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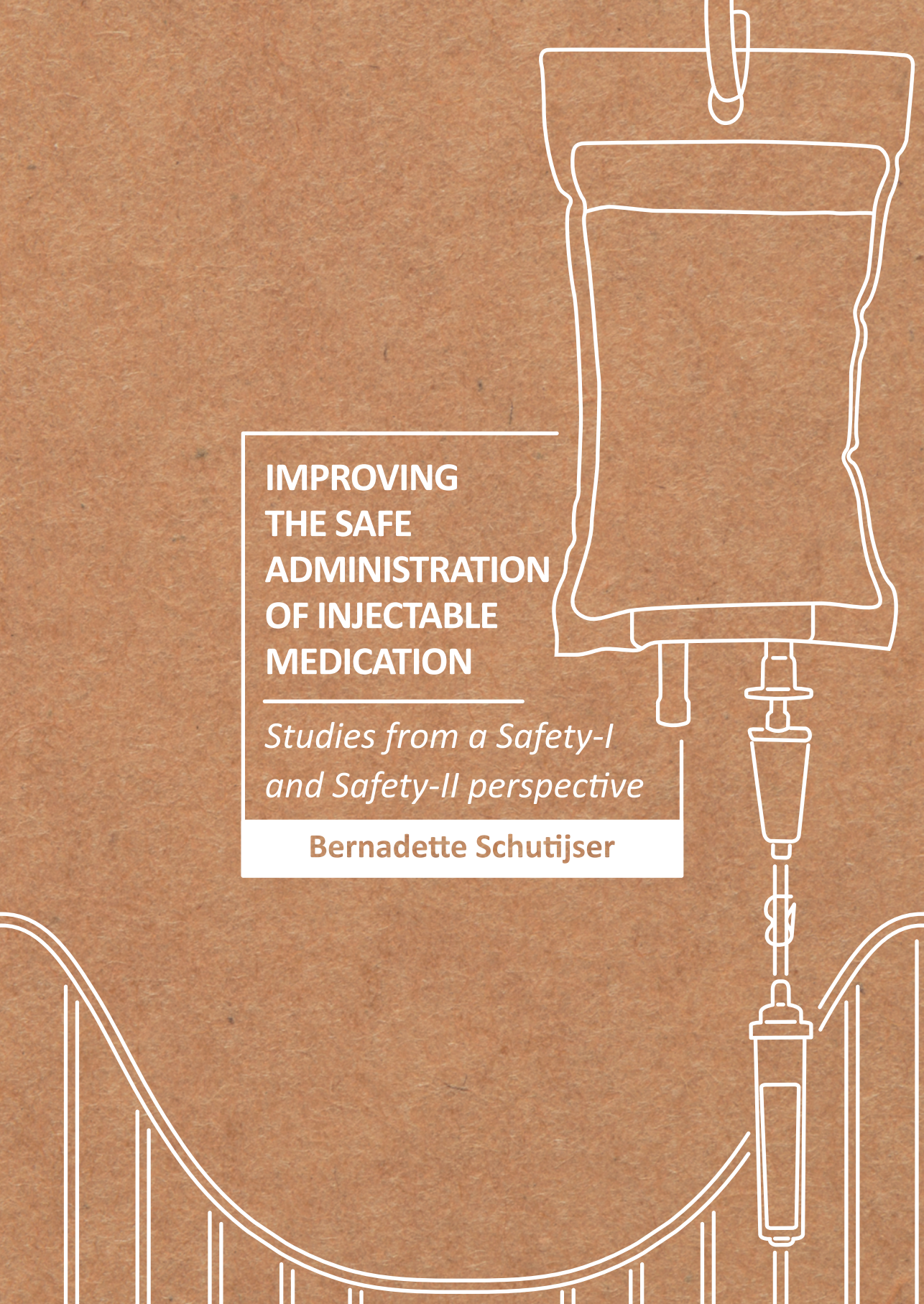
IMPROVING THE SAFE ADMINISTRATION OF INJECTABLE MEDICATION

Studies from a Safety-I and Safety-II perspective

Bernadette Schutijser



Improving the safe administration of injectable medication. Studies from a Safety-I and Safety-II perspective.

Bernadette Clara Francisca Maria Schutijser

Improving the safe administration of injectable medication. Studies from a Safety-I and Safety-II perspective.

The studies presented were conducted within the research group Safety4Patients of the Amsterdam UMC department of Public and Occupational Health / the Amsterdam Public Health research institute. The research presented in this thesis was funded by the Dutch Ministry of Health, Welfare and Sports (VWS).

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VRIJE UNIVERSITEIT

IMPROVING THE SAFE ADMINISTRATION OF INJECTABLE MEDICATION. STUDIES FROM A SAFETY-I AND SAFETY-II PERSPECTIVE.

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door

Bernadette Clara Francisca Maria Schutijser

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	dr. ir. M. Melles

paranimfen:	Petra Porte
	Marco Moesker

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Chapter 1

General Introduction

Diana (fictional case)

Diana is a nurse who has been working for over ten years in the internal medicine department of a general hospital. She has taken additional courses on lung diseases and currently she is an expert in her department. Today, she is taking care of Mrs Walters who has been admitted due to an exacerbation of her COPD. Mrs Walters suffers from shortness of breath and the physician has prescribed a furosemide infusion. Diana automatically notices the medication order in the Electronic Health Record (EHR) system. This system was implemented two years ago in the hospital, together with a barcode medication administration (BCMA) system. However, at the moment only one of the three BCMA systems has working Wi-Fi, so Diana has to wait to use a device. In the meantime, Diana prepares the medication according to the guideline and calculates the right infusion rate. She is ready to administer the medication at 4 p.m. when a physician enters the room and poses a few questions. After that, Diana continues with the medication administration and sets the infusion pump at a rate of 9.2 ml/hour. The evening shift is taken over by her nursing colleague Noelle, who checks on each patient at around 6 p.m. She suspects that the infusion rate for Mrs Walters is too high (normally the rate is around 1 or 2 ml/hour). Noelle recalculates the infusion rate, ending up with 1.2 ml/hour. She immediately adjusts the infusion pump and informs Mrs Walters that something went wrong. She also reports the incident in a digital report. The next day Diana returns to the department and reads about the incident. How could this have happened? Mrs Walters had to make several visits to the toilet, but luckily she has not sustained any permanent harm. However, Mrs Walters needs to stay an extra day in the hospital because of this incident.

Patient safety, Safety-I and Safety-II

Patient safety is still a serious healthcare issue, despite global efforts in the past 30 years.[1] Patient safety comprises the reduction and prevention of risks, errors and harm that occur to patients during the delivery of healthcare.[2] Currently, there are two perspectives when looking at patient safety: Safety-I and Safety-II.[3] Safety-I has been the standard for years and most research is done from a Safety-I perspective. It sees patient safety as a state in which 'as few things as possible go wrong', but when something goes wrong, it can result in adverse events (AEs).[3] According to Baker et al., an AE is an unintended injury that results in prolongation of a hospital admission, temporary or permanent disability or death and is caused by healthcare management instead of the patient's disease.[4] Safety-II is relatively new in healthcare and focuses on understanding how work that often goes well is done in clinical practice. It also

focuses on understanding resilience and variability in the process.[3] The main differences between Safety-I and Safety-II are that Safety-II focuses on all healthcare outcomes instead of only the negative outcomes (e.g. AEs), is more proactive and sees humans as a part of the solution instead of part of the problem.[3]

Safety-I perspective on injectable medication administration

Worldwide, approximately 43 million AEs occur every year,[5] and one in every 20 patients admitted to hospitals experiences preventable AEs.[6] The most common types of AEs occurring in hospitals are caused by medication, and are known as adverse drug events (ADEs).[6-8] Furthermore, studies show that 16-34% of all ADEs are caused by preventable medication errors.[6] The consequences of ADEs and medication errors may be considerable for a patient, such as prolonged admission or even death. The consequences of ADEs for society at large include additional costs, of up to 100,000 euros per error.[9]

In particular, ADEs with injectable medication have a higher risk of patient harm compared with non-injectable medication. Injectable medication consists of intravenous infusions and subcutaneous or intramuscular injections. Over 90% of all hospitalized patients receive some form of infusion therapy, including injectable medication.[10] Approximately 10% of all injectable medication administrations are associated with at least one error.[11] The high risk of patient harm is caused by the fact that this type of medication has an immediate therapeutic effect and can reach dangerous drug levels in a short period of time. So when injectable medication is not administered correctly, the error is often irreversible.

Keers et al. explored the causes of medication administration errors (MAEs), taking a Safety-I perspective. They pointed out that a strong theoretical focus is needed regarding the nature and complexity of these MAEs.[8] Then the key risk factors for these errors can be studied in order to develop multifaceted interventions.

Safety-II perspective on injectable medication administration

The injectable medication administration protocol can never cover all clinical practice situations. This means that in daily practice, circumstances may mean nurses are not able to follow the proceedings as intended and therefore need to adjust them to achieve their goal. This creates variation in the process. Nevertheless, administering injectable medication almost always goes well. Research on the injectable medication

administration process from this Safety-II perspective is relatively new and scarce. For example, Kaya et al. showed that Safety-II can be used to understand the complex process, in particular to reveal the non-linear interactions between different proceedings in a visual model.[12] Furthermore, another recent study shows some examples of process variability, for instance when multiple medication types cannot be administered at the same time through the same access point, when medications are infused faster, and when the thoroughness of the double check by a second nurse differs.[13] These situations can create variability further along in the process and then nurses might have to adjust or work around the protocol in order to administer the medication correctly.

Injectable medication administration in nursing practice

Administering injectable medication is a primary task of nurses. In the past decade, four main interventions changed the role of nurses in the medication administration process. First, to enhance knowledge about medication, training-related interventions have been applied, such as appointing and training dedicated nurses or arranging training led by pharmacists.[14] Second, hospitals have implemented guidelines to enhance uniformity in the medication administration process. Third, multifaceted interventions have been implemented to prevent interruptions during injectable medication administration.[15] As a consequence, there is more awareness about interruptions as a cause and contributor of medication errors.[8, 16] Furthermore, there is more awareness about multitasking and learning how to deal with interruptions.[15, 17] Fourth, information technology is increasingly used to support nurses during injectable medication administration.[14, 18] For example, a growing number of hospitals have implemented barcode medication administration (BCMA) systems. By scanning the barcode of a patient's wristband and/or the medication label, the system electronically assures that 'the right patient' gets 'the right medication'. These BCMA systems have effectively reduced some, but not all, types of medication errors.[18]

The four interventions are also noticeable in the clinical practice of our fictional nurse, Diana. She followed extra training to become an expert, works in line with the current guidelines, is aware that a physician interrupted her, and uses a BCMA system in the administration of injectable medication.

Complex process

In their efforts to improve the safe administration of injectable medication, most studies focused on single aspects of the process, for example, the organization (protocols),

tools (BCMA), and the nurses (knowledge). Yet it is widely acknowledged that ADEs are often caused by an accumulation of multiple failures in the system rather than one single event.[19] The medication process is complex,[20] and targeting just one aspect of this process is often too restrictive. A complex process contains large numbers of interacting elements, which are often nonlinear and dynamic.[21] The complexity may be especially present in unexpected interactions between the process elements. The more unexpected the interactions, the more difficult it will be to predict how processes will develop, and the more challenging it will be to improve medication safety in the long term. So it is important to understand the whole injectable medication administration system, including the complexity, in order to develop interventions.[22]

The Dutch situation

In the Netherlands, one of the first steps to improve safety in the medication administration process was the introduction of a safety management system programme. This programme was implemented between 2008 and 2012 in all Dutch hospitals and consisted of ten safety themes. One of the themes was 'safe preparation and administration of injectable medication'. It included two protocols, one for preparing and one for administering injectable medication. Today, both protocols are still the prevailing protocols; they contain 35 and 25 proceedings respectively for the safe preparation and administration of injectable medication. All proceedings are based on the 'five rights' of safe medication administration (right patient, right medication, right dose, right route, right time).[20] The implementation consisted of national conferences, a guide including advice and protocols, and training sessions about the safe preparation and administration of injectable medication. The aim of the theme was, from a Safety-I perspective, to reduce risks, errors and harm by achieving 100% compliance with both protocols.

In 2011 and 2012, Schilp et al. evaluated the extent to which the theme 'safe preparation and administration of injectable medication' had been implemented.[23] The study showed that protocol compliance was achieved in only 19% of the 2,154 observed administrations. Of the nine most important and identifiable proceedings in the protocol, the lowest compliance was observed in the following three: conducting hand hygiene, identifying the right patient and the check by a second nurse.[23] These findings gave rise to questions such as: what are the reasons for poor compliance, is the protocol feasible or too complex to follow in daily practice, and what barriers and facilitators are related to protocol compliance?

SEIPS 2.0

To understand the whole injectable medication administration system, including the complexity, the Systems Engineering Initiative for Patient Safety (SEIPS) model can be used as a theoretical framework.[22] The model was introduced in 2006 (SEIPS 1.0) and revised in 2013 (SEIPS 2.0).[24] By using SEIPS, we can understand interactions between the work system, processes (e.g. protocol compliance) and outcomes (e.g. MAEs).[22] The model includes risks related to the person (e.g. knowledge or motivation), risks related to the internal or external environment (e.g. noise or the design of departments), risks related to the organization (e.g. teamwork or policies), risks related to tools and technologies (e.g. devices or resources) and risks related to tasks (e.g. variety of tasks or autonomy). Furthermore, an adaptation phase was incorporated in the SEIPS 2.0 model.[24] With this phase, the model takes into account the fact that processes are not linear but dynamic, and that nurses need to react and adapt constantly to unexpected situations in the process (e.g. complexity). Therefore, the adaptation phase is in line with the Safety-II perspective. The Safety-I perspective is mainly reflected in the processes and outcomes phases of the SEIPS 2.0 model (Figure 1).

Hence, by describing the aspects of the work system in addition to processes and outcomes, SEIPS 2.0 is best suited to detail the whole routine clinical process in which Diana needs to function in order to ensure that the right injectable medication is administered in the right dose, by the right route, at the right time and to the right patient.

Objective

The aim of this PhD thesis is to gain a deeper understanding, from a Safety-I and Safety-II perspective, of the complex process of injectable medication administration by hospital nurses. The SEIPS 2.0 model was used as a theoretical base. By gaining a deeper understanding, we aim to reduce the risk for future patients of experiencing an injectable medication administration error during their hospital stay. To achieve this aim, we formulated two research questions:

1. What is the current nurse compliance with the protocol for safe injectable medication administration in hospitals and what is the current frequency of adverse drug events?

2. Which interactions in the work system and adaptations occur in nursing practice during injectable medication administration?

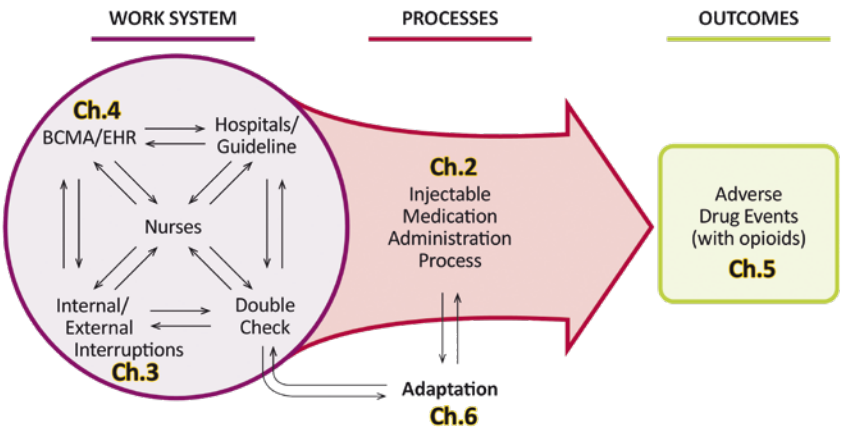

Figure 1 The injectable medication administration process from a Systems Engineering Initiative for Patient Safety (SEIPS) 2.0 perspective, incorporating the chapters of this PhD thesis. BCMA = BarCode Medication Administration, EHR = Electronic Health Record

Thesis outline

To answer these questions, we conducted five studies, which are described in **Chapters 2-6**. The first research question is addressed in **Chapters 2, 4 and 5** and the second research question in **Chapters 2, 3 and 6**. Each chapter focuses on one specific aspect in the SEIPS 2.0 model and all chapters focus on the nurse as the 'person' at the centre of the work system. Furthermore, each chapter also describes other relationships within the SEIPS 2.0 model.

Chapter 2 focuses on the process of injectable medication administration. In this observational study, we determined nurse compliance with the protocol for safe injectable medication administration. The results were compared to the first evaluation study (conducted in 2011/2012) to understand whether compliance has improved over time. Moreover, we assessed which improvement strategies hospitals implemented regarding all aspects of the SEIPS 2.0 work system.

Chapter 3 focuses on the external environment in which nurses administer injectable medication. In this observational study, we analysed the frequency, causes and factors associated with interruptions during injectable medication administration in hospitals. The data used in this study were collected during both the first and the

second evaluation of the 'safe preparation and administration of injectable medication' theme.

Chapter 4 focuses on technology used by nurses when administering injectable medication. In this cross-sectional study, we aimed to extract real-time information about nurse compliance with the protocol for safe injectable medication administration in order to create a continuous feedback loop. Therefore, we assessed whether it is feasible to monitor nurse compliance with the protocol by reusing routinely registered EHR data. We interviewed healthcare professionals about the availability of data elements in their hospitals' EHR system.

Chapter 5 focuses on undesirable outcomes in the medication process: adverse drug events (ADEs). In this study we conducted a post-hoc analysis of data collected during three Dutch retrospective patient record review studies. The goal was to provide a detailed description of the underlying nature of ADEs. This chapter focuses on one specific drug type, namely opioids, because opioids are often given by nurses as injectable medication and they have fast therapeutic effects with possibly severe or fatal patient outcomes.

Chapter 6 focuses on adaptation by nurses in the context of injectable medication administration. In this qualitative study, we focused on one of the protocol proceedings that is most likely to be omitted: the double check during injectable medication administration. We determined the extent to which work-as-imagined according to the protocol matched work-as-done in current clinical nursing practice.

Finally, the general discussion is presented in **Chapter 7**. In this chapter we answer the two main research questions, discuss the methodological considerations, and end with recommendations for future research and for current and future nurses who will be administering injectable medication.

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Chapter 2

Nurse compliance with a protocol for safe injectable medication administration: comparison of two multicentre observational studies.

B.C.F.M. Schutijser, J.E. Klopotowska, I.P. Jongerden,
P.M.M. Spreeuwenberg, C. Wagner, M.C. de Bruijne

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ABSTRACT

Objectives Medication administration errors with injectable medication have a high risk of causing patient harm. To reduce this risk, all Dutch hospitals implemented a protocol for safe injectable medication administration. Nurse compliance with this protocol was evaluated as low as 19% in 2012. The aim of this second evaluation study was to determine whether nurse compliance had changed over a 4-year period, what factors were associated over time with protocol compliance and which strategies have been implemented by hospitals to increase protocol compliance.

Methods In this prospective observational study, conducted between November 2015 and September 2016, nurses from 16 Dutch hospitals were directly observed during intravenous medication administration. Protocol compliance was complete if nine protocol proceedings were conducted correctly. Protocol compliance was compared with results from the first evaluation. Multilevel logistic regression analyses were used to assess the associations over time between explanatory variables and complete protocol compliance. Implemented strategies were classified according to the five components of the Systems Engineering Initiative for Patient Safety (SEIPS) model.

Results A total of 372 intravenous medication administrations were observed. In comparison with 2012, more proceedings per administration were conducted (mean 7.6, 95% CI 7.5 to 7.7 vs mean 7.3, 95% CI 7.3 to 7.4). No significant change was seen in complete protocol compliance (22% in 2016); compliance with the proceedings 'hand hygiene' and 'check by a second nurse' remained low. In contrast to 2012, the majority of the variance was caused by differences between wards rather than between hospitals. Most implemented improvement strategies targeted the organisation component of the SEIPS model.

Conclusions Compliance with 'hand hygiene' and 'check by a second nurse' needs to be further improved in order to increase complete protocol compliance. To do so, interventions focused on nurses and individually tailored to each ward are needed.

INTRODUCTION

Injectable medication therapy is considered an essential component of current healthcare delivery. Over 90% of all hospitalised patients receive some form of this therapy.[1] Injectable medication therapy comprises medication that is administered directly into body tissue or the circulatory system.[2] It includes primarily intravenous medication infusions and injections, but also other administration routes such as subcutaneous and intramuscular injections. The benefits of intravenous medication, such as an immediate therapeutic effect and the possibility to reach therapeutic drug levels in a short period of time, provide at the same time a high risk for patient harm.[1, 3-6] This high risk arises from the fact that errors with intravenous medication are almost irreversible. Errors with intravenous medication occur frequently during hospital admission. The probability of making at least one error at any stage of the intravenous medication process is 73%.[6] Besides, most errors occur during medication administration. These medication administration errors (MAEs) can be defined as 'deviations of a drug from a physician's prescription, the hospital's policy or the manufacturer's instructions'.[7] It is five times more likely that an MAE occurs when intravenous medication is administered compared with non-intravenous medication.[4]

Using a protocol for safe administration of injectable medication contributes to a reduction in medication errors in hospitals.[8-12] In Dutch hospitals, a protocol for safe administration of injectable medication was implemented in 2009 as part of the National Patient Safety programme.[13] This prevailing protocol contains 35 proceedings for preparing and 25 proceedings for administering injectable medication, and is based on the 'five rights' of safe medication administration (right patient, right medication, right dose, right route, right time).[3] The goal of the National Patient Safety programme is to achieve 100% compliance with this protocol. In other countries, comparable protocols have been implemented, and protocol steps such as 'patient identification' and 'hand hygiene' are generally seen as important and included in these protocols.[14-16]

Between November 2011 and December 2012, Schilp et al[17] conducted a prospective observational study in 19 Dutch hospitals to evaluate the implementation of the Dutch protocol for safe administration of injectable medication. In total, 2154 intravenous medication administrations by nurses were directly observed, monthly, during a 12-month period, and complete compliance with the protocol was observed

in 19% of the observations. The least conducted proceedings were found to be 'patient identification', 'hand hygiene' and 'check by a second nurse'. Schilp et al[17] concluded that the implementation of the protocol was inadequate and recommended that more time was needed to increase protocol implementation.

In response to the results of the evaluation study of 2012, Dutch hospitals — supported by the Dutch associations of nurses and hospital pharmacists — proposed follow-up actions to improve protocol compliance, for example, appointing an injectable medication nurse champion, whose responsibility would be to supervise the implementation of the protocol at the hospital and ward levels.[18] In addition, barcode medication administration (BCMA) systems were introduced and increasingly used in Dutch hospitals. A BCMA system enables nurses to scan the barcode on the patient's wristband and/or medication label to improve compliance with patient identification. Implementation of BCMA systems in hospitals has been associated with a decrease in MAEs.[19] Also, the protocol compliance was a focus of external safety audits by the Dutch Inspectorate of Health Care. Whether these various follow-up actions had impact on nurse compliance with the protocol for safe injectable medication administration is unknown.

Since the most recent evaluation study was conducted 4 years ago, and tracking performance is helpful in determining protocol implementation,[14] we conducted a second prospective observational study to evaluate the current implementation of the protocol for safe injectable medication administration in Dutch hospitals. In addition, we wanted to know which factors are associated over time with complete protocol compliance, since compliance can be influenced by various characteristics (i.e., organisational, individual and environmental).[20,21] Therefore, the aims of this study were (1) to determine whether complete protocol compliance and compliance with individual proceedings have changed compared with the first evaluation study conducted in 2011/2012, (2) to investigate which hospital and administration factors are associated over time with complete protocol compliance and with three individual protocol proceedings as compared with the first evaluation, and (3) to provide an overview of improvement strategies implemented by hospitals to increase protocol compliance.

METHODS

Design and setting

For the purpose of this second evaluation, a prospective observational study was conducted in 16 Dutch hospitals from November 2015 to September 2016. These 16 hospitals included one university hospital, six tertiary teaching hospitals and nine general hospitals. The hospitals were randomly selected to participate and originated from the representative (stratified on area and type of hospital) sample of 19 hospitals that participated in the first evaluation in 2011/2012. Of these 19 hospitals, 13 agreed to participate in the second evaluation. To assure a representative measurement for all Dutch hospitals and to gain a sufficient sample size for comparison with the first evaluation, three new hospitals were selected from a new random sample. The main reasons not to participate in the second evaluation were time constraints due to the implementation of a new hospital electronic health record system, and the fact that a similar measurement had recently been conducted by hospital staff. The Strengthening the Reporting of Observational Studies in Epidemiology guideline for reporting observational studies was used to enhance accurate and complete reporting of this study.[22]

Participants

Nurses working on three hospital wards — intensive care (IC), internal medicine and (general) surgery — were directly observed during the administration of intravenous medication. These three ward types were considered to be representative of protocol compliance in the whole hospital. All (trainee) nurses involved in the administration of intravenous medication on the study wards were eligible for this study. Verbal consent from the nurses and (wherever possible) the patients was obtained to conduct the observation. Nurse managers of the participating wards were fully informed about the purpose of the study. Nurses were informed about the goal of the observations (correct administration of injectable medication) but not about the specific protocol proceedings being observed, in order to prevent bias (Hawthorne effect).[23] However, nurses could be aware of the observed proceedings on the observation form, since all proceedings follow the current protocol, which is publicly accessible in all hospitals. Participation in the study was voluntary and anonymous for nurses; if a nurse did not want to participate, then he/she was not observed.

Data collection

Data collection was similar to the first evaluation study.[17] In summary, to determine complete protocol compliance and compliance with individual proceedings, direct observations were conducted for patients ≥18 years of age during the intravenous medication rounds from 06:00 to 22:00. Parenteral nutrition, intravenous chemotherapy and acute medications were not observed because for these medications other administration protocols apply. At each hospital, one trained nurse researcher (BS) conducted the observations during two consecutive weekdays. A standardised observation form was used to evaluate performances of the individual proceedings. The form included the nine most important and identifiable administration proceedings from the protocol, predetermined and described by an expert team (Table 1). All correctly conducted proceedings were marked on the observation form. Moreover, a minimum of three nurses per ward and a maximum of three administrations per nurse were observed to correct for between-person variation.

Table 1 Protocol proceedings for administering injectable medication*

Step	Explanation
1. Check medication	Checking the drug on the basis of a medication list or distribution list.
2. Prepare administration	Preparation of administration: setting pump and speed of injection.
3. Collect materials	Gathering the needed materials and checking the administration label.
4. Patient identification	Identifying the patient either electronically or by checking the name, date of birth, patient number and type of medication.
5. Hand hygiene	Hand disinfection before administration or wearing gloves during administration.
6. Check flow infusion	Checking the intravenous medication line before administering the medication.
7. Check pump mode	Checking or setting the pump mode before administering medication.
8. Check by a second nurse	Having a second nurse check the patient, medication, administration route, and administration rate.
9. Sign medication order	As the administrator, signing the medication order.

**As published in Schilp et al. (2014)[17]*

To detect a 10% improvement in protocol compliance at a 5% significance level, at least 300 observations were needed during the second evaluation (ß=0.8). This means 20-21

observations per hospital and 6-7 observations per ward. Consequently, only one data collection moment per hospital was needed and planned. During the first evaluation, data were collected during 10 moments (once a month) per hospital to follow process variation over different months and calculate an average compliance rate.

Protocol compliance

The primary outcome was the complete protocol compliance with the Dutch injectable medication protocol. Each observed intravenous medication administration was scored (0-9) and then dichotomised into complete compliance (nine safety proceedings conducted) and incomplete compliance (≤8 safety proceedings conducted).[17] The secondary outcomes were the mean number and percentage of correctly conducted individual proceedings, in particular compliance with 'patient identification', 'hand hygiene' and 'check by a second nurse'. These three proceedings were the three least conducted protocol proceedings during the first evaluation.

Factors associated with protocol compliance

To determine factors associated over time with complete protocol compliance and selected individual protocol proceedings, additional variables were registered on the observation form: type of hospital (university, tertiary, general), type of department (general surgery, internal medicine, IC), time of administration (morning (05:00-12:00), afternoon (12:00-18:00) and evening (after 18:00)), type of administration (by intravenous infusion, bolus intravenous injection or intravenous syringe pump) and name and type of medication.

Improvement strategies implemented to increase protocol compliance

To identify improvement strategies implemented by the hospitals, two short interviews were conducted with a quality and safety officer and the head or senior nurse of each ward. During the first interview conducted during the intake, questions regarding the availability of an injectable medication champion, injectable medication education programmes and interruption prevention strategies (i.e., do-not-disturb vests) were asked. The second interview followed after the observations and comprised questions regarding the availability and use of information technology to support the injectable medication administration process. In addition, local injectable medication administration protocols were collected to identify other potential improvement strategies. The identified strategies were classified according to the five components of the work system as described in the Systems Engineering Initiative for Patient Safety

(SEIPS) model: organisation, technology and tools, person, tasks, and environment.[24-26] The SEIPS model provides a comprehensive theoretical framework for understanding interactions between the components in the work system, processes (e.g., protocol compliance) and outcomes (e.g., MAEs) in healthcare.[27]

Data analysis

All results collected on the observation forms were entered in an online database: NETQuestionnaires. Descriptive statistics were used to describe hospital type, ward type, administration time, administration type and medication type. Differences between mean number of conducted protocol proceedings were tested with one-way analysis of variance statistics. Differences in the protocol compliance (complete protocol compliance: yes or no) were tested with χ^2 statistics.

To assess the associations over time between potential explanatory variables (i.e., hospital type, ward type and administration time) and protocol compliance, separate univariate multilevel logistic regression analyses were conducted for four dependent variables: complete protocol compliance (yes/no), patient identification compliance (yes/no), hand hygiene compliance (yes/no) and check by a second nurse compliance (yes/no).[28] A three-level multilevel structure was used, whereby the observations were clustered within wards and the wards within hospitals. The explanatory variables were used as independent variables. The fixed effects for the first evaluation were the average value of the intercepts. The fixed effects for the second evaluation were the regression coefficients to the extent that the second evaluation deviated from the first evaluation. In all analyses, a corrected model was used with adjustment for the other two explanatory variables.

In addition, the between-hospital and ward-level variance was split into two elements, one for the first and one for the second evaluation. Also the covariation between both evaluations was modelled at the hospital and ward levels. This resulted in intraclass correlations (ICCs) for each evaluation separately, which indicated whether the relative contribution of the hospital and ward levels differed between both evaluations. Based on the variances and covariance, the correlation between participated wards was calculated.

Descriptive analyses were conducted using IBM SPSS Statistics V.20 and the multilevel analyses using MlwiN V.2.30 (University of Bristol). The multilevel logistic models were

calculated using penalised quasi-likelihood second order (or when this failed, first order), with constrained level 1 variance. For all analyses, P values ≤0.05 were considered statistically significant.

Table 2 Descriptive statistics of IV medication observations during the two evaluation studies.

	First evaluation	Second evaluation
	2011/2012	**2015/2016**
Number of observations	2154	372
Number of hospitals	19	16
Range of observations per hospital	70-196	20-28
Type of hospital		
University	297 (13.8)	22 (5.9)
Tertiary	750 (34.8)	139 (37.4)
General	1107 (51.4)	211 (56.7)
Type of department		
Internal Medicine	643 (29.9)	129 (34.7)
(General) Surgery	771 (35.8)	112 (30.1)
Intensive Care	671 (31.2)	131 (35.2)
Other	69 (3.2)	0 (0)
Administration time		
Morning (6AM-12PM)	771 (35.8)	92 (24.7)
Afternoon (12PM-6PM)	1257 (58.4)	243 (65.3)
Evening (after 6PM)	126 (5.8)	37 (9.9)
Type of medication (most common)		
Antibiotics	1323 (61.4)	236 (63.4)
Analgesics	167 (7.8)	38 (10.2)
Gastrointestinal medication	178 (8.3)	16 (4.3)
Anesthetics	27 (1.3)	16 (4.3)
Electrolytes	83 (3.9)	14 (3.8)
Corticosteroids	85 (3.9)	11 (3.0)
Type of administration		
By IV syringe pump	29 (1.3)	48 (12.9)
By bolus IV injection	66 (3.1)	51 (13.7)
By IV infusion	2059 (95.6)	273 (73.4)

Data is presented as n (%), unless stated otherwise. IV = Intravenous

RESULTS

In total, 372 intravenous medication administrations were observed, with a range of 20-28 observations per hospital (Table 2). Most observations had been conducted at general hospitals (57%), internal medicine (35%) and IC wards (35%), during the afternoon (65%), and of administrations by intravenous infusion (73%).

Protocol compliance

Table 3 shows the mean number of correctly conducted protocol proceedings and percentages of intravenous medication administrations with complete protocol compliance during both evaluations. On average, more proceedings per intravenous medication administration were conducted during the second evaluation compared with the first evaluation: 7.6 (95% CI 7.5 to 7.7) vs 7.3 (95% CI 7.3 to 7.4) (P<0.001). However, no significant change was seen in complete protocol compliance during the second evaluation compared with the first evaluation: 22.3% (95% CI 18.1% to 26.5%) vs 19.4% (95% CI 17.7% to 21.1%) (P=0.194).

Table 3 Comparison of the first and second evaluation study in conducting the complete protocol.

	First evaluation 2011/2012	**Second evaluation 2015/2016**	**p-value**
Conducted proceedings, mean (CI)	7.3 (7.3 to 7.4)	7.6 (7.5 to 7.7)	<0.001*
Complete protocol compliance, % (CI)	19.4 (17.7 to 21.1)	22.3 (18.1 to 26.5)	0.194†

** tested by one-way analysis of variances (ANOVA) test*
† tested by Chi-Square (X^2) test, CI = 95% Confidence Interval

Three proceedings were least often conducted: 'patient identification' (80.1%), 'hand hygiene' (63.2%) and 'check by a second nurse' (47.3%) (Figure 1). Compliance rates with the other six proceedings varied between 93% and 100%.

Compliance with 'patient identification' improved significantly from 61% (95% CI 58.0% to 62.1%) in the first evaluation to 80% (95% CI 76.1% to 84.2%) in the second evaluation (P<0.001). During the second evaluation, patient identification was conducted in three ways. First, 49% of the nurses identified their patient by a physical check (e.g., asking the patient's name, and/or date of birth, or by checking information on the patient's wrist-band). Second, 16% of the nurses identified the patient by using a barcode scanner in addition to the physical check, or by only using a barcode scanner. Third, in 15% of

the observations, all on IC wards, the nurse to patient ratio was one nurse per patient. Hence, patient identification was scored as conducted in all these observations.

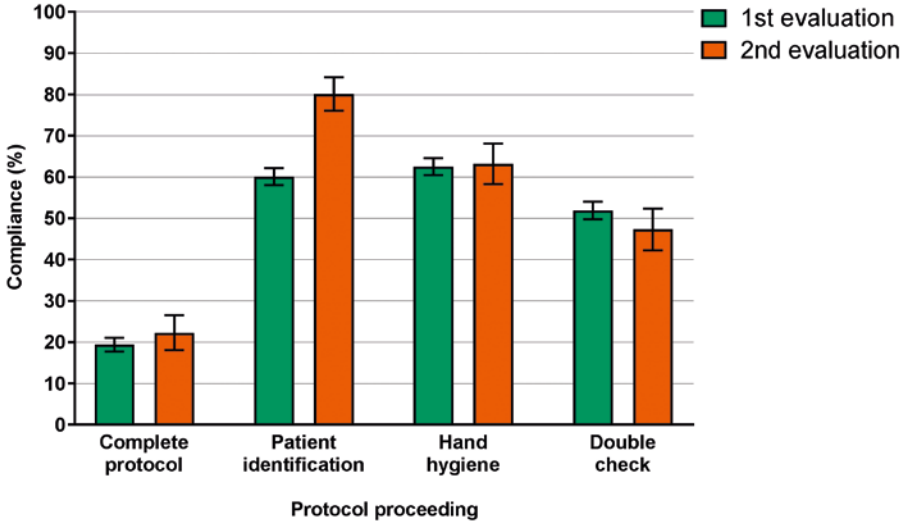

Figure 1 Compliance percentages with the complete protocol and three individual proceedings within the first (n=2154) and second (n=372) evaluations. Results are presented with 95% CI. Compliance was tested by X^2 statistics. Compliance with the six other proceedings varied between 93% and 100%, and was significantly increased for 'prepare administration', 'check flow infusion' and 'check pump mode', and significantly decreased for 'check medication'.

Factors associated with protocol compliance

The univariate associations over time between three potential explanatory variables (e.g., type of hospital, ward type and time of administration) and four dependent variables (complete protocol compliance, compliance with patient identification, compliance with hand hygiene and compliance with check by a second nurse) were investigated. A positive association was found between all three explanatory variables and compliance with 'patient identification'. Compliance with the proceeding 'patient identification' improved significantly over time for all the different administration times (morning, afternoon and evening) (Table 4), all the different ward types (IC, internal medicine and (general) surgery) (Supplementary Table 1) and in tertiary teaching hospitals (Supplementary Table 2). Other investigated hospital and administration-related variables were not associated with complete protocol compliance or compliance with the other two analysed individual proceedings. Furthermore, multilevel analyses showed that the hospital variance became very small and was estimated as 0 (Table 4).

On the other hand, ward variance increased. For example, 0% (ICC=0.00) of the total variance in the association between 'patient identification compliance' and 'administration time' can be explained by individual hospitals and 50% (ICC=49.70) by individual wards (Table 4). During the first evaluation, opposite results were found, in which the ICCs of hospital variance were high and the ICCs of ward variance were low. In addition, at the ward level, the correlation between the two evaluations was 0.52, indicating that wards having had a high compliance in the first evaluation also had a high compliance in the second evaluation. Vice versa, wards that had a low compliance in the first evaluation also had a low compliance in the second evaluation.

Table 4 Multilevel analyses of the association between administration time and compliance with the proceeding 'patient identification' during the first and second evaluation.

	First evaluation 2011/2012		Second evaluation 2015/2016	
	N	**Estimate (SE)**	**N**	**Estimate (SE)**
Fixed effects				
Patient identification in morning	771	0.19 (0.46)	92	1.97 (0.61)*
Patient identification in afternoon	1257	0.39 (0.45)	243	1.58 (0.53)*
Patient identification in evening	126	0.39 (0.55)	37	1.64 (0.76)*
Random effects				
Hospital level ICC		38.09		0
Hospital level variance		3.24 (1.21)		0 (0)
Hospital level covariance and correlation		0 (0); 0		
Department level ICC		23.27		49.70
Department level variance		1.13 (0.34)		2.40 (0.78)
Department level covariance and correlation		0.85 (0.46); 0.52		

**p<0.05, ICC=Intra Class Correlation, SE=Standard Error*

Improvement strategies implemented to increase protocol compliance

Figure 2 shows nine identified strategies implemented by hospitals with the aim to improve compliance with the injectable medication administration protocol. Most strategies were classified according to the SEIPS model as targeting the organisation component (n=3), followed by tasks (n=2) and technology and tools components (n=2). Only one intervention targeted the person and one the environment component.

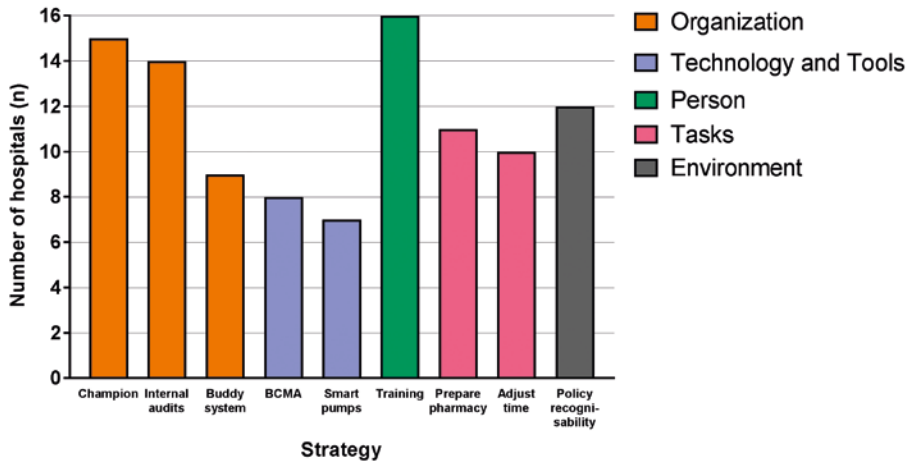

Figure 2 Identified strategies implemented by the hospitals during the second evaluation (n=16 hospitals), classified according to the individual components of the Systems Engineering Initiative for Patient Safety model (e.g., organisation, technology and tools, person, tasks, and environment). BCMA = barcode medication administration.

Hospitals implemented on average six strategies, ranging between four and nine strategies. Organisation component strategies were appointing an injectable medication champion (15 participating hospitals), conducting internal audits (14 participating hospitals) and having a buddy system in which two nurses double-check their buddies' intravenous medication administrations (nine participating hospitals). Most appointed injectable medication champions were hospital pharmacists, and the way in which this task was performed varied greatly between hospitals. BCMA systems (eight participating hospitals) and smart pumps (seven participating hospitals) were the implemented tools and technology improvement strategies. Smart pumps are infusion pumps with software that creates a library of medication administration protocols.[29] A personal component-related strategy included training and education (e.g., e-learning modules and introduction modules) for nurses to enhance their knowledge (16 participating hospitals). Task-related strategies included shifting the tasks of injectable medication preparation from nurses on hospital wards to pharmacy technicians in the (central) hospital pharmacy (11 participating hospitals) and adjusting the timing of the check by a second nurse to the beginning of a shift (10 participating hospitals). Finally, having policy regarding the recognisability of nurses during injectable medication administration (12 participating hospitals) was the only environmental component-related strategy identified. Most combined strategies were training and education, and appointing an injectable medication champion.

DISCUSSION

Compliance with individual proceedings of the Dutch protocol on administering injectable medication has improved over 4 years, but complete protocol compliance did not significantly change. In 19% of the observations in 2011/2012, the protocol was completely conducted, compared with 22% in 2015/2016 (P=0.194). In contrast to the first evaluation study, differences in protocol compliance between wards were greater, and differences between hospitals were smaller. Furthermore, according to the SEIPS model, most improvement strategies targeted the organisation component of the injectable medication administration process.

Compliance with the proceeding 'patient identification' increased significantly to an average of 80%. Using a BCMA system to electronically identify patients may have contributed to the higher compliance rate of this proceeding in our study. Taliercio et al[30] showed that nurses experience using a BCMA system to identify patients as a major advantage. In our study, a BCMA system was implemented as a strategy in eight (50%) participating hospitals and used in 16% of all observations. Since an increasing number of Dutch hospitals will implement a BCMA system in the next few years and using BCMA will be further integrated in daily nursing practice, we expect that compliance with this proceeding will further increase. A reason for non-compliance with this proceeding can be that nurses believe they know their patients well enough not to ask the patients' name and date of birth.[31] Other observational studies on medication administration reported lower compliance rates (33%-80%), but did not specify whether identification was supported by a BCMA system.[15, 16, 32-35]

Compliance with the proceeding 'hand hygiene' remained unchanged (63%). This may be explained by the lack of improvement strategies specifically targeting hand hygiene compliance in the participating hospitals. The compliance of 63% in our study is comparable with the study of Helder et al,[36] which showed a hand disinfection rate during medication administration of 58% after a mutual feedback intervention. Improving hand hygiene remains a challenge in many hospital processes, not only during medication administration. A recent review showed that the overall mean hand hygiene compliance rate after interventions was 57%.[37] Huis et al[38] explored determinants of hand hygiene improvement strategies and showed that addressing knowledge, awareness, action control and facilitation is not enough to improve hand hygiene compliance. Baseline compliance rates of hand hygiene vary strongly in the literature

(20%-60%).[39] Also, the increased compliance with hand hygiene appears temporary in most intervention studies. Huis et al[38] recommended that social influence, attitude, self-efficacy and attention (person component of SEIPS) should be taken into account in new strategies, and that they should preferably be focused on the whole nursing team.

Compliance with the proceeding 'check by a second nurse' also remained unchanged (47%). Of all four subchecks of this proceeding (e.g., 'right patient', 'right medication', 'right administration route' and 'right administration rate'), the subchecks on 'right patient' and 'right medication' were most often conducted. These subchecks are supported by barcode scanning systems while the subchecks on 'right administration route' and 'right administration rate' are not. Therefore, for these checks on route and rate of intravenous infusion, a second nurse at the patient's bedside was necessary. This is a task that depends on nurse capacity and/or workload. In theory, the check by a second nurse for all intravenous medications has become a standard and critical proceeding. Alsulami et al[40] described that most healthcare professionals prefer the double-check, but that staff shortage can prevent for correctly conducting this proceeding. In practice, we observed that increased workload, indeed, may prevent this standard. Therefore, this proceeding must be prioritised in future studies. In order to facilitate the check by a second nurse, intervention strategies such as adjusting the timing of the check by a second nurse (10 hospitals) and having a buddy system (9 hospitals) have been implemented in the participating hospitals. However, qualitative studies on the check by a second nurse showed that the focus should lie on training and education, automating the proceeding and seeing the check by a second nurse as a method to share opinions.[41]

Using the SEIPS model for classifying strategies implemented by the hospitals revealed that most strategies targeted the organisation of the injectable medication administration process. Less strategies targeted the person and environment. This is in contrast with Berdot et al, who showed that most interventions aiming to reduce MAEs targeted technology and tools (e.g., automated medication dispensing systems, BCMA systems) and the person (e.g., interactive CD-ROM program or simulation-based learning). This can be explained by the fact that Berdot et al[42] included seven studies, mostly randomised controlled trials, which had MAE rates as outcome measure. Our observational study identified current improvement strategies used in daily practice. Knowing that strategies are most often complex and multifaceted, it is recommended to determine potential barriers prior to implementing a strategy.[42] These barriers

can be found in all SEIPS components. Apparently, Dutch hospitals have been trying to overcome barriers in the injectable medication process by implementing mostly organisational strategies at the hospital level. This is, however, not enough to increase protocol compliance. Since most variations were seen at the ward level, rather than hospital level, future strategies should be tailored to individual wards. It is important to focus these strategies on individuals (e.g., nurses, patients, families) and the environment. On the other hand, the protocol itself can also be a focus for discussion. Since two evaluation studies concluded that the implementation of the protocol has not yet been accomplished, it may be necessary to take a critical look at which proceedings are essential and whether the proceedings reflect all SEIPS components.

One of the strengths of this study is that more than 20% of all Dutch hospitals participated in one of the two evaluation studies, 19 during the first evaluation and 16 during the second evaluation. This random and representative sample ensures that the results can be generalised to the Dutch hospital setting. Furthermore, similar observation list, observation procedure and training of researchers were used during both evaluations, and 13 hospitals participated in both evaluations. Therefore, we could compare the two evaluations reliably. However, several uncertainties may have limited the generalisability of our results. First, this second study comprised one data collection moment compared with 10 data collection moments in 2011/2012. As a consequence, the compliance rate reflects one moment in time, compared with an average compliance rate. Nevertheless, we conducted more than the intended 300 observations, and on this basis we think the results reflect current nursing practice. Second, almost all observations (96%) were conducted by one researcher, which could have created error of leniency or severity (i.e., rating observations, in particular, positively or negatively).[43] However, in our study, using one observer ensured that all administrations were measured in the same way and it appeared that the compliance rates were in line with previous studies. Third, no data about nurse-related characteristics (degree of education and years of experience) and workload-related characteristics (turnover rates, stability of the nursing workforce, stability of the nurse to patient ratio over the years and number of drugs to be dispensed per round per nurse) have been collected. This may have resulted in an incomplete overview of factors associated with protocol compliance. The nurse-related characteristics have not been collected because we used the same observation form as in the first evaluation, which did not include these characteristics. The workload-related characteristics have not been collected because these data appeared too complex and the way these variables are calculated varied per ward and per hospital. Fourth, not all

injectable medications were included in the observations, only intravenous medications. Since chemotherapy, and less invasive injectable medication administration routes, such as intramuscular and subcutaneous injections, are increasingly used in hospitals, it would be recommendable to also observe administration of these types of injectable medications in the future. Fifth, the fact that nurses were aware of being observed may have resulted in more compliance. As a consequence, compliance rates could have been overestimated. This so-called Hawthorne effect is a known challenge within observational studies.[44] To minimise this effect in our study, the researcher was discreet during observations and did not give performance feedback during or after observations. Finally, since the information about implemented improvement strategies was collected during two interviews, it is uncertain how well these strategies are implemented in daily practice on the wards. Therefore, this information provides only a first impression. To be able to determine associations between strategies and protocol compliance, we would recommend to perform a new study aiming to observe the execution of the mentioned strategies on the wards.

CONCLUSION

In conclusion, our results show that conducting all nine proceedings included in the protocol for safe injectable medication administration by Dutch hospital nurses remains challenging. Importantly, compliance with patient identification during intravenous medication administration has improved and implementing BCMA systems may have contributed to this finding. Therefore, further implementation of BCMA systems in hospitals is recommended. Compliance with 'hand hygiene' and 'check by a second nurse' needs to be further improved in order to increase complete protocol compliance and reduce the risk of MAEs. To improve compliance with these proceedings, other interventions are needed, preferably focused on nurses, and individually tailored to each ward.

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Supplementary Table 1 Multilevel analyses of the association between ward type and compliance with the proceeding 'patient identification' during the first and second evaluation.

	First evaluation 2011/2012		Second evaluation 2015/2016	
	N	**Estimate (SE)**	**N**	**Estimate (SE)**
Fixed effects				
Patient identification on internal medicine ward	643	-0.05 (0.51)	129	1.58 (0.64)*
Patient identification on surgery ward	771	0.27 (0.50)	112	2.13 (0.67)*
Patient identification on intensive care ward	671	0.74 (0.51)	131	1.32 (0.65)*
Random effects				
Hospital level ICC		38.42		0
Hospital level variance		3.28 (1.22)		0 (0)
Hospital level covariance and correlation		0 (0); 0		
Department level ICC		23.09		48.33
Department level variance		1.14 (0.34)		2.24 (0.75)
Department level covariance and correlation		0.83 (0.46); 0.52		

**p<0.05, ICC=Intra Class Correlation, SE=Standard Error*

Supplementary Table 2 Multilevel analyses of the association between hospital type and compliance with the proceeding 'patient identification' during the first and second evaluation.

	First evaluation 2011/2012		Second evaluation 2015/2016	
	N	**Estimate (SE)**	**N**	**Estimate (SE)**
Fixed effects				
Patient identification in university hospitals	297	0.61 (1.35)	22	2.56 (1.95)
Patient identification in tertiary hospitals	750	0.02 (0.72)	139	2.09 (0.82)*
Patient identification in general hospitals	1107	0.45 (0.61)	211	1.27 (0.68)
Random effects				
Hospital level ICC		37.53		0
Hospital level variance		3.14 (1.18)		0 (0)
Hospital level covariance and correlation		0 (0); 0		
Department level ICC		23.18		48.71
Department level variance		1.12 (0.34)		2.30 (0.76)
Department level covariance and correlation		0.82 (0.45); 0.52		

**p<0.05, ICC=Intra Class Correlation, SE=Standard Error*

Chapter 3

Interruptions during intravenous medication administration: a multicentre observational study.

B.C.F.M. Schutijser, J.E. Klopotowska, I.P. Jongerden,
P.M.M. Spreeuwenberg, M.C. de Bruijne, C. Wagner

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ABSTRACT

Aims The aim of this study was to determine the frequency and cause of interruptions during intravenous medication administration, which factors are associated with interruptions and to what extent interruptions influence protocol compliance.

Background Hospital nurses are frequently interrupted during medication administration, which contributes to the occurrence of administration errors. Errors with intravenous medication are especially worrisome, given their immediate therapeutic effects. However, knowledge about the extent and type of interruptions during intravenous medication administration is limited.

Design Multicentre observational study.

Methods Data were collected during two national evaluation studies (2011/2012 & 2015/2016). Nurses were directly observed during intravenous medication administration. An interruption was defined as a situation where a break during the administration was needed or where a nurse was distracted but could process without a break. Interruptions were categorized according to source and cause. Multilevel logistic regression analyses were conducted to assess the associations between explanatory variables and interruptions or complete protocol compliance.

Results In total, 2,526 intravenous medication administration processes were observed. During 291 (12%) observations, nurses were interrupted 321 times. Most interruptions were externally initiated by other nurses (19%) or patients (19%). Less interruptions occurred during the evening (odds ratio: 0.23 [95% confidence interval: 0.08–0.62]). Do-not-disturb vests were worn by 61 (2%) nurses. No significant association was found between being interrupted and complete protocol compliance.

Conclusion An interruption occurred in every eight observed intravenous medication administration, mainly caused by other nurses or patients. One needs to consider critically which strategies effectively improve safety during the high-risk nursing-task of intravenous medication administration.

INTRODUCTION

Interruptions during healthcare delivery are common in the daily work of nurses in hospitals, with an average of seven (range 1-42) interruptions per hour.[1,2] An interruption can be defined as "a temporary break of a human activity (initial task), with the assumption that this initial task will be resumed".[3] Interruptions can be initiated by the nurse him/herself (internal), or by other individuals or objects such as pump alarms (external). Although interruptions can positively influence nurse performance and patient care (e.g. a nurse is interrupted to hear information about the health status of the patient), most interruptions are considered as breaks with negative outcomes, such as loss of focus or delays in tasks.[4]

Background

Of all nursing tasks, medication administration is the one most interrupted.[2] Approximately 10%-66% of the nurses are being interrupted during medication administration.[5-7] The large difference in interruption frequencies between studies may be explained by differences in setting, used definitions and type of medication observed. Being interrupted has been identified as a contributing factor for a lower medication administration protocol compliance.[8,9] Lower protocol compliance has been associated with medication administration errors (MAEs) and patient harm.[5,10] In particular intravenous (IV) medication administration is considered a high-risk task, given the immediate therapeutic effects of IV medication.[11] Therefore, acquiring knowledge about the extent and type of interruptions during IV medication administration is of great importance. This knowledge can be helpful in designing interventions aimed at minimizing or preventing interruptions and medication errors related to them.

To our knowledge, only two observational studies focused on interruptions during the administration of IV medication, both conducted in North-America (USA and Canada), in single centres.[6,7] One specifically investigated the administration of IV chemotherapy and not IV medication in general.[7]

METHODS

Aims

This study aimed to determine: (a) the frequency and cause of interruptions during IV medication administration in hospitals; (b) which factors are associated with interruptions during IV medication administration; and (c) to what extent interruptions influence compliance with the prevailing protocol for safe injectable medication administration.

Design and setting

We conducted a prospective observational multicentre study with a focus on interruptions during IV medication administration. The data used for this study were collected during two national evaluation studies conducted in 2011/2012 and 2015/2016. In both studies, compliance with the protocol for safe injectable medication (which contains intravenous medication) administration was evaluated.[8,12] This protocol contains 25 proceedings for administering injectable medication and is based on the "five rights" of safe medication administration (right patient, right medication, right dose, right route, right time).[13] In total, 22 hospitals participated in the study (three university hospitals, eight tertiary teaching hospitals and 11 general hospitals). Thirteen hospitals participated in both studies, along with another six (2011/2012) and three (2015/2016) hospitals that participated in only one evaluation. The 19 hospitals in the first study were randomly selected to participate and originated from a stratified sample based on area and type of hospital. Of these 19 hospitals, 13 agreed to participate in the second study. The main reasons for non-participation in the second evaluation were time constraints due to the implementation of a new hospital Electronic Health Record system and a recently conducted comparable evaluation by own hospital staff. For the second study, three additional hospitals were selected from a new stratified random sample. The STROBE guideline was used for reporting this study.[14]

Participants

Nurses working on intensive care units (ICU), internal medicine wards and general surgery wards were directly observed during the administration of IV medication. All nurses (and trainee nurses) involved in the administration of IV medication on these wards were eligible to participate.

Ethical considerations

As this study did not fall in the scope of the Dutch Medical Research (Human Subjects) Act, the medical ethical committee waived the requirement of informed consent (protocol numbers: 2011/359 and 2015/430). Nevertheless, verbal consent from nurses and (wherever possible) patients was obtained prior to observations. Nurse managers from the participating wards were informed about the purpose of the study. Nurses were aware that they were being observed and were informed about the purpose of the observations: administration of IV medication. Nurse participation in the study was voluntary and anonymous.

Data collection

During weekdays between 6AM - 10PM, nurses on the study wards were directly observed while administering IV medication to patients >18 years of age. It involved observing all IV medications, except parenteral nutrition, chemotherapy and acute medications. At each hospital, trained external researchers conducted the observations during consecutive weekdays. During each observation, the following items were registered: (a) whether or not the administrator was interrupted during the administration; (b) whether or not the administrator was wearing a do-not-disturb vest and (c) describing the interruption in detail (free text). It was possible to be interrupted more than once during one administration.

Sample size

The sample size calculations in both evaluation studies were based on protocol compliance as outcome measure. In the first evaluation study, data were collected per hospital once a month but at 10 different moments to monitor process variation over time and calculate an average compliance rate. To detect a 10% improvement, at a 5% significance level (ß = 0.8), at least 300 observations were needed in the second evaluation study. Therefore, one data collection moment per hospital was sufficient. Although this sample size was not based on interruption related outcomes, a sample of 300 observations among at least 100 nurses was considered as high.[1]

Primary outcomes

The primary outcomes were the frequency and causes of interruptions during IV medication administration. In this study, a broad definition for an interruption was

used (Supplemental Box 2): a situation where a nurse needed to temporarily break the IV medication administration or a situation where a nurse was distracted but could ignore or process without a break in the IV medication administration.[1,3] Both situations were recognized as having negative influence on the safety of the medication administration procedure.

For the analyses of causes of interruptions, each interruption was categorized as internally or externally initiated (e.g. initiated by the nurse him/herself, by other individuals or objects).[3] Furthermore, a distinction was made between interruptions with a break and interruptions without a break (i.e. distractions). Questions from other HCP, patients and family were considered as interruptions with a break when nurses responded to these questions. Finally, causes of interruptions were categorized into human, technical or environmental.[1] Human interruptions are caused by HCP, patients, family, either directly or by means of telephone calls, since the caller initiated the call.[1] Technical interruptions are caused by alarms (e.g. pagers, infusion pumps) or operational failures (e.g. collecting additional attributes necessary to administer the medication). Environmental interruptions are caused by contextual circumstances during the administration such as noise, light, smell and crowdedness.

Secondary outcomes

Secondary outcomes were factors associated with interruptions and the influence of interruptions on protocol compliance. To determine factors associated with interruptions, four explanatory variables were registered per observation: study period (2011-2012 & 2015-2016), type of ward (general surgery, internal medicine, intensive care), moment of administration (morning, afternoon, evening) and wearing a do-not-disturb vest (yes/no). Study period was chosen as a factor because the protocol could have been implemented more thoroughly in daily practice between 2011-2012 and 2015-2016 and awareness about interruptions could have been increased. Furthermore, previous studies showed that type of ward, moment of administration and wearing a do-not-disturb vest were associated with interruptions.[15-17] To determine if protocol compliance is influenced by interruptions, protocol compliance for each IV medication administration was observed and calculated. Prior to the first evaluation study, an expert team selected the nine most critical and identifiable proceedings from the Dutch protocol on safe injectable medication administration. These nine proceedings relate to the “five rights” of safe medication administration and include: check medication order, prepare for administration, collect materials, identify the

patient, conduct hand hygiene, check infusion line, check infusion pump mode, conduct double check by a second nurse and sign the medication order. A standardized observation form was used to observe whether or not these nine proceedings were conducted correctly by the nurses. Compliance was considered complete when all nine proceedings were correctly conducted. Each administration was scored (0-9) and then dichotomized into complete and incomplete compliance (≤8 proceedings correctly conducted).[8]

Validity and reliability

The external researchers, who conducted the observations and were not employed in the hospitals, used a similar observation list during both research periods. The researchers were either nurses or research assistants with a biomedical Master's degree. During both observation periods researchers were trained in performing observations during 1 day and follow-up trainings were conducted to discuss definitions and common observation situations.[8] During the observations, nurses were unaware that interruptions were registered, to minimize the Hawthorne effect. However, nurses could know that interruptions were being observed, since preventing interruptions is highlighted in the current protocol which is publicly available. Furthermore, two researchers (BS and TM) independently and retrospectively categorized the causes of interruptions. Inconsistencies were discussed with two senior researchers.

Data analysis

Descriptive statistics were used to summarize characteristics on observation level. Since the total number of interruptions was small in both evaluation studies, combined results are presented.

To assess the association between explanatory variables and interruptions, an univariate multilevel logistic regression analysis was performed. A three-level structure was used, with observations clustered in wards and wards in hospitals. One dependent variable was used: being interrupted at least once (yes/no). The four explanatory factors (study period, ward, moment, wearing a vest) were added as independent variables. Study period was centred in such a way that both study periods were equally weighted (-0.5/0.5). Intra class correlations (ICC) indicated if the relative contribution of the hospital and ward levels differed. During the ICC calculation, all explanatory variables were taken into account.

To determine to what extent interruptions influenced protocol compliance, another multilevel analysis was conducted. In this model, the dependent variable was complete protocol compliance (yes/no) and being interrupted (yes/no) was added as an independent variable. The explanatory variables were also taken into account in this model.

Only in the descriptive analysis of causes, the distinction between an interruption with a break and an interruption without a break (i.e. distraction) was made to gain a more detailed insight.

Descriptive analyses were conducted using SPSS Statistics 20 (IBM Corporation) and the multilevel analyses using MlwiN V.2.30 (University of Bristol). The multilevel association models were calculated using Penalized Quasi Likelihood second order with constrained level 1 variance; $p \leq 0.05$ were considered statistically significant.

RESULTS

In total, 2,526 IV medication administration procedures were observed, of which 2,154 during the first evaluation study (2011-2012) and 372 during the second evaluation study (2015-2016). Since not all hospitals participated in both evaluation studies, the total number of observations in the hospitals ranged between 22-196 (median = 119). Most observations were conducted at general hospitals (52%), on general surgery wards (35%) and during the afternoon (59%) (Table 1). Do-not-disturb vests were worn by 61 (2%) nurses.

Frequency of interruptions

A total of 321 interruptions were identified (Table 1). These interruptions occurred during 291 observations of which 263 observations (90%) with one, 26 (9%) observations with two and two (1%) observations with three interruptions. Interruptions occurred most frequently in the morning (34%) and afternoon (65%). In 13 (4%) observations with an interruption, the nurse wore a do-not-disturb vest.

Table 1 Characteristics of the observations.

	Total number of observations N=2526	Observations with ≥1 interruption N=291
Type of hospital		
University	319 (13%)	41 (14%)
Tertiary teaching	889 (35%)	86 (30%)
General	1318 (52%)	164 (56%)
Type of ward		
Internal Medicine	772 (31%)	88 (30%)
(General) Surgery	883 (35%)	90 (31%)
Intensive Care	802 (32%)	103 (35%)
Other	69 (3%)	10 (3%)
Administration time		
Morning (6AM-12PM)	863 (34%)	98 (34%)
Afternoon (12PM-6PM)	1500 (59%)	188 (65%)
Evening (after 6PM)	163 (7%)	5 (2%)
Wearing a do-not-disturb vest		
Yes	61 (2%)	13 (4%)
No	2465 (98%)	278 (96%)
Complete protocol compliance		
Yes	539 (21%)	42 (14%)
No	1987 (79%)	249 (86%)

Causes of interruptions

Of 189 (59%) of all 321 interruptions, the cause of the interruption could be obtained from the observations forms. Most the interruptions were externally initiated (N = 181, 96%). Of these 181 externally initiated interruptions, 135 resulted in a break and 46 in no break (i.e. distractions) (Figure 1). External interruptions with a break were mainly caused by other nurses (N = 35, 19%) and patients (N = 35, 19%). However, distractions were mainly caused by other HCP (n = 12, 6%), for example, food delivery services to patients or by environmental situations (N = 10, 5%) (e.g. noise, crowdedness). Of eight (4%) internally initiated interruptions, six resulted in a break and were caused by operational failures (i.e. a nurse putting on gloves halfway through the administration procedure instead of at the start) and one resulted in a break and was caused by a patients' family (i.e. a nurse commenced a conversation while administering medication).

The remaining internally initiated interruption that resulted in a distraction was caused by the environment (i.e. administration of medication by a nurse in a busy hallway, where the patient was at that moment). In Supplemental Box 1, examples of other causes are described.

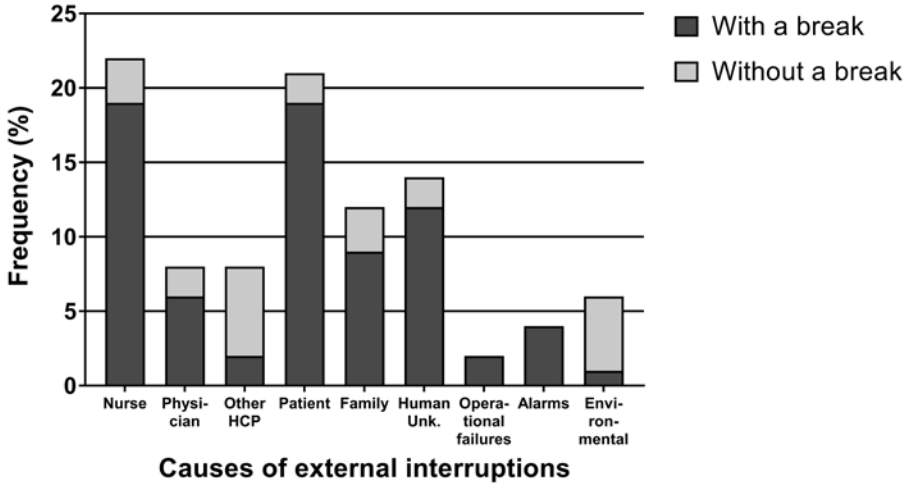

Figure 1 Causes of external initiated interruptions divided in interruptions with a break and without a break (i.e. distractions) (n=181/189). HCP = Heath Care Professionals, Human Unk. = caused by humans, but unknown which person, Phone calls were categorized as 'Human Unknown', Environmental = noise, light, smell, or crowdedness.

Factors associated with interruptions

In the first univariate analysis between independent explanatory variables and being interrupted at least once, the variable "period" appeared not significantly associated. Therefore, a second multilevel analysis was conducted without this explanatory variable, where a positive association between time of administration and being interrupted was found (Table 2). The number of interruptions decreased significantly during IV administration in the evening compared with the morning (odds ratio [OR]: 0.23 [95% CI]: 0.08-0.62). Other exploratory variables were not significantly associated with the occurrence of interruptions. In total, 20% (ICC = 19.7) of the variance in the association between explanatory variables and being interrupted was caused by differences between individual hospitals and 2% (ICC = 2.4) by differences between individual wards. This finding is supported by the number of observations with interruptions between individual hospitals: 0-37 (median = 12).

Interruptions and protocol compliance

The protocol for safe injectable medication administration was conducted completely in 14% of the observations with an interruption (Table 1), compared with 21% of the observations without an interruption. After adjusting for explanatory variables, the multilevel analysis showed no significant influence of being interrupted on the complete protocol compliance (OR: 0.85 [95% CI: 0.57-1.26]). In total, 21% (ICC = 21.4) of the variance in the association between explanatory variables and complete protocol compliance was caused by differences between individual hospitals and 13% (ICC = 12.5) by differences between individual wards.

Table 2 Multilevel logistic regression analysis of the association between explanatory variables and being interrupted at least once during IV medication administration.

Explanatory variables	Odds Ratio	95% Confidence Interval
Type of hospital		
University	1.09	0.26-4.53
Tertiary teaching	Reference	Reference
General	1.56	0.68-3.61
Type of ward		
Internal Medicine	0.99	0.65-1.51
(General) Surgery	Reference	Reference
Intensive Care	1.22	0.81-1.85
Other	1.40	0.52-3.75
Administration time		
Morning (6AM-12PM)	Reference	Reference
Afternoon (12PM-6PM)	1.10	0.81-1.49
Evening (after 6PM)	0.23*	0.08-0.62*
Wearing a do-not-disturb vest		
Yes	1.93	0.96-3.90
No	Reference	Reference

** p≤0.05*

DISCUSSION

During 12% of the IV medication administration observations in 22 Dutch hospitals, at least one interruption occurred, which was usually initiated by a colleague nurse or patients. Significantly less interruptions occurred during medication administration during evening shifts. No significant association was found between being interrupted and complete protocol compliance. Differences in interruption frequency were larger between individual hospitals than between individual wards.

An interruption frequency of 12% identified in this study is at the lower end of the interruption frequency range identified in other studies: 10%-66%.[5-7] The large difference in interruption frequency between the studies may be explained by differences in setting, used definitions and type of medication observed. In our study, only IV medication administrations were observed; nurses may be more aware of the risks associated with IV medication administration and therefore try to avoid interruptions during this high-risk task as much as possible. The outliers in the range, for example, 10%[7] and 66%[6], are both studies which focused on IV medication administration alone. In the first study,[7] only IV chemotherapy administrations were observed, which protocols are even more strict compared with regular IV medication administrations. In the second study,[6] both the administration and preparation of IV medication were observed on ICUs. Preparing medication in often busy medication rooms as well as the fact that the ICU setting is more prone to frequent care interventions may both explain high interruption frequency identified in the study of Moss et al.[6]

Human actions (e.g. nurses, patients, family, other HCP) were the major cause of interruptions in our study (85%), which is line with previous studies.[18,19] Due to a reduced number of nurses and HCP on wards after 6 p.m., this may also explain why fewer interruptions occurred during evening shifts. Since humans are the major cause of interruptions, it seems logical that do-not-disturb vests, as a tool to reduce interruptions, were introduced in various hospitals,[17,19,20] including the Netherlands. Although not mandatory in Dutch hospitals, most hospitals participating in this study stated in their protocols that such vests were implemented. A do-not-disturb vest as an intervention to prevent interruptions stems from the belief that interruptions are negative situations and, therefore, need to be avoided. We found that do-not-disturb vests were rarely worn by nurses during IV medication administration. Previous studies showed that nurse-related arguments for not wearing the vests include: disliking the

colour, disbelieving vests will prevent interruptions, thinking vests are unhygienic and hot and thinking the administration will take more time.[17,19] Since the choice of not wearing a vest seems to be based on nurses personal ideas instead of patient safety-related arguments, increasing nurses awareness regarding the consequences for patient safety could improve their acceptance of the vests. Designing a new vest, meeting nurses' needs and specifications, can also be another potential solution to addressing the low acceptance of the vests.

At the same time, nurses need to be visible,[18] need to consult people when delivering health care[7] and are key-informants for family and other HCP.[2] These aspects of nursing make nurses more prone to interruptions, forcing them to multitask.[5,19] Nurses spend 15% of their shift on multitasking.[21] Westbrook et al. found that during medication administration, 88% of the nurses conducted at least one other task.[19] In this context, a do-not-disturb vest seems not a good fit.

Another potentially effective approach are bundled interventions, which consist of a combination of do-not-disturb vests, hourly medication rounds, posters in medication rooms, patient and family education, information material, no interruption zones and triage of phone calls.[19,22,23] These interventions effectively reduced the frequency of interruptions during medication administration but were not focused specifically on IV medication and did not include dealing with multitasking or setting priorities. Therefore, our recommendation is to implement and determine the effectiveness of combined interventions aiming to reduce interruptions and simultaneously equipping nurses in dealing with interruptions, prioritizing and multitasking.

Limitations

This is the first multicentre study where interruptions during IV medication administration were determined over a 4-year period. As more than 20% of all Dutch hospitals participated in this study, this strengthens its generalizability in the Dutch hospital setting. Another strength of this study is that nurses were not aware that interruptions were being measured, giving a realistic reflection of daily practice. Also, to ensure a consistent categorization of the identified interruptions, a two-step process was followed where two researchers independently analysed causes of interruptions and in case of disagreement two senior researchers were consulted to solve it. This study also has several limitations. Data on interruptions from the first evaluation study were retrospectively analysed. Although we were able to retrieve a majority of causes for

the interruptions by analysing the information registered by the observers, 41% of the causes could not be identified. However, compared with other studies, the magnitude and type of identified causes were similar. Therefore, we are confident that our sample represents current nursing practice. Another limitation was that it was not possible to correct for the observer effect (i.e. whether one observer registered more interruptions than another observer). In both evaluation studies, most hospitals were visited by only one observer. To correct for the observer effect, at least two observers should have conducted an equal number of observations in all hospitals and each observer should have visited several hospitals. Due to practical reasons this was not included in our study design. Finally, we did not measure the consequences of interruptions in terms of MAEs and harm resulting from MAEs or estimated whether or not interruptions were avoidable. As an alternative, we evaluated consequences of interruptions on protocol compliance. As mentioned before, low protocol compliance is associated with MAEs and patient harm. In addition, the evaluation of avoidability of interruptions is hampered by a lack of consensus on this topic.[1,2,24]

CONCLUSION

To conclude, in this multicentre observational study interruptions during IV medication administration occurred in one of every eight administrations. Colleague nurses and patients are the most frequent cause of these interruptions. As do-not-disturb vests are seldom worn, one needs to critically consider what type of strategies are necessary to effectively improve safety in the process of administering IV medication by nurses. The available literature provides insufficient evidence addressing the subject of multitasking or setting priorities.[5,19] Future research should focus on implementing interventions which aims to reduce interruptions, along with equipping nurses in dealing with interruptions, prioritizing and multitasking.

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Supplemental Box 1 Examples of interruptions during IV medication administration per cause.

Nurse: The nurse received information concerning another patient from another nurse.
Physician: The physician entered the patients' room for a brief consultation with the nurse.
Other HCP: A physiotherapist had various questions for the nurse therefore causing an interruption.
Patient: The patient asked the nurse many questions.
Family: During visiting hour, the patients' family members asked the nurse many questions.
Human Unknown: The nurse was interrupted several times to answer the phone.
Operational failures: Having forgotten a necessary infusion sideline, the nurse had to return to the mediation room to get it.
Alarms: The nurses' pager is beeping because a patient in a room next door pressed on an alarm button. The nurse visited the patient and finished the administration afterwards.
Environmental: The room was occupied by more than one patient. It was clean, but also noisy due to various visitors visiting patients.

Supplemental Box 2 Operational definitions used during this study.

Concept	Definition
Interruption	A situation in which a nurse needed to temporarily break the IV medication administration.
Distraction	A situation in which a nurse was distracted but could ignore or process without a break in the IV medication administration.
Internally initiated	An interruption or distraction that is initiated by the nurse him/herself.
Externally initiated	An interruption or distraction that is initiated by other individuals or objects.
Do-not disturb vest	A colored vest with the text 'do-not-disturb' on the back, which can be worn by nurses especially during medication rounds.

Chapter 4

Feasibility of reusing routinely registered data to monitor safe preparation and administration of injectable medication: a multicenter cross-sectional study.

B.C.F.M. Schutijser, J.E. Klopotowska, I.P. Jongerden,
C. Wagner, M.C. de Bruijne

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ABSTRACT

Background Reusing routinely recorded data from electronic hospital records (EHR) may offer a less-time consuming, and more real time alternative for monitoring compliance by nurses with a protocol for the safe preparation and administration of injectable medication. However, at present it is unknown if the data necessary to calculate the quality indicators (QIs) are recorded in EHRs, or if these data are suitable for automated QI calculation. Therefore, the aim of this study was to determine the feasibility of monitoring compliance by nurses with a protocol for the safe injectable medication preparation and administration by reusing routinely recorded EHR data for the automated calculation of QIs.

Methods A cross-sectional study in 12 Dutch hospitals (October 2015-May 2016). The checks included in the currently prevailing national protocol for the safe preparation and administration of injectable medication were translated into 16 data elements required to calculate the QIs. At each hospital, one interview was conducted using a structured questionnaire to decide whether the data elements were available in EHRs. To present these results, descriptive statistics were used.

Results In total, 20 health-care professionals were interviewed and four different EHR systems were evaluated. The availability of data elements was comparable between the four evaluated EHR systems. Nine of the 16 required data elements were recorded in EHRs, eight in a structured format. The seven missing data elements were mainly related to checks such as 'gather all materials needed' or 'conduct hand hygiene'. Furthermore, changes were identified in the process for the preparation and administration of injectable medication. These changes are mostly related to the increased use of electronic medication administration registration and barcode medication administration systems.

Conclusions Reusing EHR data to monitor compliance by nurses with the currently prevailing protocol for the safe preparation and administration of injectable medication is not entirely feasible. A decision should be made on which checks should be recorded in the EHRs and which checks should be audited in order to minimize the registration burden for nurses. Moreover, the currently prevailing protocol should be revised to bring it in line with work-as-done. Our results can be used as guidance for such a revision and also for designing new QIs that can be calculated by reusing routinely recorded EHR data.

INTRODUCTION

Background

More than 90% of all hospitalized patients receive some form of injectable medication, i.e. through an infusion or subcutaneous or intramuscular injections.[1] Because of the immediate therapeutic effects, errors with injectable medication have a higher risk of patient harm.[2, 3] To prevent such errors, protocols for the safe preparation and administration of injectable medication have been established nationally and internationally.[1, 4, 5]

To monitor compliance with these protocols, most hospitals conduct periodic internal audits. An internal audit is defined as an "independent and objective assurance and consulting activity".[6] In such an audit, internal employees (peers) evaluate how the protocol is followed. Methods for this evaluation are observations, interviews, site visits, document analysis, and surveys.[7] Data collected during internal audits can be used to manually calculate quality indicators (QIs). QIs are "explicitly defined and measurable items referring to the structures, processes or outcomes of care".[8] Internal audits have been shown to improve the effectiveness of risk management, control, and governance by identifying patient safety problems.[9] However, conducting internal audits is time consuming and the audit provides only a snapshot of the compliance at that particular moment.[9] Moreover, awareness among staff of being audited can lead to biased measurements (the Hawthorne effect).[10]

Reusing data that are routinely recorded in the Electronic Hospital Record (EHR) for an automatic calculation of QIs may provide a promising alternative monitoring strategy: data can be collected in real time, and represent work-as-done, and this approach is less time consuming than conducting an audit.[11] Furthermore, such an approach may contribute to a faster plan-do-check-act cycle when quality improvement is needed. However, at present it is unknown to what extent the data that are necessary to monitor compliance with a protocol for the safe preparation and administration of injectable medication are recorded in EHRs, and whether these data are suitable for automated QI calculation.

Objective

The aim of this study was to determine the feasibility of monitoring compliance by nurses with a protocol for the safe injectable medication preparation and administration by reusing routinely recorded EHR data for the automated calculation of QIs.

METHODS

Design and setting

A cross-sectional multicenter study was conducted in 12 Dutch hospitals (October 2015-May 2016): one university hospital, seven tertiary teaching hospitals, and four general hospitals. These hospitals originated from two random samples of respectively 19 and 3 hospitals, selected for a larger study which aimed to evaluate compliance with Dutch protocols on injectable medication.[12, 13] Both samples were stratified based on area and type of hospital (university, tertiary teaching, and general). Of these, 12 agreed to participate in the current study. Hospitals participated voluntarily on the basis of willingness and availability (convenience). No criteria were used to select hospitals. However, we made sure that the most frequently used EHR systems in the Netherlands were represented in our sample. At the time of the study, 11 Dutch hospitals were using EPIC (13% of all Dutch hospitals) and 41 (47%) were using ChipSoft.[14] Also, many hospitals were in the process of selecting new EHR systems, with ChipSoft and EPIC being the most probable choices. Reasons for hospitals' non-participation in this study were that they were currently implementing a new EHR system (n=3), time constraints (n=2), and no interest (n=5).

The STROBE guideline for observational studies in epidemiology, including cross-sectional studies, was used to report this study.[15]

Participants

At each hospital, at least one health-care professional with knowledge of the functionalities within the local EHR system used during the process of injectable medication preparation and administration was invited to participate in an interview. These health-care professionals could be hospital pharmacists, quality and safety officers, or information technology (IT) experts with a medication safety background. After the hospital board gave consent for participation, we were referred directly to these health-care professionals.

Ethical considerations

The medical ethics committee of the Amsterdam UMC, Vrije Universiteit Amsterdam concluded that the study did not fall within the scope of the Dutch Medical Research (Human Subjects) Act and gave a waiver for the requirement of informed consent (protocol number: 2015/430). Nevertheless, all hospitals were asked to sign a written consent form for participation in the study and all interviewed participants were informed prior to the interview about the purpose of the study and the fact that participation was voluntary.

Data collection

We focused on two QIs within the currently prevailing Dutch national protocol for the safe preparation and administration of injectable medication in a non-acute setting: (1) the number of correctly conducted checks during the preparation of injectable medication; and (2) the number of correctly conducted checks during the administration of injectable medication.[4, 16] The Dutch protocol is comparable to other protocols implemented in other countries[17-20] and it was implemented in all Dutch hospitals in 2009. The most important and verifiable checks were translated into data elements. Data elements are pieces of information necessary to calculate QIs, for example a timestamp for medication administration or identification of the right patient.[21] For each QI, eight data elements were required to be able to calculate their outcome, i.e. compliant or not compliant (Table 1).

Second, to determine whether the data elements were recorded in the studied EHRs, a structured questionnaire was developed with 29 questions. The questionnaire was tested in a pilot interview in one hospital and changes to the questionnaire were made accordingly.

Third, in each hospital one interview was conducted by one senior researcher (JK). During the interview, the researcher filled in the structured questionnaire together with the participants. The interviews were not recorded, but the researcher took notes. Moreover, a copy of a completed questionnaire was sent back to the participant(s) to ascertain validity of the information. If needed, screenshots of EHR functionalities were collected to clarify where the data elements could be found.

Table 1 Required data elements for two quality indicators: (1) 'the number of correctly conducted checks during the preparation of injectable medication'; and (2) 'the number of correctly conducted checks during the administration of injectable medication', based on Schilp et al.[16]

Data elements	Brief explanation of data elements and the underlying check
Preparation phase	
1. Verify medication order and check guidelines	Verify the injectable medication order based on the patient's medication list and check local handbook of injectable drugs for a guideline on how to prepare the medication.
2. Create medication label	Create injectable medication label based on information from injectable medication order and handbook of injectable drugs.
3. Calculate right amount	Calculate the right amount of injectable medication to be prepared based on the patient's medication order.
4. Conduct hand hygiene and disinfect preparation surfaces	Conduct hand disinfection before preparation or wear gloves during the preparation. Make sure that the preparation surfaces are clean.
5. Gather all materials needed	Gather the materials needed for the preparation.
6. Check right ingredients and prepare the medication	Check whether the right ingredients are present (e.g. right vials or ampules of medication, and diluent if applicable) and prepare the injectable medication.
7. Sign for preparation	Sign for preparation of injectable medication immediately after completing it.
8. Check and co-sign by a second nurse	A second nurse checks whether the right injectable medication order was chosen, the right ingredients were collected, the right amount was calculated, the shelf life of the ingredients has not expired, the right preparation method was used, and the right injectable medication label was created with the right expiration date on it. The second nurse co-signs for preparation.
Administration phase	
1. Check right medication	Check the injectable medication label based on the patient's medication order list (right medication, right dose, right time).
2. Prepare for administration	Check the local handbook of injectable drugs for a guideline regarding infusion rate and right infusion route for the medication.
3. Gather all materials needed	Gather the materials needed for the administration.
4. Identify the right patient	Identify the right patient.
5. Check by a second nurse	A second nurse checks whether the right patient, medication, and time, and right administration route and rate have been chosen.
6. Conduct hand hygiene and disinfect the preparation surfaces	Conduct hand disinfection before administration or wear gloves during administration. Make sure that the administration surfaces are clean.
7. Check right infusion rate and flow	Administer the medication and set the right infusion rate (via drip or pump mode). Check if infusion is flowing correctly.
8. Sign medication order	As the administrator, sign for the administration of the medication order.

Outcomes

The primary outcome was the availability in the EHR of the data elements required to calculate the two QIs automatically. Data elements were recorded as available if that data element was recorded in the EHRs. If a data element was recorded, information was collected about the recording method (i.e. manual or automated), type of data format (i.e. structured or unstructured), and type of health-care professional responsible for recording the data element.

Data analysis

All information from the interviews, and additional information received after the interviews if applicable, was entered in an Excel spreadsheet (Microsoft Office Professional Plus 2016). For the primary outcome, the number of available data elements, the number and description of recording methods, and the description of the data format were described. Automatic computation of QIs would only be feasible if all required data elements were available in the EHR in a structured, computer-readable format. For hospital and health-care professional characteristics, we used descriptive statistics.

Table 2 Characteristics of the hospitals and health-care professionals in the study.

Characteristics	Number of hospitals (n=12) or health-care professionals (n=20)
Hospital characteristics	
Type of hospitals, n (%)	
University	1 (8)
Tertiary teaching	7 (58)
General	4 (33)
Type of EHR system, n (%)	
ChipSoft (EZIS)	3 (25)
ChipSoft (HIX)	3 (25)
EPIC	3 (25)
Siemens-i.s.h. med	2 (17)
NEXUS (xCare-EPD)	1 (8)
Health-care professional characteristics	
Type of profession, n (%)	
Hospital pharmacist	14 (70)
EHR expert	4 (20)
Quality and safety officer	2 (10)
Number of professionals per interview, median (range)	1.5 (1-4)

RESULTS

Participants

In 12 Dutch hospitals, 20 health-care professionals were interviewed (one to four professionals per hospital), of whom 14 (70%) were hospital pharmacists (Table 2). Four different EHR systems were reviewed during the interviews: ChipSoft (HIX or EZIS), EPIC, NEXUS, and Cerner/SAP. The hospitals were at different stages of post-going live, varying from a few months to several years after implementation. In nine hospitals (75%), health-care professionals worked with a fully integrated EHR system (i.e. a system in which all functionalities are placed in the same technical layer and utilize a single clinical data repository, e.g. administrative data, patient demographics, notes, vital signs, diagnoses, medication, images, and lab results).

Table 3 Availability and recording method of data elements for preparing injectable medication.

Data element	Availability, n hospitals (%)	Description of recording method, n hospitals (%)	Type of recording method	Type of data format
1. Verify medication order and check guidelines	0 (0)	n/a	n/a	n/a
2. Create medication label	8 (67)	1. Log file of printed label, 8 (67)	1. Automated	1. Structured
3. Calculate right amount	0 (0)	n/a	n/a	n/a
4. Conduct hand hygiene and disinfect preparation surfaces	0 (0)	n/a	n/a	n/a
5. Gather all materials needed	0 (0)	n/a	n/a	n/a
6. Check right ingredients and prepare the medication	2 (17)	1. Scan barcode of the ingredients, 2 (17)	1. Automated	1. Structured
7. Sign for all preparation steps	8 (67)	1. Log file of printed label, 8 (67) 2. One sign-off for all steps, 1 (8)	1. Automated 2. Automated	1. Structured 2. Structured
8. Check and co-sign by a second nurse	1 (8)	1. One sign-off for all steps, 1 (8)	1. Automated	1. Structured

n/a=not applicable

QI for the safe preparation of injectable medication

Of the eight required data elements, four (50%) were available in all the EHR systems reviewed ('create medication label', 'check right ingredients and prepare the medication', 'sign for all preparation steps', and 'check and co-sign by a second nurse', see Table 3). In all hospitals, these data elements were recorded in a structured format. All hospitals used the same recording method for three of these four data elements.

In eight hospitals (66%), injectable medication labels were automatically generated based on medication order information in the electronic medication administration record (eMAR), an application integrated in the EHR system. By printing these labels, an EHR system automatically captures the name of the nurse and a timestamp for label printing. In these hospitals, this method was used to capture the data elements 'create medication label' and 'sign for all preparation steps'. In the remaining four hospitals (33%), medication labels were created manually, and signed and checked by two nurses. In two hospitals (17%), a barcode scanner was used to verify if the right ingredients were chosen. By scanning the barcode on the ingredient's container, the EHR system automatically captures the name and strength of the ingredient and checks for mismatches with the related medication order. In these hospitals, this method was used to capture the data element 'check right ingredients and prepare the medication'. In one hospital (8%), it was possible to automatically sign off for preparation by using an identification badge. In this hospital, this method was used to capture the data elements 'sign for all preparation steps' and 'check and co-sign by a second nurse'.

QI for the safe administration of injectable medication

Of the eight required data elements, five (63%) were available in all the EHR systems reviewed ('check right medication', 'identify the right patient', 'check by a second nurse', 'check right infusion rate and flow', and 'sign medication order', see Table 4). Of these data elements, four were recorded in a structured format, and the same recording method was used for these data elements in all hospitals.

The entire registration of medication administration checks was conducted manually in one hospital (8%). In the remaining 11 hospitals (92%), nurses used eMAR. Nurses need to log into eMAR with their own login name and password in order to verify patients' medication orders and to record the administration of medication. Therefore, in these hospitals this login procedure is used to capture the data element 'sign medication order'. In two of these 11 hospitals, eMAR is used in combination with barcode scanning

technology to check for the right patient by scanning the barcode on the patient's wristband and for the right medication, dose, and time by scanning the barcode on the injectable medication label. This captures the data elements 'check right medication' and 'identify the right patient'. In four of the 11 hospitals, only the barcode scanning of the patient's wristband is operational. In 11 hospitals, a 'check by a second nurse' pop-up window is shown to capture the related data element. A second nurse needs to log into the system to complete the pop-up window. To capture the data element 'check right infusion rate and flow', all 11 hospitals use a free-text field in the eMAR system to record the related information. No data elements related to the check and second check of the right administration route and rate were identified.

Table 4 Availability and recording method of data elements for administering injectable medication.

Data element	Availability, n hospitals (%)	Description of recording method, n hospitals (%)	Type of recording method	Type of data format
1. Check right medication	4 (33)	1. Scan barcode on patient's wristband and barcode on injectable medication label, 4 (33)	1. Automated	1. Structured
2. Prepare for administration	0 (0)	n/a	n/a	n/a
3. Gather all materials needed	0 (0)	n/a	n/a	n/a
4. Identify the right patient	6 (50)	1. Scan barcode on patient's wristband, 6 (50)	1. Automated	1. Structured
5. Check by a second nurse	11 (92)	1. One signature in eMAR for all steps, 11 (92)	1. Automated	1. Structured
6. Conduct hand hygiene and disinfect the preparation surfaces	0 (0)	n/a	n/a	n/a
7. Check right infusion rate and flow	11 (92)	1. Free text field in eMAR, 11 (92)	1. Manual	1. Unstructured
8. Sign medication order	11 (92)	1. Log-in to eMAR and record administration, 11 (92)	1. Automated	1. Structured

n/a=not applicable

DISCUSSION

Our study shows that only half of the data elements required for automatic QI calculation (in order to monitor nurses' compliance with the protocol for safe preparation and administration of injectable medication), are routinely recorded in the evaluated EHR systems. Various data recording methods are used by nurses and most of these methods have the same structured format. Furthermore, we found that all four evaluated EHR systems are comparable regarding the availability of the required data elements. Therefore, monitoring compliance with the currently prevailing protocol using routinely recorded EHR data, is not entirely feasible. The current EHR systems are not fit for the purpose of monitoring compliance with this protocol.

To our knowledge, no other studies have been published of the feasibility of automated calculation of QIs related to the preparation and administration of injectable medication using routinely recorded EHR data. However, studies of other hospital processes also showed limited opportunity regarding automatic QI calculation by reusing EHR data. Chazard et al. showed in their review that only 98 of 440 QIs (22%) found in the literature could be calculated automatically.[22] In line with this review, a data requirement review of Roth et al. showed that only one third of 400 QIs studied, covering 29 conditions and preventive care, were readily accessible from the EHRs.[23] Finally, automatic calculation of a set of 10 colorectal cancer surgery QIs in a Dutch hospital was also deemed not feasible.[24]

Two key reasons why QIs cannot be easily calculated by reusing EHR data are that data are missing or unavailable,[22, 24, 25] and data are captured in an unstructured format (e.g. free-text fields).[21-23, 25-28] These limitations were also identified in our study. In particular, data elements related to checks when getting ready for preparation or administration (e.g. 'gather all materials needed') or conducting hygiene activities (e.g. 'conduct hand hygiene') were missing in EHR systems. Furthermore, the use of free-text fields for 'checking for right infusion rate and flow', hinders use of this check in automated QI calculations.

More specific to our setting and the injectable medication preparation and administration process is the fact that the protocol we used was implemented in 2009. At that time, many hospitals in the Netherlands were still using paper charts for the preparation and administration of injectable medication. The protocol is, however,

still the prevailing protocol and hospitals are inspected by the Health and Youth Care Inspectorate for compliance with this protocol. Besides, we have found that hospitals have implemented various IT tools such as eMAR and barcode medication administration (BCMA) systems in addition to EHR systems, resulting in changes in how the process of the preparation and administration of injectable medication is conducted. Therefore, in our opinion the currently prevailing protocol should be revised in order to utilize the benefits of automation in hospitals and to address possible new risks resulting from such automation.

Based on our results, we recommend taking the following three steps:

1) Revise the prevailing protocol for safe injectable medication preparation and administration to bring it in line with work-as-done. Our study shows that BCMA has additional advantages for monitoring protocol compliance. When used in combination with an eMAR, data elements are captured along with safety warnings when mismatches occur. For example, the medication order in the eMAR is checked against the information from the barcode on the patient's wristband (the right patient), the barcode on the medication label (the right medication, dose, and time), and the barcode of ingredients (the right medication ingredients). However, although use of IT has reduced risks in the process of preparation and administration of injectable medication, it has also created new risks (i.e. workarounds).[29, 30] This should be taken into account when revising the current protocol.

2) Define which checks should be recorded in the EHRs and which checks should be monitored differently so that the EHRs are fit for the purpose of automated calculation of QIs. In our opinion, there is no added value from recording checks such as 'gather all materials needed' or 'conduct hand hygiene and disinfect preparation surfaces' in an EHR. This has been confirmed by almost all interviewed participants, who indicated that these checks are not suitable for translation into data elements. Besides, the Dutch nursing organization has been trying for several years to reduce the administrative burden on nurses, because 92% of nurses argue that the registration of many activities has gone too far and is often unnecessary.[31] Other forms of monitoring are probably more appropriate for these checks, such as site visits or periodic observations.

3) Formulate new QIs. To be able to compare QI outcomes between hospitals and learn how to improve accordingly, we recommend standardizing the data elements in EHR systems that are needed for QI calculation. Several international and national information standards have been developed to achieve interoperability in health-care information. One example is the identification of medicinal products (IDMP) standard, which specifies standardized definitions of medicinal products for human use, and covers aspects about which standards to use for medication names, frequencies, doses and routes of administration.[32] Furthermore, as formulated by Nictiz, the Dutch information standard for the medication process covers aspects of how to record and exchange information with other care providers regarding prescribing, dispensing, administering, and using medication.[33] With respect to medication administration, additional guidance is provided about how to record the double check. Any information that is covered by these standards and is needed as a data element for the QIs should preferably be standardized in EHR systems according to these standards, especially given the efforts to develop such standards and their (intended) widespread use. However, as this study reveals (Table 1), there are still many data elements that are not (yet) covered by these standards, for example, elements recording that the 'right amount was calculated', 'medication label was created', 'hand hygiene was conducted' and 'right infusion rate and flow was set'. To standardize these elements, other tools could be valuable, such as the CLinical quality Indicator Formalization (CLIF) method developed by Dentler et al.[34] CLIF is an eight-step method that helps its users in transforming quality measures (often recorded in unstructured text fields) into precise queries that can be computed on the basis of EHR data. CLIF can lead to reproducible results, but input is required from trained experts with clinical and medical informatics expertise. The experts need to agree on the terminology, definitions, and registration methods for data elements and must consider these as a minimum dataset.[35] Besides data elements monitoring the quality of the process, data elements should also be considered that give insight into the safety of the process, for example the number of barcodes on ingredients and medication labels that can be scanned, or the number of mismatch pop-ups because of a wrong time window or a wrong patient.

Finally, the revised protocol should be implemented and the ability to record the data elements required for automated calculation of the (new) QIs should be configured in the EHR systems in order to make them fit for purpose. Cooperation with EHR vendors will be of added value. Future studies could then focus on monitoring nurse compliance

with the revised protocol by reusing EHR data and on gaining insight into the effects of this new approach to medication safety. Moreover, reusing EHR data for quality-of-care monitoring provides opportunities to audit and obtain feedback on the nurse's own compliance without reliance on internal or external auditors. This might encourage employees to take control and responsibility for their compliance, since compliance results, and the effects of improvement measures, are readily available.

Strengths and limitations

The strengths of our study are its random selection of 12 participating hospitals and appropriate representation of the Dutch EHR landscape (25% were EPIC hospitals and 50% were ChipSoft hospitals). Furthermore, one of our participants (MD) was a representative of the Dutch ChipSoft user group for medication processes and familiar with the possibilities and limitations of the ChipSoft EHR system. One of our researchers (JK) was in the lead of the medication processes configuration and implementation of the EPIC EHR system and was familiar with the possibilities and limitations of that system. Therefore, given the sufficient representation of EHR systems and involvement of experts, we are confident that our results give a realistic overview of the possibilities of both systems. Nevertheless, our study also has some limitations. Firstly, this study was an explorative study and relied on information provided by the participants, not on information extracted from the EHR systems. However, at the time of the study we did not know to what extent EHR systems were used to support the process of injectable medication preparation and administration and therefore which data to extract to calculate the QIs. Given these unknowns and taking into account the strict regulations regarding patient privacy when extracting data for research, we decided that the best option to meet the aim of our study (within the available time and resources) would be via interviews with local EHR experts. Besides, these experts were highly knowledgeable about the EHR systems, the protocol for the safe preparation and administration of injectable medication, and the underlying processes. Furthermore, parallel to this study, we were conducting direct observations of nurses at the same hospitals to measure compliance with the same protocol.[12] Therefore, we are confident that this combined strategy provided us with sufficient knowledge of clinical practice and how the EHR system was used in order to reliably determine whether it would be feasible to calculate injectable medication QIs by reusing data recorded in the EHRs. Secondly, since this study was conducted in 2015-2016, it is possible that the participating hospitals have since implemented a new version of their hospital's EHR system and that some data elements can now be recorded and retrieved for the automatic calculation of QIs.

However, implementing new IT tools or changes in EHR systems is often very complex and time-consuming, which suggests that our findings provide a valid overview.

CONCLUSION

Currently, reusing EHR data to measure compliance with the protocol for the safe preparation and administration of injectable medication is not entirely feasible. This finding applies across the four EHR systems reviewed. To move forward, several steps are needed to make sure that the current protocol for the safe preparation and administration practices for injectable medications is in line with work-as-done, and to establish the most appropriate monitoring strategies for measuring compliance. In our opinion, using information technology such as EHR systems, eMAR, barcode scanning, and smart infusion pumps, and reusing routinely recorded data in these systems should be pursued as ways to optimize medication safety and to support an efficient, transparent, safe, and reliable plan-do-check-act cycle.

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Chapter 5

Nature of adverse events with opioids in hospitalised patients: a post-hoc analysis of three patient record review studies.

B.C.F.M. Schutijser, I.P. Jongerden, J.E. Klopotowska,
M.J. Moesker, M. Langelaan, C. Wagner, M.C. de Bruijne

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ABSTRACT

Objective Opioids are increasingly prescribed and frequently involved in adverse drug events (ADEs). The underlying nature of opioid-related ADEs (ORADEs) is however understudied. This hampers our understanding of risks related to opioid use during hospitalisation and when designing interventions. Therefore, we provided a description of the nature of ORADEs.

Design A post-hoc analysis of data collected during three retrospective patient record review studies (in 2008, 2011/2012 and 2015/2016).

Setting The three record review studies were conducted in 32 Dutch hospitals.

Participants A total of 10,917 patient records were assessed by trained nurses and physicians.

Outcome measures Per identified ORADE, we described preventability, type of medication error, attributable factors and type of opioid involved. Moreover, characteristics of preventable and non-preventable ORADEs were compared to identify risk factors.

Results Out of 10,917 patient records, 357 ADEs were identified of which 28 (8%) involved opioids. Eleven ORADEs were assessed as preventable. Of these, 10 were caused by dosing errors and 4 probably contributed to patients' death. Attributable factors identified were mainly on patient and organisational level. Morphine and oxycodone were the most frequently involved opioids. The risk for ORADEs was higher in elderly patients.

Conclusions Only 8% of ADEs identified in our sample were related to opioids. Although the frequency is low, the risk of serious consequences is high. We recommend to use our findings to increase awareness among physicians and nurses. Future interventions should focus on safe dosing of opioids when prescribing and administering, especially in elderly patients.

INTRODUCTION

Over the past decades, prescription of opioids has substantially increased worldwide.[1,2] Moreover, the rise in addiction rates and deaths resulting from opioid overdoses has urged physicians to call out an opioid crisis.[3] In the Netherlands, the prescription of oxycodone has increased almost fivefold over 10 years (from 96,000 users in 2008 to 485,000 users in 2018).[4] This increase may however not only lead to more addiction but may also affect the number of opioid-related adverse drug events (ADEs) in hospitals.

Opioids are frequently involved in ADEs[5-7] and approximately in 2-14% of all patients.[8-12] ADEs are unintended injuries from a medical intervention related to drugs.[13] Opioid-related ADEs (ORADEs) occur frequently, specifically in pediatric,[7,14] palliative[15] and surgical patients.[10,11,16] ORADEs are often caused by errors such as omissions or incorrect dosing.[7,14,15,17] In addition, approximately 11% of ORADEs among hospitalised patients cause severe or even fatal patient harm,[18] and also due to the fast therapeutic effects of opioids. Besides these severe consequences, ORADEs lead to significantly higher healthcare costs.[9,10,16]

Our current knowledge about the incidence of ORADEs and their underlying nature is mostly based on medication-related incident reports.[7,14,15,17] However, a comprehensive patient chart review provides the most reliable information on ADEs in hospitals while incident reports suffer from severe under-reporting.[19,20] Furthermore, ORADE studies based on incident reports were usually conducted at one point in time or within one hospital or at a specific department.[7,14,15,17] The few ORADE studies based on comprehensive patient chart review were mainly conducted within a surgical population.[10,11,16]

Therefore, and also motivated by the opioid crisis, we have conducted an indepth analysis of ORADEs using data gathered during three consecutive national adverse event (AE) studies in the Netherlands in which patient record review was applied. To our knowledge, no such longitudinal multicentre study on ORADEs in a diverse inpatient population and using a comprehensive ADE detection method has been published. The aim of this study was to provide a detailed description of the underlying nature of ORADEs. By doing so, we hope to increase awareness and provide recommendations on how to prevent ORADEs in future hospitalised patients.

METHODS

Design and setting

We conducted a post-hoc analysis of data that were collected during three national retrospective patient record review studies conducted in 2008, 2011/2012 and 2015/2016. The aim of these studies was to identify AEs and ADEs in Dutch hospitals. A detailed description of the methodology used in these studies was previously published and comparable with other international AE studies.[21,22] In summary, for the 2008 and 2011/2012 studies, a random sample of 20 hospitals participated. In 2015/2016, a new random sample of 19 hospitals were selected, of which 7 had previously participated in two of the earlier studies. Both samples were stratified for hospital type and representation of urban and rural areas. In 2008 and 2011/2012, 200 patient records per hospital were randomly selected for review: 100 records of discharged patients and 100 records of in-hospital deceased patients. The 2015/2016 study was limited to 150 in-hospital deceased patients per hospital because the frequency of preventable AEs remained unchanged for in-hospital deceased patients in both the 2008 and the 2011/2012 measurements.[23-25] Records of patients younger than 1 year and of patients admitted at the departments of psychiatry and obstetrics were excluded because other expertise is necessary to detect AEs in these patients. The random selection of patient records was conducted by the participating hospitals with clear instructions of the researchers. The medical ethical committee of the Amsterdam UMC, Vrije Universiteit Amsterdam waived the requirement of informed consent (protocol numbers: 2005.146, 2009.130, 2016.282) as they found the scope of the study outside the Dutch Medical Research (Human Subjects) Act.

Review procedure: AE studies

During all three AE studies, selected patient records were reviewed for the occurrence of AEs, including ADEs. In Figure 1, a schematic overview of the review process in the national studies and this study is presented. In summary, the review process consisted of two phases. In phase 1, the records were screened for potential AEs by trained independent nurses. When predefined triggers were found, indicating an AE might have occurred, the record was labelled for an indepth review by a trained independent physician. Independent means that the physicians and nurses never had an employment contract in the participating hospitals. The physicians were highly experienced and specialised in surgery, internal medicine or neurology, and during the record review studies they had access to all information on the electronic patient records. Besides,

10% of all patient records were reviewed by two physicians to determine inter-rater reliability. Validity of this scoring system has not been tested, but it has been used widely in AE studies for over 20 years and the ratings of the system did not change in that time.[21-23,26-29] Prior to the study, both nurses and physicians had training sessions in which cases were discussed to enhance the quality and standardisation of the review process.

An AE was defined by three criteria: 1) an unintended physical or mental injury; 2) the injury resulted in prolongation of hospital stay, temporary or permanent disability, or death; and 3) the injury was caused by healthcare management rather than the patient's underlying disease.[23,27,28] An AE was scored as caused by the healthcare (causality) if the likelihood score was equal to or greater than 4 based on a 6-point Likert scale, with (virtually) no evidence (1), slight to modest evidence (2), not likely but borderline (3), more likely but borderline (4), moderate to strong evidence (5), or (virtually) certain evidence (6) of management causation. The scoring system was used in all three record review studies and the physicians made the judgements about causality and preventability based on all the available information of the patient's condition and taking into account the guidelines.

If an AE was identified, the independent physicians (hereafter: experts) assessed each AE on cause (diagnostic, surgery, non-invasive procedure, medication, other clinical activities, admission and other), preventability, possible contribution to death and attributable factors. The attributable factors were based on the taxonomy of the Eindhoven Classification Model and consisted of the main categories: technical, care, organisational, patient-related, violation and other.[30] An AE was considered to be preventable when the care given fell below the current level of expected performance of practitioners or systems. Before the physicians answered the question about preventability, they were required to respond to 13 questions to add more structure to the review process (see Supplemental Table 1), for example, if there was a complex medical history, if the patient had comorbidity and whether another physician would repeat this treatment. Preventability was also assessed on a 6-point Likert scale, with almost no evidence (1), slight to modest evidence (2), modest evidence but borderline (3), modest to strong evidence (4), strong evidence (5), or almost certain evidence (6) of preventability. A score of 4-6 indicated that the reviewer assessed the AE as having a greater than 50% chance of being potentially preventable.

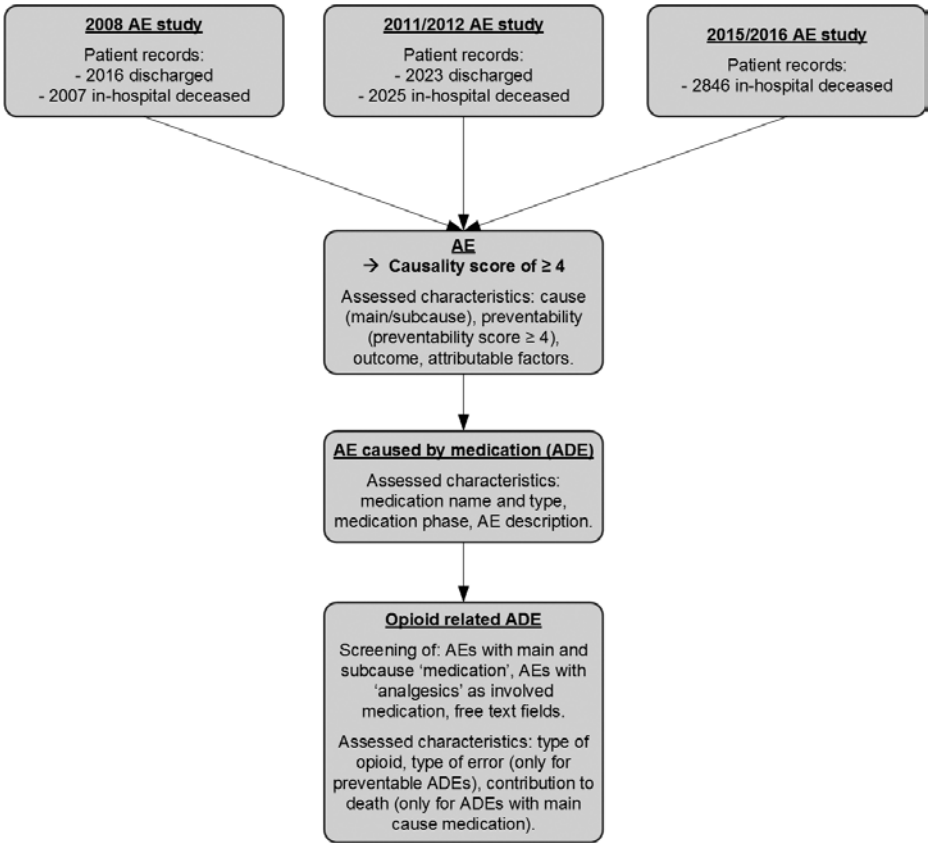

Figure 1 Overview of the three Dutch adverse event studies and our study. ADE=adverse drug event, AE=adverse event.

Furthermore, for each patient the following characteristics were registered: gender, age, length of hospital stay, urgency of admission, whether patients were terminally ill prior to the admission, the number of involved medical specialists, department of admission, type of procedure and comorbidity. The latter was divided into no, minor, moderate and severe comorbidity, and was assessed by the experts after careful review of the information on the patient record. Also, one organisational characteristic (type of hospital: university, tertiary teaching or general) and one AE characteristic (weekend or holiday at the time of the AE) were registered.

When an AE was medication-related (ADE), the following additional characteristics were registered by the experts: name and type of medication involved, medication phase, a description of the ADE and whether the ADE possibly contributed to the patient's death. The medication phases were classified into ordering, transcribing, dispensing,

administering and monitoring.[31,32] The possible contribution to the patient's death was only registered for ORADEs, with 'medication' as a main cause of the event and not for ADEs with 'medication' as a subcause.

All data were entered into a national AE database specifically designed for these AE studies.

Review procedure: ORADEs

For our study, we used the national AE database to identify ORADEs (Figure 1). One researcher (BS) conducted the screening of the database and retrieved several preselected variables: (1) AEs with the main classification cause 'medication' as well as AEs with 'medication' as a subcause; and (2) AEs with 'analgesics' as involved medication. Furthermore, two free-text fields were selected: the summary of the AEs and the preventability assessment. A second researcher (MM) independently double-checked the selection procedure.

All identified ORADEs were then classified by BS on the type of opioids involved using the World Health Organization Anatomical Therapeutic Chemical (WHO ATC) classification.[33] For the preventable ORADEs, the type of medication error was classified according to a data-driven analysis of the free-text summaries of the ADEs. The classification of ORADEs was double-checked by two senior researchers (JK and IJ) and any discrepancies were resolved by consensus.

Outcomes

To provide insight into the nature of the ORADEs, each ORADE case was summarised by gender, age of the patient (categorised in steps of 10 years for privacy reasons), type of opioid involved, attributable factors and preventability. When the ORADE was preventable, then the type of medication error and medication phase were also described. Furthermore, in order to identify risk factors, we compared the outcome variables between preventable and non-preventable ORADEs.

Data analysis

Only descriptive statistics were used in this study. Descriptives are presented as median (age and length of hospital stay) or frequency (gender, comorbidity, type of opioids and attributable factors, and so on). Patient and hospital characteristics are presented on the patient level and ORADE characteristics are presented on the AE level.

Inter-rater reliability among nurses and physicians was addressed in terms of positive and negative agreement frequencies.[34] All analyses were conducted using STATA V.14.1 and double-checked by a second researcher (MM) and a statistician (PS).

Patient and Public Involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

RESULTS

In total, 10,917 records were screened during the three AE studies. The patient records of discharged and deceased patients were equally distributed among male and female patients. Most patients were hospitalised for a non-elective procedure (Table 1). In 1150 patient records, at least one AE was detected, with a total of 1240 AEs. When detecting the predefined triggers, positive agreement between nurses varied between 76.0 and 91.5%. When detecting AEs, positive agreement between physicians varied between 53.4 and 63.3%. For assessing preventability, positive agreement between physicians varied between 71.4 and 73.3%. Overall, agreement frequencies were moderate. More detailed information about the inter-rater reliability is presented in Supplemental Table 2.

Table 1 Patient and hospital characteristics of all reviewed patient records, including adverse events per study period and discharge status.

	Study period and discharge status				
	2008		2011/2012		2015/2016
Hospital characteristics †	**Discharged**	**Deceased**	**Discharged**	**Deceased**	**Deceased**
Patient records, n	2016	2007	2023	2025	2846
General hospital records, n (%)	1013 (50)	1015 (51)	794 (39)	813 (40)	1197 (42)
Tertiary teaching hospital records, n (%)	608 (30)	593 (30)	822 (41)	820 (40)	1052 (37)
Academic hospital records, n (%)	395 (20)	399 (20)	407 (20)	392 (19)	597 (21)
	2008		**2011/2012**		**2015/2016**
Patient characteristics †	**Discharged**	**Deceased**	**Discharged**	**Deceased**	**Deceased**
Male sex, n (%)	999 (50)	1067 (53)	1027 (51)	1062 (52)	1524 (54)
Age (years), median (IQR)	62 (47-75)	77 (67-84)	63 (48-75)	77 (68-84)	77 (68-85)
Length of stay (days), median (IQR)	4 (2-8)	7 (3-14)	3 (2-7)	6 (2-13)	4 (1-11)
Non-elective admission, n (%)	1038 (51)	1708 (85)	1063 (53)	1775 (88)	2496 (88)
Admission department, n (%)					
Surgery	481 (24)	276 (14)	472 (23)	239 (12)	340 (12)
Cardiology	290 (14)	291 (15)	272 (13)	247 (12)	360 (13)
Internal medicine	364 (18)	599 (30)	365 (18)	597 (29)	876 (31)
Orthopaedics	226 (11)	33 (2)	225 (11)	26 (1)	29 (1)
Neurology	150 (7)	219 (11)	133 (7)	193 (10)	269 (9)
Lung diseases	117 (6)	259 (13)	126 (6)	300 (15)	347 (12)
Urology	109 (5)	18 (1)	111 (5)	28 (1)	23 (1)
Other	279 (14)	312 (16)	319 (16)	395 (20)	602 (21)
Underwent invasive procedure, n (%)	925 (46)	423 (21)	918 (45)	403 (20)	461 (16)
Adverse event occurrence §¶					
AE, n (%)	161 (8)	351 (16)	157 (8)	259 (12)	312 (10)
ADE, n (% within population)	37 (2)	93 (4)	40 (2)	76 (4)	111 (4)
ADE, n (% within adverse event)	37 (23)	93 (27)	40 (25)	76 (29)	111 (36)
ORADE, n (% within population)	1 (0)	7 (0)	2 (0)	8 (0)	10 (0)
ORADE, n (% within ADEs)	1 (3)	7 (8)	2 (5)	8 (11)	10 (9)

† Presented on the patient record level.
§ Presented on the AE level.
¶ Total number of AEs: 1240; total number of ADEs: 357; total number of opioid-related ADEs: 28.
AE=adverse event, ADE=adverse drug event, ORADE=opioid-related adverse drug event.

Opioid-related ADEs

Of 1240 AEs, 357 (29%) were medication-related (ADEs). In 28 (8%) ADEs, opioids were involved. These ADEs are summarised in detail in Table 2, and included 24 ADEs with 'medication' as a main cause and four ADEs with 'medication' as a subcause. The ORADEs occurred in 27 patients; one patient experienced two ORADEs. Most patients with ORADEs involved female patients (59%). The median age of the patients was 76 years (IQR: 66-83), and the median length of hospital stay was 7 days (IQR: 4-16). Most patients had moderate to significant comorbidity (70%) and had three medical specialists during the admission (78%) (Table 3).

Nature of ORADEs: preventability

According to the experts, 11 (39%) out of the 28 ORADEs were considered as potentially preventable (Table 4). Non-preventable (31%) ORADEs occurred slightly more during weekends and holidays than preventable ADEs (18%). Moreover, most preventable and non-preventable ORADEs occurred during dayshifts (08:00-17:00).

Nature of ORADEs: medication errors and phase

Of the 11 potentially preventable ORADEs, 10 (91%) were caused by dosing errors, of which 6 were during the prescribing phase (cases 1, 3, 7, 8, 9 and 10) and 4 during the administration phase (cases 2, 4, 5 and 6) (Table 2). Of the 10 dosing errors, 6 occurred in elderly patients (≥70 years) (cases 1, 3, 4, 5, 8 and 9), and 2 around patients' discharge (cases 2 and 7). The remaining one preventable ORADE (case 11) was related to incorrect decision making. Finally, the experts assessed the consequences of the ORADEs (multiple options possible). In eight ORADEs, an intervention or extra treatment was needed, in two ORADEs the patients had a prolonged hospital stay, and four preventable ORADEs possibly contributed to the death of the patient (cases 5, 6, 8 and 9).

Nature of ORADEs: attributable factors

The attributable factors involved in ORADEs were care-related (knowledge, skills, monitoring, verification and coordination of care) and patient-related (comorbidity, age, a demanding patient or a patient with an intellectual disability) (Table 4). Of preventable ORADEs, eight were care-related and six were patient-related. For non-preventable ORADEs, 3 were care-related and 10 were patient-related. However, in three of the cases of non-preventable ORADEs, the attributable factors could not be assessed by the experts due to insufficient information on the patient records.

Nature of ORADEs: medications involved

Out of the 11 preventable ADEs, 8 occurred with opioids with ATC code N02AA, which are morphine and oxycodone (Table 4). Non-preventable ORADEs occurred with opioids mainly with ATC code N02AA (morphine and oxycodone, 53%).

Table 2 Descriptions of the 28 opioid-related adverse drug events divided into preventable and non-preventable.

Case	Description†	Preventability score (1-6)‡ and type of error§
Preventable opioid-related ADEs		
Cause: dosing errors		
1	A man, 90-99 years, admitted with pain after a fall. Oxycodone for the pain was unintentionally prescribed twice instead of once and also administered twice (dose unknown). This resulted in drowsiness.	6 (prescribing error)
2	A man, 60-69 years, suffering from colon cancer and liver metastases, was admitted for optimising his analgesics medication. On returning from his weekend leave, he was diagnosed with oxycodone intoxication. During hospital stay, he received a too high dose of the opioid antagonist naloxone (1 mg instead of the ordered 0.4 mg) which caused confusion and agitation.	6 (administration error)
3	A woman, 70-79 years, admitted with a pelvic fracture after a fall. A too high dose (dose unknown) of oxycodone was prescribed and administered resulting in hypotension and drowsiness. Consequently, she needed to be transferred to the intensive care unit.	5 (prescribing error)
4	A woman, 80-89 years, admitted with malaise after a fall. During her admission she received a too high dose of morphine. In her patient record, the morphine was ordered as 'as needed' (PRN). In the medication list, the morphine was ordered '6 times a day' (dose unknown). This resulted in drowsiness.	5 (administration error)
5	A woman, 70-79 years, admitted for a plastic surgery. A high dose of intravenous administered anesthetic/pain medication (dose and medication type unknown) caused hypoventilation and a myocardial infarct. The myocardial infarct was discovered too late. She was resuscitated and ventilated. Her death was possibly caused by a hospital-acquired pneumonia.	5 (administration error)
6	A woman, 50-59 years, admitted due to an aspiration pneumonia, was administered morphine. The pump mode was set at 13 ml/hour instead of 8 ml/hour as ordered. This possibly resulted in an epileptic insult requiring ventilation.	5 (administration error)

Table 2 Descriptions of the 28 opioid-related adverse drug events divided into preventable and non-preventable.

Case	Description†	Preventability score (1-6)‡ and type of error§
7	A man, 60-69 years, readmitted to the hospital due to a collapse at home. He was previously hospitalised for treatment of rib fractures and COPD Gold IV. At discharge, the doses of fentanyl and oxycodone had been significantly increased to 20 mg 4-6 times a day. Monitoring the effects of increasing these opioid doses was not conducted.	4 (prescribing error)
8	A woman, 80-89 years, admitted with osteoporosis, received at home 5 mg morphine two times per day for her back pain. The dosage was increased to subcutaneous 5 mg four times a day during hospital stay. Three days later, a paralytic ileus was discovered. A lower morphine dose was more appropriate for this elderly woman.	4 (prescribing error)
9	A woman, 80-89 years, admitted with abdominal pain due to kidney bleeding. She received morphine injections daily, varying from 2 to 6 subcutaneous injections of 2.5 mg per day along with transdermal fentanyl 12 µg hourly. Severe hypercapnia eventually caused her death.	4 (prescribing error)
10	A boy, 0-9 years, with Down syndrome, was acutely ill due to a laryngitis. He was difficult to ventilate and received antibiotics and sedatives including opioids. He was transferred to another hospital following detubation. Here, his methadone intake was reduced resulting in a delirium (dose unknown). Initially he improved, but one day unexpectedly he was found dead. It is unclear why this patient received methadone, but reducing the methadone intake may have been the problem.	4 (prescribing error)
Cause: incorrect decision making		
11	A woman, 60-69 years, admitted for a laminectomy. Postoperatively she developed an ileus caused by severe constipation aggravated by administered morphine. Macrogol oral suspension (dose unknown) instead of an enema was given as treatment, which was insufficient to resolve, and the ileus and colon perforation occurred. Untreatable abdominal septic complications followed.	4 (unknown)
Non-preventable opioid-related ADEs		
12	A woman, 80-89 years, admitted due to total knee replacement. Postoperatively, drowsiness, hypotension and oliguria occurred, possibly caused by the epidural medication sufentanil (dose unknown). This may have led to a small asymptomatic myocardial infarct.	3 (administration error)

Table 2 Descriptions of the 28 opioid-related adverse drug events divided into preventable and non-preventable.

Case	Description†	Preventability score (1-6)‡ and type of error§
13	A man, 80-89 years, admitted with a perforated stomach ulcer and known stomach cancer. His extreme, not previously known, sensitivity to morphine postoperatively (dose unknown) resulted in recurrent apnoea.	3 (other error)
14	A woman, 60-69 years, suffering from lung cancer, was admitted with severe back and limb pain related to bone metastases. She was treated with transdermal fentanyl 300 µg/hour. This resulted in drowsiness and hypoventilation.	2 (prescribing error)
15	A woman, 80-89 years, known with breast cancer and multiple lung metastases. She received tramadol (dose unknown) for the pain, which have been stopped due to drowsiness.	2 (unknown)
16	A man, 70-79 years, admitted with severe heart failure. He received morphine 2.5 mg for the pain. As a result of increased, not previously known, sensitivity to morphine, his saturation dropped.	2 (other error)
17	A man, 90-99 years, admitted due to stroke and a lot of pain. The nurse administered 10% of the prescribed dose (dose unknown) of morphine on two occasions, which caused unnecessary suffering.	2 (administration error)
18	A man, 60-69 years, admitted for surgery due to an ileus. Postoperative complications included an exacerbation of COPD and hospital-acquired pneumonia after receiving morphine (dose unknown).	2 (unknown)
19	A woman, 60-69 years, admitted with a reoccurrence of drowsiness, hypoventilation and difficulties with waking up, which was the result of a dose of 5 mg of methadone being administered in the hospital.	2 (prescribing and administration error)
20	A woman, 60-69 years, had a blood pressure drop following the administration of morphine (dose unknown) in the recovery room.	1 (other error)
21	A woman, 70-79 years, admitted with pain related to severe Kahler disease. For the pain, she received opioids (unknown which type and dose). The opioids caused drowsiness, and because of the drowsiness she choked once. This caused pneumonia. The patient died during hospitalisation.	1 (other error)
22	A man, 70-79 years, received transdermal fentanyl and oxycodone 5 mg daily up to six times due to metastases in the hip. This caused apraxia and confusion.	1 (unknown)
23	A woman, 80-89 years, admitted for occlusion of an artery in her leg. She received a morphine infusion (0.5-1.0 mg/hour) causing hypoventilation with a good response to naloxone.	1 (administration error)

Table 2 Descriptions of the 28 opioid-related adverse drug events divided into preventable and non-preventable.

Case	Description†	Preventability score (1-6)‡ and type of error§
24	A man, 80-89 years, admitted due to obstructive laryngeal cancer, was prescribed anticoagulants. This resulted in haematoma, along with severe abdominal pain for which he received morphine (dose unknown), after which he died.	1 (other error)
25	A man, 60-69 years, admitted with an acute respiratory insufficiency due to pneumonia. He received methadone 20 mg two times per day, causing hypoventilation on two occasions. This needed to be treated with naloxone.	1 (prescribing error)
26	A woman, 80-89 years, suffered from pain due to rib fractures caused by resuscitation. She received sufentanil (dose unknown), which led to bronchospasm.	1 (unknown)
27	A woman, 70-79 years, admitted with pain related to breast cancer. During the admission, it became apparent that she had metastases along with femur and vertebral fractures. A high dose of morphine (dose unknown) was necessary to relieve her pain, which consequently resulted in a delirium.	1 (prescribing error)
28	A woman, 80-89 years, admitted due to a hip fracture and pain. For her restlessness and pain she was administered 1 mg morphine, which probably caused a reduced level of consciousness.	1 (other error)

† Patients were categorised in age groups of 10 years to avoid traceability.
‡ Preventability was scored on a 6-point Likert scale: 1=(almost) no evidence of preventability; 2=small indications for preventability; 3=preventability not very likely, less than 50% but ´close call´; 4=preventability more than likely, more than 50% but 'close call'; 5=strong indications for preventability; 6=(almost) certain indications of preventability.
§ For the judgement on preventability and type of error, the experts had access to all information on the electronic patient record and therefore to the whole context in which ADEs occurred. The types of error were prescribing error, administration error, other error (e.g. side effects) or unknown.
ADEs=adverse drug events, COPD=chronic obstructive pulmonary disease.

Table 3 Characteristics of patients (n=27) with ORADEs (n=28)†

Patient characteristics	
Patients with an ADE, n	27
Male sex, n (%)	11 (41)
Age, median years (IQR)	76 (66-83)
Length of stay, median days (IQR)	7 (4-16)
Non-elective admission, n (%)	19 (70)
Terminally ill prior to admission, n (%)	6 (22)
Total number of medical specialists, n (%)	
1	4 (15)
2	2 (7)
3	21 (78)
Primary specialisation during admission, n (%)	
Surgical	7 (26)
Non-surgical	20 (74)
Underwent invasive procedure, n (%)	9 (33)
Comorbidity§, n (%)	
No comorbidity	0 (0)
Minor comorbidity	3 (11)
Moderate comorbidity	5 (19)
Significant comorbidity	19 (70)

† Presented on the patient level.
§ The level of comorbidity was assessed by the experts after careful review of the information on patient records.
ADE=adverse drug event, ORADEs=opioid-related adverse drug events.

Table 4 Clinical context of ORADEs (n=28)†

Clinical context	Non-preventable§ ADEs (n=17)	Preventable§ ADEs (n=11)
Type of hospital, n (%)		
University, ADEs	1 (6)	1 (9)
Tertiary teaching, ADEs	6 (35)	4 (36)
General, ADEs	10 (59)	6 (55)
Weekend or national holiday (yes), n (%)	5 (31)	2 (18)
Time , n (%)		
08:00-17:00	6 (35)	5 (45)
17:00-23:00	3 (18)	0 (0)
23:00-08:00	2 (12)	3 (27)
Cannot be assessed	6 (35)	3 (27)
Type of opioids (ATC code), n (%)		
Opioid anesthetics (N01AH03)	2 (12)	1 (9)
Natural opium alkaloids (N02AA)	9 (53)	8 (73)
Natural opium alkaloids and phenylpiperidine derivatives (N02AA/N02AB, combination)	1 (6)	1 (9)
Phenylpiperidine derivatives (N02AB)	2 (12)	0 (0)
Other opioids (N02AX)	1 (6)	0 (0)
Drugs used in opioid dependence (N07BC)	2 (12)	1 (9)
Attributable factors¶, n (%)		
Technical	0 (0)	0 (0)
Care-related	3 (19)	8 (80)
Organisational	2 (13)	4 (40)
Patient-related	10 (63)	6 (60)
Violation	0 (0)	1 (10)
Cannot be assessed	3 (19)	1 (10)
Other	1 (6)	0 (0)

† Presented on the adverse event level. § Preventability was scored on a 6-point Likert scale: 1=(almost) no evidence of preventability; 2=small indications for preventability; 3=preventability not very likely, less than 50% but 'close call'; 4=preventability more than likely, more than 50% but 'close call'; 5=strong indications for preventability; 6=(almost) certain indications of preventability. Not preventable ADEs were scored at 1-3; preventable ADEs were scored at 4-6. ¶ These variables were missing for 2 patients: one in the preventable group and one in the non-preventable group. Moreover, it was possible to select more than one option for this question. ADE=adverse drug event, ATC=Anatomical Therapeutic Chemical, ORADE=opioid-related adverse drug event.

DISCUSSION

In three national patient record studies with 4-year intervals, we found 28 ADEs caused by opioids. These ADEs correspond with 8% of all identified ADEs and 0.3% of all studied patient records. Of the 28 ORADEs, 11 (39%) were assessed as potentially preventable, involving mostly morphine and oxycodone. Dosing errors during the prescription and administration phase were the most common cause of preventable ORADEs and occurred most often in elderly patients. Four preventable ORADEs probably contributed to patients' death. Finally, attributable factors for ADEs were mostly care-related and patient-related.

In this study, the percentage of ORADEs of all patient records (0.3%) was low, also in comparison with previously conducted ORADE studies that focused on large populations (11-14%).[10,11,16] However, two of these studies were based on large databases and all involved surgical patients who often receive opioids postoperatively. We focused on a broad hospitalised patient population, both surgical and non-surgical. Furthermore, the difference in ORADE occurrence might be explained by differences in the used ADE definition. For example, instead of using all ORADEs, that is, including side effects of opioids, in our study only ADEs that resulted in severe patient harm were included. This means that ADEs resulted in prolongation of hospital stay, temporary or permanent disability, or death. Furthermore, only ADEs with a causality likelihood score of equal or greater than 4 were included, which means that the experts indicated an ADE as having a greater than 50% chance of being caused by healthcare. Should we have selected the cases with causality likelihood scores of 1-3 as well, then we could determine at least 2500 additional cases on whether medication and opioids were related. However, we did not determine these 2500 cases, since we wanted to stay true to the definition of an AE (at least 4 on the 6-point Likert scale), and we did not consider it ethical to change the method of the study afterwards.

In line with previous studies,[7,14,15,17] we found that dosing errors during prescribing and administering were the main cause of preventable ORADEs. Furthermore, 60% of the dosing errors in our study occurred in elderly patients (≥70 years). In general, prescribing medication for elderly patients is challenging since polypharmacy, multimorbidity, and altered pharmacokinetics and pharmacodynamics of drugs are often present. Besides, this population will rapidly increase in the upcoming years. Specifically related to opioids, physicians also need to be aware of the higher sensitivity of elderly patients to

the effects of opioids,[35] and balancing between minimizing the risk of addiction and side effects while effectively relieving pain.[36,37] Taking into account all these factors while prescribing demands a lot from physicians during their busy daily hospital practice. A clinical decision support system (CDSS) can help physicians in this complex task by showing warnings and advice during prescribing, for example showing the most appropriate choice of medication for a given condition and/or by providing dosing recommendations. CDSS has shown to effectively reduce prescribing errors among hospitalised elderly patients[38,39] and errors with medications of which the therapeutic effects are fast, such as opioids.[40] Furthermore, a CDSS can also be effective in predicting which patients are at risk for ORADEs. Using retrospective data from gastrointestinal surgical patients, Minkowitz et al. developed a risk-scoring model to identify patients with a high risk for experiencing an ORADE based on their clinical and demographic profiles.[41] If developed specifically for elderly inpatients, such a prediction model could help physicians in determining the most appropriate and safe pain management strategy for these vulnerable patients. Finally, a CDSS could also be used to identify patients who might be suitable for pre-emptive genotyping, which involves metabolic testing prior to prescribing.[42] Patients with high levels of pain despite using high doses of pain medication or patients who experience severe side effects while using common dosing schedules may especially benefit from such an intervention.[43]

Administering opioids is a task usually conducted by nurses. The dosing errors in our study were mostly related to injectable opioids. Error-prone activities, such as calculating the concentration and administration rate,[14,17] require that nurses have sufficient arithmetic knowledge and follow the protocol for safe preparation and administration of injectable medication. However, in daily practice, some nurses have math anxiety, and on average arithmetic knowledge of nursing students seems moderate.[44,45] Besides, nurse compliance with protocols for safe administration of injectable medication is considered low (around 20%)[46,47] and needs further attention. An intervention which might help to reduce dosing errors during opioid administration is the use of smart infusion pumps. These pumps have integrated medication libraries which allow nurses to set the pump automatically to the right administration rate during administration. By doing so, the administration rate of smart pumps can be seen as a double-check of the nurses' own calculation. Smart pumps seem also effective in reducing programming errors.[48] Furthermore, educational programs for nurses about brand and generic names and pharmacology of opioids or side effects might increase their knowledge and awareness of risks related to dosing during the administration of opioids.[49-51]

Overall, we think the ORADE frequency of 8% of all ADEs and 0.3% of all studied patient records found in our study is low and acceptable. However, although the frequency is low, the risk of serious consequences is high. Thus, new contributions to prevent ORADEs in future hospitalised patients need to be identified. Using the Safety-2 perspective may offer new opportunities to do so.[52] In order to understand what happened when an adverse (drug) event occurred, it is also necessary to understand how work is done when the process goes well.[53] Since healthcare processes have become more complex nowadays, it may be helpful to visualise the current variable practice of prescribing and administering opioids from a multistakeholder perspective.[54]

Strengths and limitations

Opioids are in the top 10 of drug types that cause fatal medication errors.[8] Hence, focusing on the detailed description of the nature of ORADEs was important and necessary. Another strength of this study is that it was based on a comprehensive ADE detection method and conducted in a broad sample of all hospital admissions. Most previous studies, which described the nature of ORADEs, are based on medication-related incident reports. Furthermore, data were gathered over an extended period of time within a randomly selected sample of one-third of all Dutch hospitals.

This study also has some limitations. First, in all three AE studies, the population consisted of relatively many older and deceased patients. Therefore, it is not possible to generalise the results to all Dutch hospital population. To make the study sample more representative for the Dutch hospital population, weighting the results (i.e. correcting for type of hospital, study period and discharge status) would be a solution which has been used in previous studies of our research group. However, since the total amount of ORADEs was low, we chose not to weight our results as this had little effect and makes interpretation difficult. Second, overall agreement frequencies between physicians were moderate. This could have led to different assessments or different scores if other experts were involved. This should be taken into account when interpreting our results. However, a previous review of studies focusing on assessing AEs showed also moderate to substantial inter-rater reliability.[55] For this reason, patient records in all Dutch AE studies have been assessed by the same experts as much as possible, and over the years these experts have not become stricter or lenient in their judgement of AEs and their preventability.[56] Third, due to this low number of ORADEs, it was not possible to compare the events over the three study periods. Therefore, we cannot conclude whether the low number is a positive finding and if the occurrence of ORADEs increased

or decreased over time. Fourth, our post-hoc analysis was based on the information previously recorded by the experts in an AE database and on the assessment conducted by these physicians. Therefore, some information could be missing, and interpreting the assessment of preventability was difficult for us in one case, resulting in a non-preventable ORADE. Furthermore, this was also the reason that the harm could not be further categorised according to the National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP) Index for Categorizing Medication Errors.[57] Besides, the retrospective interpretation can also be biased by temporal views. The current opinion is that prescribing opioids should be minimised due to the harm of opioids, which is supported by updated guidelines.[58] This view changed throughout the years and may not have been recognised 15 years ago, when the focus was mainly on alleviating suffering of pain. This change in opinion may have increased alertness when prescribing or administering opioids, which could have led to less ORADEs. However, our study showed that ORADEs still occur and publishing about them could serve as a method of increasing awareness.

CONCLUSION

Only 8% of ADEs identified in our sample were related to opioids, 0.3% of all studied patient records. Although the frequency is low, the risk of serious consequences is high. We recommend to use our findings to increase awareness among physicians and nurses. Future interventions should focus on safe dosing of opioids when prescribing and administering, especially in elderly patients.

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Supplemental Table 1 Preventability, preparatory and judgment questions for physicians.

Question	Answer options
1. How complex was this case?	Very complex/Moderately complex/ Somewhat complex/Not complex/Unable to determine
2. Was the management of the primary illness (not the adverse event) appropriate?	Definitely appropriate/Possibly appropriate/ Probably appropriate/Definitely not appropriate
3. What was the degree of deviation of management of the primary illness (not the adverse event) from the accepted norm?	Severe/Moderate/Little/None
4. What was the comorbidity of the patient?	Significant comorbidity/Moderate comorbidity/Mild comorbidity/No comorbidity
5. What was the degree of emergency in management of the primary illness (not the adverse event) prior to the occurrence of adverse event?	Very urgent/Moderately urgent/Not urgent
6. What potential benefit was associated with the management of the illness which led to the Adverse Event?	Lifesaving/Curing/Life prolonging/Symptom relief/Palliation/No potential benefit
7. What was the chance of benefit associated with the management of the illness which led to the adverse event?	High/Moderate/Low/Not applicable
8. What was the risk of an adverse event related to the management?	High/Moderate/Low/Not applicable
9. Is the injury/complication a recognised complication?	No/Yes/Not applicable
10. What percentage of patients like this would be expected to have this complication?	Unable to determine (UTD)/Not applicable/<1/1%–9%/10%–24%/>=25%
11. On reflection, would a reasonable doctor or health professional repeat this healthcare management strategy again?	Definitely/Probably/Probably not/Definitely not
12. Was there a comment in the medical records indicating a need for follow-up as a result of this adverse event? (select all that apply)	No/Counselling/Psychiatric/Rehabilitation/ Routine clinical/Other/UTD
13. Did the patient have any follow-up as a result of this adverse event?	No/Counselling/Psychiatric/Rehabilitation/ Routine clinical/Other/UTD
Final judgment Please indicate to what extent there are indications that the event was preventable:	1.(Virtually) no evidence for preventability 2.Slight to modest evidence of preventability 3.Preventability not quite likely (less than 50/50, but 'close call') 4.Preventability more than likely (more than 50/50, but 'close call') 5.Strong evidence of preventability 6.(Virtually) certain evidence of preventability

Supplemental Table 2 Positive and negative agreement (%) between nurses and physicians during the adverse events studies.†‡

	Nurses		Physicians - adverse event		Physicians - preventability	
Study	**Positive agreement**	**Negative agreement**	**Positive agreement**	**Negative agreement**	**Positive agreement**	**Negative agreement**
2008	76.0	89.0	63.3	86.9	n/a	n/a
2011/2012	85.8	63.3	56.9	82.9	73.3	83.3
2015/2016	91.5	68.9	54.3	80.9	71.4	81.0

† All frequencies are separately calculated by a 2x2 table:

		Nurse / Physician 1	
		Positive agreement	Negative agreement
Nurse / Physician 2	Positive agreement	A	B
	Negative agreement	C	D

Positive agreement = (2xA) / ((2xA)+B+C) and negative agreement = (2xD) / ((2xD)+B+C).

‡ The interpretation of the Kappa is not straightforward, and it is influenced by the number of categories of each variable and the prevalence of the given scores. It is therefore possible that despite a high agreement, the Kappa is low. This occurs in studies with few adverse events. For this reason we chose to present positive and negative agreement frequencies. It helps to answer questions such as: 'if one expert finds a preventable adverse event, what is the probability that another expert will also find a preventable adverse event?'

Chapter 6

Double checking injectable medication administration: Does the protocol fit clinical practice?

B.C.F.M. Schutijser, I.P. Jongerden, J.E. Klopotowska,
S. Portegijs, M.C. de Bruijne, C. Wagner

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ABSTRACT

Objectives It is unclear how nurses adjust the double check during injectable medication administration and guarantee patient safety. We used the Functional Resonance Analysis Method (FRAM) to determine the fit between the double check according to the protocol (work-as-imagined) and clinical practice (work-as-done). We aimed to learn about process variation in order to optimize safety during injectable medication administration.

Methods A qualitative study (February-July 2018) with semi-structured group interviews. An internal medicine and a surgery ward of two Dutch hospitals participated (four wards total). We interviewed nurses about injectable medication administration practices, based on prior observations. A work-as-done model was constructed for each hospital. The work-as-imagined model was based on the Dutch protocol for safe injectable medication administration.

Results A total of 27 nurses were interviewed. In both hospitals, nurses split the double check into a digital and physical check to improve workflow. The digital check was routinely conducted. For the physical check, nurses made their own risk-impact analysis and assessed staffing, familiarity with the medication, severity of side effects, type of medication and administration route and the patients' medical condition. Based upon these criteria, nurses decided to conduct the physical double check or not.

Conclusions We identified a lack of fit between work-as-imagined and work-as-done. Nurses adjust the double check in practice by assessing the patients' and wards' situation. It is unknown whether this variability also causes patient harm. We recommend to reconsider to what extent practice variation is acceptable and safe.

INTRODUCTION

Over 90% of all hospitalized patients receive some form of injectable medication, such as intravenous infusion, subcutaneous or intramuscular injections.[1] These medications are of great value in the treatment of diseases because of their immediate therapeutic effect. However, administering them has also a high risk for patient harm, since medication errors with injectable medication are often irreversible. The likelihood of at least one error, such as wrong dose or wrong time, during the whole injectable medication process is 73%.[2] Therefore, based on the 'five rights' of safe medication administration (right patient, drug, dose, route, and time),[3] protocols for safe injectable medication administration have been established internationally. In The Netherlands, such a protocol has been implemented in 2009 and includes 25 proceedings.[4]

Yet, compliance with the protocol proceedings for safe injectable medication administration is low.[5-10] Especially the compliance with the double check proceeding is between 45 and 90% and needs improvement.[8,9,11,12] The double check is defined as "a procedure that requires two qualified health care professionals, usually nurses, who independently check the medication before administration to patients".[13] Nurses see the double check as a way to prevent medication errors.[14] Compliance with the double check proceeding in The Netherlands did not change over the years (52% in 2012 and 47% in 2016).[9] Especially logistical factors such as staff shortage lead to low compliance.[9,13]

While previous studies focused only on compliance and the absence of the double check,[5,11,15,16] extra understanding is needed about how nurses actually conduct the double check proceeding in everyday clinical practice. After all, most of the work seems to be carried out safely and without harming patients. A deeper understanding may reveal workarounds or adaptation of the proceeding while still guaranteeing patient safety. Furthermore, it may reveal a lack of fit between the protocol (work-as-imagined) and daily clinical practice (work-as-done) and provide possibilities for organizational learning to reduce the gap between work-as-imagined and work-as-done.[17]

Previous studies on other proceedings have used the Functional Resonance Analysis Method (FRAM) to evaluate complex clinical processes.[18-20] Protocols are often implemented with the Safety-I idea of preventing errors, whereby compliance is the outcome measure.[21] The lack of fit can arise because of insufficient understanding of the actual process and conditions in daily practice and how health care professionals adjust

proceedings according to variable working conditions. FRAM is a method to visualize essential activities of the work-as-done including the variability of daily practice.[22]

To the best of our knowledge, a FRAM analysis of the double check proceeding during injectable medication administration has not yet been published by others. Therefore, we used FRAM to determine the fit between the double checking proceeding according to the protocol (work-as-imagined) and clinical practice by nurses (work-as-done) in order to learn about variation in the process, adapting behaviors of nurses and identify facilitators and barriers to correct performing the double check. This knowledge is needed in order to optimize safety during the injectable medication administration process.

METHODS

Design

Between February and July 2018, we conducted a qualitative study, using observations and semi-structured (group) interviews focusing on the current daily practice of the double check during injectable medication administration. We defined the double check according to the Dutch protocol: a second nurse checks the administration on right (1) medication order, (2) medication name, (3) dose, (4) administration route, (5) administration rate, (6) patient and (7) time.[4] The second nurse needs to compare the information with the original medication order from the physician (confirmation), and calculate the right administration rate separately (independent check). Hence, the second nurse has not only a confirmative role.[17] The medical ethical committee of the Amsterdam UMC, Vrije Universiteit Amsterdam waived the requirement of informed consent (protocol number: 2018/156) as they found the scope of the study outside the Dutch Medical Research (Human Subjects) Act. Nevertheless, prior to each observation and (group) interview, oral consent was obtained from the nurses. The COREQ guideline was used to report this study.[23]

Setting

Two Dutch hospitals participated in this study, one university hospital (hospital A) and one general hospital (hospital B). The university hospital has 733 beds and over 7000 staff members and the general hospital has 277 beds and over 1500 staff members. Both hospitals were selected based on their compliance with the proceeding “double check by a second nurse”, as evaluated in a previous evaluation study.[9] Hospitals were

compliant with the double check when all 7 steps (medication order, medication name, dose, administration route, administration rate, patient and time) were conducted correctly. Thus, when work-as-done was conducted according to work-as-imagined. Since we also aimed to learn from what goes right, we selected one hospital with high compliance (100%, hospital B) and one hospital with average compliance (41%, hospital A). In both hospitals, two wards were invited to participate, an internal medicine and (general) surgery ward. All four wards participated in the previous evaluation study.[9]

Participants

For observations and interviews, all nurses (including trainees) involved in the administration of injectable medication on the participating wards were eligible to participate. Nurses were purposively invited to participate in the study by a senior nurse. For both the observations and interviews, nurses needed to be working on one of the selected wards and needed to be qualified to administer injectable medication. Participation in the study was voluntary for nurses and their information was anonymously processed.

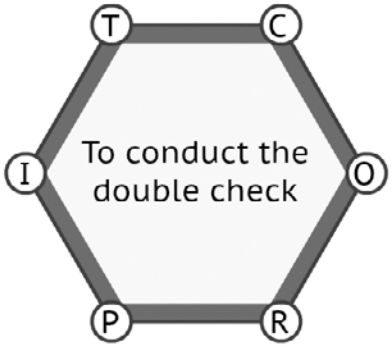

Figure 1 Example of a FRAM Function.

Functional resonance analysis method

The Functional Resonance Analysis Method (FRAM) was used to visualize essential activities of the double check process as it usually takes place.[22] This "work-as-done" model can be compared with the ideal model according to the protocol ("work-as-imagined"). The FRAM also takes into account variability, dependencies of activities and potential facilitators and barriers to correct performing the double check.[21] For each essential activity, a function (visualized as a hexagon) is created. Functions are described by a verb and need to be performed by nurses to achieve a certain goal

(i.e. to identify the patient). On each function, six aspects (Input, Output, Precondition, Resource, Control, Time) are relying (Figure 1):[22]

- Input: start of the function, for example the medication order is registered.
- Output: the result of the function, for example the administration of medication.
- Precondition: without these, the function cannot be conducted, for example the medication order is authorized.
- Resource: these are necessary during the execution of the function, for example working Wi-Fi connection to use a computer-on-wheels (COW) with a barcode scanner.
- Time: any time related restriction, for example, medication is only administered during the medication rounds.
- Control: the way the function is monitored, for example an audit every two months.

We used FRAM because the role of nurses can be seen as flexible and compensating. Nurses are often compensating for inadequacies in health care. This resilience results in adjusting to situations in practice.[24] The number of studies that used FRAM in healthcare processes are limited.[18-21,25-27] FRAM provides a unique opportunity to visualize complex processes. As compared to previous studies, FRAM can reveal which activities nurses actually do when they are double checking injectable medication. By visualizing this process with FRAM and the variability in the process, we aimed to better understand factors affecting the double check process. Besides, although individual interviews are recommended for the data-collection in FRAM studies, few studies conducted group interviews as a new method.[26,28] In our study, the work-as-done model was also constructed based on group interviews. The work-as-imagined model was based on the prevailing Dutch protocol for safe injectable medication administration.[4]

Functions in both work-as-imagined and work-as-done models were further divided in “foreground” and “background” functions: foreground functions were defined as the main and most important activities related to the double checking process. Background functions are activities related to other proceedings during injectable medication administration. Facilitators and barriers to correct performing the double check were divided in culture, technology, staff and organizational related factors and were based on a data-driven analysis. In addition, to better understand the work-as-done models, variability of the Output of foreground functions were described in (1) internal variability (i.e. variability of the function itself), (2) external

variability (i.e. variability of the work environment), (3) upstream-downstream coupling (i.e. variability from upstream functions), and (4) the manifestations of variability in terms of time (too early/on time/too late/omission) and precision (imprecise/acceptable/precise).[22] Functions with a high variability can have impact on other functions further in the FRAM model and eventually involve additional risks for conducting the process.

Data collection

We first conducted observations of nurses during injectable medication administration followed by semi-structured (group) interviews with nurses. Nurses were directly observed by using the same method as in previous observational studies by our research group.[8,9] In summary, nurses were observed while administering injectable medication to patients older than 18 years, during the medication rounds from 6 AM to 10 PM. Parenteral nutrition, intravenous chemotherapy and acute medications were excluded from the observations because for these medications other administration protocols apply. A standardized observation form was used to evaluate the nine most important and identifiable administration proceedings from the prevailing Dutch protocol (Supplement A). Correctly conducted proceedings were marked on the observation form. The findings from the observations served only as input for the interviews to give examples of proceedings with high and low compliance. Observations were not further analyzed, as no differences in the observations were found in comparison to the previous observational study.[9]

After the observations, nurses were interviewed either individually or in groups of two or three nurses. The group size depended on the availability of the nurses. For the interviews, a topic list was used, which was based on the FRAM method (Supplement B). In order to gain rich and meaningful data, examples from observations were used during the interviews and nurses were invited to reflect on these observations. One researcher (BS) conducted the interviews and a second researcher (SP) assisted and made field notes. Each (group) interview lasted approximately 30min and started with an introduction of the researchers and the goal of the interview. Also, gender and nursing experience (in years) of the participants were registered. Interviews were recorded if participants gave their consent. Two nurses refused to be recorded, one due to medical and one due to personal reasons; those interviews were transcribed directly after the interview by both researchers. Interviews were executed until data saturation was reached, providing no new information regarding the wards process of double checking. Two test interviews with independent nurses were conducted to gain more experience with the interview questions and to finalize the topic list.

Data analysis

All interviews were transcribed within a few days following the interview. Both researchers (BS and SP) individually coded all interviews through open coding and by using the six FRAM aspects as codes. Every process step during the double check was translated to a function. Then, related aspects (Input, Output, Precondition, Resource, Control, Time) were recognized from and coded per ward. Two senior researchers (IJ and JK) also coded the first two interviews in order to reach consensus about the coding method. After coding the interviews, the work-as-done model was first drafted in a FRAM model on paper, then discussed by BS, SP and IJ, and finally created with the FRAM Model Visualizer software.[29] Two overall work-as-done models were created representing the aggregated processes in both hospitals. After the data analysis, each ward was offered the opportunity to discuss the results (in a meeting) from the work-as-done model and to formulate recommendations to help eliminate identified barriers.

RESULTS

Participants

In total, 18 nurses were observed during injectable medication administration: 10 nurses in hospital A and 8 nurses in hospital B. Subsequently, 27 nurses were interviewed during 15 interviews (Table 1). Most interviewed nurses were female (81%) and median years of nursing experience was 8 years (Inter Quartile Range: 4-13 years). In both participating hospitals, nurses used electronic health records (EHR) with medication administration records and barcode medication administration (BCMA) systems during the injectable medication administration process. Data saturation was reached on all wards.

Table 1 Characteristics of the interviewed nurses (n=27).

	Hospital A (n=13)	**Hospital B (n=14)**	**Total (n=27)**
Type of ward			
Internal Medicine, n (%)	7 (54)	8 (57)	15 (56)
(General) Surgery, n (%)	6 (46)	6 (43)	12 (44)
Gender			
Male, n (%)	3 (23)	2 (14)	5 (19)
Female, n (%)	10 (77)	12 (86)	22 (81)
Years of nursing experience			
Median (IQR)	8 (5.5-9)	7.5 (4-36)	8 (4-13)

IQR=inter quartile range.

Work-as-imagined model using FRAM

The work-as-imagined model consisted of 23 functions of which 2 foreground functions focused specifically on the double check (Figure 2):

1. To administrate medication: The medication is prepared and ready for administration (Input). The medication needs to be administered at the prescribed Time. The nurse asks a second nurse for a physical double check at the patients' bedside (from Output of <To administrate medication> to Input of <To conduct the double check>). The Output is that the medication is administered and can be signed off (from Output of <To administrate medication> to Input of <To sign medication order>).

2. To conduct the double check: The second nurse checks the medication order, medication name, dose, administration route, administration rate, patient and time. The double check is considered 'complete' when all 7 steps are conducted (Supplement A) (from Output of <To conduct the double check> to Control of <To administrate medication>). A Precondition for the double check is that the medication has been ordered by a physician.

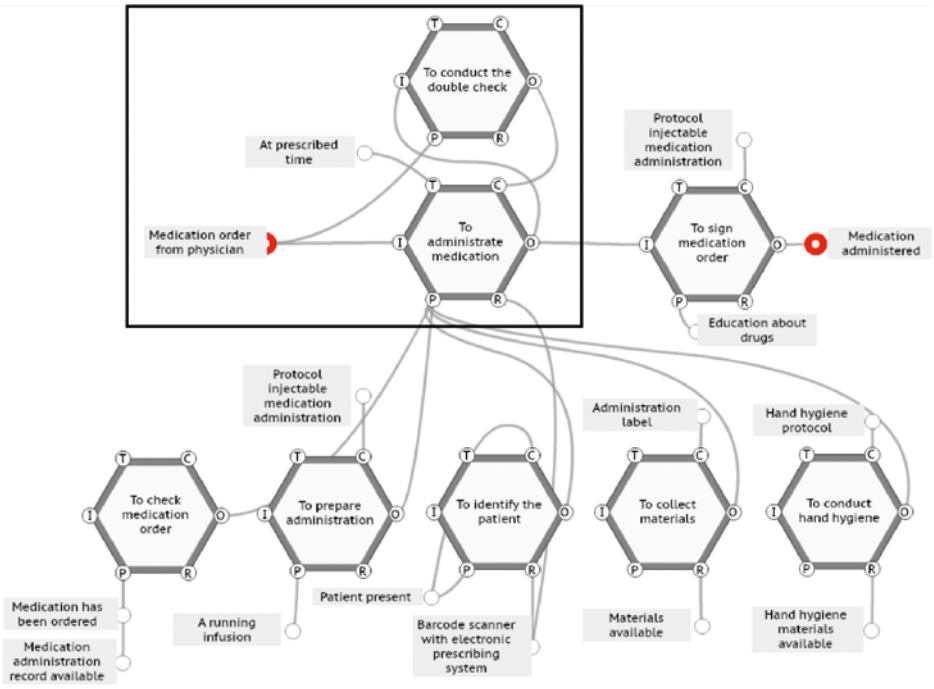

Figure 2 'Work-as-imagined' model for the injectable medication administration process.

Work-as-done model for hospital A using FRAM

In hospital A, we identified 3 additional foreground functions as compared to the work-as-imagined model. Besides, 1 of the 2 foreground functions from the work-as-imagined model was adapted in daily practice. In total, 5 foreground functions focused specifically on the double check (Figure 3):

1. To assess the situation on the ward: Medication is prepared and ready for administration (Input). Nurses assess the situation on the ward by mentally considering several criteria (Control): how frequent he/she administrated this medication previously, what the current workload is on the department, how severe the possible side effects of the medication can be, what the current medical condition of the patient is and what type of medication need to be administered by which administration route. The Output is a decision whether a second nurse is needed to conduct a physical double check.

   (IA3): "My instinct tells me that medication administered by syringe pumps, potassium and antibiotics are really high-risk medications. Therefore, I find it necessary to involve a second nurse in the double check."

   (IA6): "Anti Thymocyte Globulin for example, that is a medication with many side effects. For me, that is a high-risk medication and I handle it extra carefully. Not only during preparation, but also during administration a double check from a colleague is necessary."

2. To verify administration route and rate in the hallway or medication room: If the nurse decides that the physical double check is unnecessary, but a second nurse happens to be available in the medication room or in the hallway, the right administration route and rate will be verified orally. If no colleague nurse is available in the medication room or hallway and/or when the nurses decide that no physical double check is necessary, then the nurse proceeds to the patients' bedside.

   (IA8): "I take the medication with me and then I show it to another nurse who usually stands in the hallway with the Computer on Wheels (COW). 'I'm now going to give this medication to that patient, is that ok?' and then I sign for the medication and go to the patient."

3. To conduct digital double check: The nurse walks to the patients' bedside with a COW and a barcode scanner (Resources). Through the use of a COW, the nurse has access to the medication administration record within the EHR of the patient. The nurse executes a digital double check for 5 of the 7 steps: right patient by scanning the barcode on the wristband of the patient and right medication order, name, dose and time by scanning the barcode on the medication label. The information from the wristband and medication label is automatically compared with the information in the EHR and medication administration record. If discrepancies are identified, the nurse is alerted by a pop-up.

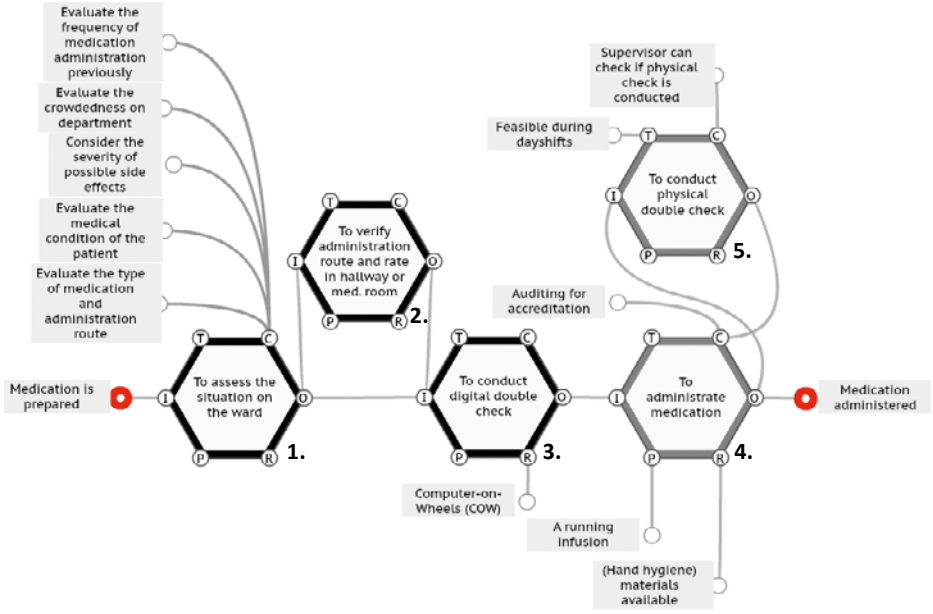

Figure 3 'Work-as-done' model for the double check procedure during injectable medication administration in hospital A. Black hexagons are new activities as compared to the 'work-as-imagined' model.

4. To administrate medication: When the digital double check has been conducted and no discrepancies have been identified, the nurse starts to administer the medication (Input). A Precondition is that the infusion is adequately running and during the administration all materials are available (Resource). When the nurse decides a physical double check is necessary, a second nurse is asked to accompany him or her. The Output is that the medication is administered.

5. To conduct physical double check: A second nurse conducts only the final 2 steps of the double checking proceeding: right administration route and rate. During the interviews, nurses provided examples of medications for which they think a physical double check is always necessary: heparin, morphine, midazolam, ketamine, potassium, furosemide, insulin and infliximab. In addition, nurses mentioned that the physical check is more feasible during dayshifts than during evening or nightshifts (Time) since during dayshifts, enough staff is available to conduct the physical double check. Finally, it is possible for ward supervisors to digitally check if the physical double check has been signed in the system (Control).

Work-as-done model for hospital B using FRAM

The work-as-done in hospital B differed from hospital A only on the check of the right patient (Figure 4). This is an extra foreground function in the model as composed to hospital A. Nurses at hospital B conduct almost always, regardless using a barcode scanner, a verbal verification of the patients' identity with the patient.

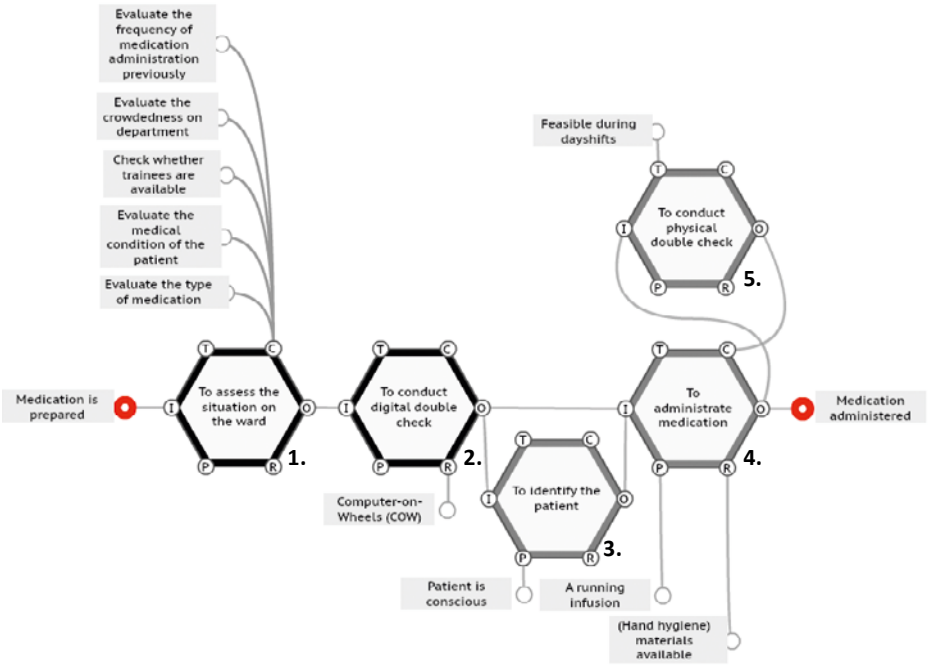

Figure 4 'Work-as-done' model for the double check procedure during injectable medication administration in hospital B. Black hexagons are new activities as compared to the 'work-as-imagined' model.

3. To identify the patient: In addition to the digital check on right patient, patients that are conscious (Precondition) are verbally asked for their date of birth. If a patient is unconscious, then the nurse starts the actual administration and this activity is skipped.

   (IB5): "At the patients' bedside you still check the patients' date of birth. You always ask that, you just have to."

In addition, during the interviews, nurses at hospital B provided examples of medications for which they think a physical double check is always necessary: prothrombin complex concentrate, gentamicin, heparin, morphine, midazolam and blood.

Differences between hospital A and B

In addition to the identification of the patient in the work-as-done model in hospital B, there are several other differences between both hospitals. In contrast to hospital A, the pharmacy department in hospital B prepares almost all scheduled injectable medication (mainly antibiotics) and nurse trainees are allowed to conduct both the digital and physical double check (after they have passed a test). Furthermore, the presence of a second nurse in hospital B is experienced as an interruption by some nurses, making it less likely that they ask a second nurse for the physical double check. On the other hand, if nurses in hospital A decided that no second nurse is needed/available for the physical double check, they still verify the administration route and rate with another nurse on the wards' hallway.

(IB1): "With a nurse trainee you are already with two and when the trainee administers the medication, I can check him/her."

Variability

Variability was mainly identifiable in the function: <To assess the situation on the ward> as this assessment is conduced depending on the opinion of a nurse involved in injectable medication administration. The criteria used for this assessment resulted in the decision whether or not a second nurse is asked for the physical double check. This decision is individually made (internal variability) and seems to relate to the subjective expertise, experience and judgement of the nurse involved. The decision either results in the execution of the physical double check further in the process or not (<To conduct physical double check>). External variability for this function seems

to relate to staffing (interns available or not), the type of department, the complexity of patients diseases on the department and to unspoken expectations between nurses regarding the assessment. The imprecise output of this function can affect the variability of downstream functions (upstream-downstream coupling). To understand the manifestations of variability in terms of time and precision; the assessment is conducted during the administration and is therefore on time. However, the outcome of the decision is imprecise due to each nurses' interpretation of the situation at that moment.

Facilitators and barriers

Facilitators and barriers to correct performing the double check can be divided into culture, technology, staff and organizational related factors. Most nurses understood why the double check is necessary and that it contributes to decreasing the amount of medication errors. Moreover, nurses believe that their team is critical, collegial and open for feedback. Electronic health records with medication administration records and barcode systems support the double check. Additionally, the availability of trainees increases the opportunity for the physical double check, since it provides more personnel. A final facilitator is that the hospital pharmacy prepares several types of medication.

However, there are also barriers. A small proportion of the nurses did not believe that the double check contributes to improved medication safety. Besides, nurses experience an increased workload due to increased clinical complexity of patient care and short admission periods. Furthermore, the COW sometimes fails to work resulting in delays in the medication administration process. Mainly, a staff shortage, in addition to a lack of time and the amount of interruptions during injectable medication administration was mentioned. A final barrier was lacking an overview of the medication preparation process by the hospital pharmacy.

(IB2): "Officially, two nurses have to go to the patient, but that does not always happen, especially due to a lack of time."
(IB5): "I have never succeeded in giving medication in a quiet environment."
(IB3): "In the past, maybe 5 patients on the ward had an infusion, now almost everyone has one."

DISCUSSION

In our study, we found a lack of fit between work-as-done and work-as-imagined in double checking during injectable medication administration. The work-as-done model is more complex and consists of more activities than the work-as-imagined model. During work-as-done, nurses split the double check into a digital and physical check. The digital check is a double check on right medication order, medication, dose, time and patient. The physical check is a double check on right administration route and rate. Nurses almost always succeed in conducting the digital double check, but not always in conducting the physical double check for every administration. Although the intention to conduct the physical double check is certainly present among nurses, several barriers result in protocol workarounds. For example, prior to the administration, nurses conduct their own risk-assessment (using various criteria) to decide whether or not a physical double check is absolutely necessary in their opinion.

This study visualized the double check process of nurses in detail. Only few previous studies focused in such detail on the double check as well, which makes our results innovative and complementary to existing results. Most studies reported that the double check process is poorly defined and that many variations of the double check process are executed in hospitals.[12,30] One detailed process description is the read-read back method from Schwappach et al.: one nurse reads out loud the medication order and another nurse verifies this on the medication label and vice versa.[15] However, this study is different from ours since it is conducted on an oncology ward and focused on chemotherapy, and the role of the barcode scanner is unclear in the various scenario's.

We found that a lack of time is a major barrier for conducting the double check proceeding during injectable medication administration. This is in line with other studies.[13,14,31] The double check, in particular the physical double check, is time-consuming and requires a second nurse at the patients' bedside.[9] With the implementation of BCMA systems, time spent on double checking has already been reduced. In hospitals with a BCMA system, the double check can always be conducted digitally for 5 of the 7 double check steps. Therefore, the risk of patient harm is already reduced during the double check process. Should it be possible to conduct the other 2 steps, right administration route and rate, by also using the barcode scanner (for example with smart pumps or a camera in the barcode scanner), then the time spent on the double check will be reduced dramatically

and the risk of patient harm will reduce further. Other facilitators to correct performing the double check, according to the nurses, that reduce the time spent on double checking are the availability of trainees and the preparation of injectable medication by the hospital pharmacy. Shifting the preparation of injectable medication from nurses on the ward to the hospital pharmacy is an emerging development. It is even estimated that using robotic devices to prepare medications in the hospital pharmacy can reduce healthcare costs and medication errors.[32]

Nurses assess the situation on the ward because of a lack of time and availability of a second nurse to conduct the physical double check for all injectable medication administrations. Criteria used for this assessment are not mentioned in previous studies, except the patients' medical condition and the type of medication.[12,13] The individual assessment by nurses can be seen as a positive and negative outcome of the lack of fit between the work-as-imagined and work-as-done. Positive because it shows the nurses' willingness to decrease risk of patient harm when administering injectable medication by using their knowledge about and experience with medication. Based on this knowledge and experience, nurses make a well-considered and substantiated decision to work around the protocol. The physical double check of 'top high-risk' medication can be seen as a good practice from which we can learn. Not following the protocol completely without making a medication error might reduce work load and fit better in practice. However, the down side of the assessment is that it relies on individual experience, knowledge and confidence of the nurse involved. Therefore, it introduces a high degree of variability in the double check process. The current protocol does not accept variability and requires that all 7 steps included in the double check proceeding are conducted independently by a second nurse for all injectable medications. Thus, if the protocol is leading, the assessment is not desirable. However, at present it is unknown if the individual assessment by nurses actually leads to errors in the injectable medication administration process. Future research should focus on this aspect and reconsider whether to continue to pursue 100% protocol compliance or accepting that variation exist and that nurses assess the situation on the ward. Besides, future research can also focus on whether the double check need to be independent or that a confirmative role is also sufficient.

To date, only a limited number of studies applied FRAM to evaluate healthcare processes.[18-21,25-27] We believe FRAM is very useful for visualizing the complexity of healthcare processes, such as the double check. The (group) interviews appeared an

effective method to gain detailed information about the work-as-done. In the future, studies focusing on this topic may learn from methodological enhancements from other FRAM studies, for example by conducting the FRAM in more than one country,[18] by analyzing the process backwards,[28] or by creating an intervention based on the FRAM models.[27] Furthermore, Shorrocks' extra dimensions work-as-disclosed and work-as-prescribed describe a grey area that can be explored more while balancing between visualizing the complex process and the ease of interpretation for nurses.[33] In total, the time investment in our study to conduct the FRAM per hospital was approximately 60 h. This is more than the suggested time investment of Damen et al., because we also conducted observations at each site.[18] The two selected hospitals differed in hospital type (general vs. university) and double check compliance rate (high vs. average compliance). A striking finding in our study is that, despite the major differences in compliance rates between the participating hospitals in the previous study,[9] the differences in the actual work-as-done process in both hospitals were small. Three factors may explain why the observed compliance in hospital B was higher in the previous study.[9] Firstly, the Hawthorne effect during observations may have had more influence on the performance of injectable medication administration than we initially thought. The interviews showed that nurses know all protocol proceedings for safe injectable medication administration considerably well and are able to reproduce them if needed. Secondly, in hospital B, trainees were allowed to conduct both the digital and physical double check which works effectively in overcoming a staff shortage. Thirdly, hospital A had a higher amount of injectable medication administrations per medication round. When many medications needs to be administered at the same time by several nurses, it is certainly plausible that they have less time to conduct the physical double check.

Strengths and limitations

To our knowledge, this is the first study that used FRAM to provide detailed information about the actual clinical process of double checking injectable medication. We determined the double check process by using a combination of observations and interviews. Since the double check is, pre-eminently, a proceeding that requires the cooperation of more than one nurse, we used the power of group interviews to invite nurses to respond to each other. However, this study also has some limitations. Firstly, this study was limited to two different wards in two hospitals. Therefore, the results cannot be generalized to all hospitals. Secondly, nurses in our sample were invited in a purposive sampling way. This may have brought bias in the results, as the nurses could

be a selected group or could be the ones with the most outspoken opinions about the double check proceeding. However, none of the nurses asked, refused to participate. Moreover, the gender and years of nursing experience varied between the nurses, which suggest that our sample was a heterogeneous group of nurses.

CONCLUSION

By using FRAM, we identified a lack of fit between work-as-imagined and work-as done for conducting the double check proceeding during injectable medication administration in two Dutch hospitals. Work-as-done revealed that, prior to conducting the double check, nurses assess the patients' and wards' situation and decide whether a physical double check is necessary or not. A physical double check is most likely conducted when a patient is vulnerable or when the medication is not frequently administered. The risk-impact analysis is individually made and may vary between nurses. It is unknown whether this variability causes patient harm. It is important to reconsider to what extent practice variation is acceptable and safe, or that the focus will still be on 100% protocol compliance. If variation due to the assessment by nurses is to be accepted, then we recommend to organize discussion meetings among nurses and the ward management to raise awareness about the assessment, the criteria and barriers and risks. Furthermore, we recommend ensuring adequate education of nurses to achieve the individual assessment. Future research should focus on the possibilities for conducting the double check solely digitally by using a barcode scanner.

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Supplement A Protocol proceedings for administering intravenous medication.*

Step	Explanation
Check medication	Checking the drug on the basis of a medication list or distribution list.
Prepare administration	Preparation of administration: setting pump and speed of injection.
Collect materials	Gathering the needed materials and checking the administration label.
Patient identification	Identifying the patient either electronically or by checking the name, date of birth, patient number and type of medication.
Hand hygiene	Hand disinfection before administration or wearing gloves during administration.
Check infusion line	Checking the intravenous medication line before administering the medication.
Check pump mode	Checking or setting the pump mode before administering medication.
Check by a second nurse	Having a second nurse check 7 steps: administration order, medication name, medication dose, patient, time, administration route and administration rate.
Sign medication order	As the administrator, signing the medication order.

**As published in Schilp et al. (2014).*[8]

Supplement B Topic list for semi-structured interviews

Definition

· Injectable medication / Double check during medication administration

Process (Input/Output)

· What is the process of administering a medication?
· Starting point / Preparation
· Order of functions
· When conducting functions
· Task division (first and second nurse) / different ways
· Opinion about process
· Manual Injectable Medication
· Next step / do you inform someone about this?

Unexpected situation(s)

· Tell about an unexpected or striking situation: acute situation, interruptions, no 2nd nurse available

Barriers (Time)

· Occupation on department (understaffing)
· Time pressure / Influence of time
· Interruptions
· Evening / night shifts / weekend shifts
· Budget / Automatic pilot

Opportunities (Preconditions/Resources)

· What is needed / arranged / present as a precondition for successful conducting double check (WiFi connection, barcode scanner, second nurse available)
· What is needed during the execution (manpower, material, software)
· And if this is not present? Examples?
· In what way contributes the double check in preventing errors?
· How do you know that all steps of the double check are conducted correctly?

Control (Control)

· Who checks the double check (guideline, work agreements, mission/vision, audits)?
· Formal procedures / supervisors / feedback, is this discussed?

Chapter 7

General Discussion

This PhD thesis focused on the safe administration of injectable medication by nurses in hospitals. Our goal was to gain a deeper understanding of this complex process both from a Safety-I and a Safety-II perspective. The Systems Engineering Initiative for Patient Safety (SEIPS) 2.0 model was used as a theoretical base. Thereby, we aimed to reduce the risk for future patients of experiencing a medication administration error during their hospital stay. In this thesis we formulated two research questions:

1. What is the current nurse compliance with the protocol for safe injectable medication administration in hospitals and what is the current frequency of adverse drug events?

2. Which interactions in the work system and adaptations occur in nursing practice during injectable medication administration?

The SEIPS 2.0 model provided a structure for determining the injectable medication administration process; it is visualized in Figure 1.

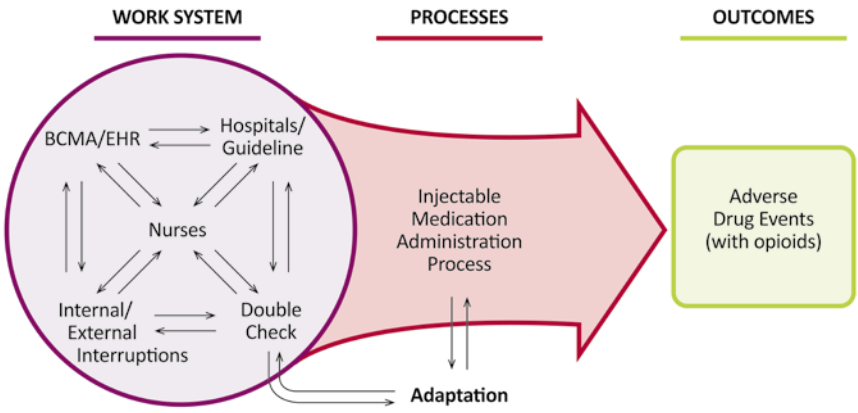

Figure 1: The injectable medication administration process from a Systems Engineering Initiative for Patient Safety (SEIPS) 2.0 perspective.
BCMA = barcode medication administration, EHR = Electronic Health Record

1. What is the current nurse compliance with the protocol for safe injectable medication administration in hospitals and what is the current frequency of adverse drug events?

This research question relates to the 'processes' and 'outcomes' phases of the SEIPS 2.0 model. The results presented in **Chapter 2** show that nurse compliance with the complete protocol (consisting of nine selected proceedings) for safe injectable medication administration is still low. Overall, no significant change was found over time (22% in 2015/2016 vs. 19% in 2011/2012). However, compliance with one of the proceedings in the protocol, 'patient identification', improved significantly from 61% in 2011/2012 to 80% in 2015/2016. The use of barcode medication administration (BCMA) systems seems to have contributed to this increase. Compliance with the proceeding 'check by a second nurse' (hereafter: double check) remained unchanged and was the least conducted proceeding (47%).

Real-time information about compliance can provide quick feedback about protocol compliance in daily practice, thereby increasing awareness and improving understanding. It was thought that it might be possible to reuse Electronic Health Record (EHR) data for this purpose. Unfortunately, our findings presented in **Chapter 4** show that such compliance monitoring is not yet feasible. Only five out of eight administration data elements are routinely recorded in EHR systems. The data elements that are not routinely registered are mainly related to checks such as 'gather all materials needed' or 'conduct hand hygiene'.

Furthermore, as shown in **Chapter 5**, the frequency of adverse drug events was substantial between 2008 and 2015/2016. Out of 10,917 patient records, 357 adverse events occurred that were related to drugs (ADEs). In our sample, 8% of the ADEs identified were specifically related to opioids. Although this percentage is low, the risk of serious consequences remains high.

2. Which interactions in the work system and adaptations occur in nursing practice during injectable medication administration?

We found several interactions and one adaptation during the injectable medication administration process. These were mostly related to the technology, tasks and environment in which nurses work and they show the difference between work-as-imagined and work-as-done.

Firstly, hospitals have implemented various technologies and tools to support the medication administration process, such as BCMA systems and smart pumps (**Chapter 2**), which have resulted in changes in the process. Scanning the barcode on the patient's wristband has made verifying the patient's identity easier and the identity can be automatically logged in the EHR.

Secondly, hospitals also implemented improvement strategies on an organizational level, such as designated injectable medication champions, internal audits and buddy systems (**Chapter 2**). The buddy system is a system in which two nurses are appointed as each other's buddy during the injectable medication administration process.

A third interaction that we identified is between nurses and the internal and external environment. **Chapter 3** showed that nurses were interrupted in 12% of the observed injectable medication administrations, mainly by other nurses and patients. One intervention to prevent these interruptions is to wear do-not-disturb vests. However, these vests were worn in only 2% of all observed administrations.

The adaptation that we identified is focused on the double check by a second nurse. **Chapter 6** showed that nurses split the double check into a digital check and a physical one. Since asking a colleague for the physical double check often takes too much time in daily practice, nurses conduct their own risk assessment (using various criteria) to prioritize the physical double check in the context of their other tasks. This trade-off reveals that nurses deviate from work-as-imagined, i.e. the protocol, if they have a reason, for example if they need to conduct other tasks that are more urgent.

Strengths and limitations

For the studies described in this thesis, we used observations, structured and semi-structured interviews and retrospective record reviews as methods to obtain the data. With these multiple data collection methods, we strived for a balanced explanation of all different aspects of the injectable medication administration process.[1] Therefore, we see this methodological triangulation, both between and within the studies, as a strength of this PhD thesis. Another strength is that we built on previous research about injectable medication administration, which made it possible to compare the results over time. Moreover, we conducted several in-depth studies of the complex environment, in particular to uncover the story behind the poor compliance percentages.

This thesis also has some limitations. Firstly, the Hawthorne effect (i.e. that nurses were aware that they were observed) may have had an influence on the compliance rate when directly observing nurses during injectable medication administration. The Hawthorne effect is a known but controversial topic within observational studies.[2, 3] Despite the fact that our researchers remained unobtrusive and did not interfere with the healthcare process during observations (**Chapters 2 and 3**), the interviews (**Chapter 6**) showed that nurses did change their behaviour when they were directly observed. As a consequence, compliance rates could have been overestimated and this must be taken into account when interpreting the results. Alternative methods that might diminish the Hawthorne effect include disguised observations and video-recorded observations.[4, 5] Yet under the current general data protection regulation, these methods may constitute an excessive invasion of the privacy of nurses and patients.

Secondly, we used data from three retrospective patient record review studies to assess the current frequency of adverse drug events. A limitation might be that adverse drug events that resulted in only minor patient harm or near misses are not always recorded in patient records. Although it has become more common to report ADEs over the last decade, there is still severe underreporting of ADEs (not only in the Netherlands).[6, 7] Therefore, this may have led to under-detection and under-recording of ADEs in the patient records. Since 2016, a new act on healthcare quality, complaints and disputes has obliged Dutch healthcare professionals to report adverse events in the patient record. This may lead to more reporting of ADEs in the coming years.

Finally, in this thesis we did not conduct studies to determine the effect of our understanding of the complex injectable medication administration process, in other words, whether our findings actually result in process improvements in clinical practice and fewer medication errors or less potential harm resulting from these errors. However, with our results, we provided an important first step by indicating where and when to intervene in the process in order to improve it.

Discussion of the main findings

By using Safety-I and Safety-II instruments, and the SEIPS 2.0 model as a theoretical base, this thesis has improved our understanding of the safety of the complex injectable medication administration process. It has also enabled us to provide evidence-based recommendations for clinical and scientific practice.

Safety-I

Using Safety-I instruments (i.e. measuring protocol compliance and measuring ADE frequency, see **Chapters 2 and 5** respectively), we have learned that standardizing a protocol comprising a large number of proceedings in a complex system does not seem feasible. Compliance with the protocol for safe injectable medication administration remains low, even after six years of implementing this protocol. Yet this applies to compliance with the complete protocol. Compliance with six of the nine proceedings is in fact high (>90%) and compliance with one of the proceedings has improved significantly thanks to BCMA technology. BCMA was implemented in half of the hospitals in our sample and use of this technology have increased since then in the Netherlands. In the USA, more than 90% of the hospitals already used BCMA by 2015.[8]

However, the changes related to the use of BCMA may also have given rise to new risks. Examples are when nurses disable alarms that might disturb patients or document the medication administration before it is administered instead of after.[9] Another example is when nurses copy the barcode onto another item (e.g. a plastic card) and scan that item instead of the barcode on the wristband to avoid disturbing the patient at night. Though these actions might be conducted from a patient-friendly point of view, they are called workarounds and occur in 66% of the administrations.[4] We did not observe workarounds, but we know that they are associated with medication administration errors.[4] Therefore, it remains important to stay focused on the implementation of BCMA systems, and in particular on possible workarounds. Uniform training in using the systems and effective communication may help to achieve successful implementation.[10]

The main reasons for low overall compliance were failures to conduct hand hygiene and arrange the double check by a second nurse. Hand hygiene remains challenging in many healthcare processes, and compliance by healthcare professionals is also around 60% in comparable studies.[11, 12] The double check consists of a digital and a physical check; the latter, the physical double check of the right administration route and rate, appeared the most difficult check to conduct. Most nurses do, however, see the importance of the double check and prefer it to single checking.[13]

Finally, the ADE incidence in hospitalized patients seems not to have decreased over eight years. This is similar to a previous review showing a heterogeneous ADE incidence

between 2000 and 2016.[14] These findings show the need for a deeper understanding, which was the reason for our study presented in **Chapter 6**.

Safety-II

We switched from focusing on Safety-I to Safety-II. The added value of Safety-II is the positive approach, learning not just from what goes wrong but also from what goes right.[15] That is also what healthcare professionals are currently looking for. Safety-II accepts the variability in care processes and focuses on the fact that nurses need to react and adapt constantly to unexpected situations in the process (e.g. complexity). We used the Functional Resonance Analysis Method (FRAM) as an instrument to visualize the work-as-done in clinical practice and to study the variability in the process (**Chapter 6**). Using Safety-II, we learned what considerations nurses take into account when conducting certain protocol proceedings, in other words, where trade-offs can be found in the process and if those trade-offs are variable and desirable. One reason why the double check is performed correctly in half of the administrations is because that nurses try to find a balance between efficiency and thoroughness. We found that nurses conduct a risk assessment to decide whether to conduct the double check or whether to skip the physical double check because of staff shortages or time constraints. These two reasons — staff shortages and time constraints — appear to be universal reasons for nurses as to why they are not able to conduct the double check in practice all the time.[13] The double check has in any case become the subject of debate in the past decade. On the one hand, nurses believe in the procedure and feel it contributes to safety,[13, 16] even if they are sometimes forced to skip the double check. This omission is unfortunately one of the leading causes of intravenous medication errors.[17] On the other hand, the effectiveness of the double check cannot completely be proven.[18] However, this does not mean that the double check is automatically ineffective and should be de-implemented. Hence, conducting the risk assessment needs more attention, since variability in clinical practice is too high to incorporate the risk assessment in the protocol.

Waefler et al. explain this balancing act by nurses as an optimum bandwidth in the Efficiency and Thoroughness Trade-Off (ETTO) (Figure 2).[19] Compliance with activities such as the double check fluctuates as a winding line instead of a straight line. If the measurement falls within the bandwidth, it is the optimum compliance one can achieve and deviations are mainly caused by random variation in the process. If the measurement is outside the bandwidth, the compliance might first be increased by

for example standardizing the protocol or training. This fluctuation makes it difficult to measure compliance accurately if it is measured at only one point in time, as we did with our observations, and calls for a more continuous measurement of compliance, or a Safety-II perspective.

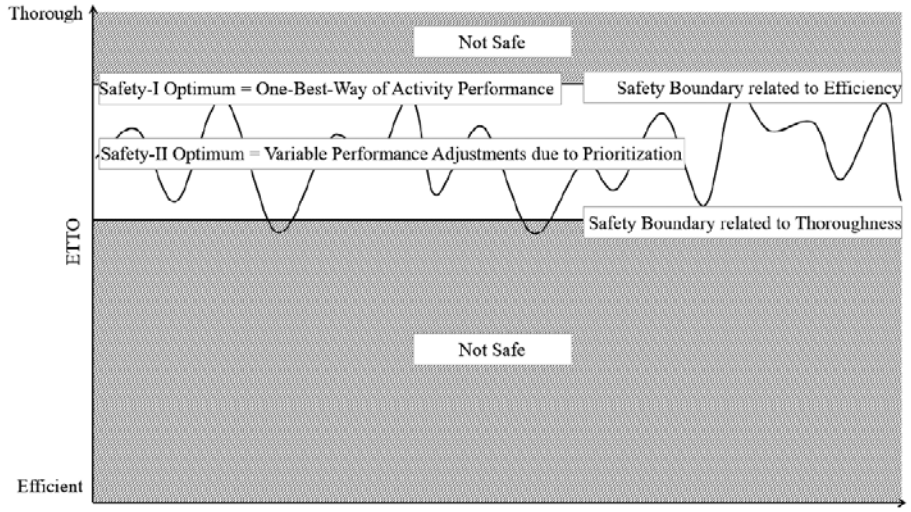

Figure 2: The optimum bandwidth of the Efficiency and Thoroughness Trade-Off (ETTO), taken from Waefler et al.[19]

SEIPS 2.0

By focusing on different aspects of the work system in the SEIPS 2.0 model (**Chapters 2 and 4**), we have learned that increased implementation of information technology in nursing practice has contributed to improved compliance with the protocol, for example, BCMA systems to identify the right patient and right medication, and EHR systems with Electronic Medication Administration Records (eMAR) to identify the right administration time. These findings are in line with previous research.[20]

When looking more closely at the environment in which nurses work (**Chapter 3**), we found that nurses are often interrupted during injectable medication administration. This does not come as a surprise since nurses are positioned at the centre of the work system and are the healthcare professionals most closely involved in the care of the patient. This inherently causes interruptions. Most interruptions are caused by humans (e.g. patients, family and other healthcare professionals).[21, 22] Although we found no significant association with protocol compliance, being interrupted has been described

as a major trigger for medication errors.[21] In order to decrease interruptions, previous studies have tested interventions such as do-not-disturb vests.[23-26] Wearing these vests has had varied success: nurses may be motivated to wear the vest as a short-term intervention, but in the long term, nurses had concerns about hygiene and felt like construction workers while wearing the vests.[24] Our study even showed that wearing a vest might increase the risk of being interrupted, although this effect was not statistically significant. As a consequence, wearing the vest may be neglected and nurses may be more likely to be interrupted.

Protocol for safe injectable medication administration

The currently prevailing protocol for injectable medication administration was implemented between 2008 and 2012. At that time, many hospitals were still using paper charts for the administration of injectable medication. We showed that there have been changes in how the injectable medication administration process is arranged due to the implementation of EHR, BCMA and eMAR systems. In other studies, the use of BCMA systems resulted in a reduction of MAEs and considerable time saving for nurses during the administration of medication.[27-29] However, this time saving did not lead to more time for the double check, but rather was used for documentation in the EHR.[28]

Furthermore, the protocol is designed as a care bundle with nine most important and identifiable proceedings to improve patient safety. Although research showed that care bundles may reduce the risk of negative patient outcomes, this is mainly based on low-quality studies and no bundle is specified for injectable medication administration in particular.[30] Also, most care bundles only have four elements and are measured in an all-or-none measurement in order to stress the importance of conducting all bundle proceedings. This means that all proceedings are equally important and have the same weight when calculating a total compliance percentage. In the injectable medication process, however, some proceedings may have more weight than others, as they may be more error prone or may cause more patient harm if omitted or not conducted in full. This may be the case for example for the double check or the actual administration of the medication, since these are the final defences before the medication reaches the patient.[17] Thus, a more compact bundle consisting of the most error prone proceedings might be more useful.

Recommendations for future research and clinical practice

The question that now arises is: how feasible is the current injectable medication administration system? Would it be possible to enhance the process by implementing more interventions or checks? And what are the possibilities given the expected increase in staff shortages in the coming years? Based on our findings, the following four recommendations should receive attention in future research and clinical practice.

1. Focus on the switch from Safety-I to Safety-II

This thesis showed that a switch from Safety-I to Safety-II is helpful to learn from trade-offs and the underlying process behind compliance percentages. Looking at adverse events and compliance alone (Safety-I) was not enough to understand and improve daily practice. The switch can be made when the protocol is implemented in a department, the proceedings are clear, nurses are well trained in administering injectable medication, and there is a need to explore the complexity of underlying processes in more detail. We used FRAM in particular as a Safety-II research method. The number of studies that use FRAM to visualize healthcare processes is expanding,[31-37] including regarding the administration of medication.[38, 39] We believe FRAM is very useful for visualizing the complexity of healthcare processes. Future studies that use FRAM may adopt methodological enhancements from other FRAM studies, such as conducting a FRAM in hospitals in different countries,[33] analysing processes backwards,[40] or creating an intervention based on FRAM models.[37] With this knowledge we can learn from the variability of processes in other contexts and it will help nurses to have a more thorough dialogue about their work-as-done. Another possible Safety-II research method that could be used to learn where to intervene in the complex process is the Resilience Assessment Grid (RAG), which aims to provide a profile (e.g. a Grid) of an organizations' ability to monitor, learn, anticipate and respond to medication incidents.[41] Moreover, excellence reporting is an upcoming trend in hospitals and can have a positive effect on the culture of a department.[42] By reporting examples of good injectable medication administration practice, people can learn about the system and what elements are contributing to that practice.

Also, more research is needed to understand the impact of the ETTO in high-risk processes such as injectable medication administration. When these are known, it can be determined how to assess them and decide which need to be prioritized, which are safe and which threaten patient safety.

Safety-II should, however, not be seen as a replacement for Safety-I. In this thesis we have learned that it is often not possible to administer injectable medication by following the prescribed protocol. While Safety-I is needed to raise awareness about the problem and root causes, Safety-II is needed to understand the complex and dynamic underlying processes in which incidents sometimes occur. Thus, Safety-I is still important because incidents are the most concrete examples of what can go wrong in healthcare, and they should be measured in order to detect relevant problems (e.g. what incidents are the most common and which have the most severe consequences). Future patient safety research should use both Safety-I and Safety-II instruments. With both Safety perspectives, it might be possible to achieve the resilient level on the safety culture ladder (Figure 3).

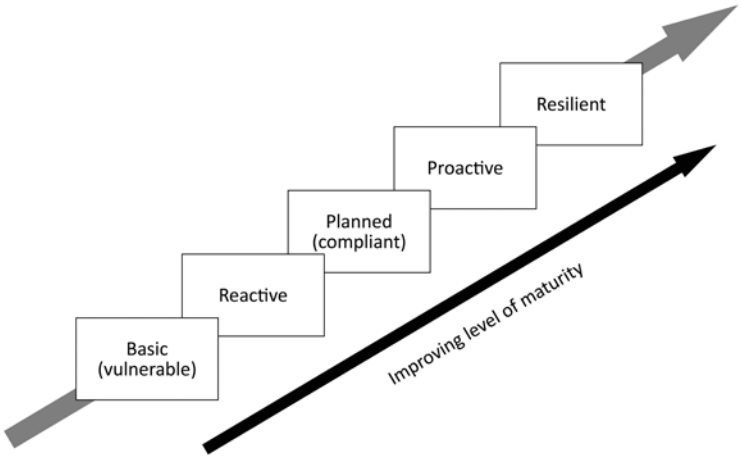

Figure 3: The safety culture journey, adapted by Hollnagel,[41] originally designed by Westrum.[43]

2. Study the patient journey by using SEIPS 3.0

SEIPS 3.0 was published in January 2020. In this new version, the patient journey has become a central focus.[44] A patient experiences the provision of healthcare often at multiple locations, delivered by multiple healthcare professionals and over a period of time. These aspects interact with each other and these steps and interactions can be described by using SEIPS 3.0.[44] We started with the SEIPS 2.0 model with nurses at the centre. This provided the opportunity to take into account variability in the injectable medication administration process. In future studies it would be interesting to use SEIPS 3.0 and determine patient experiences, emotions and views with the injectable medication administration process from a patient-centred perspective, seen in the context of the whole care process. For example, this could show how

patients can be involved in conducting the double check or how patients experience injectable medication administration at home, which is a safe alternative for example for chemotherapy.[45]

3. Revise the current protocol for safe injectable medication administration

In our opinion the currently prevailing protocol should be revised so as to utilize the benefits of automation in hospitals. Furthermore, we recommend future studies to revise the bundle and limit the number of proceedings within the bundle. A new expert group should discuss which proceedings could be dropped, which still need to be measured and which new ones should be measured. We would advise keeping the double check and hand hygiene measurements since these proceedings are still the most likely to be omitted and the most challenging in clinical practice. New proceedings that could be measured are proceedings that emerge when using the BCMA system, such as the number of mismatch pop-ups because of a wrong time window or a wrong patient.

When revising the protocol, it should also be noted that while 100% compliance is the ideal, it might not always be feasible in clinical practice. For example, in one internal medicine department it transpired that amoxicillin was a frequently administered antibiotic. The double check for this type of medication was often not conducted. Instead, nurses chose to invest their double-check time in potentially more harmful medication, such as morphine. Thus, current practice suggests that it may no longer be desirable to require a completely independent double check for all medications. As an alternative, protocols could have one part that is standard for all departments and one part that could be customized for individual departments. A requirement for this customization could be that a risk assessment must be conducted by a hospital pharmacist or another designated person, looking at which medication types are frequently administered and what the risks are related to these medications. Another requirement might be that departments should prepare by conducting a FRAM to determine their work-as-done in clinical practice and to identify their trade-offs.

4. Invest in culture-enhancing interventions

It is an illusion to think that focusing on what goes well and revising the protocol will solve all problems. Therefore, future studies should also focus more on the patient and medication safety culture. We found that nurses do not deviate from the protocol without a reason. Nurses make a well-considered and substantiated decision to deviate

from the protocol based on their knowledge and experience. We should create a culture in which their assessment can be seen as a good practice from which we can learn. We recommend focusing future research on this assessment and the effect of conducting a risk assessment on Safety-I (medication errors) and Safety-II (clinical practice).

Vision of future clinical practice

We can visualize the impact of our recommendations for Diana (the nurse in the General Introduction) in her future clinical practice. It is 2023 and Diana and her colleagues are doing their utmost to safely administer injectable medication. These excellent practices are registered in a positive routine reporting system. Diana has had training in using the barcode scanner and is now a super-user of the BCMA system in her department. She talked to her colleagues and the pharmacist about how they think injectable medication should be administered safely. This resulted in a list of high-risk medication for which they think a double check is absolutely necessary. To monitor the compliance with the most crucial protocol proceedings (e.g. the double check and patient identification), the business intelligence department created a dashboard. Unfortunately, last month an incident happened; instead of administering medication at 12 p.m., a colleague did not administer the medication at all. After that, the whole team came together to discuss what happened in their system and understand how this could have occurred. It appeared that the nurse was interrupted during the shift handover and thought the medication should only be administered when necessary. Based on this, the team decided that from now on telephones need to be given to a colleague when administering medication in order to prevent interruptions. Overall, Diana is satisfied and feels this way of working — focusing on what goes wrong ***and*** what goes well — increases medication and patient safety.

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Chapter 8

SUMMARY

Injectable medication comprises all medications that can be injected, such as intravenous infusions and subcutaneous or intramuscular injections. Over 90% of all hospitalized patients receive some form of infusion therapy, including injectable medication.[1] Administering injectable medication is also associated with an increased risk of patient harm. This high risk is caused by the fact that injectable medication has an immediate therapeutic effect and can reach dangerous drug levels in a short period of time. Besides, errors with injectable medication are often irreversible. When errors do occur, this can lead to an adverse event. An adverse event (AE) is an unintended injury that results in prolongation of a hospital admission, temporary or permanent disability or death and was caused by healthcare management instead of the patient's disease.[2] About 19-44% of adverse events involve medication, in particular at the stage of medication administration.[3-5] It is estimated that approximately 10% of all injectable medication administrations are associated with at least one error.[6]

Measuring the number of adverse events is one perspective for looking at patient safety; it is called the Safety-I perspective. Safety-I has been the standard for years and most research is done from this perspective. Safety-II is a relatively new perspective and focuses on understanding how work that often goes well is performed in clinical practice. It also focuses on understanding resilience and variability in the process.[7] The main differences between Safety-I and Safety-II are that Safety-II focuses on all healthcare outcomes instead of only the negative outcomes (e.g. AEs), and Safety-II is more proactive and sees humans as a part of the solution instead of part of the problem.[7]

Administering injectable medication is a primary task of nurses. In the past decade, the role of nurses in the medication administration process has changed due to an increase in training-related interventions, interventions that prevent interruptions, various implemented protocols and the use of information technology. Most previous studies focused on just one of these aspects of the process. However, the medication process is complex[8] and it is important to understand the whole healthcare system in which healthcare professionals work.

To increase the safety of administering injectable medication in Dutch hospitals, a protocol was implemented between 2008 and 2012. In 2020, that protocol is still

the prevailing protocol. It contains 25 steps for the safe administration of injectable medication of which nine most important and identifiable proceedings were selected by an expert group.[9] The first evaluation of this protocol was conducted in the year 2011/2012.[10] It was found that protocol compliance (achieved when all nine proceedings are conducted correctly) was achieved in only 19% of all observed administrations.[10] The lowest compliance was observed in three proceedings: conducting hand hygiene, identifying the right patient and the check by a second nurse.[10] These findings gave rise to questions such as: what are the reasons for poor compliance, is the protocol feasible or too complex to follow in daily practice, and what barriers and facilitators are related to protocol compliance?

To understand the whole injectable medication administration system, including the complexity, the Systems Engineering Initiative for Patient Safety (SEIPS) model can be used as a theoretical base.[11] The model was introduced in 2006 (SEIPS 1.0) and revised in 2013 (SEIPS 2.0).[12] By using SEIPS, we can understand interactions between the work system, processes and outcomes.[11] Furthermore, an adaptation phase was incorporated in the SEIPS 2.0 model.[12] With this phase, the model takes into account the fact that processes are not linear but dynamic, and that nurses need to react and adapt constantly to unexpected situations in the process (e.g. complexity). Therefore, the adaptation phase is in line with the Safety-II perspective.

The aim of this PhD thesis is to gain a deeper understanding, from a Safety-I and Safety-II perspective, of the complex process of injectable medication administration by hospital nurses. The SEIPS 2.0 model was used as a theoretical base. By gaining a deeper understanding, we aim to reduce the risk of future patients experiencing an injectable medication administration error during their hospital stay.

To achieve this aim, we formulated two research questions:

1. What is the current nurse compliance with the protocol for safe injectable medication administration in hospitals and what is the current frequency of adverse drug events?

2. Which interactions in the work system and adaptations occur in nursing practice during injectable medication administration?

The first research question is addressed in **Chapters 2, 4 and 5**. In **Chapter 2** we conducted a second evaluation of the protocol for 'safe preparation and administration of injectable medication'. In 16 Dutch hospitals we observed a total of 372 injectable medication administrations. Compliance with the protocol was complete when the nine most important and measurable proceedings were conducted correctly. It was found that complete protocol compliance was achieved in 22% of all administrations in 2015/2016. There had been no significant change over time (19% in 2011/2012). However, compliance with 'patient identification' improved significantly from 61% in 2011/2012 to 80% in 2015/2016. The use of barcode medication administration (BCMA) systems may have caused this increase. Compliance with 'check by a second nurse' (hereafter: double check) remained unchanged and was only 47%. To improve compliance with these proceedings, other interventions are needed, preferably focused on nurses, and individually tailored to each ward.

In the feasibility study in **Chapter 4**, we determined whether it was possible to calculate compliance with the protocol for 'safe preparation and administration of injectable medication' by reusing routinely recorded Electronic Health Record (EHR) data. The proceedings included in the protocol were translated into sixteen required data elements (eight data elements for preparation and eight data elements for administration). At twelve Dutch hospitals, an interview was conducted with healthcare professionals to decide whether the data elements were available in their EHR system. It was found that nine of the sixteen required data elements were recorded in the EHR, of which eight in a structured format. The seven missing data elements were mainly related to checks such as 'gather all materials needed' or 'conduct hand hygiene'. Reusing EHR data to monitor compliance by nurses with the currently prevailing protocol therefore is thus not entirely feasible. However, there is a need to define which checks should be recorded in the EHR and which checks should be audited. Moreover, the currently prevailing protocol should be revised to match current clinical practice. Our results can be used as guidance for such a revision.

The study described in **Chapter 5** is focused on patient outcomes, namely on the number of adverse events with medication. Thereby, we focused on one type of medication, namely opioids. We studied data from three Dutch retrospective patient record review studies in 32 hospitals (conducted in 2008, 2011/2012 and 2015/2016). In total, 10,917 patient records were assessed by trained nurses and physicians. For each identified opioid-related adverse event, we described the preventability, type of medication

error, attributable factors and type of opioid involved. In the 10,917 patient records, 357 adverse drug events (ADEs) were identified of which 28 (8%) involved opioids. Eleven were assessed as preventable. Of these, ten were caused by dosing errors and four probably contributed to the patient's death. The risk of opioid-related ADEs was higher in elderly patients. Although the frequency of opioid-related adverse events is low, the risk of serious consequences is high. We recommend using our findings to increase awareness among physicians and nurses. Future interventions should focus on safe dosing of opioids when prescribing and administering, especially in elderly patients.

The second research question is addressed in **Chapters 2, 3 and 6**. In the second evaluation study in **Chapter 2** we investigated which improvement strategies hospitals had implemented. This consisted of increased information technology to support the administration process (technology interaction), for example BCMA systems and smart pumps. Scanning the barcode on the patient's wristband makes verifying the patient's identity easier and it can be automatically logged in the EHR. Other strategies were related to the organization, i.e. the hospital (organizational interaction), for example, appointing designated injectable medication champions, conducting internal audits and implementing buddy systems.

The aim of the study in **Chapter 3** was to determine the frequency and cause of interruptions during injectable medication administration. The data were collected during both the first and the second evaluation of the protocol for 'safe preparation and administration of injectable medication'. We defined an interruption as a situation where a break was needed during the administration or where a nurse was distracted but could continue the process without a break. In total, 2,526 administrations were observed in this study. During 291 administrations (12%), nurses were interrupted at least once (environmental interaction). Most interruptions were caused by other nurses (19%) or by patients (19%). Do-not-disturb vests were worn by only 61 (2%) nurses during administration. There is a need to critically consider which strategies effectively improve safety during the high-risk nursing task of administering injectable medication.

Our final study, described in **Chapter 6**, is a qualitative in-depth study focused on the double check during the administration of injectable medication. A total of 27 nurses were interviewed in four nursing departments of two Dutch hospitals. The aim was

to determine the fit between the double check according to the protocol (work-as-imagined) and the double check in clinical practice (work-as-done). The difference between the two provides insight into the adaptation abilities of nurses. It appeared that nurses split the double check into a digital check and a physical check in order to improve workflow (adaptation). The digital check was routinely conducted. For the physical check, nurses made their own risk-impact assessment using various criteria, for example, staffing, familiarity with the medication and the patient's medical condition. We identified a lack of fit between work-as-imagined and work-as-done. It is unknown whether the variability in the process also causes patient harm. We recommend reconsidering the extent to which practice variation is acceptable and safe.

Chapter 7 contains a general discussion of this thesis. We describe our findings and reflect on these in the light of other literature. We also formulate the following four recommendations for future research and future clinical practice:

1. Focus on the switch from Safety-I to Safety-II

In this thesis, we used FRAM in particular as a Safety-II research method. We believe FRAM is very useful for visualizing the complexity of healthcare processes. Future studies that use FRAM may adopt methodological enhancements from other FRAM studies. Another possible Safety-II research method that could be used to learn where to intervene in the complex process is the Resilience Assessment Grid (RAG), which aims to provide a profile (e.g. a Grid) of an organization's ability to monitor, learn, anticipate and respond to medication incidents. Moreover, excellence reporting is an up-and-coming development in hospitals that can have a positive effect on the culture of a department. By reporting examples of good injectable medication administration practice, organizations can learn about the system and what elements are contributing to that practice.

Also, more research is needed to understand the impact of the Efficiency and Thoroughness Trade-Offs (ETTO) on high-risk processes such as injectable medication administration. If this is known, it is possible to determine how to assess the trade-offs and decide which need to be prioritized, which are safe and which threaten patient safety.

2. Study the patient journey by using SEIPS 3.0

SEIPS 3.0 was published in January 2020; in this new version, the patient journey has become a central focus.[13] We started with the SEIPS 2.0 model with nurses at the centre. This provided the opportunity to take into account variability in the injectable medication administration process. In future studies it would be interesting to use SEIPS 3.0 and determine patient experiences, emotions and views with the injectable medication administration process from a patient-centred perspective, seen in the context of the whole care process. For example, how can patients be involved in conducting the double check or how do patients experience injectable medication administration at home?

3. Revise the current protocol for safe injectable medication administration

The currently prevailing protocol should be revised in order to be able to utilize the benefits of automation in hospitals. A new expert group should discuss which proceedings could be dropped, which proceedings still need to be measured and which new ones should be measured. We would advise keeping measurements of the double check and hand hygiene since these proceedings are still the most likely to be omitted and the most challenging in clinical practice. When revising the protocol, it should also be noted that while 100% compliance is the ideal, it might not always be feasible in clinical practice. Current practice suggests that it may no longer be desirable to require a completely independent double check for all medications. As an alternative, protocols could have one part that is standard for all departments, and one part that could be customized for individual departments.

4. Invest in culture-enhancing interventions

It is an illusion to think that focusing on what goes well and revising the protocol will solve all problems. Therefore, future studies should also focus more on the culture around injectable medication administration. This thesis confirms that nurses do not deviate from the protocol without a reason. We should create a culture in which their assessment can be seen as good practice from which we can learn. We recommend focusing future research on this assessment and the effect of conducting a risk assessment for Safety-I (medication errors) and Safety-II (clinical practice).

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SAMENVATTING

High-risk medicatie omvat alle medicatie die geïnjecteerd kan worden, zoals intraveneuze infusen of subcutane en intramusculaire injecties. Ongeveer 90% van alle patiënten die opgenomen zijn in een ziekenhuis krijgen een vorm van high-risk medicatie toegediend tijdens zijn of haar opname.[1] Het toedienen van high-risk medicatie brengt ook risico's met zich mee. Met name heeft deze medicatie een snel therapeutisch effect en als er iets verkeerd gaat in de toediening, dan is dat vaak onomkeerbaar. Indien er fouten worden gemaakt bij de toediening, dan kan dit snel leiden tot schade voor een patiënt. We spreken dan van zorggerelateerde schade: een onbedoelde uitkomst die is ontstaan door het (niet) handelen van een zorgverlener en/of het zorgsysteem met schade voor de patiënt die zodanig ernstig is dat er sprake is van een tijdelijke of permanente beperking of het overlijden van de patiënt.[2]

De meeste zorggerelateerde schade met medicatie ontstaat tijdens het toedienen.[3-5] Naar schatting is ongeveer 10% van alle toedieningen met high-risk medicatie geassocieerd met ten minste één onbedoelde uitkomst (hierna: adverse event).[6]

Het meten van adverse events, naar wat fout gaat in de zorg, is één manier van het kijken naar patiëntveiligheid. Het wordt ook wel het Safety-I perspectief genoemd (Veiligheid-I).[7] Safety-I was in de afgelopen decennia de standaard en het meeste onderzoek is gedaan vanuit het Safety-I perspectief. Het Safety-II (Veiligheid-II) perspectief is relatief nieuw en focust zich op het begrijpen van het werkproces zoals dat in de praktijk plaatsvindt, vanuit de gedachte dat het vaak goed gaat. Het richt zich op de veerkracht en variabiliteit in processen.[7] De grootste verschillen tussen Safety-I en Safety-II is dat Safety-II zich niet alleen focust op wat er fout gaat (het negatieve), maar juist ook op processen die goed gaan. Safety-II is meer proactief en het ziet mensen als onderdeel van de oplossing in plaats van het probleem.

Het toedienen van high-risk medicatie is een taak die belegd is bij verpleegkundigen. In het afgelopen decennium is de rol van verpleegkundigen tijdens het toedienen van high-risk medicatie veranderd. In het bijzonder door een toename van training gerelateerde interventies, het invoeren van diverse protocollen, een toename van interventies die het aantal verstoringen tijdens het toedienen voorkomt en door steeds meer ondersteuning van informatietechnologie. In eerdere studies naar het proces van het toedienen van high-risk medicatie lag de focus met name op één van deze aspecten.

Het medicatieproces is echter erg complex,[8] waardoor het belangrijk is om het hele zorgsysteem rondom het toedienen van high-risk medicatie te begrijpen.

Om het toedienen van high-risk medicatie in Nederlandse ziekenhuizen veiliger te laten verlopen, is tussen 2008 en 2012 een protocol ingevoerd als onderdeel van het Veiligheids Management Systeem (VMS). Het VMS-protocol voor het veilig toedienen van high-risk medicatie bevat in totaal 25 handelingen die volledig uitgevoerd dienen te worden.[9] In 2020 is dit protocol nog steeds het geldende protocol. In 2011/2012 heeft een eerste evaluatie plaatsgevonden van dit VMS-thema. Hieruit bleek dat in slechts 19% van alle 2154 geobserveerde toedieningen het protocol volledig werd uitgevoerd.[10] De handelingen met de laagste naleving waren: het uitvoeren van handhygiëne, het identificeren van de juiste patiënt en het uitvoeren van de tweede controle door een andere verpleegkundige.[10] Vragen die hierdoor ontstonden waren: wat zijn de redenen voor de lage naleving, is het protocol wel haalbaar of te complex in de dagelijkse praktijk en wat zijn belemmerende en bevorderende factoren bij het naleven van het protocol?

Om het hele zorgsysteem rondom het toedienen van high-risk medicatie nog beter te begrijpen, kan het Systems Engineering Initiative for Patient Safety (SEIPS) model gebruikt worden als theoretische basis.[11] Het SEIPS (spreek uit als: sieps) model is geïntroduceerd in 2006 en herzien in 2013. Met het SEIPS 2.0 model kunnen interacties begrepen worden tussen het werksysteem, processen en uitkomsten.[11] In het SEIPS 2.0 model is ook een aanpassingsvermogen fase opgenomen.[12] Het model houdt zodoende rekening met de variabiliteit in processen en met zorgprofessionals die zich constant moeten aanpassen terwijl ze tegelijkertijd de veiligheid voor de patiënt moeten garanderen. Deze fase is dus in lijn met het Safety-II perspectief.

Dit proefschrift richt zich op het complexe proces van het toedienen van high-risk medicatie door verpleegkundigen in ziekenhuizen. Het doel is om een beter inzicht te krijgen in dit proces. Hierbij wordt gebruik gemaakt van het SEIPS 2.0 model als een theoretische basis. Uiteindelijk zal hiermee bijgedragen worden aan het verminderen van het risico op het ontstaan van toedieningsfouten met high-risk medicatie bij toekomstige patiënten.

Om dit doel te bereiken, zijn twee onderzoeksvragen geformuleerd:

1. Wat is de huidige naleving van het VMS-protocol voor het veilig toedienen van high-risk medicatie bij verpleegkundigen in het ziekenhuis en wat is de huidige frequentie van adverse events met medicatie?

2. Welke interacties in het werksysteem en aanpassingen bestaan er voor verpleegkundigen tijdens het toedienen van high-risk medicatie?

De eerste onderzoeksvraag komt aan de orde in de **hoofdstukken 2, 4 en 5** van dit proefschrift. In **hoofdstuk 2** is een tweede evaluatie uitgevoerd van het VMS-protocol voor het veilig toedienen van high-risk medicatie. In zestien Nederlandse ziekenhuizen zijn in totaal 372 toedieningen van high-risk medicatie geobserveerd. De naleving van het protocol was compleet wanneer de negen meest belangrijke en meetbare handelingen volledig waren uitgevoerd. De naleving van het volledige protocol was 22% in 2015/2016. Er bleek geen significante verandering te zijn met de eerste evaluatie uit 2011/2012 (19%). De naleving van de individuele handeling 'patiëntidentificatie' bleek echter wel significant verbeterd: 61% in 2011/2012 versus 80% in 2015/2016. Het gebruik van barcodescanners om de patiëntidentificatie uit te voeren kan voor deze stijging gezorgd hebben. De naleving van de 'tweede controle' bleef onveranderd en werd uitgevoerd in slechts 47% van de toedieningen. Op basis van de resultaten wordt geadviseerd om andere interventies toe te passen om de naleving van met name de tweede controle en handhygiëne te verbeteren. Deze interventies dienen gericht te zijn op verpleegkundigen zelf en dienen op maat gemaakt te worden voor elke afdeling.

In de haalbaarheidsstudie in **hoofdstuk 4** werd nagegaan of het mogelijk was om de naleving van de VMS-protocollen voor het veilig klaarmaken en toedienen van high-risk medicatie te berekenen door gebruik te maken van routinematig geregistreerde data uit het elektronisch patiëntendossier (EPD). De handelingen uit de protocollen werden allereerst vertaald naar zestien data-elementen die nodig waren om de naleving te berekenen. In twaalf Nederlandse ziekenhuizen is een interview gehouden met zorgprofessionals om te achterhalen in hoeverre alle data-elementen in het EPD waren terug te vinden. Negen van de zestien data-elementen bleken terug te vinden in het EPD van de ziekenhuizen. Acht data-elementen hadden een gestructureerd formaat. De zeven missende data-elementen waren met name gerelateerd aan handelingen zoals 'verzamelen van materialen' of 'uitvoeren van handhygiëne'. Het berekenen

van de naleving op basis van routinematig geregistreerde data uit het EPD is dus niet volledig haalbaar. Het is echter belangrijk om te bepalen welke handelingen in het EPD geregistreerd moeten worden en welke gemonitord moeten worden door middel van audits. Daarnaast is het nodig om het VMS-protocol te herzien om beter te voldoen aan de huidige klinische praktijk. De resultaten uit deze studie kunnen gebruikt worden als richtsnoer voor die herziening.

De studie beschreven in **hoofdstuk 5** is gericht op patiëntenuitkomsten, namelijk op het aantal adverse events met medicatie uit specifiek één medicatiegroep: opiaten. Gegevens uit drie patiënten dossierstudies uit 2008, 2011/2012 en 2015/2016, in totaal 10.917 patiëntendossiers, zijn bestudeerd door getrainde verpleegkundigen en medisch specialisten. Hierna werd de aard van de patiëntendossiers waarbij opiaten betrokken waren beschreven. De aard bestond uit het type adverse event, toe te schrijven factoren en de potentiële vermijdbaarheid. Uit deze studie bleek dat 357 adverse events met medicatie waren opgetreden. Hiervan waren 28 (8%) gerelateerd aan opiaten. Elf opiaat gerelateerde adverse events werden beoordeeld als potentieel vermijdbaar, waarvan tien veroorzaakt werden door doseerfouten. Vier adverse events met opiaten hebben mogelijk bijgedragen aan het overlijden van de patiënt. Het risico op opiaat gerelateerde adverse events was tot slot hoger bij oudere patiënten. Ondanks dat het percentage opiaat gerelateerde adverse events in deze studie laag is, blijft het risico op serieuze complicaties groot. Het is aan te bevelen om deze resultaten te gebruiken om hierover het bewustzijn bij artsen en verpleegkundigen te vergroten. Toekomstige interventies moeten gericht zijn op het veilig doseren van opiaten zowel bij het voorschrijven als het toedienen en met name bij oudere patiënten.

De tweede onderzoeksvraag komt aan de orde in de **hoofdstukken 2, 3 en 6** van dit proefschrift. In de tweede evaluatie studie in **hoofdstuk 2** is tevens onderzocht welke verbeterinitiatieven ziekenhuizen hebben geïmplementeerd. Dit betreffen steeds meer technologische hulpmiddelen om het toedienproces van high-risk medicatie te ondersteunen (technologische interactie), bijvoorbeeld barcodescan systemen en slimme infuuspompen. Met het scannen van de barcode op het polsbandje van de patiënt is het identificeren van zijn/haar identiteit makkelijker en wordt dit ook automatisch geregistreerd in het EPD. Andere initiatieven hebben te maken met de organisatie, het ziekenhuis (organisatorische interactie), door bijvoorbeeld het aanstellen van aandachtsvelders, het instellen van een buddy-systeem en het uitvoeren van interne audits.

Het doel van de studie in **hoofdstuk 3** was de frequentie en oorzaken te achterhalen van verstoringen tijdens het toedienen van high-risk medicatie. De data werden verzameld tijdens zowel de eerste als de tweede evaluatie van het VMS-protocol voor het veilig toedienen van high-risk medicatie. Een verstoring werd gedefinieerd als een situatie waarin een pauze tijdens de toediening noodzakelijk was of waarin de verpleegkundige werd afgeleid maar toch door kon gaan met de toediening. In totaal werden 2526 toedieningen geobserveerd. Tijdens 291 (12%) observaties werd de verpleegkundige verstoord (omgevingsinteractie). De meeste verstoringen werden veroorzaakt door andere verpleegkundigen (19%) of patiënten (19%). Niet-storen hesjes werden tijdens slechts 61 toedieningen (2%) gedragen. Er zal kritisch moeten worden overwogen welke interventies effectief de patiëntveiligheid verbeteren tijdens het toedienen van high-risk medicatie.

De laatste studie, beschreven in **hoofdstuk 6**, is een kwalitatieve verdiepingsstudie gericht op de tweede controle bij het toedienen van high-risk medicatie. Op vier verpleegafdelingen van twee Nederlandse ziekenhuizen zijn in totaal 27 verpleegkundigen geïnterviewd. Het doel was om een vergelijking te maken tussen het beoogde proces van de tweede controle zoals vastgelegd in het VMS-protocol (work-as-imagined) en het proces zoals dat in de dagelijkse praktijk (work-as-done) plaatsvindt. Het verschil tussen het beoogde doel en de praktijk geeft inzicht in aanpassingsmogelijkheden van verpleegkundigen. Er is gebruik gemaakt van de Functional Resonance Analysis Method (FRAM), een methode waarmee de work-as-done visueel inzichtelijk wordt gemaakt. Uit dit onderzoek is gebleken dat verpleegkundigen de tweede controle bij het toedienen van high-risk medicatie splitsen in een digitale en een fysieke controle (aanpassing). De digitale controle wordt routinematig uitgevoerd. Om te bepalen of de fysieke controle prioriteit moet krijgen, voeren verpleegkundigen een risicoanalyse uit met diverse criteria. Een voorbeeld hiervan is hoe bekend ze zijn met het toe te dienen medicijn, of er voldoende personeel beschikbaar is en wat de conditie van de betreffende patiënt is. Als conclusie kan worden gesteld dat er een verschil is tussen het beoogde proces en de dagelijkse praktijk. Het is onduidelijk of deze variabiliteit in het proces ook adverse events veroorzaakt. Overwogen moet worden in hoeverre variatie in het proces van de tweede controle acceptabel en veilig is.

Hoofdstuk 7 beschrijft de algemene discussie van dit proefschrift. Naast de belangrijkste bevindingen wordt een reflectie gegeven in het licht van andere literatuur.

Tevens worden vier aanbevelingen gedaan voor toekomstig onderzoek en de klinische praktijk:

1. Focus op de omslag van Safety-I naar Safety-II

In dit proefschrift is met name FRAM gebruikt als Safety-II methode. FRAM was erg nuttig om de complexiteit van zorgprocessen in kaart te brengen. Toekomstige studies die FRAM gebruiken kunnen methodologische verbeteringen van andere FRAM-studies benutten. Een andere mogelijke Safety-II onderzoeksmethode om te leren waar in het proces verbeteringen kunnen plaatsvinden is de Resilience Assessment Grid (RAG) waarbij een profiel wordt gemaakt van het vermogen van een organisatie om incidenten te monitoren, erop te anticiperen, ervan te leren en erop te reageren. Positief incident melden is daarnaast een opkomende trend in ziekenhuizen en kan zorgen voor een positieve cultuur. Goede voorbeelden worden gemeld om ervan te leren en om te achterhalen welke elementen daaraan hebben bijgedragen.

Meer onderzoek is ook gewenst om gericht in kaart te brengen wat de afwegingen zijn van verpleegkundigen in het toedienproces van high-risk medicatie. Wanneer deze afwegingen bekend zijn, kan men bepalen hoe ze beoordeeld moeten worden, welke afwegingen prioriteit moeten krijgen en welke veilig zijn of de patiëntveiligheid bedreigen.

2. Bestudeer de patiëntenreis met behulp van SEIPS 3.0

In januari 2020 is het SEIPS 3.0 model gepubliceerd waarin de patiëntenreis een centraal onderdeel is geworden.[13] Het is aan te bevelen om het toedienproces van high-risk medicatie in de context van het hele zorgproces ook vanuit het patiëntenperspectief nader te onderzoeken, met behulp van SEIPS 3.0. Bijvoorbeeld over hoe patiënten betrokken kunnen worden bij het uitvoeren van de tweede controle.

3. Herzie het huidige protocol voor het veilig toedienen van high-risk medicatie

Het huidige VMS protocol voor het veilig toedienen van high-risk medicatie moet worden herzien, met name om de voordelen van technologische hulpmiddelen te integreren. Daarnaast zou een expertgroep kunnen bediscussiëren welke handelingen uit het protocol nog gemeten moeten worden en welke niet. Het blijven meten van de tweede controle en het uitvoeren van handhygiëne wordt nog steeds aanbevolen; het blijken de meest lastigste en complexe handelingen te zijn.

Bij het herzien van het protocol is het van belang te realiseren dat 100% naleving weliswaar wenselijk is, maar in de praktijk niet altijd haalbaar. De huidige praktijk suggereert bijvoorbeeld dat het niet langer wenselijk kan zijn om voor alle medicatie een volledige tweede controle te eisen. Als alternatief kan het protocol twee onderdelen bevatten: één gedeelte welke een standaard aantal handelingen bevat en één gedeelte die aan te passen is per afdeling.

4. Investeer in cultuur versterkende interventies

Het is een illusie om te denken dat als we ons focussen op wat goed gaat en het protocol herzien, dat dan alle problemen zijn opgelost. De focus zou ook meer moeten liggen op de cultuur rondom het toedienen van high-risk medicatie. Dit proefschrift bevestigt dat verpleegkundigen niet zonder reden afwijken van het protocol. Aanbevolen wordt om een cultuur te creëren waarin de beoordeling van verpleegkundigen gezien kan worden als een goede praktijk waarvan geleerd kan worden. Toekomstig onderzoek zou zich moeten focussen op deze beoordeling en het effect van het uitvoeren van een risicoanalyse op Safety-I (medicatiefouten) en Safety-II (klinische praktijk).

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6 januari 2021, Driekoningen,

ABOUT THE AUTHOR

Bernadette Clara Francisca Maria Schutijser was born on the 9th of May 1988 in Zeist, the Netherlands, and lived her whole life in Driebergen - Rijsenburg. She finished her secondary school (HAVO) at the Revius Lyceum in Doorn and started her bachelor of nursing in 2005 at the Christelijke Hogeschool in Ede. She graduated in 2009 with a thesis about ethics education for nursing students. Directly after nursing school, she started her master in nursing science at the Utrecht University. She obtained her master's degree in 2012 with a thesis about the feasibility of a multi-component preadmission nursing intervention to prevent decline in older cardiac surgery patients. During and after her master program, she worked as a research nurse at the Erasmus MC (2010-2012) and the Amsterdam UMC, location AMC (2012-2015) on studies about hip osteoarthritis and chronic pancreatitis. In 2015, she started her PhD project on the safe administration of injectable medication by nurses at the Amsterdam UMC, location VUmc. This PhD project was part of the Dutch Adverse Event Study 2015-2018. From 2019, Bernadette worked on other studies while finishing her PhD thesis. She was program secretary for the Quality of Care Program of the Amsterdam Public Health research institute, worked on a guideline about preparing injectable medication with the Dutch Institute for Rational Use of Medicine and developed a stepped wedge trial within the new Dutch Adverse Event Study 2019-2022. In May 2020, she won the Anna Reynvaan Science Award for one of her PhD publications. Since september 2020, Bernadette works for SKILZ (Stichting Kwaliteits Impuls Langdurige Zorg) as a process coordinator for the development of guidelines for the long-term care. For over 20 years she is a volunteer at the Roman - Catholic church of Driebergen - Rijsenburg, first as an acolyte, later as a sacristan. Furthermore, she likes folk dancing, cycling, going to musicals and travelling to (Disney) theme parks with extraordinary rollercoasters. Since 2019, Bernadette lives together with her boyfriend Melchior van Glansbeek.

PhD - training

Bernadette followed several courses during her PhD trajectory. She trained her research and statistical skills with the courses eBROK (NFU), Scientific integrity (Amsterdam UMC, location VUmc), Practical biostatistics (Amsterdam UMC, location AMC), Regression techniques (EpidM) and Multilevel analyses (EpidM). Bernadette trained her English writing skills with the course Scientific writing in English (Amsterdam UMC, location AMC). Furthermore, Bernadette regularly visited research meetings from the department of Public and Occupational Health and from the research group Safety4Patients. She was also a member of the internal audit committee of the Amsterdam UMC, location VUmc. Finally, four times a year she had intervision meetings with other PhD fellows.

Bernadette attended several national and international congresses during her PhD trajectory where she presented her research. For example the Congress of Medication Safety, the Annual Care Days, the VU Science Exchange Day, the Annual APH Meetings, and the ISQUA Congress 2017 in London and the FRAMily Meeting 2019 in Malaga.

Bernadette provided education classes to Bachelor and Master medical students about suboptimal events, medical errors, professional secrecy, disciplinary law cases and freedom restriction. She also guided nursing and medical students during their bachelor thesis.