system.

(EHR=electronic health record, MDDD=multi-dose drug dispensing)
**Dispensing systems at pharmacies**

Pharmacists at community pharmacies play an important role in detecting prescription errors and preventing DRP [33, 61, 102]. A pharmacy dispensing information system, referred to as a dispensing system in this thesis, is a system used at pharmacies for processing and dispensing prescriptions. To dispense a prescription, pharmacies in Sweden are obliged to use a dispensing system in order to handle all relevant information. Dispensing systems are used as a support for almost all tasks performed to dispense prescriptions in outpatient healthcare, e.g. accessing the electronic prescriptions in the prescription repository, managing reimbursement for medications, and printing labels for medications. When the Swedish pharmacy market was re-regulated in 2009, Sweden moved from a one state-owned pharmacy chain to several private pharmacy companies, and four new dispensing systems emerged to replace the system that had been used at all Swedish pharmacies for more than 20 years [103].

Effective support from IT in pharmacies has the potential to facilitate safe dispensing and support pharmacists [61, 62, 104-107]. However, there are few studies that have addressed the IT system supporting pharmacists when dispensing medications at community pharmacies, most of them related to ePrescribing rather than the dispensing system [16, 95, 104, 106, 108-110].

**Clinical decision support systems (CDSS)**

Decision making in the medication management process most often refers to physicians making decisions regarding new or current treatment, but some forms of decisions are made in every step of the process and require a range of information [14]. Information and knowledge on medications can be made available in different forms, paper based or electronic, and thus can be analyzed in different ways [111]. Information or knowledge that is available in a structured electronic machine readable format may be processed and analyzed automatically by a computer and thus can be utilized in a CDSS. Information and knowledge regarding medications is continuously increasing and changing as new treatments emerge, or findings in research or clinical practice change previous recommendations [111]. However, for a clinician making decisions regarding medications on a daily basis, it is difficult or impossible to keep up with evolving knowledge and at the same time keep in mind the latest recommendations according to guidelines or health economic estimations.

The rationale for CDSS is that characteristics of individual patients are matched with a computerized knowledge base, and software algorithms generate patient specific recommendations or alerts [15, 84]. CDSS in the medication management process are used to support decisions regarding medication, facilitate evidence based medicine, reduce the incidence of DRP, and improve health care quality and efficiency [85, 112]. Nevertheless, clinicians will make the final decision; the system is merely assisting with a time efficient analysis of a mass of information. The input of patient data can be automatic via integration of patient information through e.g. an EHR, or require manual entry [85]. CDSS alerts can be delivered to the decision maker through e.g. EHR, CPOE, dispensing systems, or a separate solution. There are different types of CDSS in
the medication management process; the basic principles are shown in Figure 4 below. A common type is a system giving alerts if a potential DRP is detected in the current medication. There are also CDSS that can provide dosing instructions, treatment recommendations, or detect the need for additional treatments concerning a patient [112]. CDSS can have beneficial effects such as reduction in DRP, but results are varying [7, 8, 13, 15, 112, 113]. Effects of CDSS can be related to factors such as its implementation, design, timing of alerts, and clinical relevance of alerts as well as other social factors [114, 115].

![Figure 4. Principles of clinical decision support systems (CDSS) in the medication management process. Information on patients' current medication can be derived from different sources. Patient specific information can include e.g. age, gender, weight, diagnoses, renal and hepatic function. Drug information, knowledge and guidelines include for example recommended dosing related to different factors, drug-drug interactions, contraindications, and inappropriate drugs for older people, children, pregnant or breast feeding women.](image)

Current CDSS have various limitations in the different types of information included as well as how information is processed and alerts are presented to the user [13, 66, 116]. Many alerts from CDSS are being ignored; override rates ranging between 29–91%, with variation between different categories of alerts [117–120]. Designing an appropriate CDSS is a major challenge and an insufficient CDSS can actually do more harm than good [111, 121]. Weaknesses with current CDSS are that the systems often do not have access to an accurate and complete list of patients' medications, that the CDSS lacks important patient specific information such as renal function or weight or that this information is out of date or has to be entered manually by the
physician, or limitations in the knowledge base and algorithms. This can result in both problems that are missed or that the CDSS gives rise to an excessive amount of alerts, that may disturb the clinician rather than support him/her. Alert fatigue can be described as an excessive amount of alerts that decreases clinicians’ attention of the alerts and may result in alert override and thus the risk of important alerts being missed among the clinically less relevant alerts [114]. Other risks with CDSS are that they might diminish medical judgment, cause disturbances in clinical workflow or introduce new errors [111, 122].

In Sweden, most of the EHR systems have CDSS implemented in various ways. Some of the knowledge bases within the CDSS are provided through a national database containing medication information, called SIL (Svensk informationsdatabas för läkemedel) [123]. The knowledge bases included in SIL can also be reached online or integrated in other systems. The decision support system include recommendations from the regional drug and therapeutics committee, knowledge bases for drug-drug interactions (SFINX), drugs contraindicated in elderly, drugs during pregnancy or breast-feeding (alert for female age 13-55 years) [111, 124, 125].

Additionally, some health care providers have implemented a knowledge base providing information on drug use related to renal function (NjuRen) [126], or a CDSS for pediatric medication (ePed) or other recommendations regarding drug treatment. There are also other separate systems supporting decision making in the medication management process, such as miniQ.

The Electronic Expert Support (EES) system is a CDSS developed by Medco Health Solutions, USA, and adapted to Swedish clinical practice, and managed by the eHealth Agency. EES analyzes patients’ electronically stored prescriptions to detect DRP, including drug-drug interactions, therapy duplication, high dose, drug-disease contraindication, drug gender warning, and inappropriate drugs for geriatric or pediatric patients [127, 128]. EES is primarily intended for pharmacies where alerts can be viewed, with patient consent, by the pharmacists through a function in the information system used for dispensing prescriptions. EES is available at most Swedish pharmacies (>90%), but is currently used only in a relatively small proportion of patients. The potential value of EES alerts for physicians in health care is under discussion.

**Other health IT in the medication management process**

In addition to the technologies described above, other forms of IT can support various parts in the medication management process such as barcode medication administering, and medication cabinets for administration of medications, at hospitals, nursing homes or at home [6, 129].

As a part of patient centered care and empowerment, there are different forms of support for patients taking an active part in their medication, e.g. applications for adherence and learning. In addition, patients can access different types of personal health information, such as their health record (so far to various extents) or prescription history [130-132]. The Internet has provided new ways of communication between patients and health care providers [70-72, 133, 134].
Sources of information on medication

Different sources of information of patients’ medications are available in different settings. There may be information in health records or registers of prescribed or dispensed medications locally, regionally, or nationally. It is vital that information on the patient’s current ongoing medication is available and accurate for the patients as well as all health care professionals [8, 55, 79, 83, 135, 136]. However, health care professionals often lack accurate information, and discrepancies occur frequently and can be particularly problematic with patients with multiple medications, older patients, and the transfer of patients between different health care settings [33, 77, 78, 137, 138]. Inaccurate or unavailable medication lists/records may result in medication errors such as inappropriate prescribing (e.g. drug-drug interactions or duplicate therapy), or wrong medications being administered at hospitals, nursing homes, or taken at home [44, 139]. Physicians’ unawareness of patients’ co-medication has been described as an important cause of medication errors [33].

In Sweden, there are several different sources of information on a patient’s medication (Table 3). The different sources on patients’ medications are often incorrect and rarely correspond to each other or with the patient’s current ongoing medication [140, 141]. In the EHR, a specific prescribing module includes a medication list as well as an inpatient drug list [100]. During the past decade, by sharing an EHR system, three quarters of all counties in Sweden have implemented shared medication lists for their county council managed health care (hospital, psychiatry, primary care), sometimes including private health care providers as well [76]. There is no automatic transfer of information on patients’ medications between EHRs in different counties. Dispensing pharmacists and patients have access to the national prescription repository, including all electronically stored prescriptions in Sweden, which covers approximately 90% of all prescriptions (the remaining 10% being paper prescriptions). At pharmacies, prescriptions are dispensed from this prescription repository. Due to legal reasons for the protection of patient privacy, physicians are not allowed access to the prescription repository. Prescriptions for patients with MDDD [49, 51] are separated from ordinary prescriptions (although stored in the national prescription repository) and primarily handled using a different tool in a separate system and information is usually not automatically transferred to the medication list in the EHR. In addition, the national pharmacy register is a historic register for patients’ dispensed prescriptions during the past 15 months available for patients or health care professionals with patient consent [73]. There are registers for research and statistics; the national prescribed drug register automatically includes data at an individual level for all prescription medications dispensed [142]. There is ongoing work to plan and prepare the implementation of a nationally shared medication list in Sweden (NOD, Nationell Ordinationsdatabas) [143].

Different solutions for sharing or reconciling medication information electronically between providers have been implemented or piloted or are planned worldwide [65, 79, 89, 92, 135, 136, 144-146]. Although a shared medication list is often referred to as a path to provide safer medication by providing an accurate and complete list of patients’ medications, the consequences of a transition from a local to a shared medication list are unclear and depending on several aspects.
Table 3. Sources of information on medication in Sweden. The Swedish name primarily used for the different sources are given in brackets.

<table>
<thead>
<tr>
<th>Sources of information on a patient's medications</th>
<th>Description</th>
<th>Access</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication list [Läkemedelslistan]</td>
<td>The list of current ongoing treatment linked with electronic prescribing in the EHR. Originally, the medication lists were local and information was not transferred between different health care providers. At the time of the study, many counties in Sweden had implemented a regionally shared EHR including a shared medication list [100, 140].</td>
<td>Health care. Physicians are encouraged to give print-outs to patients.</td>
</tr>
<tr>
<td>Inpatient drug list [Ordinationslistan/Utdelningslistan]</td>
<td>A list in the EHR used when administering medications to hospitalized patients.</td>
<td>Health care.</td>
</tr>
<tr>
<td>MDDD prescriptions [Dos-recept]</td>
<td>A list of prescriptions for patients' with MDDD, which is a service in which regularly used medications are machine-packed into unit dose bags for each time of administration [50, 51]. Prescribing for these patients is managed in a separate system and information is usually not linked to the medication list in the EHR.</td>
<td>Health care, pharmacies and patients.</td>
</tr>
<tr>
<td>National prescription repository [Receptdepån/Receptregister]</td>
<td>A list of patients' electronically stored prescriptions used when dispensing prescriptions at pharmacies. Electronic prescriptions are automatically transferred to the prescription repository and stored there for the entire period of validity. If treatment is changed or terminated in the EHR, the information is not automatically changed in the prescription repository.</td>
<td>Pharmacies and patients. Print-outs are often provided to patients at the pharmacy.</td>
</tr>
<tr>
<td>The national pharmacy register [Läkemedelsförteckningen]</td>
<td>A historic register of patients' dispensed prescriptions during the past 15 months [73, 147].</td>
<td>Patients, health care providers and pharmacies with patient consent.</td>
</tr>
<tr>
<td>The Swedish prescribed drug register [Läkemedelsregistret]</td>
<td>A register of patients dispensed prescriptions held by the Swedish National Board of Health and Welfare [142].</td>
<td>For research and statistics.</td>
</tr>
<tr>
<td>National Medication Database* [NOD, nationell ordinationsdatabas]</td>
<td>A nationally shared medication list connected with the national prescription repository. Aims to capture the decisions for treatment, the medication order, rather that prescriptions. Not yet implemented.</td>
<td>Planned for health care.</td>
</tr>
</tbody>
</table>

*intended implementation

EHR = electronic health record, MDDD = multi-dose drug dispensing
Weaknesses and challenges with eMedication

Despite decades of experience and world-wide recognition of the potential benefits of IT in the medication management process, we are still struggling with major problems in the medication management process, and IT systems do not meet the expectations of efficiency and safety [14, 101]. Medication errors remain and new types of errors are revealed [5, 83, 148]. There are issues with information security [149]. IT-related incidents are reported in health care [150]. The actors in the medication management process still lack vital information or describe an information overload [67]. Knowledge and evidence is disseminated into clinical practice in an incomplete manner [1, 84]. There are frequent reports of health care professionals being unsatisfied and frustrated with the system they are using [17, 151]. There are recurrent reports of IT systems in health care not being successfully implemented, failing to meet expectations, or even being cancelled during implementation [14, 17]. The weaknesses and challenges with eMedication involve technology, social, organizational or wider political aspects, respectively.

Technology aspects, information security and continuity

Robust technology is a necessity and an enabler of a safe and efficient handling of information in the medication management process but reliability and stability of a system are affected by limitations in technical infrastructure [17, 152]. Communication and linkage between different systems are limited by the lack of technical interoperability as well as a common information structure [152]. The need for a common, structured documentation as well as requirements for basic interoperability have been mentioned in several national strategies and government documents [11, 152].

To ensure sufficient patient safety in today's health care, it is necessary that information follows the patient across providers, settings, and regional borders. A major challenge is the balancing of increased information sharing and availability on the one hand and the protection of patient integrity on the other hand. In Sweden, information exchange in health care is restricted in several ways due to legal reasons in order to protect patient privacy. The appropriateness of the legislation regarding handling of information in health care and data protection is under review by the Swedish government in order to identify any need for changes [153]. Mutual trust between the staff and patient is crucial to achieve patient safety and assumes proper protection of patient integrity; thus, management of information security in health care is essential [149, 154]. Patient safety is maintained by information availability and accuracy, whereas patient integrity is maintained by confidentiality of information [155].

There are risks for disturbances in each of the steps from manufacturing, delivery, prescribing, dispensing, and use of medications [156]. Occasionally, there are reports of system breakdowns in health care resulting in information being unavailable, health care providers not being able to document appropriately, or risk of patient harm. However, strategies for continuity during disturbances are insufficient both nationally and in...
many organizations which limit our ability to provide safe medication independent of interruptions of normal procedures or system breakdowns [156].

**Social aspects and usability**

The implementation of IT is affected by social aspects such as attitudes and concerns, resistance and workarounds, expectations, benefits, involvement and user input in design, training and support, and integration with existing work practices [17, 101]. In order to achieve maximum benefit in the medication management process, it is necessary that IT is supporting health care professionals rather than being perceived as an obstacle to providing good care in an efficient manner. An important part of developing and implementing technology in health care is usability. Usability has been defined as: "The extent to which a product can be used by specified users to achieve specified goals with effectiveness, efficiency, and satisfaction in a specified context of use" (ISO 9241-11). Despite the recognized importance, usability aspects are not always incorporated sufficiently in the design and testing of information systems in health care [151, 157-159]. If changes in work process are not considered during development and implementation, the potential benefits of IT may not be achieved [17, 18, 160]. When implementing IT in health care, there might be social challenges such as attitudes, preconceived notions, changed routines or roles for health care professionals or changes in the existing hierarchy or power structure, affecting the outcome [161].

**Organizational aspects – and regulation**

Challenges related to organizational issues when implementing IT in the medication management process include preparing the organization for change, planning, leadership and management, realistic expectations and financing, teamwork and communication, learning and evaluation [17, 19]. Although most actors in health care regard eHealth as an organizational development, the procurement of IT systems in health care is still often handled as a technical matter [152]. Benefits and cost-savings from new technology will be evident at later stages. Initially, costs and time consumed might increase but must be regarded as an investment.

The importance of eHealth, including eMedication, is increasingly recognized. In Sweden, a number of authorities are involved in regulation, supervision, and strategic activities related to the medication management process, as well as managing some of the related information sources or services. The area of responsibilities of different authorities regarding medication management, including the use of IT in the medication management process, is somewhat unclear [152, 162].

Many information systems have been implemented without sufficient quality assurance due to a sometimes immature regulatory situation, and lack of clear requirements or guidelines for evaluation of IT systems in health care [14, 18]. Drugs and medical devices (such as infusion pumps or respirators) are approved by authorities, e.g. Food and Drug Administration in the US and Medical Products Agency in Sweden, and have clearly regulated methods for quality assurance. In contrast, IT implemented in health care, although involved in many critical steps of medication management and known to directly affect patient care, are often not subject
of any independent assessment of safety and fitness for purpose [18]. Medical information systems, such as EHR, have been classified as medical devices in Sweden since 2009 [163]. As a consequence, there are demands for quality assurance, including a clinical evaluation of the intended purpose. However, it is unclear among most involved actors, including system vendors and health care organizations, as well as authorities, how this should be performed and controlled in practice [164]. On the other hand, dispensing systems at pharmacies have not qualified as medical devices in the EU [163]. The eHealth Agency (a new Swedish authority) has performed evaluations to ensure that the dispensing systems’ interface and format work correctly with the agency’s managed services and databases [165]. However, the agency’s evaluation is not an overall quality control of the dispensing system and is not a certification similar to the EC certificate used for medical devices.

**Evaluation of eMedication**

The introduction of IT in health care affects the users, working procedures, organization and outcome, and does not only have the potential to solve problems, but may also create new ones [166]. Therefore, we must evaluate the implementation of IT in the medication management process in order to ensure that it meets our expectations, delivering the desired outcome and does not create new problems [167]. Evaluation of IT in health care is in itself not a goal, instead it should be used to improve existing technology or procedures, and provide knowledge for future development, implementation, or wider strategic work. Ammenwerth et al. [166] describes evaluation in the following way:

*Evaluation is the act of measuring or exploring properties of a health information system (in planning, development, implementation, or operation), the result of which informs a decision to be made concerning that system in a specific context.*

eMedication can be studied and evaluated in different settings, using different perspectives, and methods. When evaluating IT in health care, we have to consider the environment in which IT is used and the human-computer interaction [19]. Since medication management process is complex, a holistic view with a sociotechnical perspective is often required when evaluating [14, 87, 149]. A sociotechnical approach means that the implementation outcome has organizational, technological, and behavioral explanations. There is a large gap between postulated and empirically demonstrated effects of eHealth technologies. Thus, IT is not sufficiently evaluated, and when evaluated, the results are often not disseminated [7, 15, 17, 166].
AIM

The overall aim of this thesis was to study eMedication in different parts of the medication management process.

Specific aims in the six papers were:

I. To evaluate Swedish pharmacists’ attitudes towards ePrescribing, including the transfer of ePrescriptions, electronic storing of prescriptions and mail-order prescriptions.

II. To evaluate Swedish patients’ attitudes towards ePrescribing, including the transfer of ePrescriptions, electronic storing of prescriptions and mail-order prescriptions.

III. To explore the implementation of four new information systems for dispensing at pharmacies.

IV. To describe physicians’ views on changes in accuracy, availability and confidentiality of information in the transition from local medication lists to a regionally shared medication list.

V. To analyze potential DRP detected by means of EES in patients with MDDD.

VI. To explore physicians’ perceptions on and clinical relevance of alerts generated by EES for patients with MDDD, performed actions and changes due to the alerts, and perceived benefits and needs for a CDSS providing alerts for potential DRP.
METHODS

Setting
In this thesis, four main aspects of the eMedication process are covered: electronic transfer and storing of prescriptions (Study I and II), electronic processing and dispensing of prescriptions at pharmacies (Study III), obtaining accurate information on a patient’s current prescriptions (Study IV), and decision support systems for detecting potential DRP (Study V and VI). Figure 5 shows where in the medication management each of the studies can be situated, and Table 4 provides an overview methodology for each study.

Figure 5. Overview of the thesis’ studies of the medication management process.
Table 4. Overview of the six studies in the thesis.

<table>
<thead>
<tr>
<th>Study</th>
<th>Research question</th>
<th>Study period</th>
<th>Data sources</th>
<th>Study population</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Pharmacists’ attitudes towards ePrescribing</td>
<td>April 6 – May 4, 2009</td>
<td>Web-based questionnaire</td>
<td>500 community pharmacists</td>
</tr>
<tr>
<td>II</td>
<td>Patients’ attitudes towards ePrescribing</td>
<td>September 14 – October 19, 2009</td>
<td>Postal questionnaire</td>
<td>1500 patients</td>
</tr>
<tr>
<td>III</td>
<td>Describing the implementation of dispensing systems at pharmacies</td>
<td>February – June, 2012</td>
<td>Interviews and questionnaire</td>
<td>4 system vendors of dispensing system, 13 pharmacy companies’ management and 350 pharmacists</td>
</tr>
<tr>
<td>IV</td>
<td>Physicians’ perceived consequences of shared medication list in EHR</td>
<td>September – November 2013</td>
<td>Interviews</td>
<td>7 physicians</td>
</tr>
<tr>
<td>V</td>
<td>Potential DRP detected by EES in patients with MDDD</td>
<td>March 5 – June 5, 2013</td>
<td>Register study. Prescription repository and alerts generated by EES for these prescriptions</td>
<td>180 059 patients with MDDD</td>
</tr>
<tr>
<td>VI</td>
<td>Physicians’ perception of EES alerts for patients with MDDD</td>
<td>March – November 2013</td>
<td>Interviews and physicians assessment of EES alerts</td>
<td>254 patients with MDDD and 10 physicians</td>
</tr>
</tbody>
</table>

**Study design and data collection**

Studies I-IV were performed after large scale implementation while an intervention was performed in Study VI. All studies except one involved the exploration of attitudes, perceptions, needs, satisfaction or experiences among different users of the implemented health IT, pharmacists (I, III), patients (II), and physicians (IV, VI). Study III was designed as a case study and included representatives from system vendors and pharmacy company management as well, using mixed methods to combine data from different perspectives to give insight on a unique case. Below, the methods for data collection are described.

**Questionnaire**

Questionnaires specifically developed for the study aim were used in Study I, II, and III. Two of them were electronic and sent to the respondents via their email (I, III), and one was a postal questionnaire (II). The questionnaires included statements to which respondents gave their degree of agreement on a six-point (I, II) or five-point (III) Likert-type rating scale, multiple choice questions, and open-ended questions. All questionnaires were tested among a small number of subjects representing the study population, and adjusted prior to the large-scale survey.
Interviews
Interviews (III, IV, VI) followed a semi-structured protocol with questions developed by the researchers for the specific study, with one researcher (TH) performing all interviews.

Register study
All prescribed drugs dispensed for patients with MDDD (n=180 059) during three months (March 5 – June 5, 2013) as well as alerts generated for these drugs were included in the analysis (V). Prescription data were collected from the national prescription repository.

Outcome assessment and analysis
Quantitative as well as qualitative methods were used, and combined in four of the studies (I, II, III, VI).

Quantitative analysis
Answers to the questions on Likert scales were regarded as nominal or ordinal data and analyzed accordingly (I, II, III) [168]. To study any statistical relationship between variables, two different methods were used. In Studies I, II and VI, the chi-square test was used and statistical significance set at p<0.05 (I, VI) or p<0.01 (II).

In Study V, the relationship between the number of alerts and age, gender, and the number of drugs was modelled using Poisson regression, a Generalized Linear Model with the logarithmic link function. Poisson regression is suitable for modelling count data which typically have low mean values and variances, with both the mean and variance varying with the levels of the independent variables [169]. Analysis was performed using SPSS (IBM SPSS statistics 20).

Qualitative analysis
The responses to the questionnaire in free text were analyzed and categorized using manifest content analysis methods (I, II, III) [170, 171]. Meaning units, i.e. a section of the free text answer that described one aspect related to the question, were identified for each free-text answer after reading the answers several times and subsequently grouped into categories. The categories were not predefined but emerged and changed during the analysis to best capture the meaning units identified. An individual’s answer could include several different meaning units that could be grouped into different categories. Representative quotes were chosen for each category and translated from Swedish to English. One of the researchers (TH) performed the analysis.

With the respondents’ permissions, all the interviews were recorded and transcribed (IV, VI). After completing all interviews, a qualitative analysis of manifest content was performed in order to identify physicians’ views in relation to the study questions [170, 171]. The information was sorted into the main aspects and categories. The categories were not predefined but emerged and changed during the analysis. However, the main categories identified were mostly in line with the interview questions (for example physicians’ views on how the accuracy of information had changed with a shared list in Study IV), but some categories not covered in the
questions emerged (such as perceived risks and problems with patients with MDDD in Study IV). Respondents’ answers within each main category were then further analyzed and could be divided into subcategories to capture the different views on each aspect. Representative quotes were selected and translated from Swedish to English.

The analysis and categorization of data were performed using Microsoft Office Excel (I, II) and the software QSR NVivo 10 (III, IV, VI).

**Ethical approval**

Ethical approval was granted for patient involvement and handling of sensitive data for Study II by the Regional Ethical Review Board in Linköping, Sweden (Dnr 2009-M153-09) and for Study V and VI by the Regional Ethical Review Board in Umeå (Dnr 2012-359-31M).

The ethical implications of remaining studies were considered based on the guidelines from the Ethical Advisory Board in South-East Sweden. Following advice from the committee, no formal application for ethical approval was recommended due to the nature of the information handled and the respondents included. However, we followed the guidelines from the committee regarding the information to potential participants as well as handling and presentation of data so that privacy was protected and identity would not be revealed. No incentives have been offered to the respondents.
RESULTS

Study I: Pharmacists’ perceptions of ePrescribing

Swedish community pharmacists were generally satisfied with ePrescribing (98%, 253/259). Differences in the general satisfaction could not be explained by the respondents’ age, gender, or years in practice (p>0.05). A majority of the respondents regarded ePrescriptions and electronic storing of prescriptions as being safe for patients (95% for ePrescriptions and 93% for electronic storing of prescriptions respectively), providing patient benefits (96% and 95%, respectively), and being cost-effective for the pharmacy (92% and 91%, respectively) (Figure 6). The positive aspects of ePrescribing most frequently mentioned in free text answers were being safe (72%, 187/259) and saving time (55%, 143/259). Described weaknesses were related to the dispensing system or related services being used (e.g. inconvenient to make changes or corrections, unreliable technique), a perceived gap between health care and pharmacies (e.g. different supply registers used by prescriber and pharmacy, prescriber using abbreviations different than the pharmacy), and legal limitations (e.g. prescriber cannot view, cancel or change prescriptions in the prescription repository). Pharmacists also described problems related to patients with MDDD.

Figure 6. Pharmacists’ attitudes towards ePrescriptions and electronic storing of prescriptions. Respondents (n = 259) gave their degree of agreement with statements on a six-point Likert-type rating scale where 1 represented ”do not agree at all” and 6 ”completely agree”.

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Study II: Patients’ perceptions of ePrescribing

The vast majority of patients in the study had a positive attitude towards ePrescriptions (85%, 628/739) and electronic storing of prescriptions (86%, 633/739), and regarded ePrescriptions to be safe (79%, 584/739), creating benefits for them (78%, 576/739) and promoting faster dispensing (69%, 512/739) (Figure 7). Attitudes towards ePrescriptions and electronic storing of prescriptions differed with age (p<0.01). The 25–39 years age group had the largest proportion of respondents who had a positive attitude (94%, 95/101), and the 75 years and older age group had the smallest proportion of respondents with a positive attitude (70%, 87/123). Patients storing all their prescriptions electronically were more positive towards both ePrescriptions and electronic storing of prescriptions than patients who stated they had paper prescriptions: of the respondents storing all their prescriptions electronically 92% (413/450) were positive towards ePrescriptions, compared to 59% (27/46) of the respondents who only had paper prescriptions.

The most common suggestion (n=27) for improvement was to extend the information given about the services: e.g. information about how to use the services, and the safety aspects of using them. Two of the most common comments were that the respondents had limited experience with the services (n=26) and that they did not have a computer (n=10). The study population had limited experience with mail-order prescriptions and the vast majority of the study population (79%–86%) answered with ‘do not know’, or did not answer at all the questions regarding mail-order prescriptions.

![Figure 7. Patients’ attitudes towards ePrescriptions and electronic storing of prescriptions. Respondents (n = 739) gave their degree of agreement with statements on a six-point Likert-type rating scale where 1 represented “do not agree at all” and 6 “completely agree”.](image-url)
Study III: Implementation of dispensing systems at pharmacies

The implementation of four new dispensing systems followed a strict timeframe set by political decisions, involved actors completely new to the market, lacked clear regulation and standards for functionality and quality assurance, was complex, and resulted in variations in quality. With pharmacies legally responsible for the quality of dispensing systems, there were variations in quality assurance: one system was an in-house developed product, the larger pharmacy companies had a significant involvement in the system development and testing, and the smaller pharmacy companies had to rely on the vendors’ quality management systems. It was unclear how quality assurance was shared among actors in practice, i.e. who validated what, when, and how. System vendors and pharmacy companies’ management described several different problems during the development, implementation and use of the dispensing systems including among other things: short time frame resulting in incomplete systems in use; lack of a common interpretation of applicable laws that were regarded as rather non-specific; unclear roles of different authorities, and the fact that those authorities had not always been in alignment; new dispensing system changing the workflow and requiring major adaptation and training of the staff. More than half of the pharmacists (58%, 66/115) perceived their current dispensing system as supporting safe dispensing of medications, 26% (30/115) were neutral and 15% (17/115) did not perceive it to support a safe dispensing (Figure 8). Most pharmacists (80%, 95/115) had experienced problems with their dispensing system during the previous month. The pharmacists experienced problems including reliability issues (e.g. slowness, bugs, or system crashes), usability issues (e.g. not showing information at the right time, complicated methods to undo actions or change products, and redundant steps and excessive requests to login) and missing functionality (e.g. support for advice or detecting drug-drug interactions). The EES decision support system was only available in some pharmacies and was only used infrequently at the time of the study; an active choice and consent from the patients was required to view the alerts for potential DRP. Pharmacists also described problems related to patients with MDDD.

![Figure 8. Pharmacists’ (n=115) degree of agreement (%) on a 5-point Likert scale with three statements regarding their dispensing system where 1 represented “do not agree at all” and 5 “completely agree.”](image-url)
Study IV: Physicians’ perceptions of a shared medication list

Interviews with physicians’ (n=7) showed that the transition from local medication lists to a shared medication list was perceived to increase the availability of information: from being time consuming or not possible to obtain information from other caregivers to most information being available in one place. However, there was still a risk for events limiting the availability of information, such as system breakdowns. A regionally shared medication list was perceived as having the potential to provide a greater accuracy of information but not always; the shared medication list was perceived as more complete but with an increased number of non-current drugs. Most physicians considered that the non-current prescriptions in the medication lists were primarily due to incorrect working routines. On the other hand, a shared medication list implied an increased risk of violating patient privacy, placing greater demands on IT security in order to protect the confidentiality of information. The majority of physicians had experienced few or no patients who had ever had concerns with a physician being able to access their medication information; quite the opposite, patients were usually surprised to hear that the physician had not always had access to the information. Physicians described other aspects of information risks related to information regarding patients’ medications, such as the physicians’ unclear responsibility for medication lists, the need for information other than the medication list to provide a context or a better overview, patients still often lacking information on current medications, and specific issues related to patients with MDDD (Figure 9).

Figure 9. Summary of the main findings on physicians views on changes in availability, accuracy and confidentiality in the transition to a shared medication list.
Study V: Potential DRP detected by EES

The study population (n=180,059) had 10.0 different medications (SD ±4.7, range 1-53). EES alerted for potential drug-related problems in 76% of the population with a mean of 2.2 alerts per patient (SD ±2.4, range 0-27). The older patients received a lower number of alerts compared to younger patients despite having a higher number of drugs (Figure 10). The most frequent alert categories were drug-drug interactions (37% of all alerts), duplicate therapy (30%), and geriatric warnings for high dose or inappropriate drugs (23%).

Psycholeptics, psychoanaleptics, antithrombotic agents, anti-epileptics, renin-angiotensin system agents, and analgesics represented 71% of all drugs involved in alerts (Table 5).

Figure 10. Mean number of drugs and alerts in different age groups of patients with multi-dose drug dispensing (n=180,059).

Table 5. Proportion (%) of each alert type represented by the six most common therapeutic groups of drugs in patients with multi-dose drug dispensing (n=180,059). B01=Anti-thrombotic agents, C09=Renin-angiotensin system agents, N02=Analgesics, N03=Anti-epileptics, N05=Psycholeptics, N06=Psychoanaleptics

<table>
<thead>
<tr>
<th>Alert type</th>
<th>B01 (%)</th>
<th>C09 (%)</th>
<th>N02 (%)</th>
<th>N03 (%)</th>
<th>N05 (%)</th>
<th>N06 (%)</th>
<th>Other (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug-drug interaction (n=301,018)</td>
<td>24.1</td>
<td>10.9</td>
<td>6.6</td>
<td>4.4</td>
<td>9.0</td>
<td>16.6</td>
<td>28.5</td>
</tr>
<tr>
<td>Therapy duplication (n=245,280)</td>
<td>0.4</td>
<td>1.5</td>
<td>9.7</td>
<td>10.7</td>
<td>19.5</td>
<td>17.7</td>
<td>40.5</td>
</tr>
<tr>
<td>Geriatric warning (n=128,275)</td>
<td>0.1</td>
<td>9.9</td>
<td>2.5</td>
<td>0.6</td>
<td>58.7</td>
<td>15.2</td>
<td>13.1</td>
</tr>
<tr>
<td>Drug disease inferred (n=43,319)</td>
<td>1.6</td>
<td>0.6</td>
<td>5.5</td>
<td>24.1</td>
<td>34.8</td>
<td>19.8</td>
<td>13.7</td>
</tr>
<tr>
<td>High dose (n=15,848)</td>
<td>0.8</td>
<td>0.2</td>
<td>1.7</td>
<td>1.3</td>
<td>39.1</td>
<td>14.0</td>
<td>42.8</td>
</tr>
<tr>
<td>Drug gender warning (n=668)</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Pediatric warning (n=209)</td>
<td>0.0</td>
<td>0.5</td>
<td>19.6</td>
<td>18.7</td>
<td>34.9</td>
<td>12.4</td>
<td>13.9</td>
</tr>
<tr>
<td>All drugs involved in alerts (n=734,617)</td>
<td>10.1</td>
<td>6.7</td>
<td>6.7</td>
<td>6.9</td>
<td>23.3</td>
<td>16.8</td>
<td>29.3</td>
</tr>
</tbody>
</table>
Study VI: Physicians’ perceptions of EES alerts

Patients with MDDD included in the study (n=254) received on average 11.4 different drugs (SD±3.9, range 5-23). They had a total of 740 alerts, 89% of all patients had at least one alert from the EES and the mean number of alerts was 2.9 (SD±2.3, range 0-14). Physicians perceived 68% (502/740) of EES alerts as clinically relevant, indicated an intended action for 37%, and made changes in the treatment in accordance with indicated action for 11% of all alerts. Alerts generated were therapy duplication (37.4% of all alerts, n=277), drug-drug interactions (34.7%, n=257), geriatric warnings (22.6%, n=167), drug-disease inferred (3.8%, n=28), and high dosage (1.5%, n=11) (Figure 11). Clinical relevance and likelihood to make changes in drug treatment were related to alert category and substances involved in the alert. For example more than 80% of the geriatric warnings were regarded as clinically relevant and 19% were followed by a change in drug treatment, compared with alerts for therapy duplication where only 50% were regarded as relevant and 9% were followed by changes.

Physician interviews revealed that most perceived a need for a CDSS regarding medications, that the alerts from EES could be useful in clinical practice, and that most alerts were regarded as relevant although they did not necessarily lead to a change in drug treatment. If alerts from EES should be made available for physicians they considered that it had to be in an integrated form in their EHR and some aspects should be improved.

Figure 11. Physicians’ assessment of clinical relevance (black), any intended action stated for alert (grey) and alerts for which the stated change was actually made (striped). Given as a proportion of all alerts within each alert type (%).
DISCUSSION

During the past decades, IT has been increasingly used to support the medication management process, and is necessary due to the demands of an efficient, safe, and patient centered medication, requiring certain information to be available to involved actors. However, the implementation of IT in the medication management process has proven to be a challenging task due to unfulfilled expectations [14, 17, 18].

In this thesis, we have studied the employment of IT in different steps of the medication management process during different stages of implementation with focus on the users’ perspectives. In summary, we found that IT has become a natural and necessary part of medication in Sweden but several problems remain to be solved: weaknesses with usability, functionality, and reliability of the IT systems used; insufficient patient involvement; involved actors still lack accurate and complete information as well as appropriate knowledge-based support for decision making.

ePrescribing - pros and cons

ePrescribing, including electronic storing of prescriptions, was accepted and appreciated by pharmacists and patients (I, II). Similar attitudes among physicians have been demonstrated previously in Sweden [86, 172]. Even if the vast majority of pharmacists in our study were satisfied, several weaknesses were revealed in the survey. Described weaknesses were related to the dispensing system used, lack of coordination between pharmacies, legal restriction of information access and health care and reliability; several of these are in line with those reported previously by physicians [86]. Studies from other countries support prescribers’ and pharmacists’ positive attitudes towards ePrescribing [32, 91, 173, 174]. Fewer studies have been directed towards patient attitudes [31].

The finding that ePrescribing in itself is accepted and appreciated indicates a successful implementation. Early implementation of ePrescribing paved the way with integration of the infrastructure and acted as a driving force for eMedication in a wider perspective. Electronic handling of prescriptions enables new services both for patients and health care professionals. The rather successful implementation of ePrescribing in Sweden may be due to several factors including the implementation of ePrescribing at a time when there was only one state-owned pharmacy company being a strong actor in the medication management in Sweden. Introduction of the
NEF resulted in a significant reduction of errors among electronic prescriptions [99]. Described weaknesses indicate a need for improvement of usability and reliability in the information systems used for handling prescriptions, as well as the information accessible and coordination of systems. There have been some work to identify factors with ePrescribing related to success or errors, respectively [32, 106, 167, 175-177]. The use of evidence based strategies might improve ePrescribing.

Implementation of new dispensing systems

The implementation of new information systems for dispensing prescriptions at pharmacies in Sweden was related to weaknesses of reliability, functionality, and usability that could affect patient safety (III). Some of the weaknesses with ePrescribing described by pharmacists before the re-regulation were related to the dispensing system they used (I). Similar weaknesses described with both old and new dispensing systems indicate that not all issues arose with the new dispensing systems. In addition, some of the problems identified were not directly part of the dispensing systems themselves, but rather other parts of the technical infrastructure involved in the process of dispensing prescriptions (III). This reflects the importance of ensuring the quality of each component involved in a process, as well as the interoperability between components [99].

A limited amount of research has been reported regarding information systems for dispensing prescriptions at pharmacies, and the terminology used in those studies varies [16, 95, 106, 108]. As with other health IT, dispensing systems have the potential to increase patient safety, for example by decreasing manual entry of information, increasing the availability of information, and supporting an appropriate workflow, but they can also cause problems. Technology is reported to be one of the factors that may contribute to variations in pharmacists’ prescription intervention practices, such as intervening in the event of prescribing errors and DRP, and providing counselling to patients [61]. Although these tasks are important for pharmacists’ work, the actual procedures are insufficiently regulated or defined in guidelines, and are insufficiently considered when designing a dispensing system.

The weaknesses of the dispensing systems implemented in Sweden after the re-regulation seem to result from the limited time for the development and implementation, the lack of comprehensive and evidence-based requirements for dispensing systems, and the unclear distribution of quality assurance responsibilities among involved stakeholders. Thus, there seems to be a need for information and commitment from responsible authorities.
A regionally shared medication list was perceived by physicians to increase the availability of the information about current prescriptions but may decrease the confidentiality of information (IV). A regionally shared list was considered as having the potential to increase accuracy, yet in reality, many lists were still inaccurate. Although the medication list was more complete, many physicians experienced an increased amount of non-current prescriptions. This view is in line with previous findings that regionally shared lists reduce the number of missing medications, but non-current medications remain a significant problem [141]. In addition, some issues remained unsolved with the regionally shared medication lists: the medication list still not being linked to the prescription repository, not including information on dispensing, most often not being the information source used by patients, not being shared across county borders or with municipalities, and not automatically including prescriptions for patients with MDDD. Furthermore, the issue of OTC and other non-prescription medications remains.

Several studies indicated issues related to the national prescriptions repository, such as non-current or duplicate prescriptions, and physicians being unable to access or change prescriptions (I, II, III). Since Sweden has more than 90% electronically stored prescriptions, an almost complete access to information on current prescriptions would be expected, but due to legal reasons, prescribers are not allowed to access the prescription repository in its present form. As a result, prescribers are still bound to use local or regional medication lists in their EHR. This is an example of when current regulation for protection of patient integrity is perceived to be in conflict with patient safety.

Although a shared medication list is often referred to as a path to provide safer medication by providing an accurate and complete list of patients’ medications, the consequences of a transition from a local to a shared medication list are related to several aspects. A Swedish study found that the implementation of a region-wide EHR increased accessibility and readability of information but that the EHR did not provide sufficient support, had low usability, and was time-consuming to use [101]. In the US, a shared medication list improved accuracy [136], and a similar implementation in Austria was perceived as having the potential to improve patient safety, but both studies described difficulties [135]. Internationally, there are different approaches for sharing medication information and health records, both regionally, nationally and internationally [65, 79, 89, 92, 135, 136, 144-146]. Implementing shared systems for health information has turned out to be more challenging, complex, and expensive than expected [178]. The major issues are usually not related to technology, but rather strategies, and management [145].

Accurate and available information on patients’ current medications is vital for safe medication. Thus, the implementation of a nationally shared medication list is at the core of improving eMedication. Physicians believed a nationally shared medication list would be useful, but only if the technical solution was sufficient, fit
their process, was implemented properly, and responsibilities clarified (IV). Thus, the success of a nationally shared medication list is related to several factors. Ideally, a nationally shared medication list should include all prescriptions, and the same information source should be available and used by pharmacies, patients, and municipalities. With the nationally shared medication list (NOD) being planned in Sweden, different counties would still have separate EHR systems, and information on medications would be shared through a common database that would also be linked to the prescription repository used at pharmacies. To implement a shared medication list, we recommend providing a clear description of responsibilities and routines for normal activities as well as back-up routines, considering IT security and data protection early in the development, and involving patients to improve the accuracy of the list, as well as to monitor and evaluate the implementation.

**Decision support systems are important but must mature**

It is recognized that a CDSS can be a valuable tool for physicians and pharmacists to improve safety and efficiency [6, 15, 112, 113, 179, 180]. EES is initially intended for use in pharmacies but has been proposed as a potential support in health care as well. Potential DRP were detected in the majority of patients with MDDD, on average two alerts per patient (V). In addition, we found that physicians regarded the majority of alerts (68%) as clinically relevant and several alerts (11%) were followed by changes in drug treatment (VI). The clinical relevance and likelihood to make changes in drug treatment were related to alert category and substances involved in the alerts. Most physicians perceived a need for a CDSS regarding medications, and deemed the alerts from EES as useful in clinical practice, if integrated into their EHR with some aspects improved. Physicians’ description (VI) of their need for a CDSS regarding medications is in line with the findings in another study, i.e. automatically generated alerts for severe drug-drug interactions and functions for calculating glomerular filtration rate to enable appropriate dose adjustments [66].

Appropriate decision support is important in pharmacies as well to support pharmacists in detecting potentially inappropriate prescriptions [113, 181]. At the time of the study, two of the dispensing systems had integrated EES as a support for pharmacists and many pharmacists wanted a CDSS or some support system to aid in counselling patients about their medications (III). Even among pharmacists with access to EES, the use was limited due to several factors: the decision support was regarded as complicated and time consuming, there was limited awareness of the system and had not been enough education, and viewing the alerts of the EES required an active choice as well as patient consent. However, even if pharmacists have access to an integrated CDSS, the awareness of CDSS functionalities is often limited, emphasizing the need for user training [109].

Although our studies showed that EES alerts could detect potential DRP, we cannot conclude any actual patient benefits due to the study design (V, VI). From our studies, we cannot know how well suited EES is for integration and use in health care. EES in its current form does not meet all of the current and future needs of decision support in medication management in health care [66]. A report by the Medical Products Agency
conclude that the drug-drug interaction support SFINX, currently used in health care, has several advantages compared with the corresponding knowledge base in EES [182]. Nevertheless, EES includes other knowledge bases, for example the maximum daily dose where alerts based on the dose calculated from a prescription generate an alert when the maximum daily dose is exceeded, that may be useful in health care (as well as pharmacies) and should therefore not be neglected. For the current situation in Sweden, we suggest to combine the best of available knowledge bases after thorough investigation, provided through an optimal graphical user interface and available infrastructure and solutions. CDSS for medication holds great promise but for progress we need substantial research and development. A flexible system that can continuously be developed is necessary to follow changes and progress and allowing maturation.

Ideally, a CDSS for detecting potential DRP should have a high selectivity and specificity, i.e. only give alerts that are clinically relevant and useful [114]. There are different strategies for increasing the specificity of alerts [183-185]. Patient specific information, such as renal function or other lab-values or diagnoses, should be included in algorithms [66]. The ideal CDSS should be flexible and easily adopted and further developed to allow for integration of new functions, e.g. the inclusion of genetic profiles as support for decisions on treatment and dose. In addition, alerts should be provided at the right time when the decision is being made, and in the right form [114, 122, 186]. Some users want a system that can be adjusted for different situations and different professionals according to their preferences and needs (VI). Open data in a structured machine readable format allows for utilization of knowledge bases in other settings, solutions or applications. Knowledge bases should be quality assured, continuously updated by experts according to evidence, new findings, and clinical praxis, and a plan for maintenance and responsibility for the content is also important during its entire life cycle [111].

**Multi-dose drug dispensing**

Patients with MDDD were included in the studies on EES primarily due to legal reasons only allowing physicians to view the complete drug list from the national prescription repository for this specific group of patients (V, VI). Although not a part of the study aim, issues with MDDD emerged in the other studies as well. Pharmacists described problems of dispensing and handling prescriptions for patients with MDDD in the dispensing systems (I, III). Physicians raised issues specifically regarding patients with MDDD (IV); in primary care, medications for patients with MDDD were prescribed in a separate prescribing tool with information usually not connected to the EHR, which was not always recognized at hospitals, sometimes resulting in medications from an outdated and inaccurate medication list being administered among other things.

The service of MDDD aims at improving medication safety, adherence and reduce workload in health care [187, 188]. Several Swedish studies have indicated that patients with MDDD have a lower quality of drug
treatment than other patients, an increased number of drugs after a patient’s transition to MDDD, and fewer changes in drug treatment [29, 48-50, 53]. However, problems with patients with MDDD do not seem to be the result of the dose-dispensing itself, but rather the tools and procedures for handling prescriptions being different than those used for ordinary patients and they are not integrated with each other. Some of the problems may be due to weaknesses with the systems or tools used; many problems were described after the introduction of Pascal, which is an online tool for order entry used for patients with MDDD [189]. However, some problems might simply be due to the fact that patients with MDDD often are being handled in a separate system using different procedures than for other patients. Thus, there seems to be a need for exploration of how medication quality and safety can be improved for patients with MDDD.

**Prevention of DRP requires responsibility and collaboration**

To prevent DRP it is important to have accurate information, knowledge, and cooperation, as well as clarification of responsibility among involved actors. One part in the prevention of DRP is the prevention of medication errors. Medication management and health care is not unique. There are general concepts for reducing human error and increasing safety drawn from numerous disciplines described in the report “To err is human: Building a safer health system” [190]. Several of these apply to the use of IT in the medication management process: e.g. user-centered design (building on human strengths and avoiding human weaknesses in processes and technologies), avoid reliance on memory (standardize and simplify), involving patients in their care, anticipating the unexpected (be cautious and expect errors with new technology), and improving access to accurate and timely information (information coordinated over time and across settings).

To improve patient safety, the involvement of patients in the medication process is regarded as a key strategy [77, 130]. We found that patients wanted more information about ePrescribing and safety aspects of using the services, highlighting the need for more detailed information delivered in different ways and disseminated in different settings and formats (II). In addition, we found issues related to some older people having a less positive attitude towards ePrescribing that might be related to a general resistance towards, or exclusion from, the digital society (II). Information and education to patients is important, as satisfied patients are more likely to adhere with treatment and take an active role in their own health care [74]. To achieve a collaborative relationship between patient and provider concerning medication treatment, it seems necessary to share information regarding current medication via a common medication list. Many patients are currently using the list from the prescription repositories which often does not correspond to the medication list physicians are using [191]. Patients should provide information regarding use of OTC drugs and other non-prescription drugs since these could be involved in drug-drug interactions and other DRP as well [192]. For a safe medication, the patient should be properly informed and have control of her/his drugs, and decision making should be shared. Initially, it might take more time with extended consultation and education, but patient
involvement often has positive effects in the long run [3]. Many patients want access to their health records or medication information and want to take part in treatment and providing information [73, 130, 193].

Physicians are responsible for medication, but we found variations in perceived responsibility for medication (IV, VI). Physicians’ responsibility for the accuracy and completeness of the medication list and the appropriateness of medication treatment were perceived in different ways and were unclear, in line with previous findings [55, 56] and similarly to findings with regards to medication reconciliation [57]. The responsibility of the medication list might be affected by the system for reimbursement [58]. The shared medication list does not in itself result in any formal changes in the responsibility for medications, but the shared list is a tool that enables increased opportunity for prescribers to take a greater responsibility. That physicians are not regarding alerts involving medications outside their specific competence and expertise as relevant is worrisome but also in line with other studies regarding physicians’ perceived responsibility for patients’ medications [55]. There seems to be a need for clarification regarding physicians’ responsibility for the accuracy and appropriateness of the medication list. The network for the Swedish regional drug and therapeutics committees (LOK) has recently presented their recommendations for guidelines regarding responsibility for a patient’s medication list, based on current regulation and the thesis by Pia Bastholm Rahmner [54, 194]. The recommended guidelines are specifically considering the implementation of a nationally shared medication list (NOD) and suggest that the shared medication list should be the main source of information regarding patients’ current drugs in health care, but also for pharmacies and patients themselves. The recommendations also include specific procedures for starting, changing or ending a treatment, to increase the accuracy of medication lists.

Pharmacists, nurses, and other health care professionals are also important in the prevention of DRP [33]. Pharmacists have pharmaceutical expertise with potential of improving outcome and patient quality of life by identifying, resolving, and preventing many DRP. However, presently the pharmacists seem to be an underused resource of pharmaceutical expertise, with too little focus on improving drug treatment or providing pharmaceutical care during patient encounters in community pharmacies [102, 195]. Increased recognition of the pharmacist’s role, improving the possibility for pharmaceutical counseling, and increased understanding of pharmacists work and interventions could be one part in improving medication management [61].

For an efficient collaboration and information exchange, the possibility for increased two-way communication in the medication management process should be explored [32, 94, 133]: e.g. pharmacists send a question to the prescriber regarding an ePrescription, or patients using the shared medication list to communicate which medications they are taking. Some of the weaknesses perceived in the medication management process were that there was a lack of coordination between pharmacies and physicians, in line with other studies [33, 94].
Risks with novel technology and poor usability

Although aiming at improving patient safety and efficiency, novel technology can have negative consequences for various reasons [97]. New errors or problems related to the implementation of IT in the medication management process include e.g. errors in data entry, missing or unavailable prescriptions, work-arounds, double documentation, more time-consuming work, mix-up of patients, selection of wrong medication due to how it is presented on the computer screen, frustration among users, and confidentiality breaches [5, 17, 94, 97, 101, 196]. Over-dependence on technology can be a risk in itself, e.g. if inappropriate prescribing is missed because the CDSS does not give an alert, or if a medication list is perceived as more complete than it actually is [87]. New technology can also result in changed communication and working procedures [87, 106]. Designing IT to support, and not interfere with, clinical work is a major challenge. Many systems are perceived as having low usability [101, 151, 157, 159]. A poor fit between technology and clinical workflow might cause errors, and unintended changes in the actual workflow might have unanticipated consequences [17, 87]. The pharmacist’s workflow was often perceived as having been changed by the new dispensing systems (III). Medication lists being inaccurate seemed to partly result from physicians working in different ways when using the same shared list (IV). Some issues may be related to users being unaccustomed with a particular EHR system, rather than the fact that it is a shared list. The specific technical solutions, usability of systems, implementation strategy, and routines were perceived as affecting the accuracy of information in the medication lists (IV).

Physicians and pharmacists who had experienced a large scale implementation of new IT systems described major initial problems (III, IV). End-user involvement and the possibility of changing and improving the IT system after implementation have been described as important for successful implementation and as a strategy of improving usability. The Swedish dispensing systems were developed in an iterative process and further developed substantially in the years after their introduction. The dispensing systems were described as unfinished when they were initially used which might have jeopardized patient safety (III). This study was performed early after implementation, capturing many of the early errors, corrected later on. Nevertheless, these findings suggest flaws in systems that had passed the regulatory bar at the time of the study and were used in real patient situations. The pros and cons of the iterative process, involving user feedback as part of the development, compared with standard solutions is under debate [164].

Identifying the needs that an information system should fulfill is not a trivial task. Simply asking end-users what they want and providing it to them does not necessarily result in an optimal system [18]. A major obstacle is the communication between developers and clinicians where differences in understanding and terminology may lead to systems failing to meet users’ needs [164, 197]. Observation or meeting in the clinical setting where the system is used might be a way to reach better understanding of the actual work the technology should support, including interaction between people, technology, and environment, as well as potential problems and solutions.
**Information security, continuity, and information structure**

In the endeavor to implement IT in order to increase the effectiveness and availability of information in the medication management process, patient safety and integrity have to be protected. Some of the problems in several steps of medication management seem to be related to the current regulation for information sharing in health care (I, III, IV, VI). It is important that the legislation protecting patient safety is reasonable and clear, and is adjusted to modern health care and IT systems. Physicians experienced that most patients primarily perceived the benefits of medical information to be shared between care providers (IV). However, it is important to study patients perspective on sharing information [198]. Risks of unauthorized access of information increase with the number of users and the larger amount of information stored in one place [89]. Pharmacists and physicians described disturbances where information was temporarily unavailable (I, III, IV). We should be able to provide a safe medication regardless of situation, place or time, even in a time of crisis, deviation from normal procedures or system breakdowns. Thus, there is a need for strategies for handling disturbances in the medication management process on different levels [156]. Back-up routines for system breakdowns should be provided and these should be known and practiced.

Large variation and lack of standards regarding information in health care limits the ability to share, exchange and re-use information for different purposes [14]. A large amount of the information documented in the EHR is in an unstructured free text format and there are large variations in the terms and vocabularies used. As a consequence, information is rarely re-used, although it could be valuable for clinicians as well as research [199]. The need for a common, appropriate and structured documentation has been mentioned in several national strategies and government documents [11, 152].

To continuously improve medication, it is vital that we learn from our mistakes. Therefore, reporting, collecting and analyzing data on ADRs, DRP and errors in the medication management process is important as feedback to health care professionals as well as organizations, decision makers and vendors [14, 21, 34, 200-202].

**Quality assurance of eMedication**

Sometimes IT in the medication management process is introduced without being properly tested among users [5, 14, 17, 19]. Users must be able to trust the quality of the system delivered by the vendors. Thus, when implemented in health care, IT must be combined with mechanisms counteracting errors with fatal or severe consequences.

Dispensing systems are not regulated under a specific product safety regulation as are medical devices [163]. Although pharmacy companies are legally responsible for the quality of dispensing systems, it does not seem realistic for them to conduct the quality assurance themselves, as at least some of them lack the required
knowledge, capacity, and resources [197]. Quality assurance by several stakeholders with insufficiently defined responsibilities may result in duplicated work, or worse, failure of any party to test some aspects of the system. The findings revealed some confusion regarding the evaluation of all dispensing systems by the eHealth agency. Some vendors and pharmacy companies perceived the eHealth agency to perform a broader quality assurance, when the agency in reality is responsible only for securing the connection with their own systems (III). Following the study regarding dispensing systems in Sweden, the Medical Products agency introduced a new regulation for national medical information systems, including dispensing systems, with increased requirements for quality assurance [203].

Even with systems classified as medical devices, it is unclear among most involved actors, including system vendors, health care organizations as well as authorities, how quality assurance and clinical evaluation in practice should be performed and controlled [164]. The need for increased evaluation and quality assurance of IT in health care is increasingly recognized. However, what it means, how it should be done and by whom, as well as how it should be regulated, is under discussion in different settings worldwide with many different opinions. Many argue that IT in health care should be assessed and approved in a similar process as drugs and other medical devices, while others believe in different approaches [14, 18, 163, 167, 204]. Factors complicating evaluation or certification of IT in health care includes: e.g. the complexity of many systems, difficulties in describing the intended purpose, many systems consisting of several software components from different vendors, and the heterogeneity of health care settings and users, as well as an ever changing environment they are used in. There is also a fear of strict regulation reducing innovation and limiting the flexibility and adaptability of IT systems [18, 19, 204]. Nevertheless, quality assurance of IT in each part of the medication management process, as well as clarification of responsibility among involved actors, is of vital importance.

**Methodological considerations**

When studying the implementation of IT in the medication management process there is a need to use several methods in order to cover different perspectives since the implementation concerns not only the technology itself but also social and organizational aspects, i.e. a sociotechnical perspective [19, 97, 166]. Although, important to study each component per se when studying implementation of IT, it is important to be aware of a holistic perspective, how things might affect one another and the outcome [14]. In this thesis, a variety of methods have been employed, mainly questionnaires and interviews, but also register analysis. The analyses have focused mainly on the user perspective.

**Strengths and weaknesses with study design**

Most studies were based on the subjective views of different informants, and do not represent an objective evaluation. Subjective views do not always reflect the reality; e.g. a perceived increase in safety or efficiency does
not necessarily mean that the same could be measured with an objective method, on the other hand an IT system might be perceived as lacking functionality or having low usability when the user is unaccustomed to the system or has received insufficient training. Nevertheless, subjective views are real to the user and thus may affect the outcome. Ideally, methods should be combined to include both subjective and objective measurements in an evaluation. Qualitative studies are vital to understand the complex nature of how systems are used and valued [205]. Subjective views of (actual or potential) changes and effects of IT in the medication management are widely used and can give insight of benefits, experienced problems, and need for improvements [206]. An important part in the outcome of the implementation of eMedication is the attitudes of the involved actors towards the new technology, including the perceived advantages the technology offers compared to the traditional method. Different groups of health professionals or other actors often have different needs and expectations [133, 193, 206].

Only potential DRP were detected in the studies with EES, and we cannot conclude how many of them would have cause a manifest DRP. Also, there are potential DRP that we could not detect with our method. Additionally, from our studies, we cannot draw any conclusions whether patients with MDDD are more prone to DRP compared to patients with ordinary prescriptions. Since the study had no control group, we cannot state if changes in drug treatment were due to the alerts or would have been accomplished anyhow. Nevertheless, it demonstrates a relationship between the potential DRP and changes made, i.e. it strengthens the clinical relevance of alerts, but does not show any causal relationship. To study the effects of IT such as clinical outcomes, and to know that the changes are related to the technology, randomized controlled trials are needed [8]. There was no analysis of patient outcomes and no cost-benefit analysis in this thesis.

**Limitations**

The relatively low response rate for the questionnaires might have biased the results of the study if the non-responses were not random. Pharmacists choosing to answer a web survey may perhaps have a more positive attitude towards using technology in general, compared with the total study population. In the study involving patients, we tried to minimize the risk of our results being biased towards more computer-friendly respondents by using a postal questionnaire instead of a web-based questionnaire.

In the studies with interviews, the low number of respondents is a limitation. We cannot rule out that with a larger number of respondents other aspects or perspectives could have emerged. However, we believe that the main aspects captured would not have changed substantially with more interviews.

The selection of respondents for questionnaires and interviews may also bias the results. We had problems involving pharmacists in Study III, with the number of pharmacists from different companies and different dispensing systems being unevenly distributed, making the results less representative for all pharmacists in Sweden. The selection of physicians in Study IV might also have biased the results to represent physicians more
interested in questions related to medication and IT in health care. Thus, the findings do not represent the view of physicians in general.

The register study (V) had a large population size, including all patients in the study population. The data from the prescription repository used in the study has high coverage (more than 90%) of prescription medications in the Swedish population. However, it does not cover OTC medications. The reason for using the prescription repository instead of the national prescribed drug register intended for and extensively used for research was because the algorithms in EES are implemented for analysis of prescriptions in the prescription repository. There are some important differences between the registers. However, the researchers regarded that, for patients with MDDD, the prescription repository could be used to capture current prescriptions. Findings from the studies with patients with MDDD, cannot be generalized to all geriatric or other patients as patients with MDDD differ from patients in general with ordinary prescriptions.

**General challenges when evaluating eMedication**

There is a large diversity in the methodology employed in research and evaluation of IT in health care, which is a challenge in itself. A major challenge in the evaluation of eMedication, and IT in health care in general, is the lack of common terminology which makes it difficult to find similar research and compare results. There are also vast differences between the systems, organizations, settings, regulation, and procedures between different countries limiting the generalizability of findings. Thus, a positive outcome of an IT system being implemented in one setting may not have the same effect in another setting, no matter the strength of the methodology.

Continuously changing and developing IT systems, as well as related aspects, are another challenge in evaluation. Some models and unified terminology have been proposed to facilitate analysis and comparison of eMedication systems [88, 207]. To improve future research, there is a need for further validations of the instruments or models used.

**Implications, recommendations, and future research**

Appropriate IT with sufficient quality is necessary to meet the challenges of future health care, including the medication management process. When implementing IT in the medication management process, we need to identify the advantages as well as the potential problems that may emerge in order to prevent them.

For appropriate, safe, and rational medication, we need increased availability of information in a usable form, more involved patients, and support by information systems that are usable and reliable. For this, we should make use of our experiences, learn from mistakes and successes, recognize the obstacles but also the final goal, plan the road ahead, encourage innovation but also work strategically at national level.

Below, we provide recommendations for improved eMedication in Sweden as well as suggestions for future studies.
**Recommendations for improved eMedication in Sweden**

Based on the research in this thesis, other publications and experiences, the following is recommended for improved eMedication in Sweden:

1. Improve **usability** of the IT systems in the medication management process. Determine the needs of users and let the desired working process direct technical solutions, and not vice versa.

2. Provide high quality **decision support systems** for physicians and pharmacists. Recognize the potential benefits but also the complexity in providing/implementing a good decision support.

3. Implement a **nationally shared medication** list. Provide a clear description of **responsibility** for the appropriateness of medication and accuracy of information, as well as actual procedures for keeping the information accurate. Medication for patients with MDDD should be managed in the same systems as other patients.

4. Increase **patient involvement** and education. Give patients access to the same medication list as being used in health care, and involve patients to improve the accuracy of the information.

5. Improve **continuity planning**. Provide back-up routines for system breakdowns and make sure they are known and practiced. Consider IT security and data protection early in order to protect confidentiality of information without jeopardizing patient safety.

6. **Cooperate strategically.** Joint efforts by authorities, vendors, pharmacy companies, end users and researchers are needed to avoid a gap between standardized regulatory requirements and user needs when developing health systems.

7. Facilitate improved communication and integration of systems, organizations and actors, by increased **standardization regarding interoperability and information structure**. Consider increased implementation of electronic two-way communication among actors in the medication management process and include assessment of potential benefits as well as risks.

8. Clarify responsibilities for **quality assurance** among involved authorities and organizations regarding the entire process of eMedication. Clarify who is functionally and legally responsible for which parts and how it is controlled. Improved regulation, transparent and standardized requirements are needed as well as guidelines, with the support of regulatory surveillance.

9. **Monitor and evaluate** the implementation of technology. Test the technology on a small scale before implementing it on a full scale.

10. When planning, implementing and evaluating IT in health care, it is important to consider a **holistic** view with the different aspects affecting the outcome: i.e. technology, users, and organization.
Future studies

Since health care is increasingly team based, the role of all professionals involved in the medication process has to be studied. So far, the prescribers, i.e. mainly the physicians, are well studied. There is a need for more studies on nurses, pharmacists, and other health care providers, their needs and practice patterns as they are also the frontline practitioners who are directly interacting and dealing with patients who are taking medications on a regular basis. In addition, there is a need for studies on how all health care professionals interact and how IT could support and facilitate these processes. Clearly, patients and relatives are of central importance to keep informed in order to help ensure their optimal involvement in the management of their own/patient’s medication and to maintain adherence. Here, more studies are suggested to identify success factors of how IT can improve adherence.

There is a need for studies on how IT in the medication management process affects patient outcomes as well as cost-benefit studies of IT in the medication management process. There is a need for more research on how the design and features of IT systems in the medication management process affect usability and patient safety, as well as how IT systems can support optimal working procedures in health care and pharmacies.

Future studies should compare different solutions for sharing medication information. There is a need for studies related to the implementation of a nationally shared list: how it should be integrated and implemented to best achieve the goal of complete and shared medication information, what the consequences are for information security and patient safety, and what the patients’ views are on shared information on medications.

Further studies are needed to understand the need for decision support in health care and how they should be designed as well as when and how alerts should be integrated. Clinical effects and outcomes of CDSS in clinical practice should be studied. Overrides and reasons for them should be monitored to improve systems in use.

Potential DRP should be further studied in the population including e.g. in the pediatric population. Different methods for measuring DRP should be compared and assessed.

We should also monitor effects of any regulatory actions or changes in requirements regarding the medication management process.

Researchers need to describe context and technology better to facilitate comparison [32]. Evaluation earlier in the life cycle of technology, i.e. during planning, development or implementation instead of after large scale implementation, would be valuable.
CONCLUSIONS

The conclusions from each of the six studies in the thesis:

I. Swedish community pharmacists are generally satisfied with ePrescribing, including the transfer of ePrescriptions, electronic storing of prescriptions and to a lower degree mail order prescriptions.

II. A vast majority of Swedish patients had positive attitudes towards ePrescriptions and electronic storing of prescriptions. However, a need for extended information regarding ePrescribing was identified.

III. After the implementation of new information systems for dispensing prescriptions at pharmacies in Sweden, weaknesses related to reliability, functionality and usability were identified and could affect patient safety. The weaknesses of the systems seem to result from the limited time for the development and implementation, the lack of comprehensive and evidence-based requirements for dispensing systems, and the unclear distribution of quality assurance responsibilities among involved stakeholders.

IV. Physicians perceived a regionally shared medication list as increasing the availability of the information about current prescriptions and potentially the accuracy but may decrease the confidentiality of information.

V. EES detected potential DRP in the majority of patients with MDDD. The number of potential DRP was associated with the number of drugs, age, gender, and type of medication.

VI. In most patients with MDDD, EES detected potential DRP with many of the alerts regarded as clinically relevant and some followed by measurable changes in drug treatment. The alerts from EES might be useful for physicians by providing alerts for different kinds of DRP.

In summary, we found that IT has become a natural and necessary part of medication in Sweden but several problems remain to be solved. For an improved eMedication, we need a holistic approach that combines aspects of technology, users, and organizations in development and implementation of IT as well as evaluation. The thesis suggests a need for improved sharing of information and support for decision making, coordination, and education, as well as clarification of responsibilities among involved actors in order to employ appropriate IT in the medication management process. We suggest collaborative strategic work and that the relevant authorities set up guidelines and requirements for IT in the medication management process.
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