Medication safety through information technology: a focus on medication prescribing and administering

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MEDICATION SAFETY THROUGH INFORMATION TECHNOLOGY: A FOCUS ON MEDICATION PRESCRIBING AND ADMINISTERING

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Medication safety through information technology

A focus on medication prescribing and administering

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Chapter 1

General introduction

Healthcare in the Netherlands: a growing but costly business

In the Netherlands, almost 90 billion euro's are spent on healthcare. In 2012, more than 25% (23.9 billion euro's) was spent on hospital care and is by far the largest healthcare expense[1].

Hospital care delivery in the Netherlands is changing: more patients are admitted, but stay in the hospital for shorter periods of time (**Figure 1**). More specifically, since 2000 the volume of hospital care has grown substantially: the number of hospital and day admissions increased by on average of 3% and 10% annually. The increased volume and increased cost of hospital care delivery, has resulted in almost a doubling of hospital care expenditure over the past decade (**Figure 2**). However, healthcare expenditure is finite. Providing cost conscious (accountable) care has been an important focus of the past decade: provide the best possible patient care and reduce unnecessary costs to the health care system in general[2,3] and more specifically in medication use[4,5]**.** Although total drug expenditure has decreased by 12% in 2012 (from €5.22 billion to €4.61 billion), the proportion of drug expenditure as part of the total hospital budget is increasing[6]. As a result of recent government policy, expenditure of several expensive drug classes typically prescribed by medical specialists (such as TNF-alpha inhibitors) is now part of the hospital budget. Expenditure on this drug class alone increased by 33% from €242 million to €361 million in 2011[6] with more drug classes to follow. Overall, €1.1 billion was paid from the hospital budget (4.9% of total hospital budget) in 2011, which increased to €1.5 billion (6.5% of total hospital budget) in 2012[7]. In light of these increasing budget constraints, it will become even more important to optimize inpatient medication use. Guiding prescribers to the most appropriate (cost-effective) agent, providing feedback on prescribing practices and optimizing pharmacy inventory are key components for optimal medication management.

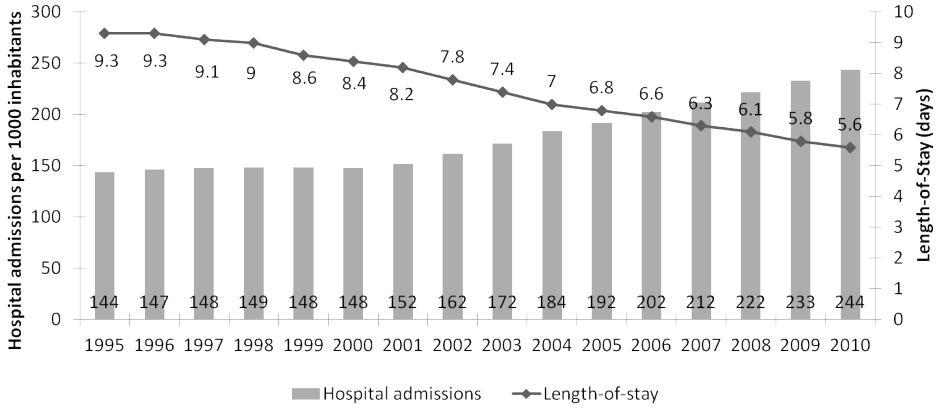

Figure 1. Hospital admissions and length-of stay 1995-20101.

Delivery of Healthcare is error prone

The 1999 US Institute of Medicine (IOM) report "To Err is human: Building a Safer Health System" initiated a worldwide focus on preventing medical errors[8]. Medication errors are the most common type of medical errors reported in hospitals[8]. In 2006, the IOM report "Preventing Medication Errors" estimated that 380,000-450,000 medication errors occur in acute care hospitals annually in the United States. In the Netherlands, a medical record study in 2004 concluded that 5.6% of patients were un-

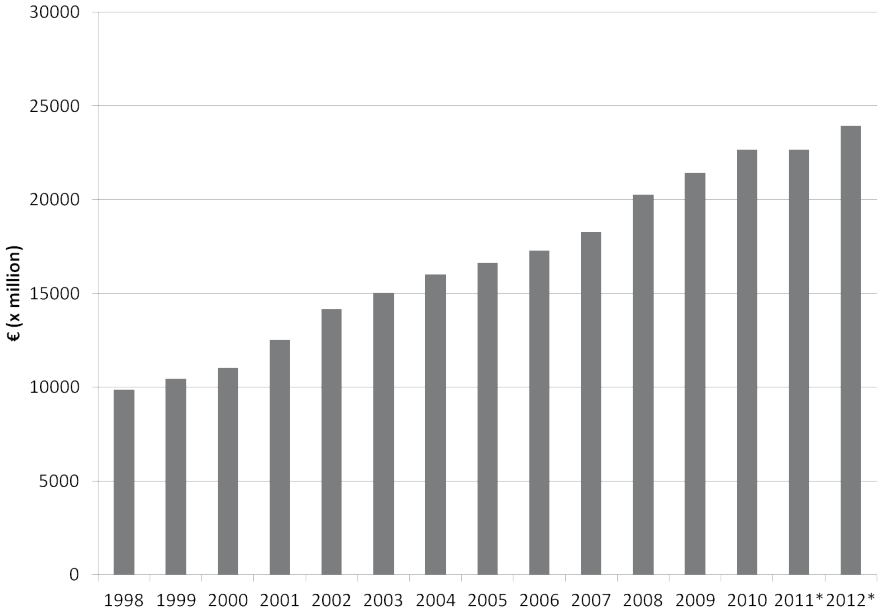

Figure 2. Hospital care expense in The Netherlands 1998-2012[1].* indicates preliminary data.

intentionally harmed during their hospital visit of which 2.3% was potentially avoidable[9]. Medication use was associated with 21% of unintentional harm, of which a further 31% was avoidable. Based on 1.3 million hospital admissions in 2004, a total of 4740 patients experience a preventable medication error with harm. In both countries, the general believe is that these numbers are underestimates[9,10].

The typical medication management process in a hospital is shown in **Figure 3**. It consists of a multidisciplinary process and a core pharmacy process. The core pharmacy process includes order verification, medication dispensing and medication distribution. Medication administration (nursing/prescribers), medication ordering (physicians or nurses/pharmacists per protocol) and monitor-

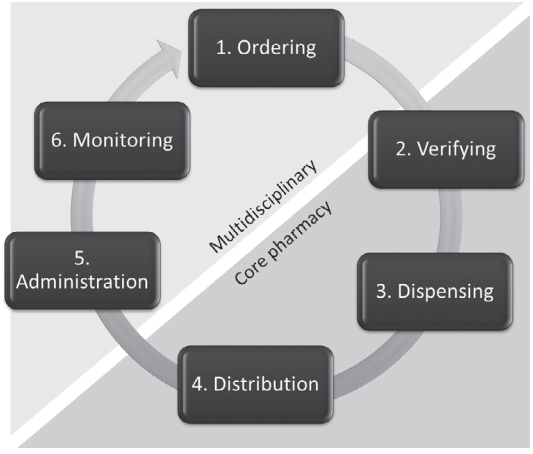

Figure 3. Hospital Medication use process[39]
This diagram is simplified for readability and shows the core processes from prescribing (ordering and verifying) medication through monitoring its effects. In general, step 2 to 4 are performed by pharmacy personnel, nurses and physicians perform steps 5 and 6 and physicians (but sometimes nurses) generally order medication.

ing (physicians, nurses and pharmacists combined) are multidisciplinary processes. Meta-analyses of medication error incidences show that prescribing errors and administration errors are the most commonly reported medication errors in hospitals worldwide[11-13]. Reports on prescribing errors vary between 7% and 60% of medication orders, 2% of patient days and 50% of hospital admissions[13-15]. Administration errors occur very frequently: when wrong administration time errors are excluded, the median error rate of administration errors was 10.5 per 100 administrations (10.5%) with an interquartile range of 7.3 to 21.7[11,12]. With few barriers to prevent them from occurring, only 2% of medication administration errors are intercepted at the patient bedside[16].

Computerized prescribing and Decision Support: proposed solution for providing safer, more cost-effective care.

A common recommendation in both Institute of Medicine reports was that errors were often the result of poorly designed systems and that healthcare facilities should rely more on information technologies to make the system less error prone. More specifically, prescribing medication orders electronically as opposed to handwritten orders (computerized physician order entry, CPOE) and improving decisions taken by clinicians through advice, alerts and reminders (Clinical Decision Support Systems, CDSS) were proposed as key interventions to prevent medication errors: *"A second important step in reducing the number of medication errors will be to make greater use of information technologies in prescribing and dispensing medications. Doctors, nurse practitioners, and physician assistants, for example, cannot possibly keep up with all the relevant information available on all the medications they might prescribe—but with today's information technologies they don't have to. By using point-of-care reference information, typically accessed over the Internet or from personal digital assistants, prescribers can obtain detailed information about the particular drugs they prescribe and get help in deciding which medications to prescribe"*[17].

The international focus on medication errors and early reports on the medication error reduction potential of CPOE[18-20] and CDSS[21-23], have resulted in widespread adoption of CPOE systems worldwide. In the US, adoption of Electronic Medical Records including CPOE and CDSS functionalities is further incentivized by the 2009 Health Information Technology for Economic and Clinical Health (HITECH) Act[24]. In 2009, on average 45% of acute care hospitals in the US have implemented CPOE, but only 3.5% mandate electronic prescribing as the only option of prescribing, resulting in on average 11% of physicians using CPOE[25]. Nevertheless, a recent review estimates that based on CPOE adoption numbers from 2008, 17.4 million medication errors are averted each year in the US by using CPOE instead of handwriting orders[26]. In the Netherlands, as of January 1st 2014, it is mandatory for all prescribers (including prescribers in acute care hospitals) to use CPOE[27]

CDSS systems can be categorized in basic- and advanced CDSS[28]: basic decision support consists of drug-drug interaction checking, drug allergy checking, drug dosing checking and duplicate therapy checking. It does not take into account other patient specific parameters such as age, lab values and concomitant medications to guide prescribers to the most appropriate drug choice. Basic decision support is relatively widely adopted in the US and the Netherlands. The Netherlands has a single national drug database (G-standard) containing information on dosing, duplicate therapy, contraindications and drug-drug interactions to enable drug safety alerting[29]. This national drug database is used nationwide as the knowledge base for all pharmacy systems and CPOEs within and outside hospitals. However, a study performed by Van Doormaal et al. did show a significant reduction in medication er-

rors but did not show an effect of basic decision support at the time of prescribing on the prevention of actual patient harm[14], indicating that more advanced clinical decision support is needed. Advanced clinical decision support includes additional medication data (administration times, dosing frequencies) and patient specific data (age, laboratory values and concomitant medication) in the decision, largely decreasing the number of irrelevant alerts. Early adopters of advanced decision support developed these systems over many years based on site specific infrastructures (so called "home grown" systems). In fact, most studies showing beneficial effects of advanced CDSS were performed in only 4 institutions in the US after years of fine-tuning and testing, limiting the external validity of the results. Advanced decision support is currently implemented in 14% of US[30] and Dutch hospitals[31].

Use of bar-code technology

Bar-code scanning technologies are increasingly adopted to reduce medication errors in the medication administration process. Bar-code-assisted medication administration (BCMA) was developed as an additional safety barrier between the nurse and the patient if a medication error reaches the patient's bedside. This technology assists the nurse in confirming the patient's identity and checks the appropriate identity, dose, time, and form of the medication. In 2009, 27.9% of hospitals in the US had implemented bar code-assisted medication administration (BCMA)[32], which increased to 50.2% in 2011[33]. In the Netherlands, BCMA technology is used in only a few hospitals. Newer applications of bar-code technology include assuring the right identity and strength of medications dispensed from the pharmacy[34,35] and assuring that medications are appropriately loaded in Automated Dispensing Cabinets on nursing units[36].

In short, the increasing discussion on quality, transparency and burden on healthcare resources results in an increased focus on improving the quality of healthcare with equal or less resources. It is well documented that the medication-use process is made safer and more efficient through the appropriate implementation of new technology. However, risks exist for making the process less safe if technology is not implemented properly. New technologies may inadvertently result in new sources of error within the medication-use system. Understanding the complicated effects new technology can have on existing processes and identifying successful strategies for implementing new technology are crucial to ensure that technological advances provide the desired benefits without creating additional unsafe or inefficient conditions. As most medication errors occur during the medication prescribing and administration processes, the aims of this thesis are to determine the effects of CPOE, CDSS and bar-coding technologies on reducing errors during and increasing efficiency of the prescribing (Part 1) and the administration processes (Part 2).

OUTLINE OF THE THESIS

Part 1: Improving medication safety through technology: focus on prescribing

There are many applications of CDSS in the delivery of healthcare. CDSS are viewed as an essential tool to increase efficiency and prevent medical and medication errors. Chapter 2 of this thesis summarizes the spectrum of CDSS applications and focuses on applying CDSS to improve medication safety. However, widespread adoption of CDSS is hampered by many barriers[37,38]. This chapter focuses on these barriers and provides recommendations for future research.

Two barriers for adoption include (1) the lack of customization options of commercially available CDSS systems and (2) the need to develop and agree upon site specific decision support algorithms. In this thesis, we studied the effects of a commercially available decision support system on several areas. In Chapter 3, we used the CDSS to determine the quality of antimicrobial prescribing in intensive care patients with renal failure in terms of dosing adjustments, duration of exposure and costs. In Chapter 4, we investigated the use of the CDSS to augment drug-drug interaction (DDI) checking based on the Dutch G-standard. We focused on refining the most frequently occurring DDI's by adding concomitant medication, administration times, patient characteristics and laboratory values to the standard G-standard DDI algorithm. We performed a Return-on-Investment analysis, comparing the costs of implementing the CDSS to the savings resulting from increased efficiency of the DDI checking task.

CPOE systems require extensive customization to facilitate safe and efficient electronic prescribing of medications. In addition, from a medication safety and efficiency standpoint it is impossible for hospital pharmacies to stock every medication that is available. Therefore most hospitals use formularies, a continually updated list of medications most commonly prescribed in the hospital, to optimize CPOE maintenance and pharmacy workflow. In Chapter 5, we describe the effects of a comprehensive formulary management system on the formulary compliance. To determine strategies to further optimize formulary compliance, we also performed a labor cost analysis identifying the most efficient scenario of managing request for nonformulary drugs. To further increase formulary compliance, we describe the effects on formulary compliance of a decision support module within a commercially available CPOE system in Chapter 6.

Part 2: Improving medication safety through technology: focus on administering

The effect of bar-code-assisted medication administration (BCMA) on medication error incidence is widely studied. However, the methodologies used in these studies vary widely. For example, different types of medication administration errors are measured in various clinical settings. In addition, there are varying reports on the effect of BCMA technology on the duration of the medication administration round. Chapter 7 reviews the literature on this subject and focuses on (1) the effects of BCMA on frequency, type and severity of medication administration errors and (2) the effect of BCMA technology on the duration of the medication administration process. To decrease the heterogeneity of future studies, this review concludes with a checklist for future research on the long-term effect of BCMA technology.

Most studies investigating the effects of BCMA technology on medication administration errors were conducted on single (general care) units with higher patient to nurse ratios. To compare the effects of BCMA technologies in different care settings in an already highly computerized hospital, we studied the effect of a commercially available BCMA system on medication administration accuracy and medication administration errors on both general and intensive care areas (Chapter 8).

Bar-code technology is not only used during bed-side medication administration. In the US, automated dispensing cabinets (ADC) are widely used to assure safe and timely access to medications on nursing units. Restocking automated dispensing cabinets is a manual process and restocking the machine with incorrect medications (so called fill errors) can have major medication safety implications. Chapter 9 describes the effect on refill errors after redesigning the ADC refill process which includes the use of bar-code technology.

The thesis ends with a summarizing discussion, conclusion and future perspectives (Chapter 10).

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Part I

Focus on prescribing

Chapter 2

Clinical Decision Support Systems in Pharmacy

Author:
Helmons PJ

Reference:
(2009) Clinical Decision Support Systems in Pharmacy in *Pharmacy Informatics*, Taylor and Francis, Boca Raton, FL.

1. Preface

This chapter discusses the impact of clinical decision support systems on medication errors. Therefore, it is important to understand the definitions of "adverse drug events" and "medication errors" before discussing clinical decision support systems. Adverse drug events (ADEs) are defined as any injury secondary to medication use [1]. These events can be divided into *nonpreventable*, *preventable*, and *potential* ADE's. Nonpreventable ADEs (also known as adverse drug reactions [ADRs]) are inherently associated with medication therapy. An example of a nonpreventable drug event is an allergic reaction following administration of a drug to a patient with no known drug allergies. Preventable ADEs are those that cause injury to the patient that could have been prevented. Using the example above, if an allergy to the drug was known, but was ignored and the administration of the drug resulted in an allergic reaction in the patient, this would be a preventable ADE. A potential ADE is an ADE that could have occurred as a result of an error, but (fortunately) did not. In the example above, if the patient was allergic to the drug and received it, but no allergic reaction occurred, this would be a potential ADE.

Medication errors are defined as any mistakes in ordering, transcribing, dispensing, administering, or monitoring of medication [1]. This is a very broad definition and while potential and preventable ADEs are all medication errors, not all medication errors are ADEs.

Both medication errors and ADEs are common, costly and cause clinically important problems [2,3]. Each year an estimated 770,000 people are injured or die in hospitals from ADEs. Approximately 28% of adverse drug events are the result of medication errors and are therefore preventable. More than half of these medication errors occur at the drug ordering stage and are the result of insufficient patient-specific information at the time of prescribing [1,4] (see Chapter 10. Avoiding Medication Errors).

This chapter starts with a case that illustrates how medication errors can result from the lack of patient-specific information. Next, the same case is presented. But this time, the healthcare provider is supported by a clinical decision support system, resulting in an entirely different scenario and patient outcome. Although this alternative scenario lacks a specific pharmacist intervention, the crucial role pharmacists play in designing and maintaining these systems will be discussed later in this chapter.

Case before clinical decision support 5:

Patient X is a 62-year-old woman with diabetes, hypertension, and borderline kidney failure. She has been seeing her primary care physician, Dr. Smith, for the past three years and has generally been pleased with her care. She arrives at the office for a visit, checks in at the front desk and then is ushered into an examination room. A few minutes later, Dr. Smith enters the room to see her. He is carrying her paper chart, and he flips through it as they discuss her current issues. After some discussion and a brief physical examination, Dr. Smith determines that Patient X has a sinus infection. He glances at the medicines she is taking and his last written note about drug allergies, and then hand-writes a prescription for an antibiotic. Patient X then leaves the office with the written prescription and takes it to her pharmacy. The pharmacist enters the prescription into his computer system, and then informs Patient X that the antibiotic is not covered on her benefit plan. The pharmacist places a call to Dr. Smith's office resulting in the prescription of an alternative antibiotic. Patient X receives the antibiotic and instructions from the pharmacist about how to take the drug and then returns home. That evening she takes the first dose of the drug – and an hour later, she develops severe vomiting. Patient X calls her doctor's office to report the new problem. When the message reaches Dr. Smith, he considers that perhaps the drug was given in too high a dose given her age and kidney function. He lowers the dose

of the antibiotic and prescribes an anti-nausea medicine. The anti-nausea medicine eventually controls her vomiting but makes her very sleepy – so much so that when she gets up that evening to go to the bathroom, she stumbles and falls, breaking her hip. She is taken to the hospital by ambulance, and undergoes surgery the next morning to have her hip stabilized with pins.

Case after clinical decision support:

Patient X arrives for her office visit. The nurse brings her to the examination room and puts a preliminary diagnosis of "sinus infection" into the computer. Dr. Smith arrives to see her a few minutes later. After examining her and confirming the preliminary diagnosis, Dr. Smith clicks a button to reveal an evidence-based recommendation on the best antibiotic options for this condition. The computer returns a list of three antibiotic choices; next to each choice is an icon indicating whether that medication is covered on Patient X's plan. The first antibiotic is non-formulary, so Dr. Smith selects the second antibiotic. The computer checks the patient's other active medications, and an alert window pops up indicating that the drug may interact with one of her diabetes drugs, resulting in vomiting (in fact, it was this interaction, not the patient's age or kidney function, that was responsible for Patient X's vomiting in the first scenario; in that scenario, the physician did not make this connection). Dr. Smith contemplates giving her a reduced dosage of the drug and treating despite the risk of vomiting. To be sure, though, he clicks a button revealing her drug history over the past 3 years. He notes that one of his partners gave a similar drug to her last year and the result was, indeed, severe nausea and vomiting. Armed with this highly relevant history, Dr. Smith cancels the drug order and selects the third antibiotic. No warnings appear this time, but the computer does recommend a reduced dosage based on her age and last measured kidney function, which Dr. Smith accepts. He confirms the prescription with a click, which directs the prescription to be electronically transmitted to the patient's local pharmacy, and also prints a concise patient's guide to the drug and its potential side effects. He reviews the prescription, dosage and potential side effects with Patient X and prepares to discharge her from the office. Before sending her home, however, he notes that the computer, which includes a full electronic health record as well as an electronic prescribing function, is recommending that the patient be placed on a cholesterol-lowering drug, based on her most recent cholesterol and LDL results and her diagnosis of diabetes; the system again shows which of the applicable drugs is on the formulary of the patient's plan. With two clicks, Dr. Smith prescribes this medication as well – again following the computer's recommended adjustment for age and kidney function. The computer also recommends a follow-up blood test (creatine kinase) after four weeks of therapy, because of the potential risk of muscle inflammation with this family of drugs. With one click, Dr. Smith orders this blood test and instructs the patient to return in four weeks to get the test done. The rest of Patient X's course remains uneventful and she recovers rapidly from her sinus infection without further incident.

2. Introduction to data, information, knowledge and decision support

2.1. *Definitions*

In pharmacy informatics, the words data(base) and knowledge(base) are often used. To better understand the definition and function of decision support systems, it is essential to understand the difference between these terms (**Figure 1**). A datum (the word data is plural) is defined as a single

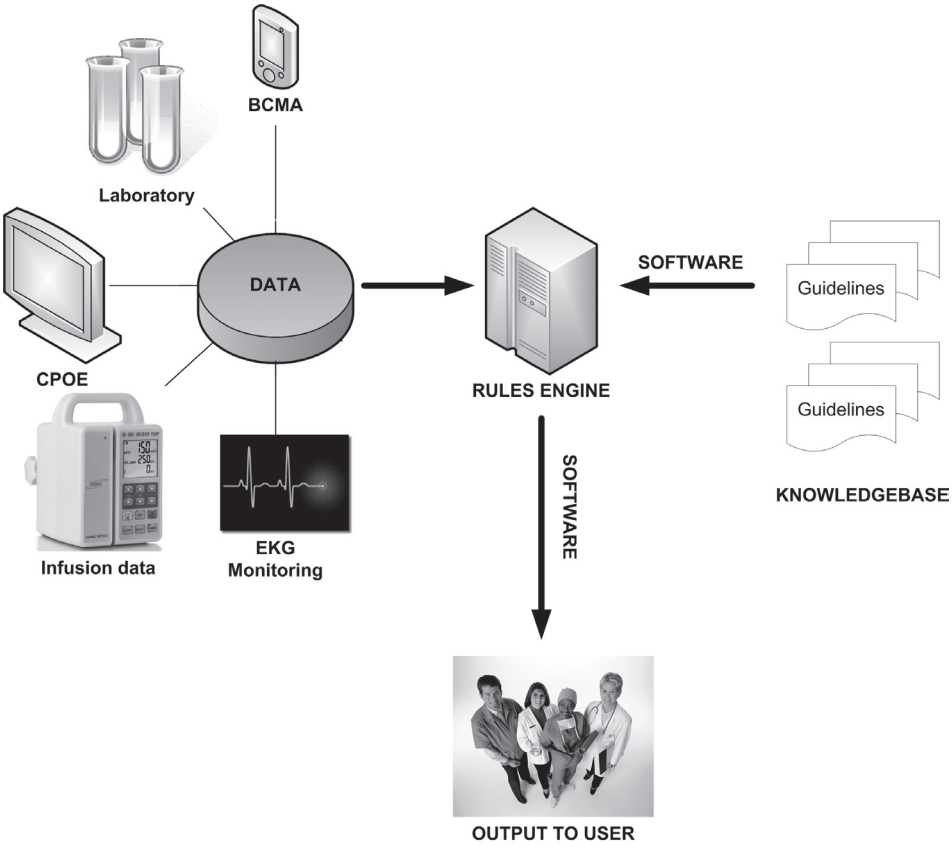


Figure 1. Elements of a CDSS.

Clinical guidelines (knowledgebase) are translated to computer interpretable decision algorithms (clinical rules). The rules engine is then used to match patient-specific information to the parameters specified in the clinical rule (for example: the current dose of a medication is matched to the renal function of the patient). If dosage adjustment is warranted according to the criteria in the knowledgebase, the user is notified.

CPOE: computerized prescriber order entry

EKG: Electrocardiogram

BCMA: bar-code enabled medication administration

observation that characterizes a relationship, in other words, it is the value of a specific parameter for a specific object (e.g., a patient) [6]. Knowledge is derived from the formal or informal analysis of data. As an example, if the result of a single measurement of a patient's blood pressure is 180/110 mm Hg, this is considered a datum. An analysis of a large number of blood pressure measurements in a population leads to the reference values of normal, high and low blood pressures. This analysis has now resulted in knowledge on patient blood pressure. A database is a collection of individual observations without any summarizing analysis. A computerized medication record is primarily a database; only data on the patient's medication are stored. However, if (medical) knowledge is added to these systems (e.g., reference values of kidney function or knowledge of interactions between medications), the computer

may apply this knowledge to aid in case-based problem solving. The system is then a *knowledge-based* system or *decision support* system.

This brings us to the definition of a clinical decision support system (CDSS) [7]: "software that is designed to be a direct aid to clinical decision-making, in which the characteristics of an individual patient are matched to a computerized clinical knowledge base and patient-specific assessments or recommendations are then presented to the clinician or the patient for a decision." These systems convert patient data, essential for the clinician to make the right decisions, into usable information at the time of decision making.

Typically, a CDSS is based on the following elements (**Figure 1**):

- Knowledge base: translates scientific knowledge (guidelines, treatment protocols) into computer-interpretable decision algorithms (clinical rules or algorithms)
- Rules engine: retrieves patient-specific data, often stored in multiple databases and checks if the criteria set in the knowledge base are met.
- Software: allows the user to create clinical decision algorithms and generates recommendations.

2.2. *Why are decision support systems needed?*

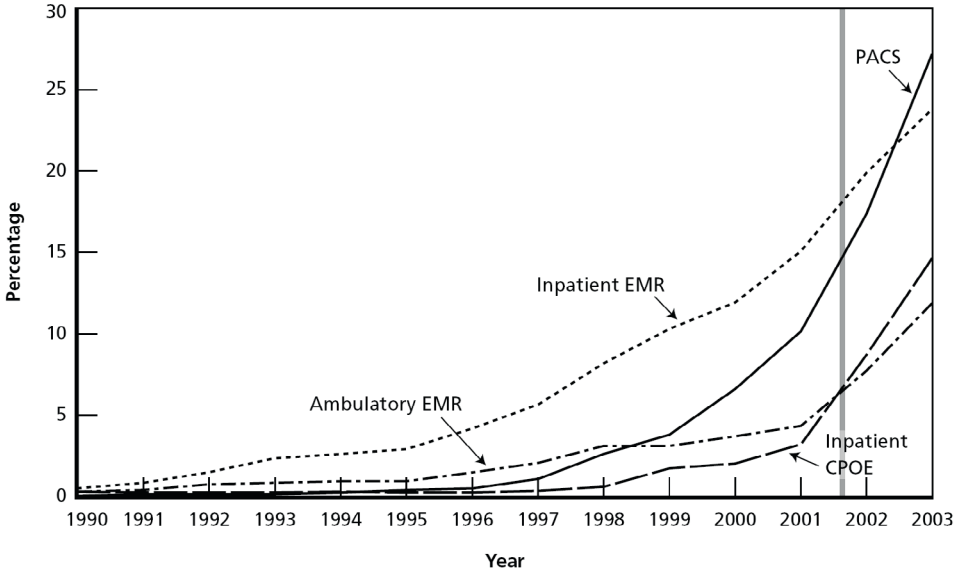
2.2.1. *Bridging the research-evidence-practice gap*

The Institute of Medicine report, "Crossing the quality chasm" has documented the gap between what health care providers know and what they do [8]. The report identified 3 types of quality problems: overuse, underuse and misuse. Misuse (errors) has been the predominant focus of attention, but it is likely that underuse or overuse of practices and resources result in a larger portion of current quality problems [9].

Surveys of clinicians indicate that a major barrier to using current research evidence is the time, effort and skills needed to access the right information among the massive volumes of research [10]. Each year, the National Library of Medicine indexes over 560,000 new scientific articles in the MEDLINE database. In addition, 20,000 new randomized trials are added to the Cochrane library [9]. This corresponds to 1,500 articles and 55 new trials per day! Even if the clinician is aware of the evidence, the clinician needs to agree, adopt and adhere to this evidence. As an example, in one study 90% of the clinicians were aware of acellular pertussis vaccination guidelines, 67% accepted the guideline, but only 35% adhered to the guideline [11]. In addition, patient acceptance of and adherence to treatment plans are often problematic. If 80% adherence to each of these stages would be achieved, this would still result in evidence based treatment of only 21% of the eligible patient population ($0.8^7 = 0.21$) [10].

2.2.2 *Increased availability of patient specific information*

Decision support systems can only be as good as the data the system is based on. The 1999 Institute of Medicine report "To err is human" has resulted in an enormous focus on medical and medication errors. Some of the conclusions of this report were that errors were often the result of poorly designed systems and that health care facilities should rely more on automation to make the system less error prone [12]. As a result, most hospitals have implemented or are implementing hospital information systems (**Figure 2** [13] and Chapter 6. Hospital Information Systems), most hospital pharmacies have imple-



NOTE: The shaded vertical line illustrates a suggested shift for the curves to reflect the "have it in place" measure of adoption.

RAND *MG409-2.2*

Figure 2. Implementation of electronic health records, CPOE, and digital storage of diagnostic images

EMR = Electronic Medical Record

PACS= Picture Archiving and Communication Systems (digital archiving of diagnostic images).

From Fonkych K, and Taylor R. The State and Pattern of Health Information Technology Adoption. http://www.rand.org/pubs/monographs/2005/RAND_MG409.pdf. 2005.With permission.

mented pharmacy information systems (Chapter 7. Pharmacy Information Systems) and most hospital nursing units use automated dispensing cabinets, limiting access to medications. In addition, medication administration errors are being addressed with bar-coded medication administration (Chapter 8. Barcoding Technology and Implementation) and intelligent ("smart") infusion pump technologies. During the last decade, computerization has led to an exponential increase of patient-specific data that can be used in decision-support algorithms. In the near future, the field of genomic medicine will provide patient-specific genomic data that can be incorporated into algorithms. Already, decision support is considered essential to integrate the vast amounts of genomic data with "traditional" parameters [14]. Some experts estimate that in just a few years primary care physicians will have to know how to employ as many as 100,000 new genetic screening tests [15], further stressing the important role of decision support.

2.2.3. *Requirement to adhere to guidelines*

The focus on quality of care and the increased availability of electronic data have resulted in greater performance requirements for health care organizations. The Joint Commission (TJC) has implemented standardized performance measures that are designed to track the performance of hospitals and

encourage improvement in the quality of care. These indicators are derived from current consensus guidelines and represent current standards of care. As an example, one performance indicator measures the percentage of patients eligible for pneumococcal vaccination that were actually vaccinated while admitted to the hospital. In 2002, 28% of patients were vaccinated; this improved to 50% in 2004 [16]. Decision support could be used to inform clinicians of these performance indicators, select eligible patients, and further improve adherence to guidelines.

2.2.4. *Current pharmacy information systems are failing*

Most pharmacy information systems currently provide some degree of basic decision support, intended to support the pharmacist in the evaluation of the patient's medication profile. Recently, 30 clinical pharmacy information systems were tested to see if they could prevent 18 unsafe medication orders. These orders had been selected because they had already caused severe adverse outcomes in patients [17]. Only 67% of these systems were directly interfaced with the laboratory system, which is essential for drug-laboratory interaction checking. This study showed that on average, only 44% of the unsafe orders were detected by these systems. Also, 50% of these systems routinely generated recommendations that were of little to no clinical value. Decision support could improve the performance of these systems by integrating additional patient-specific information resulting in more clinically relevant recommendations [5].

3. The use of decision support systems to improve quality of pharmacotherapy

3.1. *The spectrum of clinical decision support*

Decision support systems have been used to guide clinicians to the most likely diagnosis, to remind clinicians of measures to prevent disease (e.g., pneumococcal vaccination), to improve the management of disease (e.g., improving diabetes care by preventing complications) and to improve appropriate selection, dosage and monitoring of drug therapy **(Figure 3)**. This section focuses on this last category because most pharmacists will be involved in decision support as part of pharmacy information systems or computerized prescriber order entry (CPOE) systems. These systems can be categorized as basic CDSS and advanced CDSS.

3.2. *Basic decision support*

3.2.1. *Drug allergy checking*

Drug allergy checking presents an alert when a clinician orders a medication to which the patient has an electronically documented allergy. Most pharmacy systems have this functionality, because this is considered an important patient safety feature. However, these systems are often far from perfect [18]. Major shortcomings are:

1. No requirement for structured, coded entry of allergens (i.e., a controlled vocabulary. See Chapter 4. Standards & Controlled Vocabularies). This makes it impossible to be alerted to cross-reacting allergens within the same drug class and to transfer allergy information between information systems.

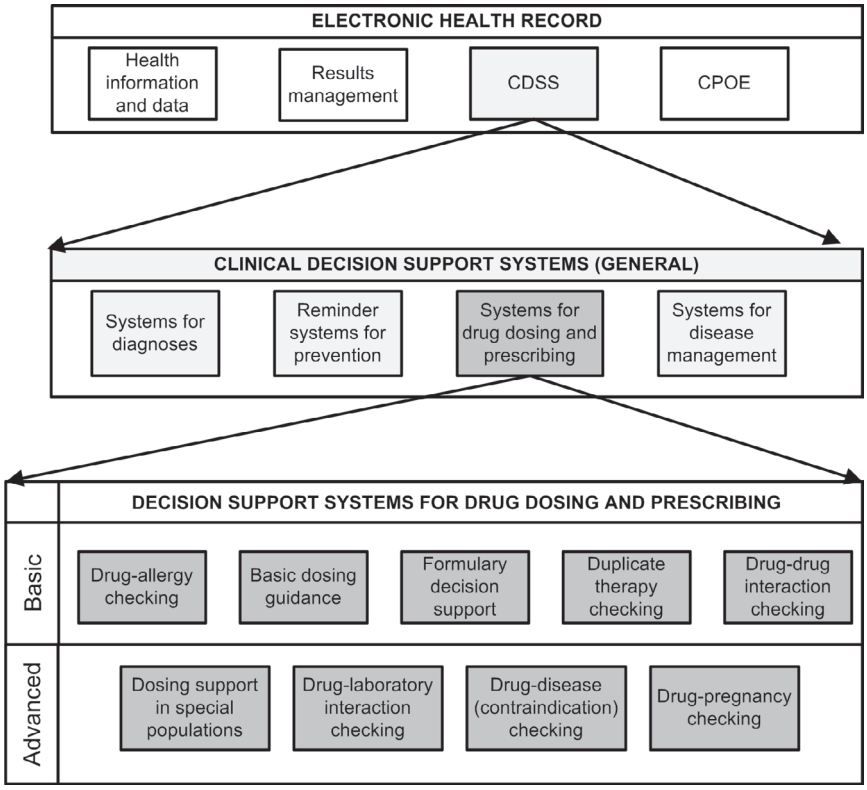


Figure 3. The spectrum of decision support 18,51,52

The first bar depicts clinical decision support systems (CDSS) as part of a patients electronic health record .The second bar depicts the different applications of CDSS in healthcare. The third bar shows the application of CDSS in pharmacy information systems.

2. If allergy data are coded, cross-reactivity data do not distinguish between a theoretical cross reactivity and an evidence-based contraindication.
3. Poor quality of allergy data in the database. A recorded allergy is often considered a definite contraindication for the patient, sometimes resulting in withholding the most appropriate therapy. However, the documented allergy can be based on a side effect (e.g., diarrhea from antibiotics) or a mild allergic reaction (e.g., minor rash from an antibiotic). Also, allergy data of a patient are seldom updated. Once an irrelevant allergy is recorded, physicians are very reluctant to delete this warning.

These shortcomings and the rare occurrence of a definite allergy in the general patient population have led to excessive, irrelevant drug-allergy alerting.

3.2.2. *Basic dosage guidance*

In non-automated ordering environments, dosage errors are the most common type of medication errors leading to preventable ADEs [1]. Susceptible patients, such as children and the elderly, are at risk

of serious dosage errors, especially overdosage [19-21]. Even basic decision support within CPOE can dramatically improve appropriate dosage of medication by:

- providing the clinician a list of patient-specific dosage parameters (often based on the age of the patient),
- drug-specific dosage parameters (based on predefined minimum and maximum allowed dosages),
- indication-specific dosage parameters. The prescriber selects the indication of a specific drug and drug dosages are automatically entered based on the selected indication.

Eliminating manual dosage entry also decreases the potential for a wrong decimal point, typographical error, or a wrong dosage unit (e.g., mg instead of μg) in the medication order.
However, apart from the patient's age, basic dosage guidance often does not take into account other patient-specific parameters, such as renal function and electrolyte levels.

A classic example is the following: a physician prescribes a normal dosage of an antibiotic for a 45-year-old patient with renal failure. No dosage alerts are generated because the patient's renal function is not used to provide dosage recommendations. In fact, had the physician adjusted the dosage appropriately in this patient, he might have been alerted of prescribing a subtherapeutic dosage. So if an error is made, no alert is generated, but if the physician prescribes the appropriate dosage, an irrelevant alert is generated.

3.2.3. *Formulary decision support*

Most hospitals try to control the rising costs of drugs by maintaining a formulary: a selection of drugs covering all therapeutic areas that can be used in the hospital. This selection is based on providing essential medications to support safe and effective care, while preventing or limiting the use of high-cost drugs with limited additional benefit. Basic decision support can improve formulary compliance by

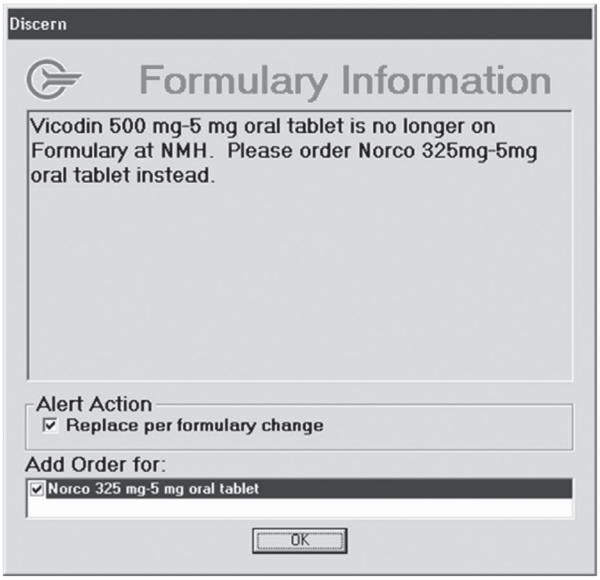


Figure 4. Formulary alert with one click correction capability
Reprinted from Kuperman GJ, Bobb A, Payne TH *et al. J Am Med Inform Assoc.* 2007;14:29-40 with permission from Elsevier.

assisting clinicians in the selection of formulary options over non-formulary options. One approach is to display a pop-up alert when the clinician attempts to order a non-formulary drug, while at the same time providing a selectable list of similar formulary medications. This approach can be very successful if alerts include clear and to-the-point guidelines with links to additional information and if noncontroversial alternatives are suggested within the same alert window **(Figure 4)** [16,22].

3.2.4. *Duplicate therapy checking*

Duplicate therapy occurs when more than one regimen of a single drug or multiple regimens of different medications with similar therapeutic effects are prescribed. It often occurs in situations in which several clinicians provide care for the same patient. Duplicate orders also originate from switching from intravenous therapy to oral therapy with the same drug, without discontinuing the original intravenous order. Therapeutic duplication is uncommon (less than 6% of all prescribing errors are duplicate orders [1]), but often results in a large number of irrelevant alerts. Prescribing multiple drugs from the same drug class is very common (and appropriate) for antimicrobials, immunosuppressants, opioids and insulin. Also, when dosage tapering occurs and different doses for the same drug are ordered, intentional duplicate orders exist in the patient's medication profile. The relatively rare occurrence of unintentional duplicate orders and the large number of irrelevant alerts resulting from basic CDSS, have caused organizations to inactivate duplicate alerting altogether [23]. Extensive customization of duplicate order checking and selective alerting are needed to prevent excessive irrelevant alerting. Examples of successful customization are limiting duplicate order checking to classes with high risks of adverse events (e.g., analgesic, cardiac, psychiatric, and endocrine medications) [23]. Also, increasing the number of relevant alerts by further customizing the alert logic is essential to prevent desensitization to all classes of alerts.

3.2.5. *Drug-drug interaction checking*

Computerized drug-drug interaction checking is one of the most frequently used types of CDSS. However, as with duplicate order checking, drug-drug interaction checking is associated with large numbers of clinically unimportant alerts. In one study, 11% of all medication orders generated a drug-drug interaction warning and clinicians overrode 88% of the interactions that the system considered a "critical" drug-drug interaction [24]. Also, clinicians categorized only 1 in 9 interactions as potentially relevant at the time of the warning [25]. Another study found that adverse consequences almost never occurred, even when the highest level of drug-drug interactions were overridden [26]. There are however a number of clinically relevant interactions that are likely to go unnoticed and lead to adverse patient outcomes because their alerts are buried in a sea of irrelevant alerts. The most important reasons for this large number of irrelevant alerts are [18]:

- Vendor-supplied drug interaction knowledge bases that have no or limited flexibility for modifications (i.e., only allow the display of the most relevant interactions).
- Flawed logic that triggers the alert: Patient-specific parameters needed to generate a clinically relevant alert are not included in the clinical rule, leading to irrelevant alerts. An example of this is the hyperkalemia warning when spironolactone (an aldosterone receptor antagonist) is prescribed together with an angiotensin converting enzyme inhibitor. This is a very common combination in patients with heart failure and leads to a large number of alerts, since the actual

potassium level of the patient is not integrated into the clinical rule. Ideally, an alert should appear only if the patient already had a high or high normal serum potassium level and the drug combination mentioned above was prescribed.

- No discrimination between the presentation of a highly clinically relevant interaction that warrants immediate action and an interaction of minor importance. A similar presentation of a serious alert (e.g., a definite allergy to penicillin) and a minor alert (e.g., "draw potassium levels within the next three days") could lead to an override of both alerts. A recent study showed that discrimination between alerts leads to a higher acceptance rate of serious alerts by clinicians [27].

The value of basic decision support could dramatically increase if these limitations were addressed.

3.3. *Advanced decision support*

Implementing decision support in a complex health care environment is a daunting task. It is therefore recommended that *advanced* medication-related decision support should be implemented only after basic decision support is in place and working well, with good user acceptance [18]. However, most studies showing important safety and financial benefits of decision support have focused on the evaluation of advanced decision support.

3.3.1. *Advanced dosage guidance*

In section 3.2.2., it was mentioned that basic decision support systems sometimes assume that patients are non-geriatric adults with normal physiologic function. However, to determine accurately what is a safe and appropriate dosage for a particular patient may require many factors to be considered. Some of these factors are: age, weight and height of the patient, the indication for the drug, renal function, liver function, fluid status, concomitant medications, genetic predisposition, and reactions to previous medications. Each of these conditions affects large patient populations: in one study, 42% of inpatients had some degree of renal insufficiency [28]. Although these parameters are not always relevant for all drugs, advanced decision support can integrate these parameters for dosage recommendations in relevant cases. In one example of advanced dosage support [29] a CDSS generated dosage recommendations of antibiotics based on the patient's age, renal function and the sensitivity pattern of the infecting microorganism. This program substantially decreased the number of adverse events, days of unnecessary therapy and costs.

3.3.2. *Advanced guidance for medication related laboratory testing*

Several categories of drugs need monitoring of their serum concentration (e.g., aminoglycoside antibiotics, digoxin and antiepileptic drugs) or of the physiological parameter it affects (e.g., the prothrombin time with anticoagulants). Decision support tools remind physicians to request the appropriate blood samples at the appropriate time. In one study, the number of antiepileptic blood levels that were drawn inappropriately decreased from 54% to 14.6% after implementing a decision support system [30]. Another study showed that alerts at the time of ordering could double physicians' rates of compliance with a variety of guidelines, including drug monitoring [31]. Integrating laboratory values with drug-drug interaction checking can greatly decrease the number of irrelevant alerts. However, access to the patient's previous laboratory results is an important prerequisite of medication-laboratory test monitor-

ing. But even when laboratory values are incorporated into the decision support system, rigorous evidence on monitoring is often lacking. Most recommendations are currently based on expert opinions or package inserts that are often non-specific (e.g., "periodic laboratory testing is recommended"), complicating the development of explicit decision support rules [32].

3.3.3. *Advanced checking of drug-disease interactions and contraindications*

Clinicians should avoid prescribing contraindicated drugs based on pre-existing disease states and other patient-related conditions. A review of drugs in the British National Formulary revealed around 1,500 contraindications between drugs or drug classes and morbidities or clinical states [33]. The most important contraindications are renal impairment and hepatic impairment. Accurate medication-contraindication checking has been a daunting task for several reasons. Similar to other categories of decision support, the information about contraindications for health care providers is often vague and not structured. For example, streptokinase, an agent used in dissolving blood clots, is contraindicated in "all conditions that are likely to be associated with existing or very recent hemorrhage[34]", without defining how likely, which conditions or what constitutes "very recent". Secondly, contraindication decision support only works when patients' diagnoses and conditions have been accurately entered as structured data into the patient's electronic health record. However, the diagnosis for a patient's admission is often not entered until the patient is discharged. Secondly, contraindications related to hepatic or renal impairment are often dependent on the degree of impairment: different alerts should be presented if a patient has severe renal failure, as opposed to moderate renal failure. And finally, no simple test is available to rate liver function impairment in a fashion similar to renal function impairment.

3.3.4. *Advanced drug-pregnancy alerting*

Drug-pregnancy alerting is an important category of advanced decision support. A small number of drugs should never be prescribed to a woman who is or might be pregnant (e.g., thalidomide, isotretinoin). Even if drug-pregnancy interactions were appropriately classified, the biggest challenge in this category of decision support would still be to accurately determine the pregnancy status of the patient. Pregnancy tests are not routinely performed on admission and many systems do not contain the results of recent pregnancy tests. Also, some systems do not update pregnancy information when the pregnancy has ended.

Not surprisingly, this category of decision support also suffers from a large number of irrelevant alerts: in one study only 10% of the drug-pregnancy alerts led to a cancellation of the offending drug, and 90% of the alerts were ignored [23]! So, in order to fully benefit from the categorization of drugs in pregnancy, electronic health records should allow clinicians to document the pregnancy status explicitly (is pregnant, might be pregnant, etc.).

4. Development of clinical decision rules and protocols

4.1. Paper protocols, clinical (decision) rules and computerized protocols (algorithms)

Clinical care is determined by clinicians' decisions and by each patient's individualized expression of his or her illness. However, most paper guidelines are far from individualized and lack specific instruc-

tions for many of the scenarios encountered in clinical practice [35]. If patient-specific parameters are not considered in medical decision making, legitimate concerns are raised about patient-invariant ("cookbook") care.

CDSS by themselves also contain different levels of individualized decision support. The basic level of decision support is generated through *clinical rules*. These rules have a typical "IF, THEN" logic: *if* a patient meets a standardized set of criteria, *then* an alert is generated. Basic clinical rules are very useful for "simple" drug-laboratory interactions, but fall short when decision support systems are used based on complex treatment guidelines. This is when *computerized protocols* are very useful. Computerized protocols are similar in structure to the decision flowcharts commonly used in paper guidelines [36], but they contain much more detail than paper guidelines and clinical rules. Computerized protocols are a combination of multiple clinical rules.

Decision support systems standardize clinical decisions for patients. This is not synonymous to "each patient receives the same treatment". As an example a clinical rule can be created standardizing the monitoring of patients receiving thiazide diuretics known to decrease serum potassium levels. The clinical rule takes current serum potassium levels and co-medication into account. In a patient with a low potassium level, the same rule will recommend addition of a potassium-sparing diuretic or potassium supplementation, while in another patient with a physiological potassium level no recommendation is generated. The clinical rule is identical but the outcome is different. This is very important since these clinical rules are now generic and if proven effective, these rules can be used by other hospitals.

4.2. *Stages in clinical decision rule and computerized protocol development* [10,37,38]

Clinical decision rules and computerized protocols are designed to help clinicians with diagnostic and therapeutic decisions. These tools help clinicians cope with the uncertainty of medical decision-making and help clinicians improve their efficiency. Because computerized protocols consist of multiple individual clinical decision rules, the essential steps in the development of individual clinical decision rules are also applicable to computerized protocols. Creating clinically relevant and effective clinical decision rules follows the six steps summarized in **Table 1**. The (obvious) first step is assessment of the need for a decision rule. An organization should ask itself, "Is there a variation in clinical practice resulting in suboptimal patient therapy; how often are clinicians currently not adhering to established (paper) treatment protocols that could decrease this variation; and can decision support be applied to tackle this problem?" If the answer is yes, then the second step is a thorough evaluation of the (paper) treatment protocols. There may be valid reasons for not adhering to a certain protocol, such as a different patient population and co-morbidities. This is why thorough evaluation (and refinement, if necessary) of the decision rule should occur prior to implementing the rule in clinical practice (step three). The next section will discuss this step in more detail. The fourth step is investigating the effects of a similar decision rule in other organizations. What were the effects? How did the rule perform? The fifth step is the requirement of the clinical rule to be cost effective. This is applicable to situations where clinical rules are developed to increase efficiency. It should be emphasized that not every clinical rule saves money! In fact, better adherence to treatment guidelines can initially generate more costs for an individual hospital, but ultimately lead to better patient outcome and decreased costs for society as a whole. An example is the requirement to treat every patient who suffered from a myocardial infarction with a beta-blocker. Increasing adherence to this guideline from 75% to 90% will initially lead to higher beta-blocker use expenses for the hospital. However, it will ultimately lead to

Table 1. Six steps in the development of a clinical decision rule
(From Stiell IG, and Wells GA. 1999. *Ann Emerg Med* 33 (4): 437-47. With permission).

Stage	Factors
1. Is there a need for the decision rule?	• Prevalence of the clinical condition in the hospitals patient population • Variation in practice leading to decreased quality of care
2. Was the rule derived according to methodological standards?	• Selection of subjects • Definition of outcome
3. Has the rule been prospectively validated and refined?	• Accuracy of the recommendations • Completeness of rules: does the tool accommodate most clinical circumstances?
4. Has the rule been previously successfully implemented into clinical practice?	• Effects that can be expected from implementing the clinical rule (if known) • Acceptance of the rule by clinicians
5. Would implementation of the rule be cost-effective?	• Is cost saving a goal of the decision rule?
6. How will the rule be disseminated and implemented	• Selection of the appropriate care area • Type of alert that is generated (obtrusive, unobtrusive)

fewer secondary myocardial infarctions and future hospitalizations. The final step is evaluating the best way to implement the clinical decision rule. Is this rule applicable to the whole hospital (e.g., dosage adjustment of antibiotics in renal function impairment) or only specific care areas (e.g., clinical rules developed to assist in the prescription or administration of oncology medication). Is it necessary to generate an instant (obtrusive) alert in the electronic prescribing system when the rule is triggered or is a weekly reminder by email or page sufficient? Involvement of all relevant clinicians (physicians, nurses, pharmacists) in all six stages of the process is critical for success.

4.3. Validating and refining rules: positive predictive value as a performance indicator

A clinical decision rule or a computerized protocol is designed to improve the quality of care. It is therefore essential to validate their output prior to implementation of the rule or protocol in clinical practice. This is especially important (and challenging) for computerized protocols because they consist of many individual decision rules with many outputs. But also after implementation in clinical practice, constant monitoring of the performance of computerized protocols is recommended. A commonly used parameter to monitor performance of a CDSS is the Positive Predictive Value (PPV) [39]. PPV is defined as: the number of clinically appropriate recommendations generated by the CDSS divided by the total number of recommendations generated. Ideally the PPV should always be 1 (or 100%) because that means the recommendations generated by the system are always appropriate. In practice, this maximum PPV is seldom obtained for several reasons: a maximum score would mean that the required data in the patient's electronic medical record is always available and correct and that the computerized protocol is always applicable to all patients. However, depending on the rule, PPVs of 80-90% are possible [39,40]. Compared to conventional drug-drug interaction checking with PPVs of about 30% [27,39,41], these PPV values are an enormous improvement.

Table 2. Electronic Medical Record Adoption (EMR), 2008 42

(From HIMSS Analytics. EMR Adoption Model 2008. http://www.himssanalytics.org/hc_providers/emr_adoption.asp. With permission)

Stage	Cumulative capabilities of EMR (Each stage includes the capabilities of the the previous stage)	2007	2008
Stage 7	Medical record fully electronic; Health Care Organization able to contribute clinical care data as byproduct of EMR. Data warehousing in use	0.0%	0.3%
Stage 6	Physician documentation (via structured templates), full CDSS, full PACS*	0.3%	0.5%
Stage 5	Closed loop medication administration (tightly coupled hospital and pharmacy systems integrated with bar coding technology at the patient's bedside	1.9%	2.5%
Stage 4	CPOE and advanced CDSS implemented (clinical protocols)	2.2%	2.5%
Stage 3	Clinical documentation (via paper flow sheets), CDSS (basis error checking), PACS data available outside of radiology	25.1%	35.7%
Stage 2	Clinical data available in electronic format, allows physician access to review and retrieve patients' results	37.2%	31.4%
Stage 1	All three ancillary major hospital data systems (pharmacy, laboratory and radiology) are installed	14.0%	11.5%
Stage 0	Some clinical automation may be present, but all three of the major ancillary systems (pharmacy, laboratory, radiology) are not installed	19.3%	15.6%
	Total hospitals surveyed	n=5073	n= 5466

5. Barriers to implementation[5]

Although the enormous potential of CDSS is clear, very few hospitals and other health care institutions have implemented a CDSS. Moreover, the necessary electronic infrastructure needed to implement a CDSS is absent in almost 20% of US hospitals [42]. The 2008 CDSS and Electronic Medical Record statistics are depicted in **Table 2**. This table shows the very low number of hospitals that have implemented advanced CDSS (stage 4 and higher), indicating that even in hospitals that capture essential patient data electronically have not achieved the next step of using these data in a CDSS. This section focuses on the barriers associated with these low adoption rates.

5.1. Lack of standards and "reinventing the wheel"

Table 3 lists ten of the most common barriers impeding widespread use of a CDSS. It is because of these barriers that the implementation (and the published research) of advanced CDSS is largely limited to 4 benchmark research institutions [43]. Especially barriers 5 and 6, "lack of standards for patient data" and "local management of the knowledge base" make widespread implementation and sharing of clinical rules and guidelines almost impossible. This has a number of important implications for institutions implementing decision support. In order to be commercially viable, commercial clini-

Table 3. Barriers to widespread adoption of CDSS
(From Teich JM *et al.* 2005. *J Am Med Inform Assoc.*;M1822.)

Barriers
1. Limited CDSS capabilities of existing CPOE products
2. Limited usability of systems and CDSS modules
3. Limited access to patient data needed to support a CDSS
4. Limited access to best CDSS knowledge
5. Local management and maintenance of the CDSS knowledge base
6. Lack of standards for data, medication dictionaries, cost calculations etc.
7. High cost and difficulty of implementation
8. High cost of use and maintenance
9. Difficulty in recognizing and objectifying value
10. Perception of increased liability if CDSS recommendations are rejected

cal decision support systems rely on limited patient data available in most hospitals (medication and laboratory data), making advanced decision support through computerized protocols impossible. As a result, advanced decision support guidelines that are effective in one institution cannot be readily implemented in other institutions. This "reinventing of the wheel" not only impedes CDSS implementation, but is also very costly.

5.2. *Concerns about quality and safety aspects of CDSS*

5.2.1. *Content issues (acceptance by clinicians of the evidence base)*

An important barrier is fear of decreased alertness of clinicians towards systems recommendations (the "the computer is always right" situation). This phenomenon is described in the literature and has led to severe patient harm in different areas [44,45]. Simply acting on systems' recommendations without considering the full clinical picture is not only dangerous, but it is also likely to occur. This is why clinical decision rules and protocols should be thoroughly validated. Also, the systems should clearly communicate to the clinician if certain areas are not covered by a specific decision algorithm. Further research is needed to minimize the risk of these unintended consequences [4].

5.2.2. *System issues (compatibility, validity, versatility)*

Most of the decision support modules are part of a CPOE system (**Figure 3**). Very few systems can be purchased as add-ons to existing systems [18]. Systems developers and vendors should be clearer about the limitations of their technologies. Often, more is expected from a system than that the system can deliver. Commercial systems are often designed with a "one size fits all" philosophy. Although probably more commercially viable, these systems are not designed to be integrated into the user's workflow and often do not provide the flexibility that is needed to better fit real-world clinical practice [46].

5.3. Gaining acceptance by health care professionals [37]:

5.3.1. Prevention of alert fatigue:

Often, an alert is intended to do more than transfer information. Alerting is about generating effect: the developers of the rule want to make sure that clinicians will act on their recommendations [46]. Current (basic) decision support systems all suffer from the same problem: they often trigger irrelevant reminders and alerts. It is no surprise that in a situation where time is a scarce resource and too many of the alerts are either irrelevant or overly predictable, irritated pharmacists and physicians disregard relevant and irrelevant alerts altogether. This is called "alert fatigue" [46] and can be prevented in several ways:

1. Develop only clinically relevant rules and algorithms: develop decision support algorithms only if the current situation is not optimal and if preliminary research has shown that decision support can improve the situation. The results from this preliminary research should be communicated to the clinicians.
2. Validate and monitor the performance of the clinical rule. Present highly clinically relevant warnings as readily identifiable and easily distinguished from other warnings [18]. An example is to have a daily email sent to draw blood samples for drug concentration measurements based on standard pharmacokinetic advice, but to have an obtrusive alert pop up or a page sent out instantly when a drug concentration is potentially toxic [4].
3. Strategies to integrate recommendations in clinical workflow:
   In general there is a lack of knowledge, from a human factors standpoint, about the best way to present specific types of alerts to providers [18]. An example is formulary management decision support. Formulary adherence greatly improved when clinicians were provided with real time alerts that included a link to an alternative and additional information as needed (FDA alerts, drug shortages, etc.) [18] (**Figure 4**). In fact, automatically providing formulary decision support to the user was the most important determinant of improved clinical practice by a CDSS [47].

5.3.2. Liability issues

An important barrier to the acceptance by health care professionals of CDSS is the perception of increased liability if the recommendations provided by the system are rejected. Again, acceptance can be increased by thoroughly validating decision support algorithms prior to implementation and always allowing the clinician a "way out." The reasons why an alert or recommendation was not followed should be captured by allowing the clinician to enter a reason. This important information is not only an essential part in the continuous performance improvement of the decision algorithm, but also serves as documentation of the clinician's decision. In addition, it is proposed that clearly stated liability considerations and appropriate liability protections should be developed and clinicians educated about this subject [5].

5.3.3. Costs

Although very few studies specifically address the cost of developing and implementing CDSS, there is no doubt that these systems are very costly. The price of a basic (out-of-the-box) CDSS starts around US$30,000. But, due to the lack of universal standards, developing and validating the clinical rules and

algorithms can cost millions [48]. Clearly, the cost-benefit ratio of these systems depends on the quality of care issues they intend to improve. Further research is warranted to identify interventions that are most cost-effective, both in direct costs (hardware and software) and indirect costs (manpower and maintenance).

6. Recommendations and future areas for research[18]

Recently, a Roadmap for National Action on Clinical Decision Support has been developed to take away the barriers mentioned in the previous sections and to improve national adoption of this potentially powerful technology [15]. The roadmap identifies three pillars that need to be in place to fully benefit from the potential of CDSS:

1. *Best knowledge available when needed in standard formats:*

The best available clinical knowledge is well organized, accessible to all and written, stored and transmitted in a format that makes it easy to build and deploy CDSS interventions that integrate the knowledge into the decision making process. Assuring adequate informatics education among clinicians is essential to reach this goal: these clinical informaticians are needed to bridge the gap between clinical and technological worlds, who speak the language of both and therefore can act as translators [46] (See Chapter 9. Pharmacy Informatics as a Career)

2. *High adoption and effective use (high compliance):*

CDSS tools are widely implemented and extensively used. Only wide national implementation of a CDSS fully exploits the potential of this technology. This means that incentives, usually financial, need to be created for organizations to implement CDSS and for benchmark institutions to share their knowledge. Also, further research is needed to optimize alerting methods and to prevent alert fatigue [18].

3. *Continuous improvement of knowledge and CDSS methods*

CDSS interventions and clinical knowledge undergo continuous improvement based on feedback, experience with the system and data that are easy to aggregate, assess, and apply.
Further research is needed to identify the best way for organizations to share alert knowledge and to edit commercial medication knowledge bases to yield clinically valuable knowledge bases [18]. Also, more research is needed to identify which member of the healthcare team (physician, nurse, pharmacist or other) is the best recipient for any particular alert, and whether physicians and pharmacists should see the same drug-related alerts.

7. Concluding remarks

This chapter is intended to provide a broad, but not an in-depth overview of clinical decision support systems. The conclusion of a 2001 Agency of Healthcare Research and Quality report stated that "the widespread implementation of successful systems is feasible and will likely become more so as pro-

viders and systems increasingly shift to computerized [health] record systems" [49]. With the increasing electronic availability of patient-specific data, sophisticated clinical decision support is not only needed, but also is within reach. Pharmacists are in a unique position to take the lead in this area. The American Society of Health-System Pharmacists acknowledges this unique position in its Statement on the Pharmacist's Role in Informatics (2007) [50]:

"Pharmacists have the unique knowledge, expertise, and responsibility to assume a significant role in medical informatics. As governments and the health care community develop strategic plans for the widespread adoption of health information technology, pharmacists must use their knowledge of information systems and the medication-use process to improve patient care by ensuring that new technologies lead to safer and more effective medication use."

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Chapter 3

Using a clinical decision support system to determine the quality of antimicrobial dosing in intensive care patients with renal insufficiency

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Reference:
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ABSTRACT

Background

The benefits on clinical practice of a clinical decision support system (CDSS) are predominantly determined by the quality of the clinical rules used in this system. Therefore, it is essential to investigate the performance and potential benefits on quality of care of these rules.

Methods

We developed a clinical rule assisting physicians in selecting the appropriate dosage according to renal function of frequently prescribed antimicrobials. In 2004, 1,788 patients admitted on the Intensive Care Unit (ICU) for more than 12 hours were included in this retrospective study. We compared the actual number of dosage adjustments without the support of the CDSS with the theoretical number of dosage adjustments determined by the clinical rule in patients with moderate (creatinine clearance (Cl_{creat}) 10-50 ml/min) and severe (Cl_{creat} < 10 ml/min) renal dysfunction. If dosage adjustment was omitted, we determined the duration of excessive anti-infective dosing and extra drug costs involved.

Results

Dosage adjustment of antimicrobials was omitted in 163 patients (86%) with moderate and 13 patients with severe renal failure (54%). Excessive exposure was most frequently detected in patients receiving fluconazole and ciprofloxacin (median duration of 6 days). On our ICU alone, more than €16,000 ($19,000) can be saved annually by adjusting the dosage according to renal function of frequently prescribed antimicrobials.

Conclusions

Despite intensive monitoring of patients on the ICU, dosage adjustment of antimicrobials is often omitted. Implementing this clinical rule has the potential to contribute to a significant improvement in medication safety and is expected to generate substantial savings.

INTRODUCTION

Clinical decision support systems (CDSS) are defined as electronic or non-electronic systems designed to aid in clinical decision making. These systems use characteristics of individual patients to generate patient-specific assessments or recommendations that are presented to clinicians for consideration [1]. The field of decision support is rapidly evolving as many hospitals are transitioning from paper based patient records to electronic health records [2,3]. In addition, increased awareness and concerns of medical and medication errors and a focus on improving the quality of healthcare have led to a widespread adoption of information technology interventions [4]. Computerized prescriber order entry (CPOE) is one of the interventions aimed at improving prescribing practices and decreasing medication errors [5]. CPOE has resulted in increased access to computer systems and consequently improved availability of electronically available patient data at the point-of-care. By adding a CDSS, this wealth of data can be effectively converted into patient specific information which enables health care providers to augment their clinical decision making skills [6,7]. High adoption, effective use, and monitoring the impact of a CDSS are key factors for successful implementation [8,9]. Minimizing irrelevant alerts and deploying decision support only when needed, are important prerequisites for high adoption rates [10]. Thus, the actual success of a CDSS in clinical practice depends predominantly on the quality and "added value" of the clinical rules implemented. Therefore, it is important to investigate the need and performance of the clinical rules used in CDSS, before implementation in clinical practice [8].

Renal insufficiency is relatively common in patients admitted to the Intensive Care Unit (ICU) [11] and is associated with a persistent high mortality in critically ill patients [12]. Furthermore, renal function in critically ill patients can change rapidly. Antimicrobials are among the most frequently prescribed drugs on the ICU [13]. Excessive dosing of antimicrobials not only increases costs but may result in a variety of adverse drug events such as diarrhea, neurological disorders (i.e. convulsions) and additional deterioration of renal function [13]. When antimicrobials are administered intravenously, excessive dosing may also increase the risk of thrombophlebitis and infection [14]. Thus, there is general consensus that dosage of antimicrobials should be adjusted according to renal function to prevent adverse drug events. In daily practice, however, these adjustments are often omitted [15] because information on renal function is not readily available at the point of care [16,17] or because clinicians are not aware of the specific dosage adjustments that are warranted in individual patients with renal failure.

Most studies on decision support systems to improve prescribing in patients with renal failure are done in the United States using decision support systems specifically designed for the local situation [18,19]. Consequently, it is difficult to extrapolate the results to a Dutch ICU, using a commercially available decision support system. On the ICU in our institution, laboratory values and medication data are electronically available in one software application. This provides an opportunity to assess the quality of antimicrobial dosing and the potential of a decision support in a highly computerized setting and in an intensively monitored patient population. Therefore, we investigated the value of a clinical rule designed to improve antimicrobial dosing in critically ill patients with renal dysfunction on the ICU in terms of dosing adjustments, duration of exposure and costs, using a commercially available CDSS.

METHODS

Study design and settings

We performed a retrospective database study evaluating the quality of antimicrobial prescribing by comparing the number of dosage adjustments without the support of a CDSS with the theoretical number of dosage adjustments indicated by the clinical rule. Furthermore, we determined the exposure of the patient to the antimicrobial in terms of duration and number of doses administered to evaluate the theoretical risk of excessive dosing. Finally, we estimated the extra drug costs involved in omitting antimicrobial dosage adjustment.

Approval by the Institutional Review Board was not required for this type of study. The study was carried out at Catharina Hospital, a 700-bed secondary care teaching hospital in Eindhoven, The Netherlands. The 21 bed-ICU uses the Intensive Care Information System (ICIS version 2.8, INAD Computers and Software BV, Eindhoven) for Electronic Medical Record (EMR) keeping and Computerized Physician Order Entry (CPOE). Laboratory results, medication and intravenous fluids, diagnoses and complications are stored in the system.

Study population

The ICIS-database of 2004, including 2,752 patients admitted to the ICU, was used for this study. This study was aimed at the ICU patient population that could receive antimicrobial therapy for a prolonged period of time. Therefore, only patients staying on the ICU for a period of more than 12 hours were included (1,788 patients).

Description of the decision support system

The clinical decision support system GASTON (Version 2.6 , Medecs BV, Eindhoven, The Netherlands) was used in this study [20,21]. GASTON is independent of the presence of a CPOE but is linked to the EMR, which allows data, stored in the EMR, to be used in clinical rules. It is also possible to perform calculations on the data stored in the database to generate new variables for use in clinical rules. For example: GASTON uses the Cockcroft-Gault formula to calculate the creatinine clearance of patients by using the variables age, weight, length and serum creatinine concentration, stored in the EMR [22]. As a result, "creatinine clearance" is an extra variable that can be used in clinical rules.

The EMR of each patient was evaluated by the CDSS every 12 hours after admission on the ICU. For example: if a patient with renal failure had received amoxicillin 1000 mg IV four times daily (QID) for 2 days, 4 alerts were generated (4 episodes of 12 hours). All alerts were manually compared to the EMR to assure that the alerts accurately reflected the true overdosing of antimicrobials. Excess dosing was calculated by multiplying the extra doses administered per day by the duration of exposure. The additional drug costs involved were estimated by multiplying the extra doses administered by the listed drug price per dose.

Description of the clinical rule

The "GASTON guideline-editor" is a user-friendly interface that presents clinical rules as flowcharts (**Figure 1**). Clinical rules are created by linking every step of the flowchart to a variable in the database

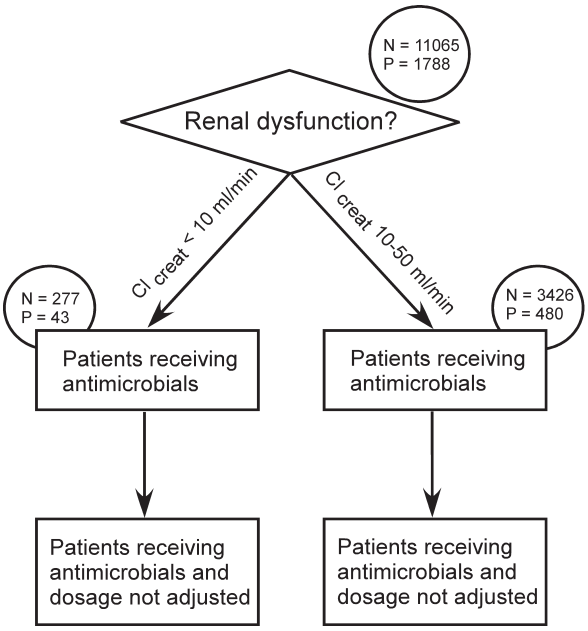

Figure 1. Identification of cases.

The clinical rule used in this study starts with selecting ICU patients based on the level of renal function impairment (diamond). Patients receiving antimicrobials are then further evaluated (rectangles). First, the total number of patients receiving a specific antimicrobial is identified (denominator). Subsequently, we determined excess antimicrobial dosing in this group (numerator). This allows calculation of the percentage adjusted and unadjusted dosages. P indicates the total number of patients evaluated in each decision step. N indicates the number of alerts in the database (as a measure of total exposure to excessive dosage).

(for example "creatinine clearance" or "amoxicillin"). By further specifying the variable (for example "creatinine clearance between 10-50 ml/min" and "amoxicillin 1000 mg every 12 hours"), the question "How often is an excessive amount of amoxicillin prescribed in patients with a creatinine clearance of 10-50 ml/min" is integrated in the clinical rule (**Figure 2**).

We selected the ten most frequently prescribed antimicrobials on our ICU that need dosage adjustment in renal failure, since these antimicrobials account for 90% of all antimicrobial prescriptions. We used the categories of renal failure and dosage adjustments specified in the antimicrobial formulary of our hospital [23], which are based on published Dutch guidelines (**Table 1**)**.** The Cockcroft and Gault formula cannot be used to calculate creatinine clearances in patients receiving renal replacement therapies [22]. In these patients, the overall creatinine clearances achieved by continuous veno-venous hemofiltration (CVVH) and hemodialysis were set at 30 ml/min and 10 ml/min respectively [24].

As a result, we defined two categories of renal failure:

1. Patients with moderate renal failure: creatinine clearance of 10 to 50 ml/min or receiving CVVH as renal replacement therapy.
2. Patients with severe renal failure: creatinine clearance of less than 10 ml/min or receiving hemodialysis as renal replacement therapy.

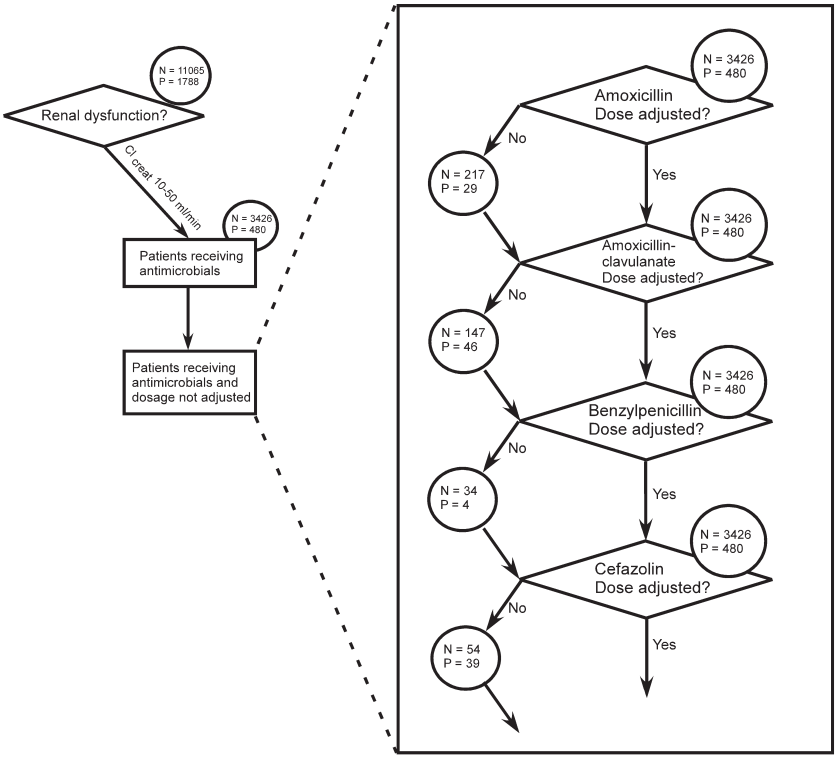

Figure 2. Calculation of exposure

As an example, the decision rule for the moderate renal failure group is shown. A total of 480 patients with moderate renal failure received at least one of the antimicrobials studied. If amoxicillin is taken as an example: 29 patients received excess doses (P=29), resulting in 217 alerts. This corresponds to a total duration of exposure of 108 days (217 episodes of 12 hours).

Table 1. Recommended intravenous dosages of the ten most frequently prescribed antimicrobials in patients with normal, moderate and severe renal failure23

Antmicrobial	Standard dosage	Dosage in moderate renal failure (CrCl 10-50 ml/min)	Dosage in severe renal failure (CrCl < 10 ml/min)
Amoxicillin	1000 mg q 6 h	1000 mg q 8 h	1000 mg q 12 h
Amoxicillin-clavulanate	1200 mg q 6 h	1200 mg q 12 h	1200 mg q 24 h
Benzylpenicillin	1 million IE q 6 h	1 million IE q 8 h	1 million IE q 12 h
Cefazolin	1000 mg q 6 h	1000 mg q 12 h	1000 mg q 24 h
Ceftazidime	1000 mg q 8 h	1000 mg 24 h	1000 mg q 48 h
Cefuroxime	1500 mg q 8 h	1500 mg q 8 h	1500 mg q 24 h
Ciprofloxacin	400 mg q 12 h	400 mg q 12 h	400 mg q 24 h
Fluconazole	400 mg q 24 h	400 mg q 48 h	200 mg q 48 h
Piperacillin-tazobactam	4500 mg q 8 h	4500 mg q 8 h	4500 mg q 12 h
Sulfamethoxazole-trimethoprim	960 mg q 8 h	480 mg q 12 h	480 mg q 24 h

RESULTS

A. Dosage adjustments

An episode of moderate renal failure was found in 480 out of 1,788 patients (27%). One hundred and eighty nine patients (39%) received at least one of the investigated antimicrobials. Cefuroxime, ciprofloxacin and piperacillin-tazobactam are excluded because no dosage adjustment is warranted for this group of patients. In 163 out of 189 patients (86%), dosage adjustments were omitted (**Table 2**). Excessive dosing was most frequently found in patients receiving ceftazidime (100%), fluconazole (100%), amoxicillin-clavulanate (94%) and cefazolin (85%).

The system identified 43 patients with severe renal failure or receiving hemodialysis. Twenty-four patients (56%) received at least one of the investigated antimicrobials. The most frequently prescribed antimicrobials were amoxicillin and cefuroxime, whereas cefazolin and ceftazidime were not prescribed at all in this group. In 13 patients (54%) the dosage was not adjusted according to renal function.

Renal function in patients receiving renal replacement therapy is more intensively monitored compared to patients who are not. Since increased monitoring is expected to result in improved dosing by physicians, we compared dosage adjustments in patients receiving renal replacement therapy to patients with renal failure but without renal replacement therapy. A total of 51 patients received renal replacement therapy. Of this group, antimicrobial dosage adjustment was omitted in 44 patients (86%), which is similar to the adjustment rate in patients with renal failure but not on renal replacement therapy (150 patients out of 181 patients (83%)).

Table 2. Overview of dosage adjustment according to renal function and extra drug costs associated with excess exposure.

Antimicrobial	Patients (unadjusted / total)		Total group		
	Moderate renal failure group	Severe renal failure group	Median exposure (days (range))	Median excess doses administered (range)	Extra drug costs (€)
Amoxicillin	29/34	3/5	3 (1-22)	3 (1-25)	524
Amoxicillin-clavulanate	46/49	3/4	2 (1-9)	4 (1-18)	1046
Benzylpenicillin	4/11	1/2	4 (1-18)	12 (4-54)	86
Cefazolin	39/46	0	1 (1-2)	2 (1-4)	386
Ceftazidime	13/13	0	4 (1-15)	15 (1-45)	4852
Cefuroxime	*	3/5	2 (1-3)	2 (2-3)	89
Ciprofloxacin	*	2/2	6 (4-8)	6 (4-8)	616
Fluconazole	17/17	0/1	6 (1-15)	6 (1-21)	8122
Piperacillin-tazobactam	*	0/1	0	0	0
Sulfamethoxazole-trimethoprim	15/19	1/4	4.5 (1-8)	9 (2-16)	668
*) No dosage adjustments are warranted in this group				**TOTAL**	**16,389**

B. Duration of exposure and associated costs

The exposure to excess antimicrobial dosage and extra drug costs associated with exposure are shown in **Table 2**. Excessive exposure was most likely to occur in patients receiving fluconazole and ciprofloxacin (median duration of 6 days). By adjusting the dosage of the most frequently prescribed antimicrobials according to renal function, more than € 16,000 ($19,000) per year can be saved on our ICU alone. Exposure to fluconazole (€ 8,122) and ceftazidime (€ 4,852) was responsible for 80% of these extra drug costs.

DISCUSSION

Our study shows the value of a clinical rule designed to improve antimicrobial dosing in patients with renal failure. Dosage adjustment of antimicrobials are often omitted, leading to prolonged exposure to excessive antimicrobial doses and is associated with substantial costs.

One explanation could be that information of a patient's renal function is not readily available when antimicrobials are prescribed [16,17]. However, this is unlikely in our study since serum creatinine concentrations are stored in the same system used to prescribe antimicrobials. A second explanation could be that physicians are unaware of the need and specific guidelines for dosage adjustment in patients with renal impairment. In fact, default dosages of frequently prescribed antimicrobials are pre-defined in ICIS and it is common practice to select this default (unadjusted) dosage. Because of this, it is very unlikely that the low degree of antimicrobial dosage adjustments is attributable to a single prescriber.

Our study has several limitations. First, the results of retrospective database research are only an estimate of the benefit that can be achieved by a decision support system. Therefore, additional (prospective) research in our clinical setting is needed to show that this system lives up to its expectations. Second, only the ten most frequently prescribed antimicrobials were studied, but this clinical rule can be applied to all drugs where dosage reduction in renal failure is indicated. Third, when therapy is very short, one could argue that dosage adjustment in patients with renal failure is not required. Indeed, the *initial dose* of antimicrobials is identical to patients with normal renal function, because the volume of distribution is not altered. In this study, this could have been the case for fluconazole and sulfamethoxazole-trimethoprim, where both dose and dosing interval recommendations were used in the clinical rule. However, this does not apply to the results of the other antimicrobials where only dosing interval adjustments were used. Finally, patient side effects and outcome were not studied, because data of relevant side-effects due to exposure to high dosages of antimicrobials were not systematically stored in the database. At the time of our study, the medical records of our patients were only electronically available on our ICU. Therefore, we were not able to detect any side effects that could have occurred after discharge from the ICU. But even if these data were available, causality assessment remains very difficult in critically ill patients. Therefore, our calculations of the potential savings of this clinical rule did not include potential savings arising from the reduction in adverse drug events or prolonged stay on the ICU. Despite these limitations, our findings are consistent with the findings of Evans et al. on a United States ICU where 53% of intensive care patients receiving antimicrobial therapy was exposed to excessive dosing [19].

Although this study shows that successful implementation of a CDSS to improve antimicrobial prescribing could lead to decreased costs, it should be emphasized that cost reduction is of minor importance compared to the improved quality of care that can be achieved by implementing such a system. Also, failing to adjust antimicrobial dosage is not simply due to negligence of the health care

provider, but to flaws in the system the provider works in. As an increasing amount of data is electronically stored in databases, implementing decision support at the time of decision making seems to be the logical next step to convert this data into ready-to-use, patient specific information. Indeed, increasing availability of patient specific information at the time of prescribing could lead to a significant improvement of appropriate dosing of renally cleared and/or nephrotoxic medication [18,19,25]. However, extrapolating results achieved in other institutions can be challenging. In fact, most studies indicating a positive effect of decision support are performed in only four benchmark institutions in the United States, using "home grown" decision support systems [26]. As a result, difficulty in recognizing the value of a CDSS is considered to be one of the major barriers to widespread effective use of CDSS [27].

Overall, we conclude that a clinical rule designed to improve antimicrobial dosing detected a high prevalence of unadjusted antimicrobial dosage in intensive care patients with renal failure. As determining the need for a clinical decision rule is pivotal for successful implementation of a CDSS, the retrospective approach described here can be used to quantify its value.

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Chapter 4

Drug-drug interaction checking assisted by clinical decision support: a return on investment analysis

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ABSTRACT

Purpose

Drug-drug interactions (DDIs) are very prevalent in hospitalized patients. This study determines the number of DDI alerts, time savings and time investment after identifying clinically relevant DDIs and adding clinical decision support.

Materials and methods

The 29 most frequently occurring DDIs were evaluated for clinical relevance by a multidisciplinary expert panel. Four DDIs appeared upon prescribing and were retrospectively evaluated by pharmacists, 17 DDIs were only evaluated by pharmacists and 8 DDIs were found not clinically relevant. DDI evaluation by pharmacists was further enhanced using computerized decision support. During Phase 1, CDSS assisted DDI checking was implemented, but all DDIs continued to appear to both the pharmacist and prescriber. During Phase 2, CDSS assisted DDI checking remained in place, but only relevant DDIs appeared to both the pharmacist and prescriber. Both conventional DDI checking as CDSS assisted DDI checking were performed on the same patient population by the same pharmacist. In each phase, duration and number of alerts were compared. In addition, time investment of implementing and configuring the CDSS was compared to the time saved using CDSS assisted DDI-checking.

Results

CDSS assisted DDI checking resulted in a daily decrease of DDI checking duration from 15 to 11 minutes (P=0.044) and from 15.5 to 8.5 minutes (P=0.001) in Phase 1 and Phase 2 respectively. The number of daily alerts decreased from 65 to 47 in Phase 1 (P=0.03) and from 73 to 33 alerts in Phase 2 (P=0.003). Almost 298 of the 392 hours required to implement CDSS assisted DDI checking were invested by pharmacists. An annual time savings of 30 hours yields a return-on-investment of 9.8 years.

Conclusion:

CDSS assisted DDI checking results in a 45% reduction in time spent on DDI checking and a 55% reduction of the number of alerts, yielding a return of investment of almost 10 years. However, our approach can be used to refine other drug safety checking modules, increasing efficiency of the drug safety checking task without the need to add more pharmacist staff.

INTRODUCTION

Drug-drug interactions (DDIs) are very prevalent among hospitalized patients: up to 65% of inpatients are exposed to one or more DDIs and 41–70% of patients are discharged with a potential interacting drug combination[1-4]. There is limited evidence on the patient safety consequences of DDIs. In one study, 44 patients were discharged with a potentially severe DDI, resulting in only one readmission within two months[3]. However, an increased risk of mortality was observed in a cohort of elderly inpatients when exposed to at least two potentially severe DDIs[4]. A recent study investigated the consequences of the interacting drug combination of clarithromycin and dihydropyridine calcium antagonist: the investigators found that not only co-prescribing these interacting medications was common but also that co-prescription was associated with a higher risk of hospitalization with acute kidney injury, hypotension, and all-cause mortality[5].

To mitigate these risks, most computerized prescriber order entry (CPOE) systems include drug-safety software, consisting of drug-dosing, duplicate-therapy and drug-drug interaction checking modules. In The Netherlands, drug-drug interaction checking in pharmacy and electronic prescribing systems is based on the G-Standard, a national knowledgebase[6]. The G-Standard evaluates DDIs on relevance and provides recommendations to both prescribers and pharmacists based on their practice setting (outpatient or inpatient). However, the G-Standard does not apply additional information (such as concomitant medication, laboratory values and administration times) to the drug-drug interaction checking algorithm. In addition, drug-safety checking is typically performed when a medication is first prescribed or when an existing order is modified, while the deleterious effects of DDIs typically occur days or even weeks after first prescribing the medication. This results in frequent and often irrelevant alerts for prescribers and an inefficient drug-drug interaction checking process by pharmacists. In a Dutch study, medication safety software based on the G-standard resulted in 176 alerts after entering 515 orders (34%). DDI alerts were both the most prevalent (98%) drug safety alerts and the most frequently overridden (91% of alerts)[7].

Clinical decision support systems (CDSS) can be used to augment DDI checking practices. A clinical decision support system (CDSS) is defined as "software that is designed to be a direct aid to clinical decision making, in which the characteristics of an individual patient are matched to a computerized clinical knowledge base resulting in patient-specific assessments or recommendations"[8]. Gaston (Medecs BV, Eindhoven, The Netherlands) is a commercially available clinical decision support system. Details of this system are described elsewhere [9,10]. It is used in a number of Dutch hospitals as a clinical rule engine to facilitate drug surveillance efforts. At our institution, Gaston is used to evaluate all active medication orders for DDIs of each non-ICU inpatient three times per day. As a result, the potential deleterious effect of an interaction can be monitored over time. In addition, the CDSS adds clinical laboratory values, concomitant medication, patient demographics and administration times to the drug-drug interaction algorithm. These variables are commonly stored in hospital databases and determine the clinical significance of many frequently occurring DDIs. Manually retrieving these parameters is common practice when evaluating DDIs, but is an inefficient and labor-intensive process. Therefore, we hypothesize that adding clinical laboratory values, concomitant medication, patient demographics and administration times to the basic DDI checking algorithm results in fewer alerts, more relevant alerts and increased efficiency without sacrificing quality of care. This study compares the number of DDI alerts of conventional DDI checking with CDSS assisted DDI checking and quantifies pharmacist time investment associated with configuring this novel method of DDI checking and benefits in terms of pharmacist time saved.

METHODS

Setting

St Jansdal Hospital is a 341 bed general hospital with 18,573 patient admissions and 369,808 outpatient visits in 2012. It has a capacity of 6 cardiac monitoring and 6 ICU beds. CPOE is fully implemented in both the inpatient and outpatient setting. The ICU has implemented a dedicated ICU prescribing and monitoring system that is currently not interfaced with the hospital CPOE system or the CDSS. Therefore, the ICU is excluded from this study. St Jansdal hospital has achieved stage 4 (CPOE and decision support implemented) of the Electronic Medical Record Adoption Model of the Healthcare Information and Management Systems Society (HIMSS) [11]. The Department of Pharmacy employs the following staff relevant to this study: 3.67 FTE hospital pharmacists, 1.78 FTE IT-pharmacists, 1.37 FTE quality assurance officers.

Intervention

The DDI refinement approach is shown in **Figure 1**. Ideally, DDIs should be prevented at the time of prescribing to minimize the likelihood of patient exposure. Therefore, we first evaluated if DDIs could be prevented by smart CPOE ordering (e.g. predefined orders or order sets). For example, we minimized the occurrence of absorption interactions caused by calcium preparations by predefining calcium orders to be administered at 22.00u as most interacting drugs are administered in the morning or during the day.

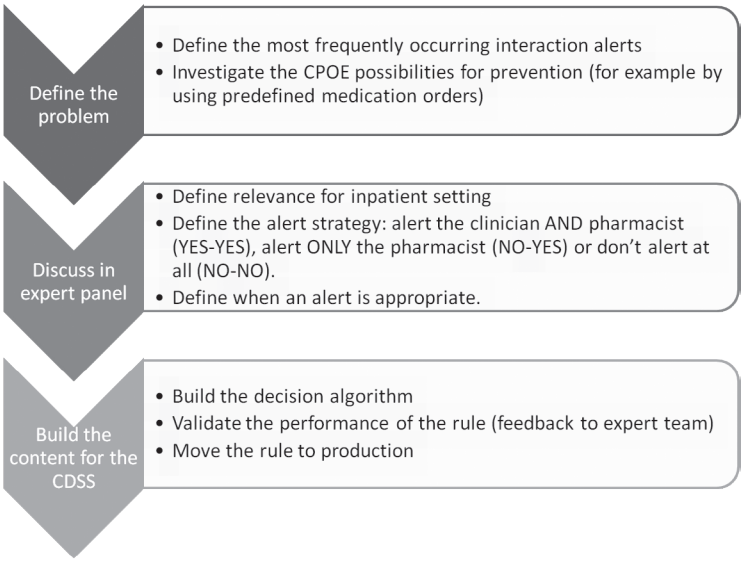


Figure 1. Schematic representation of the DDI refinement approach

During Phase 1, the 29 most frequently occurring interactions were refined using the CDSS when possible, but no alerts were suppressed. During Phase 2, only the YES-YES alerts were shown at the point of prescribing and the pharmacist reviewed the YES-YES and NO-YES interactions. The NO-NO interactions were suppressed for both the pharmacist as the prescriber, but remained visible in the patient medication profile as a yellow exclamation mark.

Assessment of relevance of most frequently occurring DDIs in the inpatient setting

In addition to improving efficiency of DDI checking by pharmacists, a second goal was to decrease the number of irrelevant alerts at the time of prescribing. Log files dating back one month were analyzed to identify the most frequently occurring DDIs (**Table 1**). A total of 29 interactions accounted for 86% of total alerts and were assessed by a multidisciplinary expert panel consisting of a hematologist, nephrologist, geriatrician, cardiologist, rheumatologist, neurologist, pediatrician and hospital pharmacist. DDIs were categorized in three groups: (1)YES-YES interactions: pop-up alerts are shown to both the prescriber at the moment of prescribing and the pharmacist. This strategy applies when an interaction should be prevented at the time of prescribing. (2) NO-YES interactions: no alert is presented to the prescriber, but only a yellow exclamation mark indicating a DDI is present, is shown on the medication profile. However, pharmacists review and correct the order if needed. This strategy applies when an interaction should be prevented, but a lag time of a maximum of 24 hours is acceptable. (3); NO-NO interactions: only a yellow exclamation mark is shown in the medication profile at the moment of prescribing, but the pharmacist will not review the interaction. These interactions are considered not clinically relevant for the inpatient population.

Conventional DDI checking by pharmacists

Conventional DDI checking was based on the national Dutch G-standard and occurred after initiating or modifying a medication order. In both instances, a pop-up alert is presented to the prescriber and the alert is logged for pharmacist review. DDI log files were generated, emailed to the pharmacist on call and reviewed three times daily (10.30AM, 1PM and 3.30PM). Any interventions were recorded. Additional variables required to determine the significance of a DDI were manually retrieved. For example, when a potassium sparing diuretic was prescribed with a potassium salt, the most recent potassium value was manually retrieved from the hospital's electronic medical record (EMR).

CDSS assisted DDI checking by pharmacists

Three times per day (at 10.30AM, 1PM and 3.30PM) all active medication orders of all inpatients were evaluated using the CDSS Gaston. Out-of-the box, the standard DDI checking software based on the G-standard is included in the CDSS and is updated monthly. Consequently, the same conventional DDI alerts are initially generated. However, Gaston also includes laboratory data, concomitant medication, medication order details (such as administration times) and patient demographics. Consequently, many of the frequently occurring DDI-alerts can then be refined using a user-friendly guideline editor **(Figure 2).** Using the same example: when a potassium sparing diuretic is co-prescribed with a potassium salt, an alert will only be generated when the latest potassium level exceeds 5 mmol/l **(Figure 2)**.

CDSS assisted DDI-checking was implemented in two phases: during Phase 1, all DDIs were still presented to both the prescriber and pharmacist, but for pharmacists additional decision support was applied using the variables mentioned above.. During Phase 2, only the YES-YES interactions are shown to the prescriber and the YES-YES and NO-YES interactions are shown to the pharmacist who then again used CDSS assisted DDI checking when possible to manage the alerts. NO-NO interactions no longer resulted in an alert for the prescriber and were not shown to the pharmacist.

Table 1. Evaluation by expert panel of frequently occurring DDIs.

YES prescriber-YES pharmacist: DDI alert evaluated by both prescriber and pharmacist.

NO prescriber-YES pharmacist: DDI alert only evaluated by pharmacist.

NO prescriber-NO pharmacist: DDI-alert not evaluated by both prescriber and pharmacist.

Numbers behind brackets: national G-Standard DDI number

YES prescriber-YES pharmacist	NO prescriber-YES pharmacist	NO prescriber-NO pharmacist
Ssri's/venlafaxine + tramadol (4227)	Thyreomimetics + antacids/ calcium (3433)*	Betablockers + nsaid's (272)
Cumadins + allopurinol (523)	Raas-inhibitors + diuretics (19)	Cumadins + (es)omeprazole (8494)
Cumadins + amiodarone/ propafenone (531)	Nsaid's (excl. coxib's) + corticosteroids (2046)*	Selective betablockers + insulin (302)
QT-prolonging agents + QT-prolonging agents ('arizona') (6297)	Raas-inhibitors + nsaid's (27)	Betablockers + orale blood glucose lowering agents (3964)
	Cumadins + antibiotics (ex. cotrim/ metron/cefam.) (566)	Simvastatine/atorvastatine + cyp3a4-inhibitors (2445)
	Diuretics + nsaid's (1155)	Non selective alpha blockers + betablockers/calcium antagonists (78)
	Raas-inhibitors + potassium or potassium sparing agents (35)*	Non selective beta blockers + betamimetics (310)
	Salicylates antitrombotic + nsaid's (ex ibuprof) (7951)*	Clopidogrel + omeprazole/ esomeprazole (8036)
	Nsaid's (ex Coxib's) + serotonergic agents (3360)*	
	Ssri's/venlafaxine/duloxetine + thiazides (5851)*	
	Cumadins + salicylates antitromb. (up to 100 mg) (3026)*	
	Cumadins + thyreomimetics (2380)	
	Cumadins + nsaid's (736)*	
	Simvastatin + ticagrelor (9903)*	
	Bisfosfonates + antacids/iron/ calcium (2135)*	
	Iron + antacids/carbonates (140)*	
	Potassium + Potassium sparing diuretics (1066)*	

* DDIs refined using CDSS. The following DDIs were also refined, but were not evaluated by the expert panel as they were not (as) frequently occuring: Quinonolones + Antacids (906), Quinolones + Calcium/bismutoxide (914), Quinolones + Iron (922), Thyreomimetics + Iron (2364), Trimethoprim + Raas-inhibitors/spironolactone (9962), Acetazolamide + Diuretics (Potassium-excreting) (2127)

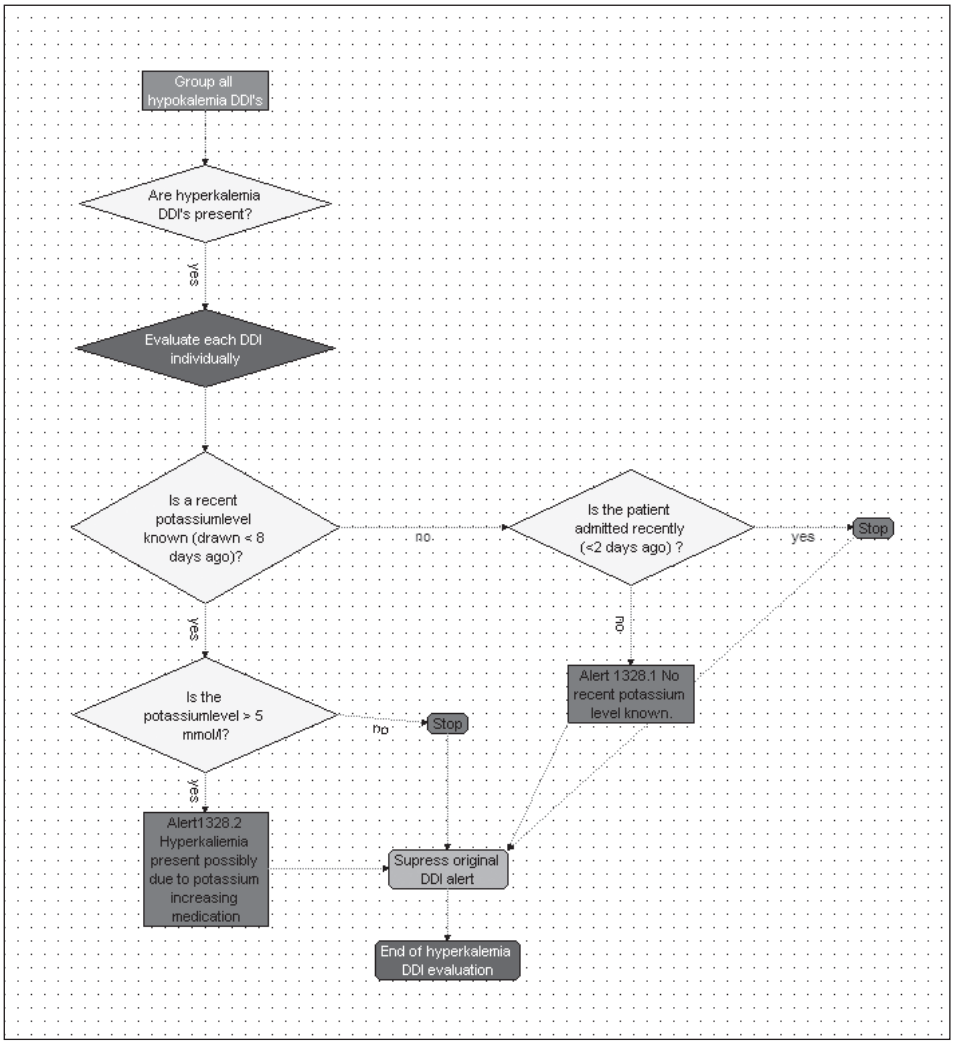


Figure 2. Screenshot of a CDSS assisted DDI algorithm

Top rectangle: grouping step, groups DDIs with similar effects. As a result, multiple DDIs can be refined with one clinical rule. Light grey diamond: decision step, only yes and no decisions are allowed. Dark grey diamond and bottom square: start and end of a "loop": each patient's active medication is evaluated multiple times for each DDI in the group. For example: if 2 DDIs are present resulting in potential hyperkalemia, the clinical rule does not stop after evaluating the first DDI, but continues with the second DDI. Dark grey square: refined alert, which is presented to the pharmacist for evaluation. Dark grey "stop" oval: guideline remark to highlight the end of a decision step. Light grey oval: "Activity step": suppresses the original alert generated by basic DDI checking. CDSS-assisted DDI checking evaluates all active medication orders three times daily. Consequently, many more alerts will initially be generated compared to conventional DDI-checking where only alerts are generated when an order is initiated or revised. Therefore CDSS assisted DDI checking is configured to (1) suppress conventional DDI alerts which were evaluated as not relevant during the previous DDI checking episode and (2) to suppress conventional DDI alerts of those DDIs that were refined using the CDSS (the final step of each CDSS assisted DDI algorithm). As a result, only relevant (refined) alerts (grey boxes in the algorithm) are presented to the pharmacist.

Data-collection

Investment

Time investment for development, configuration, presentation and training activities was assessed by analyzing calendar events. The activity categories are shown in **Table 2** and are in line with a previous study evaluating the costs of implementing a CDSS assisting in renal dosing [12].

Table 2. Time investment of implementing CDSS assisted DDI checking.

Category	Subcategory	Total time (hours)	Pharmacist time (hours)
Project management	Developing and approving Business Case	9	9
	Identifying staff and introducing them to the project	18	9
	Developing and approving project plan	9.5	7
	Meetings	19	18.5
	Designing process and procedures for developing CDSS components	13	13
	Meetings	4	4
	Presentation for interested parties	9.5	9.5
System purchase	Discussing and approving quote	8.5	6
Preparing contents of the CDSS	Selecting most frequently occurring interactions	5	5
	Clinical rule build/configuration	13.5	13.5
	Constructing and reviewing rules for inclusion in the CDSS	2	0.5
Informatics (IT) project management	Hard- and software configuration	3.75	0.75
	Meetings	5.5	1.5
	Backup procedures	1	1
Testing and implementing	Implementing new workflow	6.75	5.75
	Troubleshooting before go-live	3.5	3.5
	Backup procedures	27	0.5
	Validation	74	68.5
	Training users	5	5
	Troubleshooting after go-live	10	10
Programming	Hard- and software configuration	0.5	0.5
	Clinical rule build/configuration	143.5	105.5
TOTAL		**391.5**	**297.5**

Return

During both phases of the study, the pharmacist on call first performed conventional DDI checking by reviewing DDI alert log files and subsequently performed the same task in the same patient population by reviewing the alerts generated by the CDSS. The time required to retrieve relevant laboratory values or other medication order or patient characteristics was included in the time measurement. The time required to follow up on DDI alerts (e.g. call a physician, change a medication order) was not included in the time measurement. Start and finish times of the DDI checking task and number of DDI alerts were recorded for each method. Total daily time spent was calculated for each method by subtracting the start time from the finish time of each DDI checking session.

Sample size calculation and statistical analysis

Calculation of data collection days required to adequately power this study was based on an pre-study time measurement of 3 days of conventional DDI checking. On average 9.3 minutes were spent daily on conventional DDI checking. Assuming, an α of 0.05 and a power of 80%, at least 12 data collection days were required to detect a reduction of 3 minutes (33%) after implementation of CDSS assisted DDI checking.

In each phase, time investment and number of alerts of conventional DDI-checking were compared to CDSS assisted DDI checking. Data were entered into spreadsheets (Microsoft Excel 2010, Redmond, WA) for initial analysis and summary statistics. NCSS 2007 (Version 07.1.20 Kaysville, UT) was used for statistical tests. The two-sided Wilcoxon Rank-Sum Test for difference in medians was used to compare the daily time spent on DDI checking, as this outcome variable was not normally distributed. Assessment of statistical significance of the number of DDI alerts during Phase 1 and Phase 2 was conducted using the two-sample t-test for continuous data. The a-priori level of significance was set at 0.05.

RESULTS

A total of 61 DDI checking sessions over 21 weekdays were analyzed during Phase 1 and 41 DDI checking sessions over 14 weekdays were analyzed during Phase 2. More DDI checking sessions were included in Phase 1 as the effect of CDSS assisted DDI checking on duration and number of alerts was expected to be less. Each pharmacist performed a median of 15 DDI checking sessions (range 15-18) during Phase 1 and 10 DDI checking sessions (range 6-16) during phase 2.

The 29 DDIs evaluated by the expert panel accounted for 83% and 79% of total alerts in Phase 1 and Phase 2 respectively, which is similar to the 86% found in the pre-study analysis of DDI log-files **(Figure 3)**. Conventional DDI checking resulted in 28 and 11 interventions during Phase 1 and Phase 2 respectively, and required manual data collection 247 and 179 times.

Performance of the CDSS

A total of, 18 DDIs were refined using additional variables in the CDSS: 6 DDIs requiring modification of administration times, 4 DDIs requiring monitoring of potassium levels, 2 DDIs requiring monitoring of sodium levels, 5 DDIs requiring gastric ulcer prophylaxis and 1 requiring drug dose checking (**Table 1**).These DDIs accounted for 24% of conventional alerts in both phases (**Figure 3**). Concomitant medi-

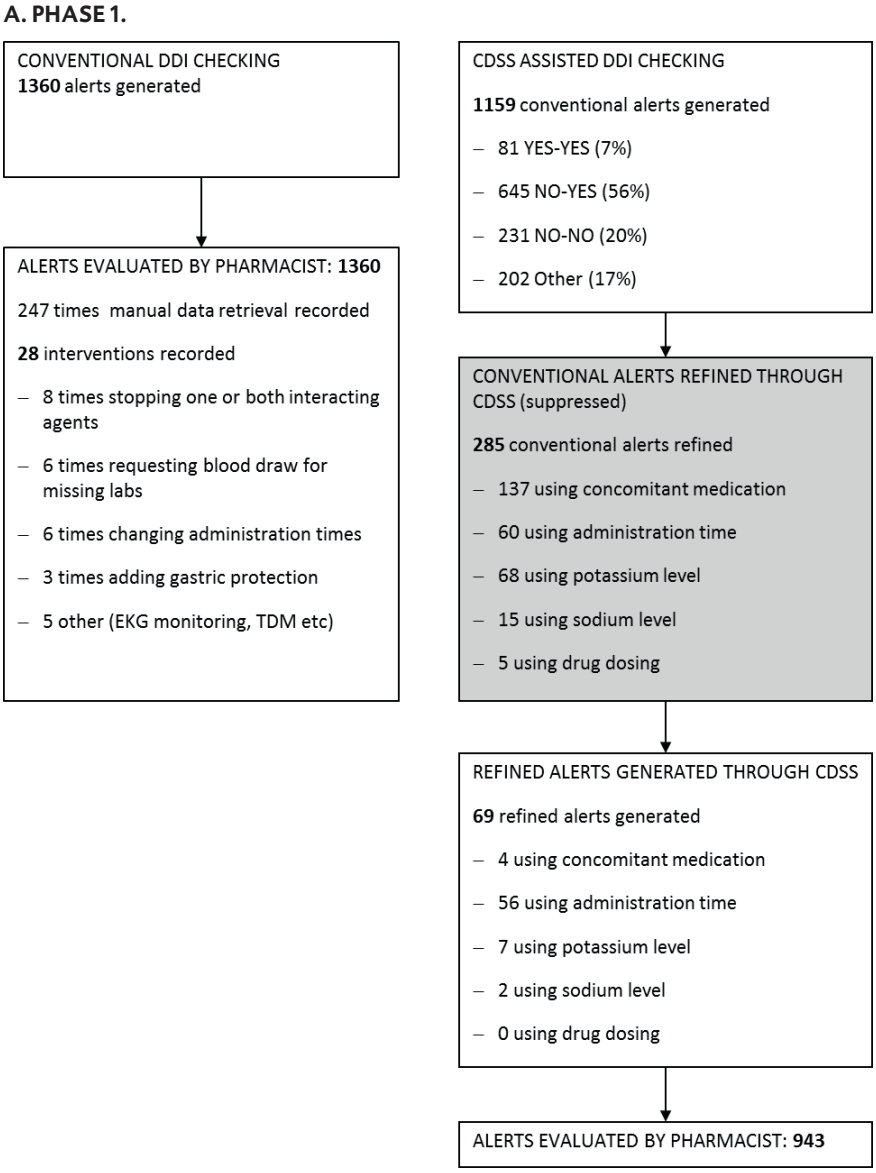
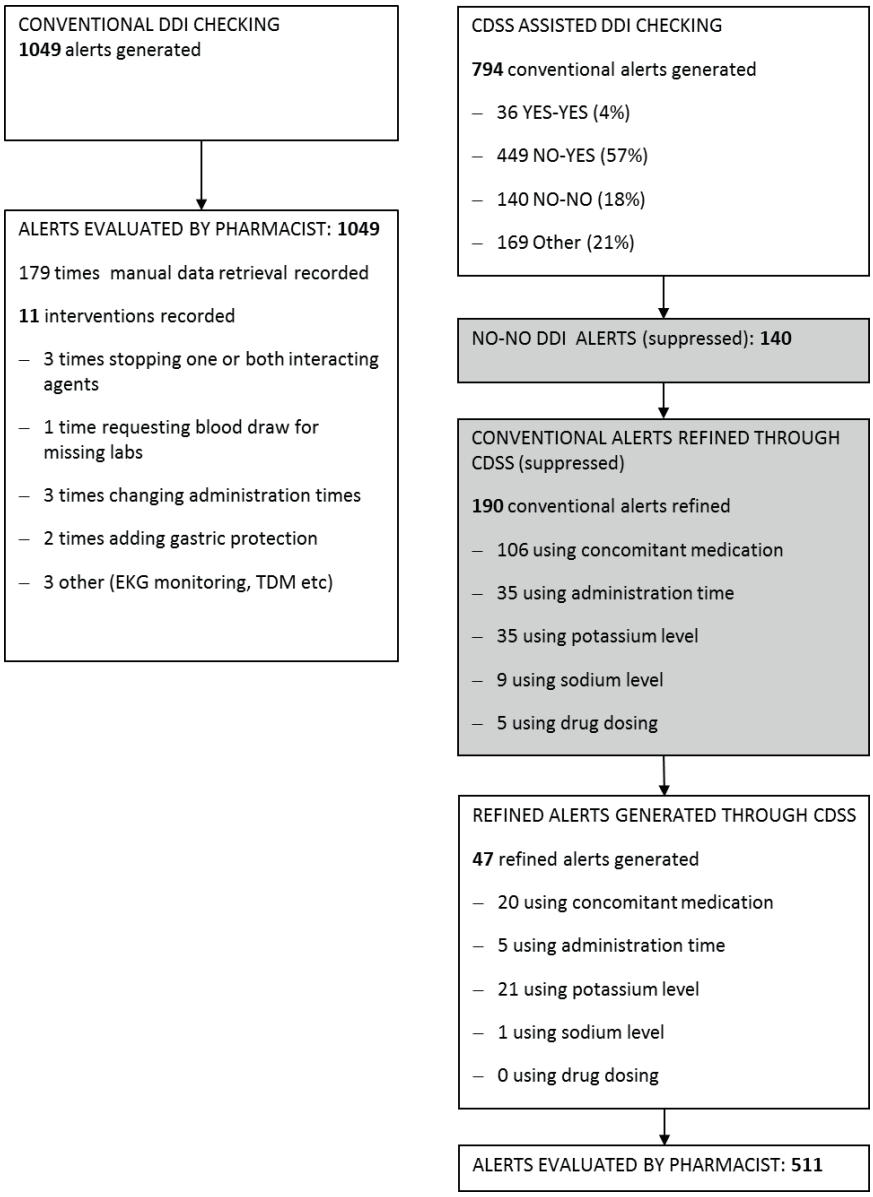


Figure 3. Alerting behavior conventional and CDSS assisted DDI checking.

A. Phase 1: All alerts were displayed to both pharmacists as clinicians.

B. Phase 2: Only YES-YES alerts were displayed to both clinicians and pharmacists. NO-YES alerts were only displayed to pharmacists. NO-NO alerts were suppressed for both practitioners. Only pharmacists benefited from CDSS assisted DDI checking in both phases.Grey boxes indicate alerts suppressed by the CDSS. As an example: during Phase 1, 1159 conventional alerts were generated using the CDSS; 285 conventional alerts could be refined using the additional variables in the CDSS and were suppressed. 69 alerts were subsequently generated after refinement, yielding a total of 1159-285+69 = 943 alerts to be evaluated by the pharmacist.

B. PHASE 2.



cation was the most frequently used variable to refine conventional DDI alerts (48% and 56% in phase 1 and phase 2 respectively), followed by potassium levels and administration time in both phases (grey boxes in **Figure 3**). DDIs refined using administration times resulted in the most remaining alerts (81%) in Phase 1, as opposed to DDIs requiring potassium level (45%) potassium in Phase 2. Overall, the CDSS decreased the number of conventional alerts generated by 18 DDIs by 76%.

Duration of the DDI checking task (Figure 4A).

Duration of the DDI checking task and number of alerts of conventional and CDSS assisted DDI checking are compared in **Figure 4**. Daily duration and number of alerts of conventional DDI checking did not differ during both phases of the study. The duration of evaluating DDI alerts was similar for conventional DDI checking and CDSS assisted DDI checking in both phases at 4 alerts per minute. CDSS assisted DDI checking resulted in a 4 minute and 7 minute decrease of the DDI checking duration from 15 to 11 minutes per day (P=0.044) and from 15.5 to 8.5 minutes per day (P=0.001) in Phase 1 and Phase 2 respectively.

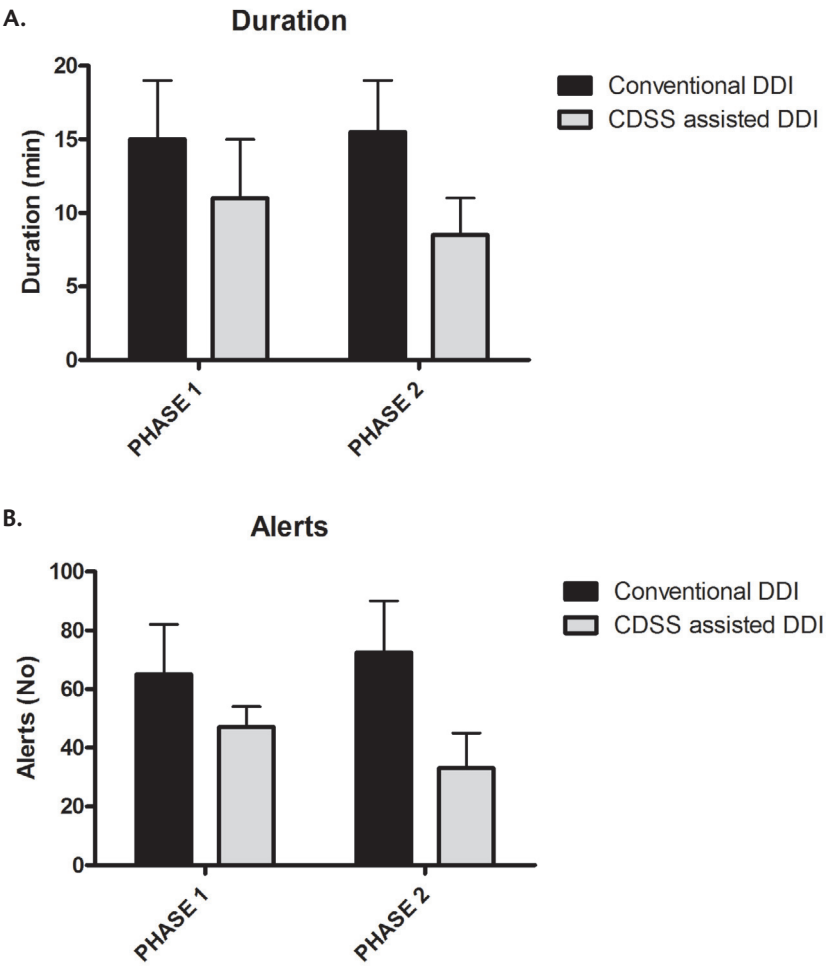


Figure 4. Daily duration (A) and number of alerts (B) of the DDI checking task per phase.

Number of alerts generated (Figure 4B)

After implementation of CDSS assisted DDI checking, the number of alerts evaluated by pharmacists decreased by 18 from 65 to 47 alerts per day in Phase 1 (P=0.03) and by 40 from 73 to 33 alerts in Phase 2 (P=0.003). In Phase 2, we suppressed the NO-YES and NO-NO alerts for prescribers, accounting for 449 (57%) and 140 (18%) alerts respectively (**Figure 3B**).

Return-on-investment analysis

The time investment of implementing CDSS assisted DDI checking is shown in **Table 2**. Almost 392 total project hours were required to configure the CDSS for DDI checking. Almost 298 hours (76%) were invested by hospital pharmacists who performed the DDI checking task. CDSS assisted DDI checking decreases the duration of the DDI checking task by 7 minutes per weekday. Using 260 weekdays in a typical year, 30 hours are saved yearly after implementing CDSS assisted DDI checking. Our approach yields a return-on-investment of 9.8 years in a setting where on average 70 DDI alerts per day are generated, of which 20% is considered not clinically relevant and 24% can be refined using the additional variables described above.

DISCUSSION

In our setting, only 29 DDIs accounted for over 80% of conventional DDI alerts. CDSS assisted DDI checking of 18 DDIs decreased the number of generated alerts and the duration of DDI checking. This effect was more pronounced after suppressing clinically irrelevant alerts for pharmacists and prescribers (8 DDIs). An additional 17 DDIs were suppressed for prescribers, resulting in a 74% decrease in total DDI alerts at the point of prescribing.

Based on a calculation of pharmacist time spent on implementing and configuring the CDSS, the return-on-investment is almost 10 years if the CDSS is only used for DDI checking in a setting that is similar to ours. Return-on-investment will be shorter if the proportion of conventional DDIs that can be refined using the CDSS is increased. For example, if the QTc interval would have been electronically available as an additional variable in our CDSS, an additional 68 DDI alerts requiring a check of the QTc interval could have been refined in our study, eliminating the need for labor intensive manual data retrieval. Return-on-investment will also be shorter in larger institutions with a higher patient census, as suppressing clinically irrelevant DDI's leads to a larger decrease of DDI alerts. Furthermore, return-on-investment is shorter if CDSS assisted DDI checking results in a decreased duration of evaluating a DDI. For example, at the time of our study the duration of evaluating DDI alerts was similar for conventional DDI checking and CDSS assisted DDI checking in both phases at 4 alerts per minute. We are currently implementing DDI checking by technicians, who are now authorized by our medical staff to change administration times when absorption DDIs occur. This increases the number of DDIs that can be evaluated by pharmacists.

Additional medication safety checking features (such as drug dosing in renal function checking) are also included in the CDSS software, again based on the national G-standard. The approach used to augment DDI checking, can easily be applied to efficiently add these additional medication safety checking activities, without adding additional staff. To our knowledge, this is the first study evaluating the return-on-investment of CDSS assisted DDI-checking based on a national DDI database. In a study by Field et al., almost 925 hours were required to implement a CDSS assisting in renal dosing[12]. An

advantage of their system is that renal dosing alerts appear at the time of prescribing, while our CDSS provides recommendations retrospectively three times daily. Alerting the clinician at the time of prescribing could lead to increased efficiency. More importantly, adequate follow up on real time alerts at the time of prescribing prevents potential patient harm, as the clinician is stopped when prescribing a potential harmful drug combination. However, when evaluating the most frequently occurring DDIs, we concluded that an intrusive pop-up at the time of prescribing is not required for many DDIs, as the clinical effects of these DDIs do not occur instantaneously. For example, hyperkalemia as a result of a DDI typically occurs one week after prescribing the combination, making an alert at the time of initiating an order less relevant. In addition, alert fatigue is caused by many more alerts than only DDI alerts: duplicate therapy checking and drug-dosing checking are typically also included in CPOE drug safety software increasing the likelihood of missing a relevant alert at the time of prescribing. In any case, the investigators estimated that even if real time alerting functionality would have been included out-of-the-box in their CDSS, still 475 hours would have been required for configuration, 80 hours more than what was spent in our setting. Also, no additional staff was hired by pharmacy or by other departments of the hospital to implement the CDSS.

Our study has several limitations: first, we did not compare the interventions resulting from conventional DDI checking with the interventions resulting from CDSS assisted DDI checking. However, both systems are based on the same national DDI checking database and CDSS assisted DDI checking was extensively validated before use. No differences in DDI checking performances were found during validation. Therefore, we concluded that both systems detected the same potential harmful DDIs, but CDSS assisted DDI-checking detected these DDIs more efficiently. Of note, per pharmacy procedure, pharmacists are instructed to record any modifications in therapy and discussions with prescribers. No differences in the number or type of recorded interventions were observed.

Second, potential time investment and time savings of other practitioners (prescribers, pharmacy technicians) were not included. Almost all alerts generated by conventional DDI checking are overridden at the point of prescribing [7,13]. In Phase 2 of this study, we configured the CPOE to suppress NO-YES alerts and NO-NO alerts for prescribers, resulting in a 74% reduction in the number of pop-up alerts at the point of prescribing. This could have resulted in some time savings for the physician, but physicians were instructed to pay extra attention to the alerts that remained. This could have offset the initial time savings of suppressing NO-YES and NO-NO alerts.

Third, the costs of the CDSS (€ 20,000) were not included in the analysis, as this study was set up as a return on investment of pharmacist time.

This study has several strengths: both methods of DDI checking were performed on the same patient population at the same time. Consequently, seasonal changes in patient acuity, length-of-stay, pharmacy and physician staffing could not have influenced any effects. In addition, multiple pharmacists performed DDI checking, increasing generalizability of the time savings. Pharmacists served as their own control. Next, both number of alerts and DDI checking duration were similar during the conventional DDI checking periods in Phase 1 and Phase 2. This suggests a valid baseline measurement of conventional DDI checking. Last, the frequently occurring interactions included in this study are representative of a typical inpatient population and are in line with previous DDI studies in the Netherlands[7,13]. Van der Sijs et al. evaluated the reasons for overriding DDI alerts in a large academic medical center and included 24 DDI's that were overridden more than 10 times in one month[13]. Thirteen DDI's were also included in our study and accounted for 69% of total overrides in their setting. A panel of prescribers and pharmacists recommended on average 30% of the time that these 13 DDI alerts are

suppressed altogether, but no study participants unanimously agreed that hospital-wide suppression of a specific DDI alert could occur safely. The investigators did find a positive correlation between the number of alerts overridden and the number of clinicians recommending suppression of the alert, but cautioned against turning off DDI alerts altogether. In our setting, 11 of these 13 DDI's were suppressed for prescribers but only 4 were suppressed for both pharmacists and prescribers. An additional 5 DDI's were refined using the CDSS. Our approach provides additional options for efficient DDI checking and safely turning off DDI alerts for only the prescriber or for both prescriber and pharmacist.
In conclusion, CDSS assisted DDI checking results in a 45% reduction in time spent on DDI checking and a 55% and 74% reduction of the number of alerts for pharmacists and prescribers respectively, yielding a return of pharmacist time investment of 9.8 years in a general hospital non-ICU setting. Our approach can be used to optimize DDI checking practices, reduce alert fatigue and refine other drug safety checking modules such as renal and conventional drug dosing checking. This allows for expanding drug safety checking practices without adding more pharmacist staff.

Acknowledgments

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Chapter 5

Systematic formulary management combined with a pharmacy labor cost analysis augments formulary compliance

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ABSTRACT:

Purpose

Hospital drug formularies guide prescribers to the safest, most cost-effective agents for treating medical problems. There are conflicting reports on what the optimal formulary management strategy is in terms of safety, productivity, and cost. We evaluated the effects on formulary compliance of a comprehensive hospital formulary management system. We included a pharmacy labor cost analysis to identify the most efficient scenario of managing nonformulary drug requests.

Methods

The formulary management system consisted of monitoring nonformulary medication use, reviewing formulary medication use annually and providing periodic feedback. Workflow scenarios for nonformulary medication requests were identified. Pharmacy personnel were interviewed to obtain the probability of occurrence of each scenario and time involved. Labor costs were determined by multiplying the time spent on each activity by the corresponding salaries.

Results

Nonformulary medication use decreased from 17.8 to 5.9 nonformulary initiations per 100 admissions over a 3 year period ($P<0.001$). Time and labor costs associated with managing nonformulary medication requests and labor costs varied from 4 to 69 min and $3.68 to $27.28 depending on the scenario used. Automatically converting to a formulary alternative is the least labor-intensive option ($4.40 per request), followed by changing to a formulary alternative after consulting the prescriber ($9.92).

Conclusion

This formulary management system improves formulary compliance. Use of therapeutic interchange protocols is the least labor intensive option of managing nonformulary medication requests. A similar approach in other institutions could identify other successful formulary management strategies resulting in increased efficiency and quality of the hospital medication-use process.

INTRODUCTION

A formulary is a continually updated list of medications and related information, representing the clinical judgment of physicians, pharmacists, and other experts in the diagnosis and/or treatment of disease and promotion of health[1]. Many hospitals worldwide create drug formularies to improve patient care, help control medication costs and increase efficiency. In the US, hospitals are required to maintain a formulary to comply with regulatory standards[2]. The Pharmacy and Therapeutics (P&T) committee is typically responsible for managing the formulary system. It is the multidisciplinary, evidence-based process employed by an organization to select and use medications that offer the best therapeutic outcomes while minimizing potential risks and costs for patients[3]. Drug formularies are considered an important tool to guide prescribers in choosing the safest, most cost-effective agents for treating medical problems. It is generally accepted that well-designed formularies lead to increased efficiency and improved medication safety[4]. This is intuitive, as adding a medication to the formulary requires a thorough evaluation of safety, efficacy and costs by the P&T committee. Also, limiting the number of drugs in a therapeutic class decreases the potential for errors as a result of sound-alike medications, while increasing the familiarity of the drug to prescribers. The Institute for Safe Medication Practices (ISMP) even recommends that P&T committees should discourage the prescribing of new medications that have not gone through the formulary addition process[5].

It is, however, impossible to create a formulary that covers every clinical scenario. As a result, it is also a regulatory requirement in hospitals in the US to have a mechanism in place to obtain a nonformulary alternative when use of a formulary medication is not in the best interest of the patient[6]. This leads to an interesting paradox:

- A closed formulary could lead to increased use of nonformulary medications (NFM). Increased use of NFM may result in excess expenditure and may cause delays in initiating treatment due to lack of product availability[7]. Patient safety may also be compromised by errors in prescribing, dispensing or administration due to unfamiliarity with a NFM. In addition, changing the patient's home regimen to the formulary alternative for a typical 4 day hospital stay has been shown to induce medication errors[8-10]. A potential advantage of a closed formulary is that fewer medications have to be evaluated for formulary addition, which is a resource-intensive activity.
- An open formulary could lead to multiple therapeutic duplications in one drug class. Inexperienced prescribers, require more training in safe and rational prescribing at the start of their clinical practice[11,12]. More medications on formulary could then potentially lead to more medication errors, as prescribers have to become familiar with more medications. As formulary agents are generally kept in stock, an open formulary leads to a larger inventory. A larger inventory might lead to more waste as a result of expiration of infrequently used medications.

As a result of this paradox, the cost-effectiveness of formularies continues to be debated[13-17]. The latest studies in this area argue against a very limited inpatient formulary: expanding the number of formulary items within a few drug classes would allow for a reduction in expenses, an improvement in patient satisfaction, and more time for pharmacist to participate in other patient care activities[7,15,17].

The inpatient formulary at University of California San Diego Health System (UCSDHS) reflects this philosophy. As an example, UCSDHS has all 9 angiotensin converting enzyme inhibitors (ACEi) and 5 out of 6 angiotensin receptor blockers (ARB's) on formulary. During a visit of our institution, ISMP has commented on this practice and recommended decreasing the number of items in these drug classes, based on the general assumption that including fewer medications on formulary improves medication safety. This observation by ISMP, concerns about NFM overuse by hospital leader-

ship, and the requirement by The Joint Commission to review the hospital formulary at least annually resulted in an increased focus on formulary management practices.

UCSDHS includes a 511 bed academic medical center, consisting of 2 locations. UCSDHS achieved stage 7 of electronic medical record (EMR) adoption[18] which includes an enterprise wide electronic medical record, computerized prescriber order entry (CPOE) and barcode-assisted medication administration. The medical center includes most medical specialties excluding pediatrics, a Level 1 trauma center and a Level 3 Neonatal Intensive Care Unit. Prior to July 2008, medications were added to the formulary through a structured approval process through the P&T committee. Medications were only removed from the formulary if the requestor specifically indicated during the approval process that the new agent should replace the current formulary agent. No structured monitoring of formulary adherence existed. From July 2008 onwards, we implemented a continuous monitoring system consisting of the following components: (1) daily review of active inpatient NFM orders by a formulary management pharmacist for the possibility of substitution or switching to a formulary alternative, (2) monthly review of the aggregated NFM use data by the Pharmacist-in-Chief and the Chair of the P&T committee, (3) semi-annual review of the formulary compliance dashboard described below by the P&T committee and (4) annual review of usage data of medications currently on formulary by the P&T committee.

The aims of this study are to determine the effects on formulary compliance after implementing a comprehensive hospital formulary management system, and to identify the most efficient scenario of managing nonformulary drug requests through a pharmacy labor cost analysis to further optimize formulary compliance.

METHODS

Measuring formulary compliance:

A metric best describing formulary compliance was intended to incorporate the following principles: (1) the metric should accurately detect formulary compliance: as the metric increases, more decisions are made for NFM use, resulting in lower formulary compliance. (2) The metric should detect monthly trends in the use of individual NFM. (3) The metric should correct for hospital census as increased census could influence the number of NFM requests.

Therefore, we developed a formulary compliance dashboard consisting of two reports. First, a graph showing monthly formulary compliance using the absolute number of NFM therapy initiations

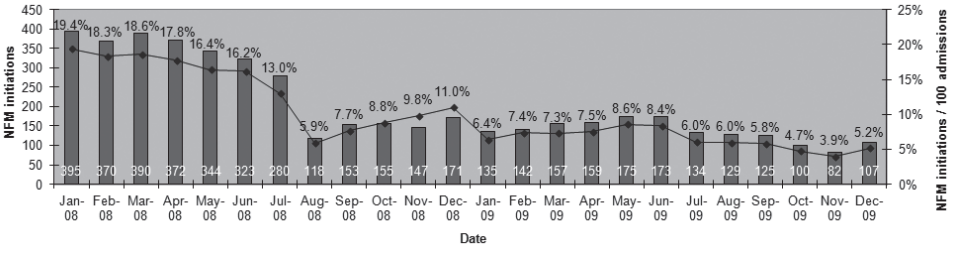

Figure 1. Example of the bar-graph on the formulary compliance dashboard indicating the total number of monthly nonformulary medication initiations (bars and white numbers) and the number of monthly nonformulary medication initiations per 100 admissions, expressed as percentages (diamonds and line).

DRUG CODE	PRIMARY_NAME	Jul-09	Aug-09	Sep-09	Oct-09	Nov-09	Dec-09	Grand Total	Details	Follow up
12112	FISH OIL DHA:120MG/EPA:180MG	5	10	5	5	9	10	44	Formulary addition is planned pending nutraceutical supply chain review.	Nutraceutical product supply chain review to be completed.
11361	OLMESARTAN MEDOXOMIL	4	7	9	5	5	8	38	Drug class review completed: all continuation of home therapy	None
11632	RANOLAZINE	11	7	8	5			31	Added to the formulary	none
10953	DUTASTERIDE	6	4	4	2	4	7	27	All continuation of home therapy. Finasteride is on formulary.	Drug class review planned.
11445	LEVALBUTEROL (XOPENEX HFA)	4	7	6	3		3	23	Use has decreased by 80%. Some patients with Cystic Fibrosis are passionate about their inhalers.	None
8474	TIZANIDINE HCL	1	4	5	5	3	4	22	Requested input from pain specialist (1/20/10):"We use it fairly frequently in outpatients. It is more sedating than baclofen so I usually give it at bedtime. It is also great for opioid withdrawals. Difficult to say if it is any better than baclofen but some patients prefer it.	Requested submission of formulary addition request. Not yet received.
8753	ESOMEPRAZOLE MAG TRIHYDRATE	4	2	5	6	2	2	21	Pharmacy has substitution authority: prescribers switched in September and October because of FDA warning about potential interaction with clopidogrel.	None
7858	OMEPRAZOLE	4	2	6	4	3	2	21	Pharmacy has substitution authority: prescribers switched in September and October because of FDA warning about potential interaction with clopidogrel.	None
11137	ALFUZOSIN	3	7	1		3	3	17	All continuation of home medication.	None
6637	DARVOCET-N 100	4	3	3	2	2	1	15	All continuation of home therapy.	See P&T meeting December 2009. Follow up with Howell service planned.
6816	DOXAZOSIN MESYLATE	5	3	2	1	1	3	15	All continuation of home medication	Add to formulary
7388	LEVOFLOXACIN	2	3	2	2	1	2	12	Most patients receive levo for CF. 1 patient continuation of home UTI regimen 1 patient for "lung/prostate"	None

Figure 2. Example of medication-specific dashboard report highlighting trends in prescribing of nonformulary medications. Highlighting of different colors is used for medications initiated in 5-10 patients and in more than 10 patients.

(#) and the number of NFM therapy initiations/100 admissions **(Figure 1)** and a report highlighting usage trends of individual medications using color coding **(Figure 2).** Specific recommendations for those nonformulary items that were initiated in 10 patients or more during a 6 month period were discussed at the P&T committee meeting.

Using this dashboard, we compared formulary compliance prior to implementation of the formulary management system (January-July 2008) to compliance of 6 consecutive six-month periods from July 2008 through June 2011 after the formulary management system had been in place for over 2 years. Formulary compliance was expressed as the average number of nonformulary medication initiations per 100 admissions during this six-month time period.

Pharmacy labor cost analysis:

Labor costs associated with managing NFM requests at UCSDHS were identified by creating a decision model (TreeAgePro 2009, Williamstown, MA) of the following scenarios:

1. The NFM order is cancelled: no drug is dispensed or patient uses own supply
2. The NFM is automatically converted to an equivalent formulary alternative per a P&T approved protocol without the need to consult the prescriber.
3. The NFM is converted to a formulary alternative after consulting the prescriber
4. The NFM is dispensed and may or may not have to be repackaged

If an alternative drug is dispensed, the medication can be stored in the central dispensing area of the inpatient pharmacy or can be available in the automated dispensing cabinet in the patient area. Nonformulary medications are not regularly stocked in the inpatient pharmacy and are only available in the patient area if another patient recently required the same NFM.

Table 1. Variables included in the model

	Description	Default Value
Salaries ($/min)	Buyer	0.5
	Pharmacist	0.92
	Technician	0.37
Buyer labor (min)	Buyer labor for ordering NFM	5
Pharmacist labor (min)	Automatic conversion	4
	Switching to FM alternative	10
	Using nonformulary medication from inpatient pharmacy	11
	Using nonformulary medication from same area	11
	Using nonformulary medication from outpatient pharmacy without repackaging	11
	Using nonformulary medication from outpatient pharmacy requiring repackaging	14
	Ordering nonformulary medication not requiring repackaging	11
	Ordering nonformulary medication requiring repackaging	14
	No drug is dispensed	14
Technician labor (min)	Automatic conversion	15
	Switching to formulary alternative in inpatient pharmacy	15
	Using nonformulary medication inpatient pharmacy	15
	Using nonformulary medication from outpatient pharmacy without repackaging	20
	Using nonformulary medication from outpatient pharmacy requiring repackaging	50
	Ordering nonformulary alternative not requiring repackaging	20
	Ordering nonformulary alternative requiring repackaging	50
	No drug is dispensed	10
Probabilities	Formulary product available on same floor as patient	0.8
	Nonformulary medication available in patient area	0.05
	Nonformulary medication stocked in inpatient pharmacy	0.4
	Nonformulary medication stocked in hospital or outpatient pharmacy	0.8
	Necessity of repackaging nonformulary medication	0.8

Within each scenario, the probabilities of having to perform the task and the average time spent on each task were estimated by interviewing three staff members of each job-title who regularly perform these activities (e.g. three technicians, buyers and pharmacists), similar to the method previously used by Sweet et al[17]. Our goal was to develop a general model that can be used by other hospital pharmacies. Therefore, we obtained the US national average hourly wages for each job title from the Bureau of Labor Statistics, National Compensation Survey[19], and did not include institution-specific salaries and fringe benefits in the model.

The labor costs of each employee type were then determined by multiplying the average total minutes spent on each activity by the corresponding average UCSDHS salaries per minute. The variables included in the model are listed in **Table** 1. The following variables were excluded from the model: (1) labor costs associated with ordering NFM through alternative distribution channels as this occurs very rarely, (2) labor costs associated with procurement of formulary medications as formulary agents are typically in stock, (3) costs associated with medication errors as a result of changes in the patient's outpatient medication regimen as they are difficult to quantity and typically occur after discharge and (4) working hours as at our institution, night pharmacists receive the same salaries as daytime pharmacists, but are compensated through more time off ("7 on, 7 off" schedule).

Data sources/statistics

From 2008 to 2011, prescribers used a CPOE system to enter medication orders. This system was interfaced with the pharmacy information system (Siemens Pharmacy, Malvern, PA) and medication details (formulary status, dose, administration route, etc.) and costs were retrieved using MS Access (Microsoft Corp., Redmond, WA) queries. From March 2011 onwards, UCSDHS implemented an enterprise wide Electronic Medical Record (EpicCare, Verona, WI) from which medication and cost data were retrieved. Further analyses of the data were done using MS Excel (Microsoft Corp., Redmond, WA). Assessment of statistical significance of formulary compliance between the pre – and post management system time periods were conducted using the two-tailed t-test for continuous data (NCSS 2007, Kaysville, UT). The a priori level of significance was 0.05.

RESULTS

Formulary management system

Implementing a comprehensive formulary management system resulted in a 67% increase in formulary compliance by decreasing the use of NFMs from 17.8 nonformulary initiations per 100 admissions in January to June 2008 to 5.9 nonformulary initiations per 100 admissions from January to June 2011 ($P<0.0001$) (**Table** 2). Specific examples of P&T actions as a result of the formulary management system, were the evaluation and addition of frequently used NFM to the formulary and improving adherence to therapeutic interchange protocols.

Pharmacy labor cost analysis

The labor cost analysis decision tree is shown in **Figure 3**. Overall time and labor costs associated with NFM requests are summarized in **Table** 3. Time commitment and labor costs for each individual sce-

Table 2. Formulary compliance: Jan 2008-June 2011

Metric	Jan to Jun-08	Jul to Dec-08	Jan to Jun-09	Jul to Dec-09	Jan to Jun-10	Jul to Dec-10	Jan to Jun-11
Total nonformulary medication initiated	2194	1024	941	677	664	672	799
No of patient admissions	12,339	10,967	12,399	12,782	12,673	13,560	13,444
No nonformulary medications initiated /100 admissions	17.8	9.4	7.6	5.3	5.2	5.0	5.9

Table 3. Labor costs for managing requests for nonformulary medications

Strategy	Time associated in minutes*	Overall costs ($)
Automatic conversion	4-19	4.79
Change to formulary medication	10-25	10.31
No drug dispensed	19	16.58
Dispense nonformulary medication	11-69	24.44

*'Time spent by pharmacy personnel involved (pharmacist, technician, and buyer) for scenario's ranging from best case (medication is available In patient area, no repackaging necessary) to worst case (medication needs to be ordered and repackaged).

nario vary from 4 min and $3.68 if a therapeutically interchanged drug is available in the patient area, to 69 min and $27.28 when a NFM is dispensed that has to be ordered and repacked. More specifically, every scenario where a NFM is dispensed is more labor intensive than changing a medication to the formulary alternative ($10.12-$27.28) unless the NFM is already available on the patient's floor ($10.12). However, this is a rare occurrence as our current policies do not allow NFM's to be regularly stocked in the inpatient pharmacy or on the floor. Overall, automatically converting a NFM to a formulary alternative results in the lowest time commitment of pharmacy staff (4-19 min) and the lowest costs of labor ($4.40). Changing to the formulary alternative after having to consult the physician is more labor intensive, but formulary alternatives are typically available on the patient's floor resulting in a relatively low time commitment (10 min). Dispensing a NFM is the most labor intensive option ($20.07) as these medications generally need to be ordered and repackaged.

DISCUSSION

The formulary management system described in this study increased formulary compliance by 67%. Furthermore, we showed that automatically converting nonformulary medications to the formulary equivalent per P&T approved protocols is the most labor efficient way of managing nonformulary drug requests.

The results from this study can be used to develop an efficient process for handling NFM requests in the inpatient setting. Continuous monitoring of nonformulary prescribing and periodic review of trends is an essential part of formulary management [20]. A formulary compliance dashboard using ap-

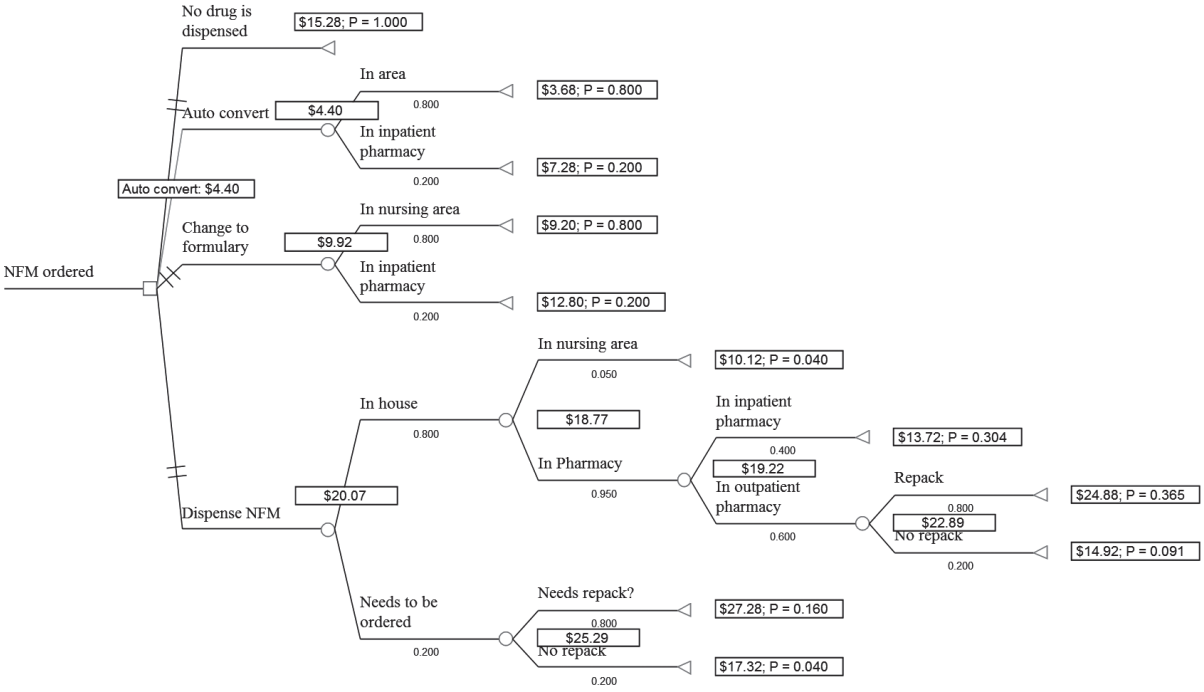

Figure 3. Decision model comparing scenario's of managing NFM requests.

Decision model comparing various scenarios for managing requests for nonformulary medications. The square represents a choice node for the four scenarios. Circles represent chance nodes, and triangles represent final outcomes with associated average labor costs and final probabilities (P values). P values also appear for each branch beyond the chance nodes. Costs adjacent to chance nodes represent average labor costs for entire branches of the model. The preferred option is to automatically convert to a formulary medication. The non-preferred options are indicated by a double line after the choice node..

propriate monitoring metrics is the first step in the development of such a system. At our institution, a monitoring system based on the metrics evaluated in this study has identified omissions in the formulary leading to legitimate use of NFM. However, this system also detected irrational prescribing practices at our institution such as the use of topical diphenhydramine preparations (associated with hypersensitivity reactions), use of levalbuterol (a costly analogue of the equivalent formulary agent albuterol) and use of topical antiviral creams (which are considered ineffective). In addition, our formulary management system includes a review of usage patterns of formulary agents. This feedback mechanism allows for early detection of infrequently used formulary medications, which are then removed from formulary. Education of prescribers and pharmacists of potential therapeutic interchange opportunities, expanding the number of therapeutic interchange authorities, a continuing focus on NFM use by the P&T committee, as well as an annual review of the formulary, have resulted in a more rational formulary that matches prescribing patterns without excessively and irrationally expanding the formulary. For example, UCSDHS's formulary contained 2923, 3029 and 2562 items in November 2007, April 2009 and July 2012 respectively. We initially included nonformulary drug costs in our dashboard. However, we found that these costs were not an accurate metric of formulary adherence (data

not shown). In fact, more money was spent on NFM after implementation of the monitoring system, than before. Investigation showed that legitimate use of costly nonformulary chemotherapeutic and biological agents in only a few patients leads to substantial fluctuations in costs. These fluctuations were not an accurate indicator of non-adherence to our policies, but rather a reflection of the large differences in drug costs within nonformulary prescribed medications. Overall, NFM drug costs account for less than 1% of total inpatient drug expenditure.

In contrast, pharmacy labor costs associated with managing NFM could be substantial. The most labor efficient scenario results in only 4 min additional labor, while the most labor intensive scenario results in over an hour additional work. The additional time gained by optimizing this process can be used for more patient specific activities such as patient counseling and monitoring. Any request for an NFM is a deviation from the normal medication-use process in the hospital. This can have important medication safety implications. As an example, NFMs have not undergone a thorough review by the P&T committee, which generally involves a risk assessment of its use in the hospital. Second, clinicians infrequently prescribe and administer these medications and are less aware of monitoring criteria and other precautions associated with the medication.

The analysis done in this study is largely in line with a previous analysis performed by Sweet et al. in 2001[17]. They also identified automatic substitution as the least labor intensive method of dealing with NFM requests. However, not dispensing any medication (or having patients bringing in their own medication) was the second least costly option in their analysis, while in our setting changing to a formulary alternative was the second least costly option. This difference can be explained by the adoption of bedside barcoding technology by UCSDHS. This technology requires that every medication unit of use should contain a barcode as every medication needs to be barcode scanned prior to administration. In both studies, pharmacists had to visually inspect all medication patients bring with them to the hospital. At UCSDHS, pharmacists and technicians are also required to prepare and affix a barcode to the medication. This is a labor intensive process resulting in additional costs.

The labor cost analysis has its limitations. First, we used interviews to determine the time spent on each task, and did not validate the responses using objective time measurements. This approach was selected for practical reasons: the time spent on the same task can vary widely and multiple measurements would have been required. We assumed that employees regularly performing the task could accurately estimate the duration of each task. This approach was also used in a previous labor cost analysis[17], which allows for comparison of the results.

Second, labor costs by physicians and nursing staff were excluded from this analysis. However, including those labor costs is unlikely to have changed the outcomes of the analysis. At the time of the study, pharmacists reentered the order if a medication could be automatically converted to the formulary alternative without contacting the physician. Likewise, physicians spent equal amounts of time discussing NFM requests with the pharmacist regardless of the outcome of the discussion.

Third, including only labor costs in the model can be viewed as a limitation. An additional factor for evaluating NFM use is the cost of expiration of medications. As an example, if a specific NFM can only be ordered in a package size of 10 vials, and the patient only requires 2 vials, it is likely that the other 8 vials of the product will eventually expire as most NFM are rarely used. The decision to order the NFM is influenced by the cost of the specific medication, as patients may be more likely to use their own medication in case of an infrequently used, high cost item. We excluded this factor from our analysis for the following reasons; first, our goal was to develop a general model to evaluate different formulary management options. A general model would not be feasible if we included costs of expired

medication, as they are directly related to the acquisition costs of the medication. Second, 85% of NFM requests at our institution concerns oral medications. A previous study at another institution showed an average cost difference of only $0.39 between oral NFM and the formulary alternative[17]. This marginal cost difference would not be a factor in the majority of the decisions to order NFM.

Last, this study was not set up as a Return-on-Investment analysis. Consequently, we did not include the costs of developing and using the formulary management system. In our institution, no additional pharmacist staff was hired for this project and semi-annual review by the P&T committee resulted in a 15 minute agenda item every 6 months. Nevertheless, systematic formulary management is a requirement for accreditation by The Joint Commission and future research should be conducted to quantify the impact of this requirement on institutions.

This study addresses a practical problem in many institutions maintaining a formulary. In 2011, a survey was conducted to evaluate formulary management practices[21]. Forty-six of the 52 respondents (88%) reported tracking nonformulary use. However, the authors acknowledged that it was not possible to compare nonformulary use between institutions as various metrics were used. The limited data required to create a formulary compliance dashboard as reported here (medication name, formulary status, admission number) are readily available and retrievable in most pharmacy information systems and hospital wide electronic medical records. In fact, during this study the pharmacy department migrated from a pharmacy information system to an enterprise wide electronic medical record. Even though the data used in the dashboard were obtained from a different source, the same metrics remained readily available. As a result, this change had no implications for the dashboard. Adoption by more hospitals of a similar dashboard based on the same metrics results in powerful benchmarking opportunities. This allows for identification and dissemination of successful formulary management strategies in other institutions resulting in increased efficiency and quality of the hospital medication-use process.

CONCLUSIONS

A comprehensive formulary management system as described results in increased compliance to a formulary that matches the needs of the institution and minimizes the number of nonformulary medication requests. Expanding pharmacists therapeutic interchange authorities is the least labor intensive way of managing NFM requests. If this is not possible or desired, adding the most frequently used NFMs to the formulary is the second least costly option.

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Chapter 6

Decision support at the point of prescribing increases formulary adherence

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Kosterink JGW, Daniels CE

Reference:
Drug Safety (Submitted).

ABSTRACT:

Objective

Many hospitals worldwide use drug formularies to improve medication safety and efficiency. Therapeutic interchange allows clinicians to substitute nonformulary items for the preferred agent. We configured formulary decision support included in a commercially available electronic medical record (EMR) to guide prescribers to the preferred formulary agent at the time of prescribing. This study evaluates formulary non-adherence before and after implementing an EMR with decision support enforcing therapeutic interchange.

Materials and method

This retrospective observational study evaluates formulary non-adherence before and after implementation of therapeutic interchange alerts. Pop-up alerts appeared displaying the formulary alternative and equivalent dosing as soon as a therapeutically interchanged agent was selected. Formulary non-adherence was assessed for a 6-month period at baseline and at two 6-month periods after implementation.

Results

Overall formulary non-adherence decreased by 65% from 3.5% at baseline to 1.2% in the second 6-month intervention period ($p<0.001$). Formulary non-adherence decreased most in the intranasal steroid drug class (12%), followed by the non-barbiturate sedatives and hypnotics class (5%).

Discussion

Our findings support the use of EMR's with similar decision support functionality to improve and monitor formulary adherence without the need to develop or purchase additional decision support tools.

Conclusion

Formulary non-adherence of 8 therapeutically interchanged drug classes decreased after implementing an EMR including formulary decision support.

INTRODUCTION:

Drug formularies are maintained by many hospitals worldwide and are viewed as an important tool to guide prescribers in choosing the safest, most cost-effective agents for treating medical problems[1]. It is generally accepted that fewer drugs on formulary lead to increased efficiency and improved medication safety[2]. Therapeutic interchange is defined as the dispensing of a drug that is therapeutically equivalent but chemically different from the drug originally prescribed[3]. In many hospitals, therapeutic interchange protocols allow for automatic substitution to the preferred agent by the pharmacist without having to contact the prescriber. Therapeutic interchange is widely used to limit the number of drugs on formulary and is the least labor intensive way of managing nonformulary drug requests by pharmacists[4,5].

At University of California San Diego Health System (UCSDHS), adherence to the formulary is monitored using a comprehensive formulary adherence monitoring system[5]. An important part of this system is semi-annual review of nonformulary medication prescribing trends and proposed actions by the Pharmacy and Therapeutics (P&T) committee. In general, adherence to UCSDHS therapeutic interchange protocols is high, but in some therapeutic classes, adherence could be further improved. w

Clinical decision support (CDS) systems are defined as "any electronic system designed to aid directly in clinical decision making, in which characteristics of individual patients are used to generate patient specific assessments or recommendations that are then presented to clinicians for consideration"[6]. Applying clinical decision support to computerized prescriber order entry systems (CPOE) can be very successful in achieving improved formulary adherence[7,8]. A CDS can guide physicians to the appropriate alternative when a therapeutically interchanged medication is prescribed**.** Successful guidance is dependent on the following factors: clearly written "to-the-point" guidelines with links to additional information, and offering a non-controversial alternative within the alert window[9-14]. A recent review investigating the features of effective CDSS concluded that systems requiring the practitioner to give a reason for overriding advice were more likely to succeed than systems missing this feature[15]. Factors associated with poor adherence are the lack of an offered alternative, or strong provider beliefs about the medication, even if those beliefs are not necessarily supported by the available evidence[8].

In February 2011 UCSDHS implemented Epic (version 2010, IU4, Verona, WI), an enterprise wide Electronic Medical Record (EMR) which includes a CPOE system with CDS functionality. One of the features is a pop-up window listing the recommended alternative and equivalent dosing information when a therapeutically interchanged drug is ordered. This study evaluates adherence to the formulary of 8 therapeutic classes, before and after adding decision support at the point of prescribing facilitating therapeutic interchange.

METHODS

This is a retrospective before and after observational study conducted at UCSDHS, a 511 bed Academic Medical Center, consisting of 2 locations. UCSDHS achieved stage 7 of electronic medical record (EMR) adoption[16] which includes an enterprise wide electronic medical record, computerized prescriber order entry (CPOE) and barcode-assisted medication administration. The medical center includes a Level 1 trauma center, a Level 3 Neonatal Intensive Care Unit and most medical specialties excluding pediatrics. All inpatient areas of the medical center were included in this study except the Emergency Department, as the EMR was not implemented in this area at the time of the study.

Each therapy initiation with a nonformulary drug is a deviation from normal workflow with potential medication safety and efficiency implications[5]. In addition, prescribing of nonformulary medications for which therapeutic interchange protocols exist should be particularly discouraged, as the P&T committee specifically indicates that each nonformulary member of a therapeutically interchanged drug class is equivalent to the formulary alternative. Nevertheless, nonformulary medications of the following therapeutically interchanged drug classes accounted for 30% of nonformulary medication initiations during the pre-intervention period and were included in this study: intranasal steroids, nonbarbiturate sedatives and hypnotics, proton pump inhibitors, histamine (H_2) antagonists, respiratory

Table 1. Characteristics of the therapeutically interchanged medications

Drug class	Place in therapy	Administration route	Therapeutically interchanged medications	Formulary alternative	Baseline formulary non-adherence (%)
Intranasal steroids	Allergic rhinitis	Nasal inhalation	beclomethasone budesonide flunisolide fluticasone furoate mometasone triamcinolone	fluticasone	13.3
Nonbarbiturate sedatives and hypnotics	Insomnia	Oral	eszopiclone zolpidem CR	zolpidem	6.6
Anti-adrenergic agents - peripherally acting	Benign Prostatic Hyperplasia	Oral	alfuzosin	tamsulosin	4.0
Proton pump inhibitors	Gastric ulcer, GERD	Oral	dexlansoprazole esomperazole omeprazole pantoprazole rabeprazole	lansoprazole	3.7
Fluoroquinolones, systemic	Anti-infective	Oral	levofloxacin	moxifloxacin	3.6
Sympathomimetic bronchodilators	Asthma/COPD*	Inhalation	levalbuterol	albuterol	2.7
Respiratory inhalant combinations	Asthma/COPD*	Inhalation	budesonide/ formoterol	fluticasone/ salmeterol	2.6
Histamine (h2) antagonists	Indigestion, GERD**	Oral	cimetidine nizatidine ranitidine	famotidine	0.6

*COPD: chronic obstructive pulmonary disease.
**GERD: Gastroesophageal reflux disease

inhalant combinations, sympaticomimetic bronchodilators, systemic fluoroquinolones and peripherally acting anti-adrenergic agents. Further details of these drug classes are shown in **Table 1**. Therapeutic interchange alerts were built for all nonformulary medications in each class, directing the prescriber to the appropriate formulary item and corresponding dose (**Figure 1)**. The alert was obtrusive (a pop-up window at the time of ordering) and was built as a hard stop; if a physician specifically wished to proceed with the original order, a phone-call to the pharmacist was required with justification. If approved, the pharmacist entered the nonformulary order and documented the reason for approval.

Prescribing data from July 2010 to December 2010 were used as pre-intervention data. The EMR was implemented in February of 2011. To assess a long-term effect of the therapeutic interchange alerts, post-intervention data were collected during two 6 months periods, March-August 2011 (POST-1) immediately following the implementation and September 2011-February 2012 (POST-2) to evaluate the longer-term impact of the intervention. Non-adherence was expressed in relation to other agents in the same drug class. For example: non-adherence to proton pump-inhibitor (PPI) therapeutic interchange protocols is calculated as follows: absolute number of nonformulary PPI-initiations/total number of inpatient PPI-initiations.

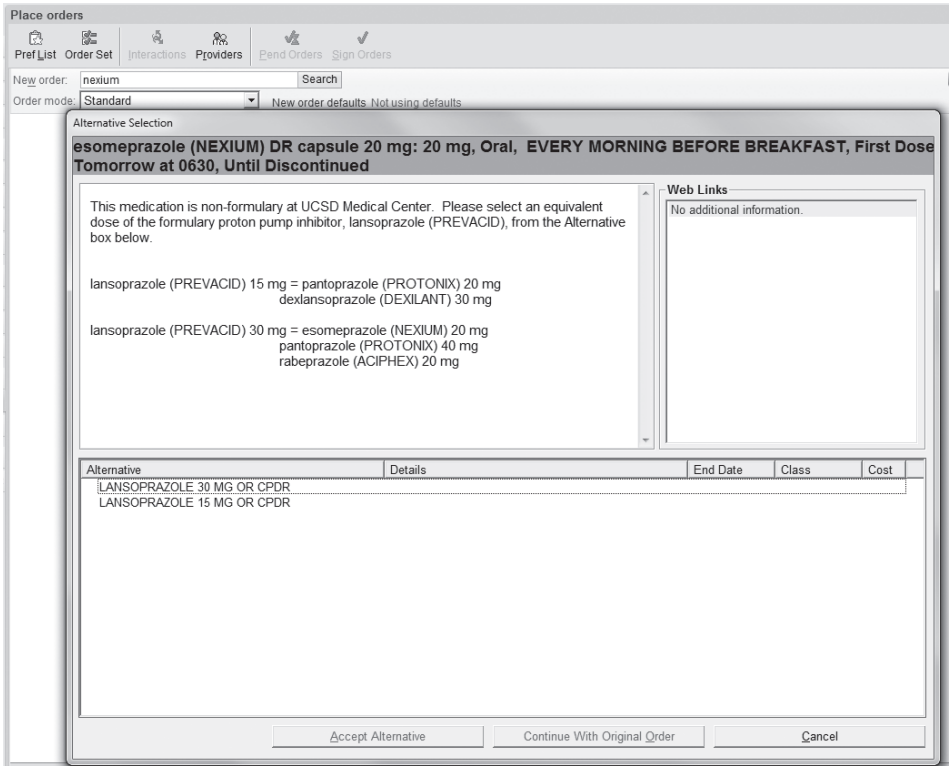

Figure 1. Screenshot of the therapeutic interchange alert for the proton pump inhibitor esomeprazole.

The alert displays equivalent dosing for each member in the drug class. After selecting the appropriate alternative, the prescriber can proceed with the alternative order with one click. When therapeutic interchange protocols exist, the button "continue with original order" is not available for prescribers but it can be selected by pharmacists.

Formulary non-adherence after each 6 month period was compared to the pre-intervention period. Data were entered into spreadsheets (Microsoft Excel 2010, Redmond, WA) for initial analysis and summary statistics. NCSS 2007 (Version 07.1.20 Kaysville, UT) was used for statistical tests. Chi-square analysis was used to compare formulary non-adherence before and after the intervention. The a-priori level of significance was set at 0.05.

RESULTS

Characteristics of the therapeutically interchanged drugs are listed in Table 1. Baseline formulary non-adherence varied from 13.3% in the intranasal steroid drug class to only 0.6% for the H_2-antagonist class. Formulary non-adherence and number of nonformulary initiations before and after implementation of therapeutic interchange alerts are shown in **Figure 2.** Formulary non-adherence decreased in most drug classes after implementation of the therapeutic interchange alerts (POST-1) and the effect persisted during the second post-intervention period (POST-2) **(Figure 3)**. The exception is the peripherally acting anti-adrenergic class, where non-adherence increased during POST-1 and subsequently

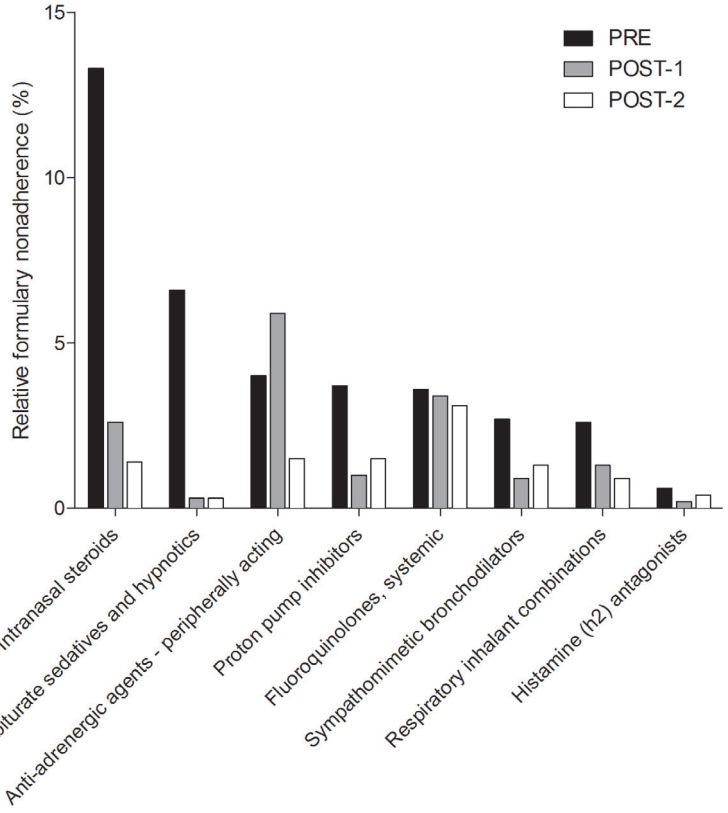

Figure 2. Formulary nonadherence before (PRE) and after implementation of formulary therapeutic interchange decision support (POST-1 and POST-2). Numbers above bars indicate absolute number of nonformulary medication initiations.

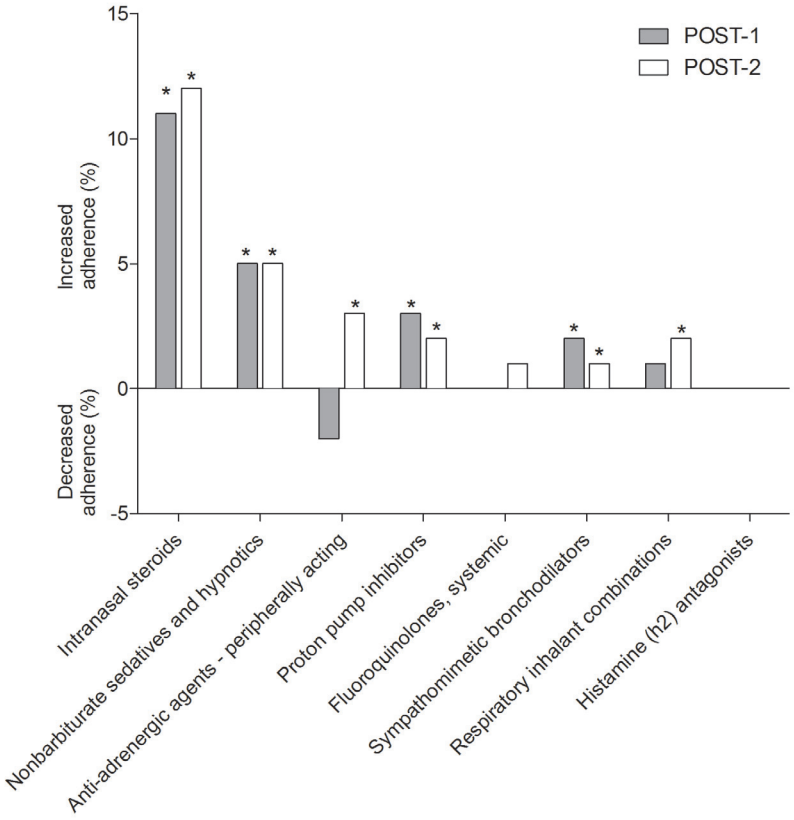

Figure 3. Change in formulary non adherence compared to baseline after implementation of formulary therapeutic interchange decision support. * indicates a statistically significant difference at P<0.05.

decreased sharply during POST-2. Upon investigation of this outlier, we found that no therapeutic interchange alert had been built for this drug class at the end of the first post-intervention period. During the second post-intervention period the alert was in place, and a decrease in formulary non-adherence of 3% was also observed in this drug class (p=0.018). Overall, formulary non-adherence in these eight therapeutically interchanged drug classes decreased by 65% from 3.5% at baseline to 1.3% and 1.2% during the POST-1 and POST-2 periods (<0.001). We observed the largest decrease in formulary non-adherence (11% in the POST-1 and 12% in the POST-2 periods) in the intranasal steroid drug class, followed by the non-barbiturate sedatives and hypnotics class (5% in both time periods, **Figure 3)**.

DISCUSSION

Formulary non-adherence decreased in most therapeutically interchanged drug-classes after implementation of formulary decision support at the point of prescribing. The only exception is the histamine (H_2) antagonist drug class, where we found no change in formulary non-adherence. The effect was most profound for the intranasal steroid and nonbarbiturate sedative drug classes where baseline non-adherence rates were relatively high (13.3% and 6.6% respectively). This difference in effect is likely

explained as prescribing practices had the highest room for improvement in the intranasal steroid and nonbarbiturate sedative drug classes, as opposed to the histamine (H_2) antagonist drug class. Overall, baseline non-adherence to therapeutic interchange alerts was already very low in our institution. This may be attributed to the implementation of a comprehensive formulary management system in 2008[5]. The formulary management system consisted of monitoring nonformulary medication use, reviewing formulary medication use annually and providing periodic feedback. Using dashboards, systematic trends in nonformulary prescribing of therapeutically interchanged drugs were detected early and regularly reported to the P&T Committee. The continuous focus on nonformulary prescribing likely increased pharmacist awareness of therapeutic interchange protocols. However, a reactive approach by pharmacists to correct an order for a therapeutically interchanged medication is less efficient than the prescriber entering a correct order initially. In addition, if a pharmacist did not correct the order for a therapeutically interchanged medication, the reactive approach could have medication safety implications: therapeutically interchanged medications are typically not available on the patient floor which could result in a delay of therapy. These risks are prevented by facilitating the selection of the appropriate alternative by the physician at the time of prescribing.

This study has several limitations. First, this was an observational study in which the effect on prescribing practices was followed over time, after implementation of an enterprise wide EMR which included formulary decision support. The observed effect could be the result of factors outside of the therapeutic interchange alert intervention. However, this is unlikely as we unintentionally included a negative control in our study. The therapeutic interchange alert for the anti-adrenergic agent drug class was not implemented until the second intervention period. This drug class was the only drug class where initially an increase in formulary non-adherence was observed and non-adherence subsequently decreased after the alert was implemented. Second, we did not measure clinical outcomes such as adverse events or medication errors as a result of therapeutic interchange, which could be viewed as a limitation. These consequences should be the subject of further research. However, we focused in this study on improving adherence to therapeutic interchange protocols as this is common practice in hospitals nationally and internationally[3].

Our results are in line with other studies implementing formulary decision support. Teich et al. demonstrated an impressive increase from 12% to 95% in prescribing the preferred H_2-antagonist over an 8 week period. This effect persisted at 1-year and 2-year follow-up measurements[8]. However, most studies reporting the effect of clinical decision support on outcomes are done with locally developed ("home grown") systems, implemented and expanded over many years[7,8]. This is considered a major barrier to implementation of a CDS[17,18]. To our knowledge, this is the first study reporting the effect of formulary decision support included in a commercially available EMR that has been widely adopted by many hospitals in the US and abroad. Another strength of this study is that formulary non-adherence further decreased in a setting where non-adherence to the formulary was already low. Our approach can be used by other institutions using EMR's with the same or similar decision support functionality to improve and monitor formulary non-adherence without the need to develop or purchase additional decision support tools.

Acknowledgments

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Part II

Focus on administering

Chapter 7

Effects of bar-code assisted medication administration (BCMA) on frequency, type and severity of medication administration errors: a review of the literature

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Jansen MMPM.,
Helmons PJ

Reference:
Eur J Hosp Pharm Sci Pract 2012;19: 489–494.

ABSTRACT

Bar-code-assisted medication administration (BCMA) is increasingly adopted as an additional tool in the prevention of medication administration errors. This literature review summarizes the evidence behind the effects of BCMA technology on medication safety. Although most studies show an error reducing effect of BCMA technology, compliance with the new technology after implementation of this technology and the long term effects on error reduction are often not assessed. Most importantly, the effect of medication error reduction on patient outcomes is limited.

INTRODUCTION

The medication distribution process is an important source of medication errors. Medication error rates reported in literature vary widely depending on the methodologies and definitions used. A recent review summarized the prevalence of medication errors as follows: 5.7% of administrations (range 0.038–56.1%, n = 31 studies), 1.07 errors per 100 patient-days (range 0.35–12, n = 9) or 6% of patients hospitalized (range 0.93–24%, n = 7)[1]. Most errors originate in the medication administration process (median 53%, range 9-90.7%) [1]. With few barriers to prevent them from occurring, only 2% of medication administration errors are intercepted at the patient bedside[2]. Bar-code-assisted medication administration (BCMA) is increasingly adopted as an additional barrier in the prevention of medication administration errors. In 2009, 27.9% of hospitals in the United States had implemented BCMA[3], which increased to 50.2% in 2011[4].

BCMA technology is developed to improve compliance with checking the 5 rights of medication administration: right patient, right route, right drug, right dose and right time. The right patient is identified by matching the unique bar-code on the patient wristband to the patient information in the electronic medication administration record (eMAR). The right drug, right dose, right dosage form and right time are checked by matching the bar-code on every unit- or multidose medication to the information in the eMAR. In a 2009 position statement, the American Society of Health-System Pharmacists encouraged health systems to adopt BCMA technology to improve patient safety and the accuracy of medication administration and documentation[5]. Most studies evaluating the effect of BCMA on medication administration errors have been conducted in the United States. However, this technology is also used in European countries, including Denmark, Italy and the Netherlands[6] and in 2006, the Council of Europe Expert Group on Safe Medication Practices also encouraged the use of electronic systems to improve the safety of medication administration[7]. In June 2010, the general assembly of the European Association of Hospital Pharmacists called for the implementation of bar-coded single dose-packed dugs in national and European regulations[8].

While BCMA as a tool in the prevention of medication administration errors makes intuitive sense, there is limited evidence demonstrating the effect of this intervention on medication administration errors and patient outcomes. In addition, increased workload is a commonly voiced concern by nursing staff as the use of bar-coding technology can potentially result in a longer duration of medication administration. Therefore, this review of the literature focuses on the following: (1) what is the effect of BCMA on frequency, type and severity of medication administration errors and (2) what is the effect of BCMA technology on the duration of the medication administration process?

METHODS

Study selection

In May 2012, a PubMed search was performed to select studies investigating at least one of the following topics: the effect of BCMA on the rate or severity of medication administration errors or studies evaluating the effect of BCMA on the duration of administering medication. Only studies with a prospective design and in which observational techniques were used to measure medication errors and/or administration time were included. The detailed search criteria and selection procedure of the 10 articles included in this study are shown in **Figure 1**[9-18]. We also reviewed the reference lists of the

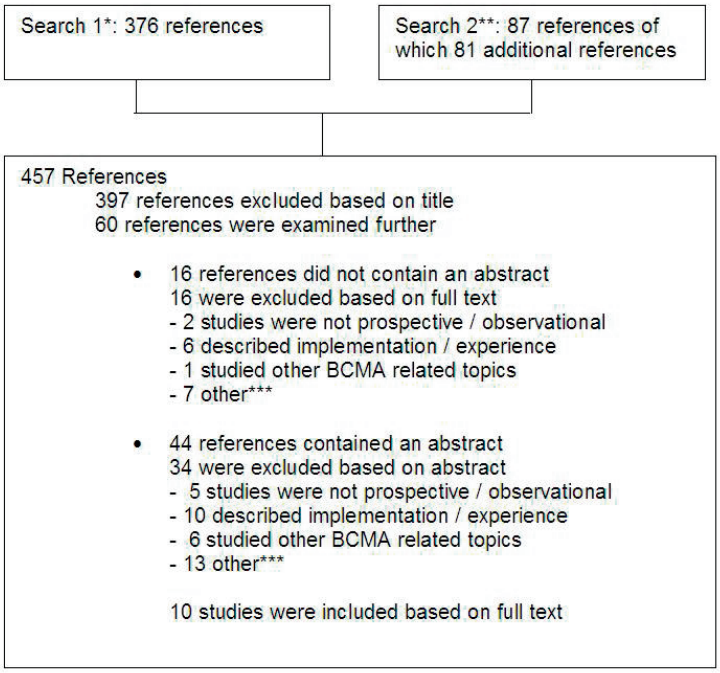

Figure 1. Details on performed literature search

* Search 1: ("automatic data processing"[MeSH Terms] OR ("automatic"[All Fields] AND "data"[All Fields] AND "processing"[All Fields]) OR "automatic data processing"[All Fields] OR ("bar"[All Fields] AND "code"[All Fields]) OR "bar code"[All Fields] OR "barcode"[All Fields]) AND ("pharmaceutical preparations"[MeSH Terms] OR ("pharmaceutical"[All Fields] AND "preparations"[All Fields]) OR "pharmaceutical preparations"[All Fields] OR "medication"[All Fields]) AND ("organization and administration"[MeSH Terms] OR ("organization"[All Fields] AND "administration"[All Fields]) OR "organization and administration"[All Fields] OR "administration"[All Fields])

** Search 2: ("pharmaceutical preparations"[MeSH Terms] OR ("pharmaceutical"[All Fields] AND "preparations"[All Fields]) OR "pharmaceutical preparations"[All Fields] OR "medication"[All Fields]) AND verification[All Fields] AND ("technology"[MeSH Terms] OR "technology"[All Fields])

*** The category "other" includes review articles, describing articles on BCMA and/or technology, summary of a research published in another journal, perspective, editorial, letter to the editor.

Table 1: Study characteristics

Study	Type of ward	Hospital	Setting pre intervention
Paoletti et al.12	Cardiac (telemetry) Medical-surgical	20-bed cardiac ward 36-bed medical surgical ward in a general hospital, Lancaster, United States	Decentralized cabinet distribution system Handwritten order Handwritten paper MAR
Poon et al.11	ICU Medical Surgical	35 units in a 735-bed tertiary academic medical center, Boston, United States	CPOE MAR transcribed by nurses
Franklin et al.9	Surgical	28-bed ward in a teaching hospital, London, United Kingdom	Stock cupboards and two drug trolleys. Drug prescription on paper MAR
Helmons et al.10	ICU (medical-surgical) Medical-surgical	13- and 20-bed ICU 22-, 26-bed medical surgical ward in a 386-bed academic teaching hospital, San Diego, United States	Unit-based ADCs CPOE Printed paper MAR manually updated
DeYoung et al.17	ICU	38-bed medical ICU in a 744-bed community teaching hospital, Grand Rapids, United States	ND
Morriss et al.14	NICU	36-bed ward in a children's hospital, Iowa city, United States	Handwritten orders entered by pharmacist in pharmacy information system Paper MAR on which orders were transcribed and administrations recorded
Ros et al. Wesselink et al.20,21	Neurologic	42-bed ward, community teaching hospital, Apeldoorn, the Netherlands	Dispensing to the ward from pharmacy by drug trolley CPOE EMAR with manual confirmation of administration

*ND= not determined

Setting post intervention	Other points of interest	Observation period
Decentralized cabinet distribution system Handwritten order EMAR with pharmacist order entry BCMA	1.5 year surveillance data	ND*
CPOE EMAR BCMA	Transcription errors Severity classification of potential adverse drug events 2 year surveillance data (in supplement)	2-4 weeks before and 4-8 weeks afterwards. 4 hour observation of staff nurses on 35 observed units
Automated dispending cabinet (ADC) and two electronic drug trolleys CPOE bar-code scan used to confirm drug-identity when loading medication into drawer ADC and for patient identification eMAR with manual confirmation of administration	Prescribing errors Staff time spent on medication tasks Potential severity assessment of observed errors	3-6 months before and 6-12 months afterwards. Sample of 56 drug rounds before and 55 afterwards (including nights and weekends) during a 2-week period
Unit-based ADCs CPOE EMAR BCMA	Medication administration accuracy Time spent on medication tasks	One month before three months after implementation. During week and weekend days focus on medication round 9 a.m.
Handwritten or pre-printed orders EMAR with pharmacist order entry BCMA	-	One month before and four months afterwards. 24 hours a day during four days.
Handwritten orders entered by pharmacist in pharmacy information system EMAR bi-directionally interfaced with pharmacy information system BCMA	Severity assessment of observed preventable ADEs	19 consecutive weeks before implementation than one month after implementation during 31 weeks
Bedside assortment picking (BAP) cart CPOE EMAR BCMA	Time spent on medication tasks	1 year and 8 months before and 3 months afterwards. Three daily medication rounds during 21 days.

selected articles. This revealed one full text article[19] of an abstract we already selected[13]. In addition, we included a study that met the above mentioned criteria and was published in this journal and a Dutch pharmaceutical journal, not indexed in PubMed[20,21]. As a result, a total of 11 studies were included[9-12,14-21].

Settings and intervention

The studies were conducted on wards with different levels of care and in organisations with varying medication use processes (**Table 1**).

Implementation of BCMA was accompanied by the implementation of an electronic medication administration record (eMAR) in all studies. In 2 studies, the introduction of BCMA was accompanied by additional interventions, such as simultaneously implementing bedside assortment picking (**Table 1**)[9,20]. In all studies, error rates were calculated using the same formula: total errors divided by the sum of observed administrations and omissions. In the study by Franklin et al., barcode technology was used to stock the automated dispensing cabinet and assure the correct identity of the medication. At the bedside, BCMA was then used to assure the correct identity of the patient[9].

RESULTS

Error frequency

Error rates before and after implementation of BCMA are summarized in **Table 2**.

As wrong-time errors are generally considered to be less severe[22], results are reported as total errors and errors excluding wrong-time errors. Baseline error rate varied between 5.8% and 25.3% if time errors were included and between 1.6% and 27.3% when time errors were excluded. Most studies show a 30-50% reduction of medication administration errors after implementation of BCMA when time errors are excluded. However, implementation of BCMA does not result in a consistent reduction when time errors are included.

Error type

The type and number of error categories varied between studies. Error categories that were assessed in at least three studies and are expected to be reduced by BCMA are omissions, wrong drug errors, unauthorized drug errors, wrong dosage form errors and extra dose errors. Only one study did not find a reduction in unauthorized drug errors and omissions, wrong drug and wrong dose errors even increased[17]. Wrong dose errors also increased in the ICU setting in the study by Helmons et al[10]. Wrong dosage form errors and extra dose errors increased in the study by Ros et al[20].

Wrong route errors are not expected to be influenced by BCMA and wrong time errors only partially. Reduction of these errors was inconsistent among studies. Most studies were underpowered to identify statistically significant differences within individual categories.

Overall it seems that wrong time errors are the most frequently occurring[11,12,17,20].

Table 2. Number of observations and error rates before and after BCMA implementation.

Study	Ward type	No. Observations		Frequency of errors incl. time errors		change from baseline		Frequency of errors excl. time errors		change from baseline	
		Baseline	Post BCMA	Baseline	Post BCMA		P	Baseline	Post BCMA		P
Paoletti et al.12	Cardiac telemetry	308	318	25.3%	19.2%	24.1%	0.065	1.6%*	1.6%*	0.0%	0.959
Poon et al.11	Medical	2008	2232	ND	ND	ND	ND	5.3%**	3.8%**	28.5%***	ND
Paoletti et al.12	Medical-surgical	320	310	15.6%	10.0%	35.9%	0.035	6.3%*	2.9%*	53.5%	0.045
Franklin et al.9	Surgical	1473	1139	7.0%	4.3%	38.6%	p=0.005	ND	ND	ND	ND
Helmons et al.10	Medical-surgical	888	697	10.7%	8.2%	23.6%	ND	8.0%	3.4%	56.9%	ND
Poon et al.11	Surgical	3528	3856	ND	ND	ND	ND	9.8%**	5.4%**	45.1%***	ND
De Young et al.17	ICU	775	690	19.7%	8.7%	56.0%	P<0.001	3.6%	4.2%	-16.3%	ND
Helmons et al.10	ICU	374	394	12.6%	13.5%	-7.0%	ND	11.0%	9.9%	9.7%	ND
Poon et al.11	ICU	1187	1230	ND	ND	ND	ND	27.3%**	16.5%**	39.5%***	ND
Morriss et al.14	NICU	46090	46308	6.7%	8.0%	-14.7%***	ND	ND	ND	ND	ND
Ros et al.20	Neurology	3814	4300	5.8%	7.0%	-20,4%	<0.03	1.7%	0.8%	48.5%	<0.0008
Poon et al.11	Overall	6723	7318	16.7%****	12.2%****	27.3%	0.001	11.5%	6.8%	41.4%	<0.001

ND= not determined

*Excluding time and technique errors

**Frequency calculated based on numbers presented in original publication (no of errors per ward type/no. of observed doses per ward type x 100%)

***Reduction calculated based on numbers presented in original publication.

****Only time errors

Error severity

Adverse Drug Events (ADEs) are defined as an injury resulting from the use of a medicine or omission of an intended medicine[23]. This definition includes adverse drug reactions and harm from medication incidents. As a result, medication errors resulting in harm are considered ADEs. An error that could potentially lead to harm is a potential ADE. One study[14] assessed the severity of observed ADEs and two studies[9,11] categorized the potential severity of observed administration errors (**Table 3**).

Morriss et al. found that BCMA reduced the risk of preventable ADEs drug events by 47%[14]. Poon et al. showed a 50.8% reduction of potential adverse drug events[11]. In this study, the reduction in many of the potential adverse drug events could be attributed to improved medication administration documentation[11]. Franklin did not find a reduction in error severity[9].

Table 3. Severity of observed errors or (potential) ADEs pre and post implementation of BCMA.

Study	Outcome measure	Baseline	Post BCMA	% Change from baseline	P
Poon et al.11	Percentage clinically significant potential ADE	1.8	0.9	48.5	<0.001
	Percentage serious potential ADE	1.3	0.6	54.1	<0.001
	Percentage life-threatening potential ADE	0.03	0.01	53.9	0.34
Franklin et al.9	Mean score of potential error severity *	2.7	2.5		0.39
Morriss et al.14	n/1000 doses of preventable adverse drug events**	0.86/1000 doses	0.43/1000 doses	47	0.044

* scoring on a scale from 0 to 10, 0 labelled as no effect, 10 labelled as death

**severity was assigned using the NCC MERP index. All preventable ADEs were assigned class E (temporary harm that required intervention) except 5 cases assigned to class G because it was not possible to exclude permanent harm

Duration of medication administration

The general idea that the use of BCMA technology is time consuming for nursing staff is considered a barrier to implementation. Seven studies addressed this topic (**Table 4**)[9,10,15,16,18,19,21]. Two studies[9,10] evaluated the time spent by nursing staff to complete the medication administration task, while three[15,16,21] studies measured the duration of each administration. Two studies determined the percentage of total nursing time spent on medication administration by using either the time and motion method[13] or the work sampling method[18]. No increase in medication administration time was found. Poon et al.[19] noticed a shift in the percentage of time spent on each medication administration task e.g. a management of physician orders decreased but verifying patient identity and inefficient waiting increased. Three studies found a reduction in time spent on medication administration[9,15,16].

Poon et al.[19] and Dwibedi et al.[15] also found that after implementation of BCMA the time spent on direct patient care activities increased.

Table 4. Results of studies evaluating the influence of BCMA on time spent on medication administration related tasks

Study	Outcome measure	Baseline	Post BCMA	P
Franklin et al.9	Mean (range) duration of each drug round (min)	50 (15-105)	40 (16-78)	0.006
Helmons et al.10	Median (range) duration of a medication administration round on medical-surgical ward(min)	10 (1-30)	10 (1-50)	ND
	Median (range) duration of a medication administration round on the ICU (min)	12 (1-58)	13.5 (1-53)	ND
Wesselink et al.21	Mean duration of administration per drug (min) drug round 8.00 a.m. drug round 12.00 a.m. drug round 5.00 p.m.	 0.906 1.848 1.249	 1.050 1.596 1.198	 <0.006 <0.282 <0.616
Poon et al.19	Percentage of time spent on administering medication Percentage of time spent on direct patient care	26.9% 26.1%	24.9% 29.9%	0.16 0.03
Dwibedi et al.15	Mean duration of administration activity (sec) Mean duration of time spent on direct patient care (sec)	59.8 47.4	45.5 182.3	0.01 <0.0001
Tsai et al.16	Mean working time for oral medication administration (sec)	36.49	18.42	ND
		Paper group	BCMA group	
Huang et al.18*	Percentage of time spent on medication related tasks Percentage of time spent on direct patient care	25.0% 28.2%	17.4% 28.1%	<0.001

* Cross-sectional design as opposed to a before-after design

ND= not determined in original publication

DISCUSSION

The effect of BCMA on medication error rate is variable among the studies included in this review. BCMA-technology seems to decrease the incidence of medication administration errors when excluding time-errors. However, the studies included in this review are heterogeneous.

First, the number and types of administration errors included in studies vary. In some studies error categories that are not reduced by BCMA are included (e.g. technique errors, wrong route errors). This influences base line error rate and dilutes the overall effect size of BCMA technology[9-11,21]. Second, the study setting has an effect on baseline prevalence of medication errors and therefore on the potential effect after implementation of BCMA. As an example, medication in an ICU is generally administered intravenously in an area with a higher nurse-to-patient ratio. Indeed, observation of medication administration in an ICU setting resulted in the detection of different types of medication errors compared to observations performed on a general medicine ward[10]. Furthermore, medication use processes varied among the different study settings (**Table 1**), for example drug dispensing by pharmacy, use of traditional ward stock or use of automatic dispensing cabinets.

Next, there is a difference between studies in time of observation (e.g. continuous observation or observing specific medication rounds). As the time of the medication administration round is a determinant for medication errors[24,25], the moment of observation could influence baseline error rate.

In two studies[9,20] the intervention comprised of more than BCMA and an EMAR. It is not possible to contribute the error reductions either to BCMA-technology or to the other intervention (e.g. automated dispensing cabinet)[9,20].

The degree of implementation of the technology is of importance to the results. Shortcomings in design, implementation and workflow integration encourage workarounds[11,19,26]. Therefore current study results might reflect the impact of the technology in the context of its implementation rather than the impact of the technology itself[19].

Not all studies evaluated user compliance with the new technology. As a result, workarounds could have influenced the effect of BCMA on medication administration errors. Helmons et al. and Paoletti et al. reported on the compliance rate which was around 90%[10,12]. Poon et al. reported that 20% of the drugs administered using bar-code eMAR technology was given without the bar-code scanning step during the study period[11]. However, no studies evaluated which errors detected in the study were the result of non-compliance.

Although the goal of BCMA is to enhance medication safety, studies that evaluate the prevention of (potential) harm after implementation of BCMA are limited[9,11,14]. Only two studies showed a reduction in the severity of (potential) ADEs[14,19]. These limited data support the beneficial effects of BCMA and eMAR on patient outcomes. Evidence on the long term effect and safety of BCMA is also limited. However, this information is important as workarounds evolve over time. The duration of the positive effects of BCMA on medication administration errors varied from one month after implementation to twelve months after implementation. Paoletti et al. and Poon et al. reported data on long term medication administration error warnings after BCMA implementation. In both studies the number of warnings remained constant during a respectively 1.5 and 2 year period after implementation of BCMA suggesting a long term effect of this technology in the detection of medication errors[12,27].

BCMA did not increase the time spent on medication administration. This is a reassuring finding as nursing staff are concerned about the time consuming aspects of BCMA technology. A successful

Design:
- longitudinal design, measurements periodically, during at least a week, in a period before implementation and a follow up period of more than 2 years after implementation
- 24/7 observation
- disguised observation method
- sufficient power to test for statistical significance in individual error categories
- include different ward types

Intervention:
- limit intervention to BCMA and eMAR

Outcome measures:
- medication errors expected to be influenced by BCMA
- scoring of severity of observed errors

Information on confounders:
- BCMA compliance rate
- try to measure workarounds
- analysis of origin of the observed errors
- description of the implemented BCMA process including percentage realisation of preconditions (e.g. percentage of barcoded unit-doses)

Figure 2. Checklist for future research on the long term effect of BCMA technology on the error frequency and severity

implementation of BCMA is the culmination of judicious planning, design, testing, training and support that occurred before, during and after BCMA deployment[19]. Therefore, the degree of implementation of BCMA technology is an important variable in studies evaluating the effect of BCMA.

This review of the literature generally found a positive effect of BCMA on decreasing medication errors without increasing medication administration time. However, these results are difficult to interpret because of the variability in study design, intervention

and reporting of outcome measures and confounders. We created a study design and reporting checklist as a guide for future research in this area (**Figure 2**). Although we realise that conducting a study that meets all of these criteria will not be easy.

CONCLUSION

The results from this review generally support the medication administration error reducing potential of BCMA-technology up to one year after implementation without indications of increasing nursing time spent on medication administration. Current studies however do not always mention user compliance and degree of implementation, factors narrowly related to the effectivity of BCMA-technology and necessary to ascertain what the maximum achievable effectivity is. Future research should focus on the long term effects of BCMA on medication error reduction, the causes of errors after BCMA implementation, the effects on nursing workflow and the harm prevented by this technology.

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Chapter 8

Impact of bar-coded medication administration (BCMA) on medication administration errors and accuracy in multiple patient care areas: a before-and-after study.

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Reference:
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ABSTRACT

Purpose

The effects of a commercially available bar-code medication administration technology on six indicators of medication administration accuracy and nine types of medication administration errors in distinct patient care areas were studied.

Methods

This study was set up as a prospective before-and-after study on two medical-surgical units, one medical intensive care unit and one surgical intensive care unit, using a validated observation methodology. Nursing staff were observed one month before and three months after implementation of a commercially available bar-coding technology during one month data-collection periods.

Results

On the medical-surgical units, 888 and 697 medication administrations were observed pre-and post implementation. Improved adherence to patient identification policies was observed (decrease in non-adherence from 13.4% to 6.9%). More distractions of the nursing staff occurred (from 15.5% to 25.2%) and medication was less frequently explained to the patient (not providing an explanation increased from 10.9% to 14.9%). Although an increase in time errors was observed (from 2.7% to 4.7%), total medication errors did not change. If time errors were excluded, medication errors decreased by 58% (from 8.0% to 3.4%). On the intensive care units, 374 and 394 medication administrations were observed pre-and post implementation. Charting after medication administration improved (from 24.4% to 6.7% non-charted medications). Total medication errors and time errors did not change.

Conclusion

In this study, a general medication administration accuracy tool was used to determine the effect of bar-coding technology on medication administration accuracy and errors in multiple patient care areas. If time errors were excluded, medication administration errors decreased on the medical-surgical units, but not on the intensive care units. Also different effects on medication administration accuracy were observed. This study demonstrates that patient care areas have differential benefits from bar-coding implementation.

INTRODUCTION

The landmark Institute of Medicine Quality Chasm series "To Err is Human" (2000)[1], "Crossing the Quality Chasm" (2001)[2] and Preventing Medication Errors (2007)[3] has resulted in a major focus on medical and medication errors. The key points from the latter report are: medication errors are very common and costly and most strikingly, much of the considerable patient harm that is caused by medication errors is preventable. The administration of medication is one of the most error prone steps of the medication use process with 34% of all errors originating from this phase [4]. In addition, less than 2% of the medication administration errors are intercepted at the patient bedside[4]. Bar-coded Medication Administration technology (BCMA) is developed as an additional safety barrier between the nurse and the patient if a medication error reaches the patient's bedside. This technology assists the nurse in confirming the patient's identity and confirms the appropriate identity, dose, time and form of the medication ("the five rights"). The number of hospitals using BCMA technology is increasing; while in 2002 only 5% of hospitals with 300-399 staffed beds had implemented this technology, this had increased to 17.9% in 2005[5]. Although organizations such as the Food and Drug Administration (FDA), the Healthcare Information and Management Systems Society (HIMSS) and the American Society for Health-Systems Pharmacists (ASHP) have urged to adopt BCMA and the Institute for Safe Medication Practices considers BCMA a "mature technology" [6], there have only been a few studies that investigated its effects on medication errors. In addition, these studies were conducted in different settings limiting the external validity of the results. Some studies were conducted in only one or two general care area's (medical surgical and cardiac telemetry units) [7,8], without additional implementation of computerized prescriber order entry (CPOE)[8] or using an institution specific ("homegrown") BCMA system [8,9]. Others focused on warning and alert data as a surrogate marker for certain types of medication administration errors prevented by the BCMA system[10,11].

The evaluation of BCMA should not be limited to determining the effect on medication administration error prevention, as implementing BCMA has important implications for nursing workflow as well. An average of 25% of nursing time is spent on medication-related activities[12] and the error prevention potential of BCMA is greatly diminished if the technology does not support nursing workflow. Already, numerous workaround strategies after implementation of BCMA have been described[13-16], illustrating the need for assessment of medication administration accuracy in addition to medication administration errors after implementation of BCMA. Directly observing medication administration is the most efficient and practical medication error detection method and produces valid and reliable results[17-19]. Therefore, the objective of this study was to determine the effect of a commercially available BCMA system on medication administration accuracy and medication administration errors on two patient care area's (general and intensive care) in a highly computerized setting using a validated observation methodology.

METHODS

Setting

This study was conducted on two medical surgical units (22 and 26 beds) and two intensive care units (one 13 bed medical intensive care unit (MICU) and one 20 bed surgical intensive care unit (SICU)) of a 386 bed academic teaching hospital. The maximum nurse-to-patient ratio was 1:4 on the medical-

Table 1. Study unit characteristics

	Medical-surgical unit 1		Medical-surgical unit 2		MICU		SICU	
	Pre-BCMA	Post-BCMA	Pre-BCMA	Post-BCMA	Pre-BCMA	Post-BCMA	Pre-BCMA	Post-BCMA
Study period	Sep 2007	Feb 2008	Sep 2007	Feb 2008	Nov 2007	March 2008	Nov 2007	March 2008
Daily occupancy (%)	82	86	78	81	84	94	97	93
Total patients discharged	119	93	202	149	13	14	19	31
Length-of-Stay (days)	4.6	5.8	4.5	5.1	7.3	15.4	9.0	11.5
Career nurses (%)	75	82	98	90	87	86	90	89
Nurse vacancy rate (%)	11	4	-6	-8	0	8	10	15

surgical units, 1:2 on the MICU and 1:2 on the SICU. Additional study unit characteristics during the pre- and post intervention periods are summarized in **Table 1**.

CPOE has been implemented throughout the hospital. This system is bidirectionally interfaced with the pharmacy information system, eliminating transcription of medication orders by the pharmacy. Pharmacists' service to the medical-surgical units consists of continuous centralized order validation and daily presence of a clinical pharmacist on the units. On the MICU and the SICU, specialized clinical pharmacists are stationed on both units daily. Medication dispensing is facilitated by unit-based automated dispensing cabinets. High volume medication administration times are 9 am, 12 pm, 6 pm and 9 pm, with the majority of medications being administered during the 9 am medication pass.

Intervention

Before BCMA implementation, the patient specific medication administration record (MAR) was printed once daily and served as a paper reference for the medication administrations due and completed for that day. The hospital's CPOE system needed to be regularly checked for new or modified medication orders. Any changes needed to be transcribed on the paper MAR as this document was used to retrieve medication from the automated dispensing cabinet.

BCMA technology (Medication Administration Check™ using Med Administration Check version 23.04.9, Siemens, Malvern, PA) was implemented in our hospital from May 2007 to February 2008. Both medical-surgical units "went live" in October 2007, the SICU and the MICU followed in December 2007 and January 2008 respectively. BCMA is based on an electronic medication administration record (eMAR), accessible on computers throughout the hospital, including the medication storage room and each patient room. The BCMA system is integrated with the Pharmacy Information System and interfaced with the CPOE system. This allows the eMAR to be automatically updated when new orders are entered in the CPOE system or existing orders are modified. The BCMA software displays medication due at a certain time in the "active work list", used to retrieve medication from the automated dispensing cabinet. In the patient's room, the nurse uses the bedside computer to select the appropriate eMAR and confirms patient identity by scanning the barcode on the patient's wristband

(*right patient*). By scanning the bar-code on each dosage form, the additional 4 rights (*right medication, right form, right dose, right time*) are matched to the patient's eMAR. Staff was trained on the new technology by completing a mandatory training program consisting of an online training module and hands-on training sessions on the floors.

Study design

This study is set up as a prospective, before-and-after observational study. Data on all outcome measures were collected one month before and 3 months after BCMA implementation, during one month data collection periods. Observations were scheduled on both weekdays and weekends. We predominantly focused on the morning (9 AM) medication round, as the majority of daily medication administrations on the study units took place at that time.

Data collection instrument

We used the medication administration accuracy indicator of the California Nursing Outcomes Coalition (CalNOC). CalNOC is the largest ongoing statewide nursing quality database project in the nation and engages approximately 150 hospitals in nursing quality database development, benchmarking and research efforts. Additional information on CalNOC and CalNOC's quality indicators is published elsewhere[17].

CalNOC's medication administration accuracy indicator was made available to other hospitals in July 2006. The indicator contains a medication administration error detection component, which is adapted from a nationally recognized observational medication error detection methodology developed by Barker and Flynn[14,16,18]. An observed medication administration error is defined as any discrepancy between the medication administered to the patient and the medication ordered on the patient's medical record[11,18]. The indicator also uses identical subclasses of medication administration errors (**Table 2**). However, the CalNOC tool also contains six medication administration accuracy indicators reflecting error prone process variations (Table 2). Some of these accuracy indicators have been

Table 2. CalNOC Medication administration accuracy tool variables

Medication administration errors	Medication administration accuracy indicators
Unauthorized drug	Medication is not compared to MAR before administration.
Wrong dose	Distraction or interruption of the nurse during medication administration
Wrong form	Medication is not labeled at patient bedside
Wrong route	Two forms of patient identification are not checked
Wrong technique	Medication is not explained to the patient during administration
Extra dose	Medication is charted on the MAR or eMAR immediately after administration
Omission	
Wrong time	
Drug not available	

proven effective in other studies that focused on quality of medication administration[19] or workaround scenario detection after bar-coding technology[20,21]. Currently, 29 hospitals are using CalNOC's medication administration error and accuracy indicator for study and/or quality improvement purposes and upload their data to the CalNOC database on a monthly basis. The CalNOC database is available to all participating hospitals for benchmarking purposes and currently contains data of 116 medication administration observation periods.

The duration of the medication administration process of each patient was also recorded. To assess compliance with the BCMA technology, additional information (medication name, strength, route and override reason) were collected if the bar-coding technology was not used or could not be used.

Study procedures

Two pharmacists and four pharmacy students were trained to unobtrusively perform the observations. Training consisted of studying the medication administration accuracy indicator manual provided by CalNOC. Adequate knowledge of study procedures was assured by attending a 2 hour review session of CalNOC's training manual and study procedures, developed by one of the pharmacists. The data-collection sheet provided by CalNOC was modified to allow faster data collection and to accommodate the additional variables unique to this study. Usability of the data-collection sheet and interrater reliability were assessed during two pilot observation sessions on one medical-surgical unit. During the first pilot session, the two pharmacist-observers simultaneously observed a single nurse and the data collected was used to assure interrater reliability between the two pharmacist-observers. During the second pilot session, two groups of three student-observers and one pharmacist-observer observed the medication administration by one nurse, each group on a different medical-surgical unit. Interrater reliability between the student-observers and the pharmacist-observer was assured by comparing observation data of each student with their peers.

Prior to the start of the observations, the study team informed the nurse managers and nursing staff of each unit of the purpose and methodology of the study. Practical issues such as the proposed observation schedule, situations that were excluded from observations and the informed consent procedure were discussed. To prevent interference with nursing workflow, a maximum of two observers could be assigned to each study unit during the observation sessions. However, a nurse was only accompanied by one observer during the medication administration round.

Since nurses and not patients were the subject in our study, informed consent from the patient was not required by the Institutional Review Board of our organization. After contacting the nurse at the beginning of the medication administration round, explaining the purpose of the study, emphasizing that no personal information of the nurse was collected and participation in this study was entirely voluntary, verbal informed consent of the nurse was obtained. Observer interaction with the patient was limited to explaining the nature of the study and the presence of the observer. If the patient was uncomfortable with the presence of the observer at the bedside, the observer left the room and no data were collected. Medication administrations during emergencies (e.g. "code blues") were also excluded from this study. The observers were instructed to intervene if they witnessed actions of the nurse that could lead to a medication administration error.

Observers arrived on the nursing unit approximately 1 hour prior to the scheduled medication administration time as nursing staff were allowed to administer medication 1 hour before to 1 hour after the scheduled administration time. The observation period started when a nurse entered

the medication room and began retrieving medication from the automated dispensing cabinet. The identity, strength, and dose of the medication taken out of the cabinet were recorded by the observer. The route, infusion rate (when applicable) and the medication administration accuracy indicators were assessed at the patient bedside. After completion of the medication administration, the observer returned to the medication room and followed additional nurses until the medication administration period on this floor was completed. Medication administration errors were assessed by comparing the observed medication administered to the medication intended for that patient. Before the intervention, the intended medication was derived by photocopying the paper MAR of each observed patient as well as retrieving the medication data in the electronic medical record. After the intervention, the medication data in the patient electronic medical record was interfaced with the eMAR, resulting in a continuously updated eMAR. Thus after the intervention, the intended medication was derived from the information in the eMAR only. The medication administration error rate was calculated by dividing the number of errors by the total opportunities for error (OE). OE's are defined as the sum of observed administrations and omitted medications. As wrong time errors are generally considered less severe than other errors[22], overall results are reported as total errors and errors excluding time errors.

Sample size calculation and statistical analysis

Medical-surgical units

The number of observations needed to adequately power this study was based on the results of a similar study investigating the effect of BCMA on medication errors in a similar patient care area [8]. Assuming a similar baseline error rate of 6.3%, an α of 0.05 and a power of 80%, we needed to observe at least 654 medication administrations pre- and post BCMA implementation on both medical surgical units combined to detect a similar 54% decrease in medication administration errors.

Intensive care units

Depending on the type of medication errors, medication administration error rates in an intensive care setting using observational methodologies vary between 6.6 and 54%[23-25]. Two of these three studies were conducted in European ICU's. Therefore, we used the medication error rates found by Kopp et al.[23] in our sample size calculation, as the setting of this study was similar to ours. Assuming a similar baseline error rate of 20%, an α of 0.05 and a power of 80%, we needed to observe at least 262 medication administrations pre- and post BCMA implementation on both ICU's combined to detect an expected 54% decrease in medication administration errors.

Data were initially entered into Excel (Microsoft Office Excel 2003) spreadsheets for initial analysis and summary statistics. Stata 10 (StataCorp, LP, College Station, Texas) was used for power calculation and additional statistical tests. For categorical (nominal) data, the X^2 test was used or if 5 or less data points were analyzed, statistical analysis was done using Fischer's Exact test. Continuous data were analyzed using the unpaired t-test. A P-value of less than 0.05 was considered statistically significant.

RESULTS

Observation characteristics

The pre- and post intervention characteristics are summarized in **Table 3**. On the medical-surgical units, all observation characteristics were similar pre- and post BCMA except for a slight increase in topical medication administrations after BCMA. On the intensive care units, observation characteristics differed more: we observed less subcutaneous administrations but more intravenous piggyback

Table 3. Observation characteristics pre- and post BCMA

	Medical-Surgical units			Intensive Care units		
Variable	**Pre-BCMA**	**Post BCMA**	**P**	**Pre-BCMA**	**Post BCMA**	**P**
Total OE[a]	888	697		374	394	
Median OE's per patient (range)	5 (1-14)	5 (1-16)		5 (1-11)	4 (1-14)	
OE's per administration route (%)						
Per os	736 (82.9)	581 (83.4)	NS[b]	255 (68.2)	261 (66.2)	NS
Subcutaneous	60 (6.8)	35 (5.0)	NS	35 (9.4)	22 (5.6)	0.046
IV-piggyback	34 (3.8)	19 (2.7)	NS	38 (10.2)	72 (18.3)	0.001
IV-bolus	18 (2.0)	19 (2.7)	NS	30 (8.0)	22 (5.6)	NS
IV-large volume	5 (0.6)	0 (0)	NS	1 (0.3)	0 (0)	NS
Intramuscular	1 (0.1)	1 (0.1)	NS	0 (0)	0 (0)	NA[c]
Topical	21 (2.4)	29 (4.2)	0.042	5 (1.3)	8 (2.0)	NS
Miscellaneous	0 (0)	0 (0)	NS	10 (2.7)	9 (2.3)	NS
Observations at 9 AM (%)	839 (94.5)	651 (93.4)	NS	329 (88.0)	389 (98.7)	<0.0001
Observations at 12 AM (%)	2 (0.2)	0 (0)	NS	0 (0)	0 (0)	NA
Observations at 6 PM (%)	47 (5.3)	46 (6.6)	NS	32 (8.6)	5 (1.3)	<0.0001
Observations at 9 PM (%)	0 (0)	0 (0)	NA	13 (3.5)	0 (0.0)	<0.0001
Proportion of observations sessions conducted on weekends (%)	6.2	7.2	NS	6.7	2.5	0.006
Median duration of medication administration in minutes and seconds (range in minutes)	10:00 (1-30)	10:00 (1-50)	NS	12:00 (1-58)	13:30 (1-53)	NS

[a] OE= opportunity for error

[b] NS= not significant

[c] NA= not applicable

[d] Examples of observations of the miscellaneous route of administration: rectal, ocular and nasal preparations.

administrations during the post BCMA period. Also, post BCMA more observations were conducted during the 9AM medication round resulting in fewer observations during the 6PM and 9PM medication rounds. Finally, after the intervention fewer observations were conducted during the weekend.

Medication administration accuracy

Baseline medication administration accuracy was higher on the medical-surgical units compared to the ICU's. On the medical surgical units, three medication accuracy indicators changed after introduction of BCMA; improved ID-checking compliance after BCMA implementation was offset by more distractions and interruptions and less explaining of the medication administered to the patient (**Table 4**). These three indicators did not change on the intensive care units. However, implementation of BCMA resulted in improved charting and labeling of medication on the ICU's.

Table 4. Medication administration accuracy pre- and post BCMA

Indicator	Medical-Surgical units			Intensive Care units		
	Pre-BCMA (%)	Post BCMA (%)	P	Pre-BCMA (%)	Post BCMA (%)	P
Distraction or interruption during medication administration	127 (15.5)	169 (25.2)	<0.0001	104 (29.5)	113 (30.3)	NS[a]
Two forms of ID are not checked	110 (13.4)	46 (6.9)	<0.0001	104 (29.5)	90 (24.2)	NS
Medication is not explained to patient[b]	88 (10.9)	93 (14.9)	0.045	53 (31.2)	50 (32.3)	NS
Medication is charted immediately after administration	74 (9.0)	56 (8.4)	NS	86 (24.4)	25 (6.7)	<0.0001
Medication is not labeled at patient bedside	17 (2.0)	7 (1.1)	NS	25 (7.1)	12 (3.2)	0.026
Medication is not compared to MAR before administration.	4 (0.5)	9 (1.3)	NS	3 (0.8)	0 (0)	NS

[a] NS = Not significant

[b] Medication is considered adequately explained if at least the name of the medication is mentioned to a conscious patient.

Medication administration errors

Medication administration error data are shown in **Figures 1 and 2**. We found a baseline medication error rate of 10.7% and 12.6% on the medical-surgical units and ICU's respectively, corresponding to 8.0% and 11.0% if time errors are excluded. Although we did not find a significant decrease in total error rates on the medical-surgical units and even observed an increase in time errors after BCMA implementation, the error rate excluding time errors decreased by almost 58% after BCMA implementation on this floor **(Figure 1)**. Substantially fewer omitted medications and a decrease in the number of medications that were unavailable at the time of administration, contributed to this effect **(Figure 2)**. In contrast, we did not find any differences between the overall error rate (12.6% pre- and 13.5% post BCMA), the error rate excluding time errors (11.0% pre- and 9.9% post-BCMA)**(Figure 1)** and the error types after BCMA implementation **(Figure 2)** on the ICU's.

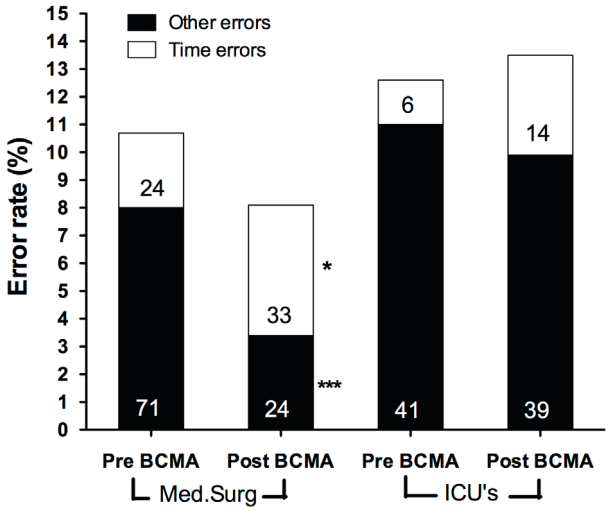

Figure 1. Total errors in the medical–surgical units and intensive care units (ICUs) before and after bar-code-enabled medication administration (BCMA) implementation. Numbers in bars indicate absolute numbers of errors, * indicates p < 0.05, * indicates p < 0.0001.**

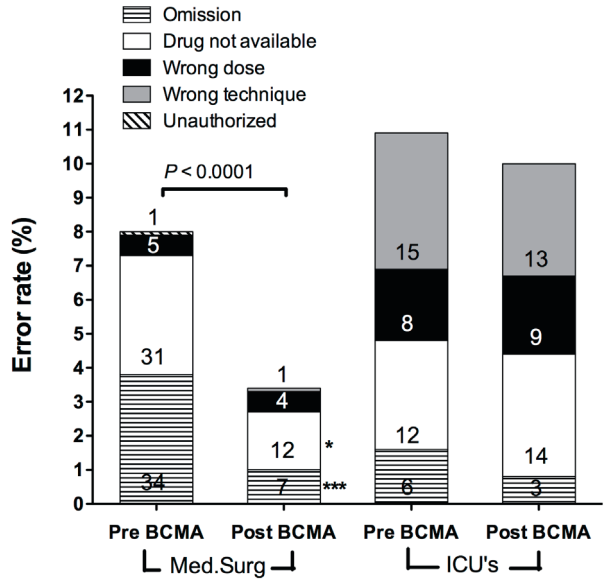

Figure 2. Types of errors excluding wrong-time errors before and after bar-code-assisted medication administration (BCMA) implementation. Error rates were calculated by dividing the number of errors by the total opportunities for error (observed administrations plus omitted medications). Numbers in bars indicate absolute numbers of errors, * indicates p < 0.05, and * indicates p < 0.0001.**

DISCUSSION

We used a general medication administration accuracy and error assessment tool, designed for use in multiple hospitals and in different care areas, to investigate the effects of a commercially available BCMA system on two medical-surgical units and two ICU's. This tool is specifically developed to allow comparison of medication administration accuracy between hospitals with different levels of automation. Therefore, this tool contains general medication administration accuracy indicators and multiple medication administration error categories. However, the effect of bar-coding technology on medication administration accuracy is reflected in only a limited number of accuracy indicators (improved ID checking, improved charting after administration and having the MAR available at the patient's bedside while administering medication). Also, bar-coding technology is specifically aimed at decreasing the following error types: unauthorized drug, wrong form, wrong dose, wrong route, extra dose and omissions. This tool will only show a decrease in medication errors if a large number of these error types are present at baseline. This explains the difference in medication administration error reduction of BCMA technology between medical-surgical units and intensive care units. Omissions were the predominant error type on the medical-surgical units but not on the ICU's. As a result, the 58% reduction of total errors excluding time errors on the medical-surgical unit can be largely explained by the decrease in errors of omission. However on the ICU's, only few errors of omission were detected at baseline. Even though these errors decreased by 50% (from 6 to 3 errors), the low prevalence of this type and other types of errors susceptible to improvement by BCMA technology, resulted in a non significant decrease of the total administration errors.

On the medical surgical units, the number of time errors increased after BCMA implementation. It is unlikely that the observed increase in time errors is a result of a longer duration of the medication administration round BCMA implementation as the median duration of medication administration on these units did not change after bar-coding implementation and varied widely per patient (see **Table 3**). Similarly, no change was observed after BCMA implementation on the ICU. These findings are in line with results of a recent study specifically set up to detect differences in nursing time spent on medication administration after BCMA implementation, which also failed to show a difference[26].

In addition, we found a 61% decrease in the number of medications not available on the medical surgical units at the time of administration. A possible explanation could be the implementation of a new hospital wide automated dispensing cabinet refill policy. However, this seems unlikely as the new policy resulted in fewer daily refills of the automated dispensing cabinets which theoretically could lead to more unavailability errors. Also, this was a hospital wide policy change and we would have observed similar decreases on the ICU's. More likely explanations are changes in pharmacy procurement practices and thorough checks of bar-code readability upon arrival of new inventory in the pharmacy as a result of the BCMA implementation. Different types of medication used on the ICU's as opposed to the medical-surgical units (**Table 3**) could explain the differences between the patient care areas.

Nurses were very often distracted during medication administration: one out of six and almost one out of three medication administrations were interrupted on the medical surgical units and ICU's respectively. After BCMA implementation we found an increase in the number of interruptions on the medical-surgical units but not on the intensive care units. It is unlikely that this is caused by BCMA implementation as there are no obvious differences between the pre- and post observation periods that could explain this. Although decreasing the number of interruptions and distractions should always be a priority during medication administration, it will never be fully eliminated (especially in critical care areas). It

is therefore reassuring that BCMA is now in place to prevent medication administration errors resulting from these interruptions.

On the medical-surgical units, BCMA implementation resulted in increased compliance to the hospitals ID checking policy. On the ICU's no difference was observed. Current policy requires two forms of ID to be checked (verbally confirming the patient's name and scanning the barcode on the patient's wristband). On the ICU's, baseline compliance with this policy remained low after BCMA implementation. One reason could be that most patients are unconscious and verbally verifying the patient's identity is impossible. The second method, visually checking the patient name and medical record number on the wristband in addition to scanning the wristband was often not performed as nurses were assigned to the same patient during the entire day. This accuracy indicator is probably less suitable for intensive care situations where the nurse to patient ratio is very high. However, checking two forms of ID is a National Patient Safety Goal[27] and failing to do so has led to patient harm even after BCMA had been implemented[28].

After BCMA implementation, medication was less frequently explained to the patient on the medical surgical units. This could be due to an increased duration of the medication administration process on these units, but warrants further investigation.

On the ICU's, charting compliance after medication administration greatly improved. Baseline charting compliance was low on the ICU's and as BCMA technology is specifically designed to facilitate this process, this indicator was expected to improve.

CalNOC's medication administration accuracy tool allowed us to monitor medication accuracy and errors on different care areas, using indicators of multiple error prone steps of the medication administration process. This is important as implementation of bar-coding technology can cause improvements on one error prone process but could have unintended consequences on others[13,20,21,28,29].

However, this study has its limitations: the observational methodology has been criticized for causing altered behavior of the observed subject (the "Hawthorne" effect). This effect has been shown to be negligible if the observers meet the following criteria: they should be experienced, objective, unobtrusive and nonjudgmental[14]. In our study, almost half of the observations were done by fourth year pharmacy students who could be considered non experienced observers. However, the expected change in behavior of the nursing staff would be improved medication administration accuracy and less errors, as nursing staff were aware of the purpose of the study.

Second, we did not match the route of administration of the pre-intervention observations to the post-intervention observations as this proved to be very impractical. As a result, the distribution of the observed routes of administration was different between the pre- and post-intervention periods (**Table 3**). In addition, the high volume of medication administrations during the 9 AM medication round resulted in the majority of the observations conducted during this round. Also, the observer who conducted 50% of the observations was also responsible for most of the data entry. However, it is unlikely that this biased our results as data integrity was assured by using an automated data-checking tool developed by CalNOC. Third, error assessment was done by the observers immediately after each observation and not by independent researchers. In addition, we did not assess the severity of the administration errors detected but based our error assessment on the rigid error definitions of CalNOC. Last, the post BCMA assessment was done 3 months after implementation which could be considered too short. However, other studies evaluating the effects of technology on healthcare also used a three month implementation period [30-32]. We assured appropriate use of BCMA- technology by assessing scanning compliance during the post-BCMA observations. Compliance rates were 89% on the medical surgical units and 94% on the ICU's, similar to compliance rates found in other studies investigating BCMA technology[8,13].

Despite these potential limitations, we found error rates that are in line with other studies, using similar methodologies and definitions of medication administration errors. Paoletti et al. found pre-implementation error rates on a 36 bed medical-surgical unit of 6.3% excluding time errors[8]. Another study investigating the impact of a closed loop electronic prescribing and administration system on administration errors on a 28 bed general-surgical unit, found an error rate of 8.6% if time errors were excluded[7]. Although baseline error rates on the ICU's were lower than expected (12.6% vs. 20%), our study was still adequately powered to detect a 50% decrease after BCMA implementation.

To our knowledge, this is the first study showing major differences of the effects of BCMA technology on medication administration accuracy and errors in different patient care areas.

Although we found a similar decrease in medication errors on the medical-surgical units as previously reported, we did not detect any differences on the ICU's. Also, we observed different changes in medication administration accuracy indicators between the two patient care areas. Recently, similar decreases in medication administration errors and improvements in accuracy were reported in a subset of 7 California hospitals, using the same CalNOC medication accuracy indicator[33]. These improvements were achieved by focusing on adherence to protocols and increased auditing. Their results and the effects shown in our study emphasize that implementing BCMA forces organizations to take a closer look at the whole medication administration process. This by itself can generate important improvements. Implementing BCMA technology has been shown to be a cost-effective intervention[30] and makes empirical sense. However**,** the results of other hospitals using the CalNOC methodology indicate that improving current systems by adhering to protocols and educating staff can generate similar results[33].

In summary, this study shows a significant decrease in medication administration errors on medical-surgical units, but not on intensive care units after implementation of bar-coding technology. We also demonstrate different effects on medication administration accuracy when these patient care areas are compared.

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Chapter 9

Redesigning the automated dispensing cabinet refill process decreases medication refill errors

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ABSTRACT

Purpose

The effects of automated dispensing cabinets (ADC) on medication safety are not well defined. Recent guidelines recommend having a process in place to assure accurate refill of the medications stored in ADCs. A wholesaler-to-ADC direct refill program, consisting of prepackaged delivery of medications and bar-code assisted ADC refilling, eliminates manual product selection of medication from pharmacy stock and aids in correct product placement within the ADC.

Methods

This prospective before-and-after study describes the effect on medication refill errors after implementing a wholesaler-to-ADC direct refill program. Medication refill errors were defined as an ADC pocket containing the wrong identity, strength or form of the medication.

Results

We observed a 77% decrease in ADC refill errors from 62 per 6,829 refilled pockets (0.91%) to 8 per 3,855 refilled pockets (0.21%, p<0.0001).

Conclusion

Redesigning the ADC refill process using an wholesaler-to-ADC direct refill program significantly decreased ADC refill errors

INTRODUCTION

Most acute care hospitals in the United States use automated dispensing cabinets (ADC) as the core of their medication distribution system. In 2008, an ASHP survey of 527 hospitals showed that 82.9% use ADCs[1]. If hospitals with less than 100 staffed beds are excluded, the adoption rate further increases to 95-98.7%[1]. ADCs offer a variety of benefits to the organization and the user, such as secure and timely access to the most commonly used medications in a specific patient care area and more accurate tracking and charge capture of the medications used.

However, the effects of ADCs on medication safety are less well defined and several reports indicate that incorrect use or design of ADCs result in medication errors[2,3]. ADCs were the source of almost 15% of all medication error reports, received by the Pennsylvania Patient Safety Reporting System (PA-PSRS) since its inception in 2004[3]. In addition, 123 medication errors associated with the use of

ADCs have been reported to the United States Pharmacopeia-Institute for Safe Medication Practices Medication Error Reporting Program (USP-ISMP MERP) since 1971[3].

In 2008, the Institute of Safe Medication Practice (ISMP) identified 12 core processes to ensure safe use of ADCs[4]: (1) provide an ideal environmental conditions for the use of ADCs, (2) ensure ADC system security, (3) use pharmacy profiled ADCs, (4) identify information that should appear on the ADC screen, (5) select and maintain proper ADC inventory, (6) select an appropriate ADC configuration, (7) define safe ADC restocking processes, (8) develop procedures to ensure the accurate withdrawal of medications from the ADC, (9) establish criteria for ADC system overrides, (10) standardize processes for transporting medications from the ADC to the patient's bedside, (11) eliminate the return of medications directly to their original ADC location, and (12) provide staff education and competency validation. At the beginning of this study, our processes were aligned with some, but not all of the core processes. Most importantly, almost all ADCs in the acute care setting required pharmacist review and approval prior to ADC dispensing of medications and subsequent administration to the patient (core process #3). Our institution also predominantly used single drug pockets. These pockets contain only one specific medication (core process #6). Single drug pockets decrease the opportunity for fill errors as only one medication compartment opens once the product to be refilled is selected, as opposed to multiple drug pocket drawers which contain multiple medication compartments. In addition, our institution had standard safeguards in place to assure appropriate stocking of the ADC (core process #7) such as a mandatory checks of any drug product to be refilled before it leaves the pharmacy and an additional pharmacist check after refilling the product in the ADC. However, we continued to experience ADC refill errors. This prospective before-and-after study describes the effect on medication refill errors after implementing a new ADC refill process, designed to assure accurate restocking of the ADC.

METHODS

Setting

This study was conducted in designated acute care areas of a 386 bed academic medical center. We included the ADCs in the general medicine units, the infant special care unit and the surgical and burn ICUs and IMU's in this study. These areas contained a total of 27 ADCs (Pyxis MedStation™, CareFusion, San Diego, CA). These areas predominantly rely on the ADC for medication distribution. More than 90% of medications billed to the patient in these areas are stored in the ADC.

The typical configuration of the ADC in the acute care areas is a cabinet containing predominantly single drug pockets and some multiple drug pocket drawers, a refrigerator unit, and an ADC tower containing bins to store large items.

At the time of the study, orders were entered by the prescriber in the computerized provider order entry system (CPOE) that was interfaced with the pharmacy information system. Medications may only be administered after the orders have been reviewed by a pharmacist. The pharmacy information system was interfaced with the ADC. As a result, the nurse would only view the medications that are active for each patient.

ADCs were restocked by technicians twice daily (morning and evening), by manually retrieving ("picking") the medications to be restocked from the pharmacy inventory. Pharmacists visually checked the contents of the picked medications before the product left the pharmacy and again after the pockets were restocked. However, the time period between the technician refill of the ADC and

the second pharmacist check is variable, depending on the availability of the pharmacist to perform the double check. As a result, our ADC restocking process was suboptimal (core process #7). Manual retrieval of medications from pharmacy inventory is not only a time consuming process, but it also allows for human error. In addition, the lag time between refill and check of the ADC is a potential vulnerability as unchecked (and potentially incorrect medications) remain available for retrieval by nursing.

Intervention

In September 2009, the inpatient pharmacy implemented a wholesaler-to-ADC direct refill program offered by our wholesaler. Only unit of use packaged medications are available through this program. **Figure 1** shows the process before and after redesign of the ADC refill activity. The wholesaler-to-ADC refill program is offered to hospital pharmacies at an additional charge. In the redesigned process, pharmacy technicians no longer have to manually select most of the ADC refill order from the central pharmacy supply and the pharmacist no longer has to check the selected product prior to refilling the ADC. Additionally, the software from the wholesaler-to-ADC direct refill program automatically creates a recommended order when the inventory of a pocket containing medication in the program falls below the pre-specified par-level. The wholesaler prepackages and delivers the ordered medications in an ADC pocket specific bag, containing sufficient medication to fit the pocket and a barcode containing the identity of the contents. When refilling the ADC, the pharmacy technician scans the barcode on the ADC pocket specific bag, and the corresponding pocket automatically opens. This eliminates the error prone step of manually browsing for the product in an alphabetized list. The double check of the identity and condition of the refilled medication at the ADC by a pharmacist remained required before and after the intervention.

Design, sample size calculation and statistical analysis

The floor pharmacists performing the post ADC refill check collected medication refill errors before-and-after redesign of the refill process. Performing ADC refill checks is part of the pharmacist's routine workflow. However, data collection for this study was voluntary. Medication refill errors were defined as an ADC pocket containing the wrong identity, strength or form of the medication. We also included a check of the expiration date of the medications as the prepackaging step by the wholesaler could result in shorter dated medications. After each post ADC refill check, the pharmacist filled out a data collection form capturing the date, ADC location, duration of the post ADC refill check and details of any fill errors (**Figure 2**). Electronic reports from the ADC were used to capture the number of pockets checked by each pharmacist. Last, we used electronic reports to document the type of pockets associated with an error. We based our sample size calculation on a previous study in a similar sized hospital that used a similar ADC system and refill process [5]. Of the 2,858 pockets inspected, this study found a misfill rate of 2.3%. Based on a similar baseline misfill rate of 2.3% and a power of 80%, we initially calculated that 6,600 pockets would need to be inspected to detect a misfill error reduction of 30%. An interim analysis during the post-implementation phase showed a much larger error reduction of more than 70%. It was then decided that sufficient data had already been collected for the study to be adequately powered. Data collection post-intervention was subsequently halted after 3,855 pockets had been included in the study

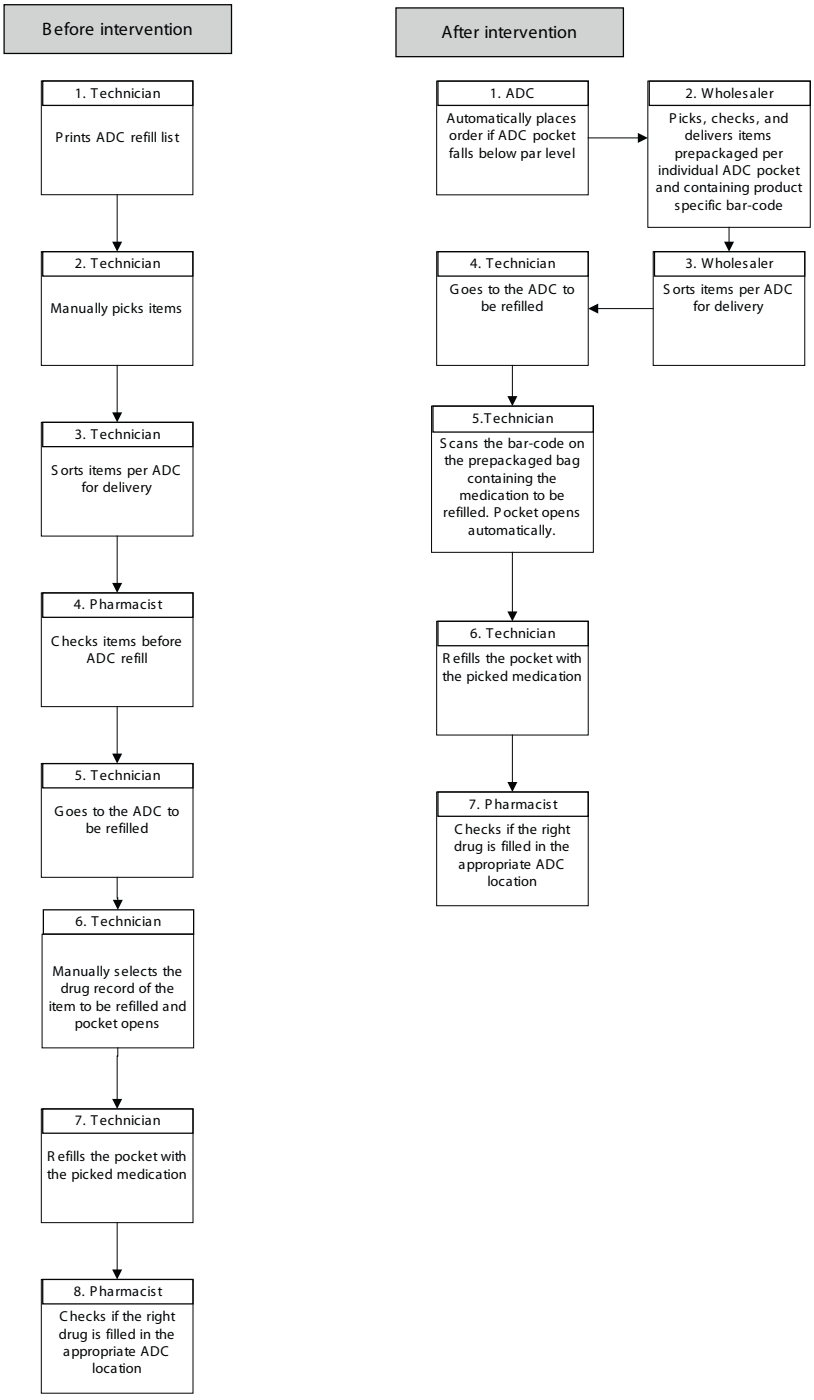

Figure 1. Redesign of the ADC refill process before and after implementation of a wholesaler-to-ADC direct refill program

ADC Error Data Collection Form - Please return to John Doe or Jane Doe when complete	Date:				Start time:	RPh:
	Pyxis Machine Name:				Stop time:	How many times were you interupted?
	Error type					
	Wrong drug	Wrong strength	Wrong form	Expired med	Error details (Medication Involved in Error - Name, Strength, Form)	

Figure 2. Data collection form

Data were entered into spreadsheets (Microsoft Office Excel 2007) for initial analysis and summary statistics. Stata 10 (StataCorp, LP, College Station, Texas) was used for the power calculation and additional statistical tests. The X^2 test was used to compare error rates before and after the intervention. Continuous data were analyzed using the unpaired t-test. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 6,829 pockets in 26 ADC's and 3,855 pockets in 24 ADC's were respectively inventoried 5 months pre- and 18 months post distribution process redesign. Since we relied on voluntary data collection by the pharmacists assigned to the unit during a fixed data collection period, refill data during the pre- and post-intervention periods were not collected from one and three ADC's respectively. Data collection characteristics were similar during both periods (**Table 1**), with one exception: during

Table 1. Pre- and post-intervention data collection characteristics

	Pre distribution process redesign	Post distribution process redesign	P-value
No. of pockets checked	6,829	3,855	NA[a]
Type of pocket Cubie (%) Non cubie (%)	 3,500 (51%) 3,329 (49%)	 2,821 (73%) 1,034 (27%)	P <0.0001
No. of ADC's (%)[b]	26 (96%)	24 (89%)	NS[c]
Median number of pockets per ADC (range)	169 (3-773)	109 (1-537)	NS
Median number of pockets per Rx Check (range)	6 (0-47)	6 (0-50)	NS
Median duration of Rx-Check in minutes (range)	3 (0-23)	2 (0-38)	NS

a NA= not applicable

b The areas included in our study contained 27 ADCs. Since we relied on voluntary data collection, not all ADCs were included.

c NS= not significant

the post intervention period, medications were more frequently stored in a single drug pocket than pre-implementation (73% vs. 51%, P<0.0001). We observed a 77% decrease in ADC refill errors from 62 per 6,829 refilled pockets (0.91%) to 8 per 3,855 refilled pockets (0.21%) (P<0.0001). The predominant error type detected before the intervention was the incorrect medication (wrong identity, strength or form) in the ADC pocket **(Table 2)**. Of the 54 incorrect medications found before the intervention, 38 (70%) were loaded in a multiple drug drawer.

After the intervention, 3 of the 5 incorrect medications (60%) were loaded in a multiple drug drawer. We found 3 instances of expired medication before and only 1 expired medication after the redesigned process.

DISCUSSION

We found a 77% decrease in ADC refill errors after redesigning the ADC refill process using a wholesaler-to-ADC direct refill program, without increasing the frequency of expired medication. These results should be viewed in light of the study's limitations. This study required extensive data collection, because medication refill errors are rare. Therefore, data were collected by different pharmacists during the pre- and post-intervention period, as part of their routine workflow. Twenty-nine pharmacists collected data during the pre-intervention period, compared to 16 pharmacists during the post-intervention period. Eleven pharmacists collected data during both time periods. This could have lead to differences in the consistency of data collection. However, the post ADC refill functionality of the ADC was used to measure refill accuracy, which is identical for every ADC. This should result in only minor data collection variance, and would not account for the large decrease in ADC refill errors. In addition, the baseline ADC refill error rate in this study (0.91%) is similar to the rate reported by Klibanov et al. (2.3%), further strengthening the validity of our results[5].

Table 2. Pre- and post-intervention error rates

	Pre distribution process redesign No. (%) of errors	Post distribution process redesign No. (%) of errors
Wrong identity	30 (48)	1 (13)
Wrong strength	16 (26)	4 (50)
Wrong form	8 (13)	0 (0)
Expired medication	3 (5)	1 (13)
Othera	5 (11)	2 (25)
TOTAL	62	8

a Examples of other errors are: non-medication items such as broken glass found in the drawer, loose dividers in the matrix drawer or technical issues.

Second, a separate effort to decrease ADC refill errors in our hospital was focused on increasing the use of the less error prone single drug pockets when storing medication in the ADC. As a result of these efforts, medications were more frequently stored in single drug pockets post-intervention than during the pre-intervention period. Scanning the wholesaler prepackaged medication barcode at the ADC automatically opens the correct single drug pocket, making it almost impossible to refill the incorrect pocket. Multiple drug pocket drawers, however, are more prone to errors as these pockets do not contain a lid. Our process requires an additional scan of the barcode in the specified pocket inside the multiple drug pocket drawer as an added safety feature. It is possible to misplace a medication in the compartment without performing a second scan. During the time of the study, we were not able to measure scanning compliance when refilling the ADC, which would have quantified this limitation. However, it is unlikely that this potential workaround influenced the results of this study: omitting the second scan requires the user to cancel the entire barcode-assisted refill process and resume the refill using a much more labor intensive manual process.

Third, the redesigned ADC refill process eliminates two error prone steps: (1) medications are no longer manually collected by the pharmacy technician in the inpatient pharmacy, but are delivered to the ADC prepackaged per pocket. (2) Pharmacy technicians no longer have to browse through an alphabetized list on the screen of the ADC for the appropriate pocket. Scanning the barcode on the prepackaged bag automatically opens the appropriate ADC pocket. We did not measure if sending the wrong product or incorrect placement in the ADC caused the ADC refill error. Therefore, we cannot conclude if wholesaler-to-ADC prepackaging or the use of bar-code assisted ADC refilling prevented the most errors.

Not all medications are available through the wholesaler-to-ADC program. Even though we observed a decrease of incorrect medication errors (wrong identity, wrong strength and wrong form), we obtained only 28 (47%) of the medications involved in incorrect medication errors through this program. At the time of the study only medications obtained through the wholesaler-to-ADC program were available for barcode assisted ADC refilling as only these products contained a barcode, scanable at the ADC. The decrease in medication errors of medications not obtained through the wholesaler-to-ADC refill program, could potentially be attributed to other changes of the redesigned process.

Nevertheless, we are planning to expand barcode assisted ADC refilling to all medications stocked in the ADC to fully benefit from the error reduction potential of bar-coding technology.

CONCLUSION

A redesign of the ADC refill process using a wholesaler-to-ADC direct refill program decreased ADC refill errors. The process described here is one approach to reduce medication distribution errors in the acute care environment.

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Chapter 10

A. Summary, general discussion and future perspectives

The landscape of the delivery of hospital care is changing: the aging population results in more patients being admitted to hospitals, but are discharged sooner. These demographic changes result in an increasing strain on healthcare budgets and a continuing focus on "doing more with the same". In addition, these changes lead to a different way of delivering healthcare, with a decreased focus on "stone" (e.g. large hospital facilities with many inpatient hospital beds), but an increased focus on information technology facilitating rapid patient turnover. In this thesis we described and investigated the consequences of several information technology interventions in hospitals (clinical decision support systems and bar-code technology) on the medication prescribing (Part 1) and administration (Part 2) processes. We focus on both quality of care aspects (e.g. quality of antimicrobial dosing in Chapter 3, medication administration errors in Chapter 8, automated dispensing cabinet refill errors in Chapter 9) and efficiency aspects (e.g. cost of excess antimicrobial dosing in Chapter 3, return on investment of CDSS assisted drug-drug interaction checking in Chapter 4 and workflow optimization in Chapters 5 and 9).

Part 1: Improving medication safety through technology: focus on prescribing

Chapter 2 describes the many applications of clinical decision support systems in pharmacy. We highlight the increasing adoption of electronic medical records and the vast amounts of data that are becoming electronically available. Chapter 2 also illustrates the need to convert these vast amounts of data to knowledge that is available to the clinician at the point of decision making. We also describe the shortcomings of our current information systems, the many barriers to adoption of effective clinical decision support and the three "pillars" that need to be in place to fully benefit from the adoption of decision support: 1. availability of knowledge in standardized formats, 2. high adoption and effective use 3. continuous improvement of knowledge and decision support methods[1].

Gaston, a commercially available decision support system was used in **Chapter 3** to investigate the quality of antimicrobial prescribing in the ICU. We found that even in an ICU setting, where medication and renal function data are readily available at the point of care, 86% of patients with moderate renal failure and 54% of patients with severe renal failure were exposed to excess dosing of antimicrobials. Almost €16,400 in drug costs can be saved annually if these antimicrobials are appropriately prescribed. A limitation of this study is that the CDSS was used retrospectively. As a result, the "real-world" effect of this system on outcomes and clinical workflow was not determined. But this study addressed the most important question in the development of a clinical decision rule: "Is there a need for this decision rule?"[2]. Clearly, the answer is "yes"!

In **Chapter 4**, the CDSS Gaston was used to assist in drug-drug interaction (DDI) checking. The national drug-drug interaction database (G-standard) is fully integrated in Gaston, which allowed for a direct comparison between conventional DDI checking and CDSS assisted DDI checking. Our approach was based on the observation that only 29 DDIs caused more than 90% of DDI alerts. We assembled a multidisciplinary expert team who evaluated these DDIs for clinical relevance and the need to alert the physician at the point of prescribing. The CDSS was then used to further increase the relevance of 18 DDI alerts by adding additional patient or medication specific parameters (such as laboratory values and administration times) to the standard DDI algorithm. No less than 14 of these 18 interactions were refined using only 4 clinical rules: 1 gastric-protection rule (6 DDIs), 1 hyperkalemia rule (3 DDIs), 1 hypokalemia rule (3 DDIs) and 1 hyponatremia rule (2 DDIs). This suggests that adding concomitant medication, sodium and potassium values to conventional DDI checking results in

a substantial decrease of irrelevant alerts. In Phase 1, we evaluated all alerts (including the clinically irrelevant alerts), but used the CDSS where possible to increase the efficiency of the DDI checking process. In Phase 2, the CDSS continued to be used, but clinically irrelevant alerts were suppressed for both prescriber and pharmacist and some less acute DDIs were only shown to pharmacists. This resulted in a reduction of DDI alerts by 28% and 55% in Phase 1 and Phase 2 respectively. We conducted a return-on-investment analysis in a setting with on average 70 DDI alerts per day, of which 20% is considered not clinically relevant and 24% can be refined using CDSS. CDSS assisted DDI checking decreased daily DDI checking duration by 4 minutes in Phase 1, and by 7 minutes if clinically irrelevant DDI alerts were suppressed (Phase 2). Almost 298 of the 392 hours required to implement CDSS assisted DDI checking were invested by pharmacists. An annual time savings of 30 hours yields a pharmacist time return-on-investment of 9.8 years. This might seem a marginal effect of CDSS assisted DDI checking, but efficiency can be further increased if a similar approach is applied to other modules in the G-standard such as renal dosing and drug-dosing checking. For example, G-standard contains many drugs with renal failure as a contraindication. In our institution, 29 drugs account for almost 92% of conventional renal failure alerts. G-standard contains specific dosing recommendations for only 15 of these drugs. Recommendations of the other drugs include cautions for side effects and slowly increasing dose, which are frequently not relevant for the clinical setting. Suppressing these 14 drugs, would decrease the number of conventional renal dose checking alerts by 72%. Further irrelevant alerting of the remaining 28% can be prevented if dose and dosing frequency are added to the decision algorithm using a CDSS. Efficiency can be further improved by identifying the appropriate route of alerting. Conventionally, all alerts are shown to the prescriber at the time of order entry and to the pharmacist for review. By identifying those alerts that require immediate action at the time of prescribing, less acute alerts can only be reviewed by pharmacy. And within pharmacy, further efficiency can be gained if less severe alerts with relative standard actions (such as changing administration times and adding gastric protection per protocol) are handled by technicians. In addition to increasing efficiency of the drug safety checking process, return-on-investment can be shortened by preventing excessive drug dosing using a CDSS and thereby decreasing drug expenditure. For example, we show in Chapter 3 that almost €17,000 could be saved annually on an intensive care unit alone when antimicrobial drug dosing is adjusted for renal function.

In short, the approach and time savings described in Chapter 4 serve as a catalyst for efficient implementation of other medication safety checking modules such as renal dosing checking without requiring additional staff.

Chapter 5 investigates the optimal formulary management strategy, which is an interesting paradox in hospital pharmacy. On the one hand, the hospital's formulary (and pharmacy inventory) should contain a large number of medications to assure immediate access and minimize medication errors resulting from changes in medication upon admission and discharge. On the other hand, large number of medications on formulary could potentially result in more medication errors as prescribers have to become familiar with more medications. In addition a larger pharmacy inventory results in more waste as a result of expiration of infrequently used medications. With the increasing adoption of computerized physician order entry systems (CPOE), an increased number of formulary items also requires increased maintenance of predefined orders and order sets. In Chapter 5, the development, implementation and results of a comprehensive formulary management system are described. We showed that continuous monitoring of nonformulary medication use, annual review of formulary medication use and providing periodic feedback to prescribers resulted in a 67% decrease in nonformulary medi-

cation use over a three year period, without increasing the number of items on formulary. Continuous monitoring of formulary compliance is essential to maintain a formulary that matches the need of the institution, and also optimizes CPOE order set maintenance. Last, our formulary compliance dashboard is based on data readily available in most hospitals (medication name, formulary status and admission number). If our approach is adopted by other institution, formulary compliance can be compared among institutions. These benchmarking opportunities could lead to the identification and dissemination of successful formulary management strategies in other institutions. Also in Chapter 5, we conducted a pharmacy labor cost analysis to identify the optimal strategy of managing requests for nonformulary medications. Automatically converting a nonformulary medication to the formulary alternative (known as therapeutic interchange) is the least labor intensive option of managing nonformulary medication requests. This pharmacy labor costs analysis is site specific and depends on CPOE functionality and adoption of other technologies. For example, it was more labor intensive in our study setting to allow the patient to use their own outpatient medication, than to call the prescriber and convert the patient to the hospital formulary alternative. BCMA was implemented throughout the hospital and required all medication used in the hospital to have a scannable barcode. Creating and affixing barcodes on medication brought into the hospital was more labor intensive than calling a physician. In a setting without BCMA, allowing the patient to use their own supply would have been less labor intensive. Nevertheless, automatically converting a patient to the formulary alternative through therapeutic interchange protocols is the least labor intensive way of managing nonformulary medication requests. The formulary compliance dashboard described in Chapter 5 identified suboptimal adherence to the therapeutic interchange protocols already in place at the time of the study. A decision support module which was part of a newly implemented electronic medical record provided opportunities to improve adherence, which we describe in **Chapter 6**. When ordering a therapeutically interchanged non formulary medication, a pop-up alert guides the prescriber to the equivalent alternative, which can be ordered by one mouse click. The pop-up alert is configured as a hard-stop and requires the prescriber to call the pharmacist to continue with the original order. Formulary compliance increased after implementation of therapeutic interchange alerts in 8 drug classes in a setting where baseline formulary adherence was already high. To our knowledge, this is the first study showing increased formulary adherence after implementing formulary decision support that is part of a widely used commercially available electronic medical record.

Part 2: Improving medication safety through technology: focus on administering

In **Chapter 7**, we reviewed the literature on the effects of bar-code assisted medication administration (BCMA) on frequency, type and severity of medication administration errors. We also summarized the reported duration of the medication administration task, as increased workload of nursing staff is a commonly voiced concern of BCMA implementation. Already in 2006, the Council of Europe Expert Group on Safe Medication Practices encouraged the use of electronic systems to improve the accuracy of medication administration[3] and in 2009, the American Society of Health-System Pharmacists encouraged hospitals to adopt BCMA[4]. In the Netherlands, a few hospitals are using BCMA technology, but most hospitals are implementing electronic charting of medication administration. As the use of bar-code technology to assure the right medication is given to the right patient makes intuitive sense, implementing BCMA also seems the logical next step in The Netherlands. However, in our review of the literature only 11 studies met the search criteria of a prospective design, using observa-

tional techniques. In general, the results from this review support the medication administration error reducing potential of BCMA technology up to one year after implementation, without indications of increased nursing time spent on medication administration. But the effect of BCMA on medication administration errors varies substantially among studies and among study setting (ICU versus general ward). In addition, most studies lack essential data on long term effects, user compliance and degree of implementation. This review of the literature illustrates that the body of literature supporting the effects of bar-coding on medication administration errors is small and that bar-coding is by no means a "mature technology" as was stated by the Institute for Safe Medication Practices already in 2002[5].

In **Chapter 8** we not only investigated the effect of BCMA on medication administration errors on both intensive care (ICU) as medical-surgical units, but we also evaluated medication administration accuracy indicators using a validated observation methodology. We found an overall 68% decrease in medication administration errors on medical-surgical units, but no effect in the ICU. In addition, we observed different effects on medication administration accuracy indicators when comparing these patient care areas. For example, compliance with patient identification procedures (checking two forms of ID) improved significantly on the medical surgical units, but no improvement was found on the ICU. In addition, the spectrum of medication administration errors varied in different areas of the hospital: omitting medication administrations was the most prevalent error on the medical-surgical units which is an excellent target for detection by BCMA. On the ICU however, wrong technique errors were the most prevalent, on which BCMA has no effect. These differences make sense as medical-surgical areas have far smaller nurse to patient ratio's compared to ICU's and different types of medication administrations. Our study demonstrates that BCMA technology is not a one-size-fits-all solution to prevent medication administration errors in an inpatient setting.

In 2008, 83% of US hospitals used automated dispensing cabinets (ADC's) as their primary method of drug distribution, which increased to almost 90% in 2011[6,7]. In **Chapter 9**, bar-coding technology was used to assure correct restocking of ADC's. ADC refill errors are relatively rare, but can have major consequences as multiple patients can be exposed to the wrong medication. By using a wholesaler-to-ADC direct refill program, the drug quantities required to refill an ADC pocket are prepackaged by the wholesaler including a bar-code. By scanning the bar-code, the right pocket in the right ADC automatically opens, almost eliminating human error. This approach provides an additional barrier for medication errors to reach the patient. In this study, we showed a 77% decrease in ADC refill errors. Even though ADC's are present in 9 out of 10 US hospitals, this study was only the second investigating the prevalence of ADC refill errors. The refill error detection methodology used in this study can be used by other institutions to identify other safe ADC restocking processes, which is a core process to ensure safe use of ADC's[8].

Conclusions and directions for future research

Part 1: focus on prescribing:

The recent guideline of the Royal Dutch Medical Association (KNMG) mandates that as of January 1st 2014, every prescriber in the Netherlands uses CPOE or has a plan in place assuring full implementation of this technology by January 1st 2015[9]. In addition, each CPOE system should have at a minimum the following functionalities based on the national standard: 1. drug-drug interaction checking, 2. al-

lergy checking, 3. duplicate therapy checking, 4. contraindication and other patient specific parameter checking[9].

The healthcare inspectorate of The Netherlands already announced to audit prescribers on adherence to this guideline[8]. However, basic decision support based on the national G-standard is plagued by many and often irrelevant alerts. In addition, basic decision support is applied at the time of initiating or modifying a medication order, while deleterious effects to the patient often occur days or even weeks later. Chapter 3 and 4 describe the great potential of advanced clinical decision support systems for renal dosing checking and drug-drug interaction checking respectively, eliminating irrelevant alerts and adding additional functionality. In addition, medication safety checking was applied to all current medication orders twice daily (Chapter 3) or 3 times daily (Chapter 4). This allows for detection of delayed effects. Another major advantage is that drug-drug interaction checking and renal failure contraindication checking modules in the CDSS Gaston are based on the national G-standard which is updated monthly. G-standard integration facilitates maintenance and allows for rapid creation and dissemination of clinical rules. In addition, Gaston has a grouping functionality by which similar interactions are evaluated using 1 common clinical rule. For example: 14 of the 18 interactions evaluated in Chapter 4 were refined using only 4 clinical rules: 1 gastric-protection rule (6 DDIs), 1 hyperkalemia rule (3 DDIs), 1 hypokalemia rule (3 DDIs) and 1 hyponatremia rule (2 DDIs). Updating these refined clinical rules would be greatly facilitated if DDIs receive a "grouping earmark" in the G-standard. For example, a new DDI requiring gastric protection would automatically be added to the gastric protection clinical rule, eliminating irrelevant alerts. This is currently under discussion with G-standard.

The CDSS Gaston used in this thesis provides recommendations retrospectively. In other words, suboptimal prescribing has to occur first, before decision support is applied. Ideally, relevant decision support should occur at the time of prescribing when needed, but should be suppressed when delayed effects occur. The national G-standard and most CPOE systems do not distinguish between acute effect and delayed effect alerting, which would greatly reduce the number of irrelevant alerts. We used a multidisciplinary expert panel to discuss the relevance of immediate alerting. However, additional research is needed to identify criteria for immediate and delayed alerting and identify the appropriate receiver of the alert (prescriber, nurse, pharmacist or technician). By adding this information to the G-standard, other institutions do not have to reinvent the wheel.

One national G-standard for medication safety checking is an essential prerequisite for effective decision support[10]. In the Netherlands, we are very fortunate with the quality and wide adoption of the G-standard. Further optimizing G-standard to allow for clinical rule based medication safety checking has already been initiated. The approach described in Chapter 4 is an example of how rapid introduction of CDSS assisted DDI-checking can be achieved in the Netherlands. In the United States, combating alert fatigue by improving the functionality of DDI checking software is becoming increasingly important as the adoption of CPOE systems for all prescribers is (similar to The Netherlands) stimulated by the federal government. A national effort has been initiated to improve drug-drug interaction checking software[11]. This project is federally funded by the Agency for Healthcare Research and Quality (AHRQ) and has the following goals: (1) develop an ongoing process for DDI evidence integration into clinical decision support systems, (2) recommend standards for DDI classification for CDS and (3) establish basic standards for communicating DDI information within CDS. The infrastructure already in place in The Netherlands has not gone unnoticed, as a Dutch clinical pharmacist has been selected as a member of the scientific steering committee of this project[12]. The logical next step in the United States is to adopt CDSS assisted DDI checking similar to current developments in the Netherlands.

Maintaining CPOE content such as order sets is essential to benefit from the full CPOE potential. One approach to effective maintenance of drug records within CPOE systems and consequently effective pharmacy inventory management was described in Chapter 5. The formulary management dashboard described in this chapter, was developed in a hospital in the US, but is now also implemented in St Jansdal Hospital Harderwijk. Adoption by more hospital pharmacies creates important benchmarking opportunities of inventories of hospital pharmacies and detects best practices. Substituting the formulary alternative for non-formulary medication is common practice in hospitals worldwide. Selecting the equivalent formulary alternative at the point of prescribing optimizes this practice. Therefore, any hospital CPOE system should include therapeutic interchange alerting functionality at the point-of prescribing (Chapter 6).

Part 2: focus on administering

Medication administration errors can be especially harmful as there are few barriers to prevent them reaching the patient. BCMA technology adds an additional safety barrier. This is a costly technology, requires repackaging activities by pharmacy personnel and has varying effects on overall medication administration errors depending on the type of hospital unit (Chapter 8). In Chapter 7 we show that the body of evidence supporting the long term effects of this technology on medication administration errors is lacking. In addition, data on the deleterious effects of medication administration errors on patient outcomes are lacking. Nevertheless, adoption of BCMA is rapidly increasing in the United States where hospitals are willing to spend millions to prevent a rare error (the "better safe than sorry" mentality). Objective data of and further research on the consequences of medication administration errors on patient outcomes are needed to support adoption of costly BCMA technology in the Netherlands. In Chapter 9, we describe the use of bar-coding technology to assure correct restocking of ADC's. In the United States, Automated Dispensing Cabinets (ADCs) can be considered a mature technology, with over 95% of hospitals with 100 beds or more using ADCs as the primary method of drug-distribution. In the Netherlands, only a handful hospitals use ADCs, and most of them only use this technology in designated patient care areas, such as the emergency department or the intensive care unit. However, ADC adoption as the primary method of drug distribution is likely to increase in The Netherlands. ADCs assure that a large selection of medication is available on the patient floor, which will be increasingly important when more patients stay in the hospital for a shorter duration. In addition, the functionality of these systems is closely linked to the implementation of CPOE as so called "profiled" ADC's only allow a nurse to retrieve and administer a medication when an active order is present in the CPOE. The ISMP guidelines assuring safe use of this technology as described in Chapter 9 are based on medication errors that have resulted in patient harm and should be adopted by every hospital worldwide currently using ADCs[13]. In addition, these guidelines and the accompanying self-assessment are a perfect starting point for hospitals currently evaluating the use of this technology.

To summarize, the requirement to use CPOE for medication prescribing opens many doors for implementing technologies aimed at increasing medication safety in the areas that are most critical; medication prescribing and administering. This thesis can help in selecting and configuring these technologies and measuring its effects on these critical steps in the hospital medication use process.

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Chapter 10

B. Nederlandse samenvatting

Inleiding

De demografische ontwikkeling in Westerse landen en de ontwikkelingen in de manier waarop zorg wordt verleend, zorgen ervoor dat het aantal mensen dat in het ziekenhuis wordt opgenomen toeneemt maar korter in het ziekenhuis verblijven. De uitgaven aan gezondheidszorg nemen toe met als gevolg een continue focus om meer te doen met hetzelfde. Ziekenhuizen investeren niet alleen meer in "stenen" (grote ziekenhuizen met een grote beddencapaciteit), maar focussen ook op het implementeren van (informatie) technologie om meer patiënten op een veilige, kwalitatief hoogwaardige en efficiënte manier te behandelen. Verder is er sinds het verschijnen van het rapport «To err is human» in 1999 een toegenomen focus ontstaan op het voorkomen van medische fouten binnen de gezondheidszorg. Medicatiefouten zijn de meest voorkomende medische fouten: een voorzichtige schatting uit een Nederlandse studie uit 2004 was dat van elke 18 patiënten die wordt opgenomen in het ziekenhuis er 1 patiënt onbedoelde schade oploopt. In 21% van de gevallen is medicatiegebruik de oorzaak en in nog eens een derde van de gevallen bleek de schade vermijdbaar. De meeste fouten ontstaan bij het voorschrijven en toedienen van medicatie. Het toepassen van informatie technologie wordt gezien als een belangrijke stap om de veiligheid van medicatiegebruik binnen het ziekenhuis te verhogen.

In dit proefschrift beschrijven we de effecten van verschillende informatie technologieën (elektronische voorschrijfsystemen, klinische beslissingsondersteunende systemen (CDSS) en de toepassingen van barcodering) op het voorschrijven (deel 1) en toedienen (deel 2) van medicatie. We onderzoeken met name de kwaliteit van de zorgverlening (bijvoorbeeld het te hoog doseren van antimicrobiële middelen bij patiënten met nierfunctieproblemen in Hoofdstuk 3, fouten in het toedienen van medicatie in Hoofdstuk 8 en het vullen van geneesmiddeluitgifte apparatuur met verkeerde medicijnen in Hoofdstuk 9) en efficiency aspecten (geneesmiddelkosten van antibiotica in Hoofdstuk 3, return-on-investment van het gebruik van een systeem dat wisselwerkingen tussen geneesmiddelen bewaakt (interactiebewaking) in Hoofdstuk 4 en het optimaliseren van werkprocessen in Hoofdstukken 5 en 9).

Deel 1: Focus op het voorschrijven van medicatie

Door de toepassing van steeds meer informatie technologie in het ziekenhuis, worden steeds meer medische gegevens elektronisch vastgelegd. De uitdaging is om deze grote hoeveelheid data om te zetten naar bruikbare informatie die de zorgverlener op het juiste moment kan gebruiken. Beslissingsondersteunende systemen (Clinical Decision Support Systems, CDSS) zijn hiervoor noodzakelijk en zijn gedefinieerd als "software die de zorgverlener ondersteunt bij het nemen van medische beslissingen door individuele patiëntgegevens volgens klinische beslisregels (clinical rules) te combineren en patiënt-specifieke aanbevelingen te genereren. In **Hoofdstuk 2** beschrijven we de vele toepassingen van dergelijke systemen in de gezondheidszorg. We beschrijven ook de tekortkomingen van onze huidige systemen (te veel, vaak irrelevante en aspecifieke meldingen) en de vele barrières om deze systemen effectief toe te passen. Drie belangrijke barrières zijn (1) de beschikbaarheid van medische kennis in gestandaardiseerde vorm, (2) meer en effectievere toepassing van deze systemen en (3) continue verbetering van de klinische beslisregels binnen deze systemen. In **Hoofdstuk 3** gebruiken we het CDSS *Gaston* om de kwaliteit van het doseren van antibiotica op de afdeling Intensive Care (IC) te onderzoeken. Op deze afdeling worden patiënten intensief gemonitord en waren medicatie en nierfunctie gegevens in hetzelfde elektronisch dossier beschikbaar. Toch vonden we dat 86% met

een matige nierfunctiestoornis en 54% van patiënten met een ernstige nierfunctiestoornis werden blootgesteld aan te hoge doseringen van antibiotica, vermoedelijk omdat voorschrijvers niet actief werden geattendeerd op deze informatie. Per jaar kan er op deze afdeling bijna €16.400 aan antibioticumkosten worden bespaard als er beter rekening wordt gehouden met de nierfunctie bij het doseren van deze middelen. In deze studie werd het CDSS retrospectief gebruikt om achteraf de dosering van antibiotica te correleren aan de nierfunctie. We weten dus niet of deze besparing ook daadwerkelijk wordt behaald als het CDSS in de dagelijkse praktijk wordt geïmplementeerd. Maar deze studie beantwoordt wel een essentiële vraag bij het gebruik van klinische beslisregels, namelijk: "Is deze beslisregel wel echt noodzakelijk en relevant voor de klinische praktijk?". We kunnen hier volmondig "ja" op antwoorden.

In **Hoofdstuk 4** is het CDSS *Gaston* wel in de klinische praktijk geïmplementeerd om ongewenste wisselwerkingen tussen geneesmiddelen (zogenaamde geneesmiddelinteracties) efficiënter te monitoren. In Nederland wordt hiervoor een nationale database gebruikt, de G-Standaard die maandelijks wordt geupdate. Deze database bevat informatie of geneesmiddel A samen gebruikt mag worden met geneesmiddel B en zorgt voor een melding voor voorschrijver of apotheker op het moment van het voorschrijven van een ongewenste geneesmiddelcombinatie. De G-standaard betrekt echter geen andere patiëntkarakteristieken bij deze beslissing wat leidt tot een groot aantal irrelevante meldingen. De conventionele interactiebewakingsdatabase van de G-Standaard is volledig geïntegreerd in het CDSS *Gaston*, maar dit systeem bevat ook laboratorium uitslagen en overige patiënt- en geneesmiddelkarakteristieken (zoals leeftijd, geslacht en overige medicatie). We vergeleken de tijdsinvestering van de ziekenhuisapotheker en het aantal interactie meldingen van conventionele interactiebewaking met interactiebewaking ondersteund door *Gaston*. Beide methodes werden uitgevoerd op dezelfde patiëntenpopulatie en door dezelfde ziekenhuisapotheker, waardoor deze persoon diende als zijn eigen controle. Deze studie was gebaseerd op een nulmeting waarbij wij vonden dat slechts 29 interacties meer dan 90% van de conventionele interactiemeldingen veroorzaakten. We stelden een multidisciplinair expert team samen bestaande uit een ziekenhuisapotheker, cardioloog, neuroloog, internist-nefroloog, internist-hematoloog, geriater, reumatoloog en kinderarts. Het expert team beoordeelde vervolgens deze 29 interacties op relevantie voor de ziekenhuissetting en indien klinisch relevant de noodzaak om een melding op het moment van voorschrijven te laten verschijnen. Slechts 4 van de 29 interacties werden beoordeeld als JA voorschrijver-JA apotheker (meldingen van interacties waarbij direct op het moment van voorschrijven schade aan de patiënt kan optreden), 17 interacties werden beoordeeld als NEE voorschrijver-JA apotheker (meldingen van interacties die klinisch relevant kunnen zijn, maar vaak nog niet op het moment van voorschrijven) en 8 interacties werden als NEE voorschrijver-NEE apotheker beoordeeld omdat ze niet relevant waren voor de klinische setting. De ziekenhuisapotheker kon vervolgens bij 18 interacties de additionele patiënt- en geneesmiddelkarakteristieken in het CDSS *Gaston* gebruiken om het aantal interactiemeldingen te verminderen en de relevantie te verhogen. Deze studie was opgebouwd uit 2 fasen: in Fase 1 werden alle interactiemeldingen getoond aan zowel de voorschrijver als ziekenhuisapotheker, inclusief de meldingen van interacties die door het expert team als klinisch niet relevant werden beschouwd. De ziekenhuisapotheker gebruikte vervolgens het CDSS *Gaston* bij de uitvoering van de interactiebewaking. In Fase 2 bleven de ziekenhuisapothekers het CDSS gebruiken voor de interactiebewaking, maar werden de NEE voorschrijver-NEE apotheker meldingen onderdrukt voor zowel de voorschrijver als ziekenhuisapotheker en werden de NEE voorschrijver-JA apotheker meldingen onderdrukt voor de voorschrijver. In Fase 1 werden 28% minder interactiemeldingen gegenereerd wat verder afnam tot 55% van het aantal conventionele meldingen

in Fase 2. Dit resulteerde in een afname van de duur van interactiebewaking van respectievelijk 4 en 7 minuten in fase 1 en 2. In totaal waren er 298 ziekenhuisapotheker-uren nodig om het CDSS Gaston volledig te configureren om interactiebewaking op een patiënt specifiekere wijze uit te kunnen voeren. Dit levert een return-on-investment (ROI) op van 9,8 jaar om interactiebewaking ondersteund door beslissingsondersteuning te implementeren in een setting waarbij dagelijks ongeveer 70 conventionele interactiemeldingen worden gegenereerd en waar bij ongeveer 1 op de 4 meldingen extra patiënt- of geneesmiddelkarakteristieken kunnen worden betrokken. Deze relatief lange ROI kan worden opgevat als een marginaal effect van het toepassen van beslissingsondersteuning bij conventionele interactiebewaking. Echter, de landelijk G-Standaard bevat meerdere modules om veilige medicatiegebruik te bevorderen, zoals doseringscontrole en het monitoren van juist gebruik van geneesmiddelen bij patiënten met een nierfunctiestoornis. Het CDSS Gaston kan ook bij deze modules op identieke wijze worden toegepast om de conventionele doseringscontrole of bewaking van patiënten met een nierfunctiestoornis efficiënter te maken. Als voorbeeld: slechts 29 geneesmiddelen veroorzaken meer dan 90% van de conventionele meldingen bij patiënten met een nierfunctiestoornis. De meldingen van slechts 15 geneesmiddelen bevatten specifieke doseeradviezen, de overige 14 geneesmiddelen veroorzaken meldingen die waarschuwen voor het optreden van bijwerkingen of het langzaam insluipen wanneer het geneesmiddel voor het eerst wordt voorgeschreven. In een klinische setting waarbij patiënten goed worden gemonitord zijn deze conventionele meldingen zelden relevant. Als alleen de meldingen zouden worden onderdrukt van deze 14 geneesmiddelen, zou het aantal conventionele meldingen direct met 72% verminderen. Relevantie van de overige 28% kan vervolgens worden verhoogd als door gebruik van een CDSS patiënt of geneesmiddelspecifieke informatie (zoals dosering en doseerfrequentie) worden betrokken bij de conventionele melding. Een efficiëntere manier van medicatiebewaking kan verder worden gerealiseerd, als apothekersassistenten op een geprotocolleerde wijze relatief eenvoudige meldingen kunnen afhandelen. Samengevat, de aanpak beschreven in hoofdstuk 4 kan worden gebruikt om de efficiëntie van de huidige medicatiebewaking te verhogen, of om de medicatiebewaking uit te breiden binnen de huidige bemensing.

Ziekenhuizen behandelen een groot aantal patiënten gedurende een vaak korte periode. De medicatie die in de thuissituatie wordt gebruikt, wordt vaak gecontinueerd tijdens ziekenhuisopname om medicatiefouten rondom opname en ontslag te voorkomen. Het is echter onmogelijk en onwenselijk om alle mogelijke medicatie te allen tijde beschikbaar te hebben in het ziekenhuis. De meeste ziekenhuizen hanteren daarom een formularium: een lijst met de meest gangbare geneesmiddelen die past bij de patiëntenpopulatie van het ziekenhuis. Elektronische voorschrijfsystemen (EVS) maken het mogelijk om snel volledige medicatieopdrachten te genereren en medicijnen die vaak samen worden voorgeschreven voor te definiëren. Deze standaardisatie verhoogt de medicatieveiligheid en betekent tijdswinst voor de voorschrijver. Hoe meer middelen het formularium bevat, hoe meer de winst van standaardisatie verloren gaat en hoe meer onderhoud er aan het EVS moet plaatsvinden. In **Hoofdstuk 5** beschrijven we de ontwikkeling, implementatie en resultaten van een formularium management systeem. Continue monitoring van middelen die buiten het formularium worden voorgeschreven (zogenaamde niet-formularium middelen), een jaarlijkse analyse van het gebruik van formularium middelen en terugkoppeling van voorschrijfpatronen naar de voorschrijver veroorzaakte een reductie van 67% van het aantal middelen dat buiten het formularium werd voorgeschreven. Deze reductie werd bereikt over een periode van 3 jaar, zonder een toename van het aantal formularium middelen. We ontwikkelden een parameter om het voorschrijven volgens formularium te meten en stelden een dashboard samen om voorschrijfpatronen inzichtelijk te maken. Dit dashboard is gebas-

eerd op gegevens die in vrijwel elk ziekenhuis elektronisch beschikbaar zijn (zoals geneesmiddel naam en formularium of niet-formularium status). Als meerdere ziekenhuizen een dergelijk dashboard gaan gebruiken, kunnen formularia vergeleken worden tussen verschillende ziekenhuizen. Op deze manier kunnen succesvolle formularium management strategieën worden geïdentificeerd.

In hoofdstuk 5 beschrijven we ook een arbeidskostenanalyse met als doel de optimale manier te identificeren om binnen de ziekenhuisapotheek om te gaan met niet-formularium voorschriften. Hoewel dergelijke kostenanalyses afhankelijk kunnen zijn van de werkprocessen binnen de ziekenhuisapotheek en binnen het ziekenhuis, kwamen wij tot dezelfde conclusie als een eerder onderzoek in een andere setting: geprotocolleerde therapeutische substitutie is de meest optimale manier om niet-formularium voorschriften om te zetten naar een formularium alternatief. Op deze manier kan een voorschrift worden gewijzigd in een equivalent formularium alternatief zonder contact met de voorschrijver. In de meeste ziekenhuizen bestaan dergelijke "substitutieprotocollen" al, maar vaak worden deze substituties pas uitgevoerd wanneer het voorschrift de ziekenhuisapotheek bereikt. In **Hoofdstuk 6** beschrijven we de toepassing van een beslissingsondersteunings systeem dat onderdeel is van een commercieel beschikbaar elektronisch voorschrijfsysteem, waardoor de arts op het moment van voorschrijven van een niet-formularium artikel direct het equivalente formularium alternatief krijgt getoond. De arts kan vervolgens met één muisklik het voorschrift omzetten naar het formularium alternatief. Het was voor de voorschrijver niet mogelijk om het niet-formularium middel voor te schrijven, tenzij telefonisch contact werd opgenomen met de ziekenhuisapotheker. Na configuratie van deze functionaliteit, verminderde het aantal niet-formularium voorschriften in alle 8 geneesmiddelgroepen. Deze studie is de eerste studie waarbij het effect van deze vorm van beslissingsondersteuning, onderdeel van een marktleidend elektronisch medisch dossier, structureel is aangetoond en gekwantificeerd.

Deel 2: Focus op het toedienen van medicatie

In **Hoofdstuk 7** hebben we de wetenschappelijke literatuur samengevat over het gebruik van barcodering bij het toedienen van geneesmiddelen binnen het ziekenhuis, zogenaamde barcode assisted medication administration (BCMA). Door het scannen van de barcode van de medicatie en de barcode op de polsband van de patiënt, kan de medicatie die elektronisch is vastgelegd in het elektronisch voorschrijfsysteem bij die patiënt worden vergeleken met de medicatie die op dat moment wordt toegediend. We beschrijven de effecten van BCMA op de frequentie van voorkomen, de ernst en het type toedienfouten. We hebben ook gefocust op de tijd die verpleegkundigen nodig hebben om medicatie toe te dienen aan patiënten, omdat we de veel gehoorde klacht dat medicatietoediening met BCMA technologie meer tijd zou kosten wilden objectiveren. Al sinds 2006 adviseren Europese en Amerikaanse instanties het gebruik van BCMA om de toediening van medicatie veiliger te maken. In 2011 gebruikte meer dan de helft van Amerikaanse ziekenhuizen deze technologie en de toepassing ervan in Nederland lijkt ook een logische keuze in de strijd tegen toedienfouten. Echter, wij vonden slechts 11 studies in de wetenschappelijke literatuur waarbij de effecten van BCMA werden beoordeeld op basis van observaties van een groot aantal geneesmiddeltoedieningen, wat wordt beschouwd als de gouden standaard voor dit soort studies. Over het algemeen reduceerde het gebruik van BCMA gedurende maximaal 1 jaar het aantal toedienfouten in deze studies, zonder een relevant effect te zien op de tijd die verpleegkundigen nodig hebben om geneesmiddelen toe te dienen. Maar we vonden ook een sterk wisselend effect tussen de verschillende studies en de afdelingen binnen het ziekenhuis (in-

tensive care versus verpleegafdeling). Bovendien ontbraken in de meeste studies essentiële gegevens over de lange termijn effecten, mate van implementatie en correcte gebruik van deze technologie. Dit overzicht laat zien dat er een beperkt aantal studies zijn die de effecten van BCMA op medicatieveiligheid objectiveren. BCMA is dus in geen geval een "uitontwikkelde technologie", zoals al wel in 2002 is genoemd door het gezaghebbende Amerikaanse Institute for Safe Medication Practices.
In **Hoofdstuk 8** beschrijven we niet alleen de effecten van de implementatie van BCMA op toedienfouten op meerdere afdelingen binnen het ziekenhuis (zowel intensive care als verpleegafdelingen), maar we onderzochten ook de nauwkeurigheid van medicatietoediening op basis van een gevalideerde observatie methode. BCMA resulteerde in een indrukwekkende 68% afname van medicatie toedienfouten op de verpleegafdeling, maar we vonden geen effect op de intensive care afdeling. Ook het soort medicatie toedienfouten verschilde tussen verpleegafdeling en intensive care: voor implementatie van BCMA was de meest voorkomende toedienfout het vergeten toe te dienen van medicatie. Barcodering kan dit type fout eenvoudig voorkomen. Op de intensive care was de meest voorkomende fout echter het op een verkeerde manier voor toediening gereed maken van medicatie (bijvoorbeeld het niet dragen van handschoenen bij het klaarmaken van parenteralia): BCMA implementatie heeft geen effect op dit type fouten. Als laatste vonden we verschillende effecten op indicatoren van de nauwkeurigheid van de medicatietoediening na implementatie op deze afdelingen. Bijvoorbeeld op de verpleegafdeling verbeterde het controleren van de juiste identiteit van de patiënt na implementeren van BCMA, maar zagen we geen verschil in deze parameter op de intensive care. Een mogelijke verklaring voor de verschillende effecten van BCMA per type verpleegafdeling is de verschillende ratio's tussen het aantal patiënten per verpleegkundige. Deze studie toont aan dat het implementeren van BCMA niet een one-size-fits-all oplossing is om medicatie toedienfouten binnen het ziekenhuis te voorkomen.

In 90% van de ziekenhuizen in de Verenigde Staten worden geneesmiddeluitgifte apparaten (zogenaamde Automated Dispensing Cabinets, ADC) op de afdeling gebruikt als belangrijkste methode om medicatie gecontroleerd (beheersbaar) op een ziekenhuisafdeling op te slaan en te verstrekken. Deze apparaten zijn te vergelijken met een snoep- of frisdrankautomaat, waarbij een groot aantal verschillende medicijnen is opgeslagen in een afgesloten apparaat. Deze technologie is vaak gekoppeld aan het elektronisch voorschrijfsysteem in het ziekenhuis, waardoor verpleegkundigen alleen maar medicatie kunnen verkrijgen en toedienen wanneer deze ook daadwerkelijk is voorgeschreven. Een belangrijk aspect van de veiligheid van de geneesmiddelvoorziening door middel van ADC technologie is het vullen van het apparaat met de correcte medicatie. Deze ADC vulfouten zijn gelukkig relatief zeldzaam, maar ze kunnen grote gevolgen hebben. Meerdere patiënten kunnen namelijk worden blootgesteld aan de verkeerde medicatie. In **Hoofdstuk 9** beschrijven we de effecten op ADC vulfouten na implementatie van een nieuwe manier van beleveren van geneesmiddelen door de groothandel. De nieuwe werkwijze maakte het handmatig verzamelen van medicatie om de ADC te vullen door de ziekenhuisapotheek overbodig, omdat de groothandel de medicatie al voorverpakt per apparaat aanlevert, inclusief een barcode. Naast een efficiëntie slag voor de ziekenhuisapotheek, zorgde deze barcode voor een veilige procedure om de ADC te vullen: het scannen van de barcode zorgde namelijk voor dat het juiste vakje van de ADC automatisch opende, zonder dat deze handmatig uit een alfabetische lijst met medicatie moest worden geselecteerd. Deze extra barrière resulteerde in onze studie in een 77% afname van ADC vulfouten. Deze studie was de tweede studie die de prevalentie van ADC vulfouten heeft onderzocht. Het vullen van de ADC wordt gezien als een kritische stap in het gebruik van een ADC. De vulfout detectie methode die wij hebben gebruikt in deze studie kan worden gebruikt door

andere ziekenhuizen om de prevalentie van vulfouten te benchmarken met onze resultaten andere effectieve methoden om ADC's te vullen te identificeren.

Samenvattend: sinds 1 januari 2014 is het voorschrijven van geneesmiddelen via een elektronisch voorschrijfsysteem verplicht in Nederland. Bovendien zijn er eisen gesteld aan welke medicatiebewakingsmodules het elektronisch voorschrijfsysteem moet bevatten en dat deze moeten voldoen aan de nationale standaard. Het elektronisch voorschrijven van medicatie is een essentiële voorwaarde om technologieën te implementeren die als doel de medicatieveiligheid te verhogen tijdens de meest kritische stappen van het medicatiegebruik in ziekenhuizen, namelijk het voorschrijven en toedienen van medicatie. Dit proefschrift helpt bij het selecteren en configureren van deze nieuwe technologieën en biedt methodes om de effecten op medicatieveiligheid te meten.

Chapter 11

Curriculum Vitae

Pieter Helmons was born in Eindhoven in 1976. He grew up in Valkenswaard, The Netherlands and completed secondary school (Gymnasium) at Hertog Jan College in Valkenswaard. He graduated from Utrecht University School of Pharmacy in 2001. After working in community pharmacy for 2 years, he completed the mandatory 4-year hospital pharmacy residency required to practice hospital pharmacy at Catharina Hospital Eindhoven in 2007. The final year of this residency, Pieter specialized in using clinical decision support technologies to improve medication safety in the Intensive Care, failure modes and effects analyses and workflow improvement.

In February 2007, Pieter moved to La Jolla, California in the United States and continued his career as a postdoctoral researcher at University of California San Diego (UCSD) Skaggs School of Pharmacy and Pharmaceutical Sciences, supervised by Prof. Charles Daniels. He investigated the effects of bar-coding technology on medication safety at UCSD Health System in San Diego and completed the licensure exams and intern hours required to practice pharmacy in California. From February 2009 to October 2011, Pieter worked as Pharmacist Specialist Pharmacoeconomics at UCSD Health System. He specialized in the use of benchmarking databases and identified multiple cost-savings opportunities by comparing UCSDs drug use patterns with other similar hospitals. During this period, Pieter completed the UCSD Clinical Research Excellence through Supplementary Training (CREST) Masters Program, aimed at empowering clinicians to become better researchers. He was also appointed Assistant Professor at UCSD Skaggs School of Pharmacy and Pharmaceutical Sciences and lectured in the Pharmacy Informatics and Applied Pharmacoeconomics courses. After returning to the Netherlands in 2011, Pieter currently works as a hospital pharmacist in St Jansdal Hospital Harderwijk. He is responsible for the safe and effective use of the Automated Dispensing Cabinets in the hospital, implementing effective and efficient medication use monitoring, formulary management and drug distribution practices. He is a member of the hospitals Information Technology Steering Committee, currently tasked with implementing a new hospital-wide Electronic Medical Record. Pieter is a member of the Medication Management Committee of the Dutch Society of Hospital Pharmacists. He co-organized the Dutch Hospital Pharmacy Days in 2012 and 2013. Pieter lectures in the Applied Pharmacoeconomics Course supervised by Prof. Maarten Postma the University of Groningen School Of Pharmacy.
Pieter lives in Leusden, is married to Nina van Sorge and has 3 children: Lars (4), Mijke (3) and Fiene (3 months)

Curriculum Vitae (Nederlands)

Pieter Helmons werd op 27 mei 1976 geboren in Eindhoven. Hij groeide op in Valkenswaard en ging naar het Gymnasium van het Hertog Jan College in dezelfde plaats. Hij studeerde farmacie aan de Universiteit Utrecht en behaalde zijn apothekersdiploma in 2001. Na het voltooien van de registratiefase tot openbaar apotheker in Apotheek De Ronde Venen in Mijdrecht, ging Pieter in opleiding tot ziekenhuisapotheker in het Catharina Ziekenhuis te Eindhoven. In het laatste jaar van deze opleiding specialiseerde Pieter zich in het verhogen van de medicatieveiligheid door het gebruik van beslissingsondersteunende systemen op de Intensive Care, failure mode and effects (FMEA) analyses en optimalisatie van werkprocessen. In januari 2007 behaalde hij zijn registratie als ziekenhuisapotheker en in februari van dat jaar emigreerde Pieter naar de Verenigde Staten om zijn carrière voort te zetten als postdoctoraal onderzoeker bij Dr. Charles Daniels aan de University of California Skaggs School of Pharmacy and Pharmaceutical Sciences in La Jolla, California. Hij onderzocht daar de effecten van barcodering op de prevalentie van medicatie toedienfouten in het UCSD Health System in San Diego en voltooide de registratie examens en stage uren die vereist zijn om als apotheker werkzaam te zijn in California. Pieter werkte vervolgens van februari 2009 tot oktober 2011 als Pharmacist-Specialist met aandachtsgebied farmacoeconomie in de ziekenhuisapotheek van UCSD Health System. Hij specialiseerde zich daar in het gebruik van benchmarking databases en identificeerde een groot aantal kostenbesparingen door het vergelijken van het geneesmiddelgebruik van UCSD Health System met andere vergelijkbare ziekenhuizen. In deze periode voltooide Pieter het UCSD Clinical Research Excellence through Supplementary Training (CREST) Masters curriculum om medische professionals te trainen in het uitvoeren van praktijk en klinisch onderzoek. Pieter werd benoemd tot Assistant Professor bij UCSD's Skaggs School of Pharmacy en Pharmaceutical Sciences en verzorgde colleges op het gebied van Pharmacy Informatics en toegepaste farmacoeconomie. Na zijn terugkeer naar Nederland in 2011, is Pieter gaan werken als ziekenhuisapotheker in het St Jansdal Ziekenhuis in Harderwijk. Hij is verantwoordelijk voor veilig en effectief gebruik van de automatische geneesmiddeldistributie apparaten in het ziekenhuis, verbeterde de efficiëntie en functionaliteit van de medicatiebewaking en is verantwoordelijk voor het formulariummanagement en geneesmiddeldistributie. Pieter is lid van de Programmaraad ICT van het ziekenhuis die op dit moment een nieuw ziekenhuisinformatiesysteem en elektronisch medisch dossier selecteert. Pieter is lid van de commissie geneesmiddelmanagement van de Nederlandse Vereniging van Ziekenhuisapothekers. Hij was lid van het organiserend comité van de Nederlandse Ziekenhuisfarmacie dagen in 2012 en 2013. Pieter verzorgt het college Toegepaste Farmacoeconomie van Prof. Maarten Postma aan Faculteit Farmacie van de Rijksuniversiteit Groningen. Pieter woont in Leusden, is getrouwd met Nina van Sorge en heeft 3 kinderen: Lars (4), Mijke (3) en Fiene (3 maanden).

Chapter 12

Dankwoord (word of thanks)

Het dankwoord behoort tot een van de meest gelezen onderdelen van het proefschrift, maar wordt ironisch genoeg vaak als laatste geschreven. Dit proefschrift is daarin geen uitzondering. Om te voorkomen dat ik iemand vergeet, wil ik beginnen met iedereen te bedanken die een bijdrage heeft geleverd aan de hoofdstukken gebundeld in dit proefschrift: co-auteurs, ziekenhuisapothekers (in opleiding), artsen, studenten, apothekersassistenten en verpleegkundigen. Maar uiteraard wil ik een aantal van hen specifiek benoemen in dit dankwoord.

Allereerst mijn beide promotores, Prof. Dr. J.G.W. Kosterink en Prof. Dr. C.E. Daniels.

Beste Jos: hoewel ik niet in Groningen heb gestudeerd en voorheen alleen voor de opleidingsdagen toxicologie het UMCG van binnen had gezien, durfde jij het aan om mij, als recent geremigreerde Nederlands-Amerikaanse ziekenhuisapotheker, die farmacie heeft gestudeerd in Utrecht en is opgeleid tot ziekenhuisapotheker in Eindhoven, te begeleiden. Tijdens onze eerste ontmoeting waren we het direct eens over hoe mijn portfolio op dat moment kon worden omgezet in een promotie. Het maandelijkse promotie overleg in het UMCG was niet alleen erg efficiënt en stimulerend , maar was ook gewoon een heel goed excuus om de stad Groningen beter te leren kennen. Hoe je het begeleiden van promovendi combineert met het professorschap, hoofd van de ziekenhuisapotheek van het op een na grootste ziekenhuis van Nederland en tennis op topniveau is mij een raadsel. Maar je nam altijd ruim de tijd voor ons overleg en wist altijd de belangrijkste verbeterpunten in de manuscripten te benoemen. Nogmaals enorm bedankt en ik hoop in de toekomst nog veel met je samen te kunnen werken.

Dear Chuck: I owe you my career in the US. You recognized the potential of a Dutch hospital pharmacist first for UCSD's Skaggs School of Pharmacy and later for UCSD Health System. This is by no means straightforward as you were not familiar with the level of hospital pharmacy in The Netherlands and had to take my word for it. After our first meeting in 2006, I instantly felt at home in California and at UCSD and I was very fortunate that Nina felt the same way about working for Prof. Nizet, making our move to California a reality. When I mentioned to you during that first meeting that I would not pursue licensure as a California pharmacist as "we would only stay for 2 years", you frowned and advised to rethink that decision. I am so glad I did as not only we stayed for almost 5 years, but this also started off our research collaboration which still continues. I am particularly proud of how we were able to witness the large number of medication administrations required to detect medication administration errors, without the availability of additional staff. You mentioned the possibility to make this study a residency project and recruit students. They pulled it off and I am very proud of the result, included as Chapter 8 of this thesis. When a large data collection effort was yet again required for the Cardinal Assist Safety in Healthcare through Information Technology project (CASH-IT), we used a similar approach and asked our floor pharmacists to collect the data during their daily check of the automated dispensing cabinets. After 2 weeks the staff showed their appreciation of their new role as data collectors, as the bin that we set up to collect the data-collection sheets had been renamed from CASH-IT to CA-SHIT. Nevertheless, we pulled it off and the result is included as Chapter 9 of this thesis. These examples indicate how you can come up with creative solutions to challenges and exploit the additional possibilities when research is combined with clinical practice. I recall how proud I was when you announced at the May 2011 P&T committee meeting that "Pieter was late for a good reason". That standing ovation of all committee members when you announced that I had obtained American citizenship is one of the many things I will never forget. It was with pain in my heart that I left UCSD in 2011 and I am pleased we not only stayed in contact but also were able to collaborate further.

I am extremely proud of the result! Thank you again for your continuing support and I sincerely hope you enjoy yourself in the Netherlands.

Let me just continue in English to thank my first paranimf, Phil Anderson. Phil, you were my office mate at UCSD when I arrived and I will never forget the remark your wife Veronica made when we came over for dinner: "Of all the people Phil could have shared his office with, he got stuck with the only person in the world who shares his sense of humor". I remember the emails you sent entitled "Don't open this in front of the students, seriously!" and I remember the contents even better. Nevertheless, (or should I say, In addition to that), you are a great professional and a great manuscript editor. I am pleased we collaborated on Pharmacy Informatics, one of the first study books focusing on the importance of informatics in current pharmacy practice. It sure made me a better writer. Thank you for your friendship and being my wingman during my thesis defense.

En dan mijn tweede paranimf: Claartje. De keuze als paranimf was voor mij direct duidelijk. Op een of andere manier zijn onze carrières onlosmakelijk met elkaar verbonden en mede aan jou heb ik het vervolg van mijn carrière in Nederland te danken. Of zou je in elk Nederlands ziekenhuis aan de slag kunnen na één gesprek via Skype? Op professioneel vlak hebben we aan twee woorden genoeg en zijn we het altijd erg snel eens. En blijkbaar kunnen we ook niet meer dan 4 km hemelsbreed van elkaar af wonen. Het werd helemaal eng toen we ons huis lieten verbouwen door dezelfde aannemer, die zei: 'je moet van die hoge plinten nemen net als Claartje heeft, staat erg chique". Ik had nog nooit op jouw plinten gelet, maar voordat ik er erg in had zei ik "doe maar, moet goed zijn". En hij had gelijk, staat geweldig. Als je de volgende keer bij mij komt, zou ik maar op de plinten letten, dan voel je je helemaal thuis… Lieve Claartje, enorm bedankt voor jouw vriendschap, het geweldige werkplezier dat je me dagelijks geeft en jouw steun tijdens mijn verdediging.

Uiteraard ook een speciaal dankwoord voor de leden van de beoordelingscommissie, Prof. Dr. A.C.G. Egberts, Prof. Dr. H.J. Guchelaar en Prof. Dr. M.J. Postma. Beste Toine, Henk-Jan en Maarten. Het verzoek tot beoordeling van het manuscript werd aan jullie aangeboden rond de jaarwisseling: binnen 1 uur hadden jullie positief gereageerd om toe te treden tot de beoordelingscommissie en na 9 dagen was de goedkeuring een feit. Hartelijk dank voor jullie tijd en de interesse die jullie hebben getoond voor dit proefschrift.

Ook wil ik mijn collega's van het Ziekenhuis St Jansdal bedanken. Beste Frans, ook jij durfde het aan om een Nederlandse ziekenhuisapotheker na 5 jaar in de Verenigde Staten in dienst te nemen. Bovendien heb je mijn ambitie om te promoveren vanaf het begin ondersteund. Ook heb je samen met de andere ziekenhuisapothekers een bijdrage geleverd aan de tot standkoming van dit proefschrift door gedurende enkele weken tijdens de drukke dagdienst op twee verschillende manieren medicatiebewaking uit te voeren. Ik durfde dat bijna niet van jullie te vragen, maar jullie hebben zonder enig commentaar direct toegestemd om op deze manier aan mijn promotie bij te dragen. En Edith, zonder dat jij het wellicht beseft, heb jij dat ene "eureka" moment veroorzaakt dat tijdens het doen van onderzoek zo belangrijk is. Jij bent degene die tijdens de uitleg van de nieuwe manier van medicatiebewaking zei: "waarom maak je niet 1 clinical rule van alle interacties met dezelfde afhandeling? Bijvoorbeeld 1 rule van alle interacties die maagbescherming behoeven. Op deze manier kun je meerdere interacties in een keer valideren en zijn aanpassingen veel makelijker door te voeren". Briljant! Ook waardeer ik jouw continue kritische blik over het functioneren van Gaston. Ik begrijp dat ik deze waardering niet altijd laat blijken, maar jij houdt me continu scherp en haalt het beste in me naar boven. Ga vooral hiermee door!

Een dankwoord is geen dankwoord zonder het benoemen van het geweldige werk dat de apothekerassistenten van het Ziekenhuis St Jansdal dagelijks doen. Jullie zijn de ogen en oren van de ziekenhuisapotheker en als jullie een "niet pluis gevoel" hebben, dan is er eigenlijk altijd wel een serieus probleem. Ook zorgen jullie dagelijks voor een erg prettige werksfeer en hebben jullie me het grootste compliment gegeven dat mogelijk is: "Pieter, dat Gaston he, dat werkt echt goed. Maar, kunnen we niet wat meer meldingen krijgen…".

Ook wil ik de voorschrijvers van het St Jansdal ziekenhuis hartelijk bedanken voor hun feedback om de medicatiebewaking in het ziekenhuis te optimaliseren. In het bijzonder wil ik de medisch specialisten benoemen die zich vrijwillig hebben opgegeven om deel uit te maken van het expert team Gaston. Beste Rene, Margreet, Geriska, Kwok Wai, Amanda, Judith en Mariska: jullie hulp om de medicatiebewaking opnieuw in te richten, heeft niet ons niet alleen meer mogelijkheden gegeven om medicatiebewaking uit te voeren, maar heeft het proces ook efficiënter gemaakt voor de voorschrijver en de ziekenhuisapotheek. En we zijn nog maar net begonnen… Ik kijk er naar uit om op een vergelijkbare manier de doseringscontrole en controle op geneesmiddelgebruik bij gestoorde nierfunctie in te gaan richten.

Verder wil ik de Raad van Bestuur en de Directeur Financiën van het Ziekenhuis St Jansdal bedanken voor het ondersteunen van mijn ambitie om te promoveren. Beste Albert, Jan en Jan: optimalisatie van ICT processen in het ziekenhuis is een vereiste voor kwalitatief hoogwaardige zorg, maar dat hoef ik jullie niet uit leggen… Dank jullie wel voor jullie visie en het feit dat jullie deuren altijd open staan voor overleg.

En dan diegenen die medicatiebewaking d.m.v. clinical rules op basis van de G-standaard mogelijk hebben gemaakt, Prashant Nannan Panday en Paul de Clercq. Beste Prashant, door jouw pionierswerk konden we in het Ziekenhuis St Jansdal een vliegende start maken met het implementeren van beslissingsondersteuning. Jij was de drijvende kracht achter de integratie van de interactie- en nierfunctiebewakingsmodules van de G-standaard in het beslissingsondersteund systeem Gaston. Hierdoor waren de meest gehoorde barrières voor ziekenhuizen die willen starten met beslissingsondersteuning voor ons niet van toepassing: wij hoefden het wiel niet opnieuw uit te vinden en "slechts" de bestaande evidence based richtlijnen te verfijnen. Maar nog veel belangrijker: het is geweldig om met iemand met dezelfde visie van gedachten te wisselen. Dank je wel voor het delen van jouw ideeën en prettige samenwerking. En dan Paul. We kennen elkaar dit jaar 10 jaar. Jij bent het gezicht van de firma Medecs en zeker niet de standaard ICT systeem verkoper. Jij maakt de veel gehoorde kreet "we willen een partner zijn voor onze klanten om de zorg te verbeteren" echt waar. Implementatie van een nieuwe manier van medicatiebewaking is pionierswerk en vraagt niet alleen veel van het ziekenhuis maar ook van de ICT leverancier. Ik hoop nog vele jaren met je samen te kunnen werken. Maar… wellicht is het bezoeken van het St Jansdal met de auto misschien toch wel een betere optie, gezien de betrouwbaarheid van de NS. Hopelijk ben je op tijd voor de verdediging van mijn proefschrift"…

Ook wil ik drie personen specifiek benoemen uit het Catharina Ziekenhuis in Eindhoven: Erik Korsten, Arnout Roos en Rene Grouls. Jullie hebben mij vroeg in mijn carrière kennis laten maken met beslissingsondersteuning en meegedacht over de toepassingen van deze veelbelovende technologie in het ziekenhuis. Arnout, ik herinner me nog levendig dat je tijdens een onderzoeksoverleg op jouw kamer op de IC op een papiertje een stroomschema schetste, waarbij je zei:"het zou toch mooi zijn dat je bij elke stap in een clinical rule kunt zien welke patiënten de bewuste stappen hebben doorlopen". Ook weer zo'n "eureka" moment want deze "audit trail" gebruik ik nu dagelijks om nieuwe clinical