Pharmaceutical care in surgical patients: Tools for measurement and intervention

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Assessing and improving the quality of pharmaceutical care is a major issue in hospitals nowadays. Medication safety strategies are being developed and widely introduced in hospitals to reduce medication-related harm. In general, medication safety strategies are based upon processes, patients, or pills or a combination of these three “P’s”; a so-called multifaceted approach. Considering the medication process, an example of a hospital-wide strategy to reduce prescribing errors is the introduction of CPOE systems with or without CDS or the use of barcode technology to reduce medication administration errors. For transfer errors, medication reconciliation at discharge of the patient from the hospital can be introduced. The patient-specific strategies are mostly aimed at high-risk populations such as the elderly, ICU patients, or pediatric patients. For example, the introduction of a QI set to assess the care of vulnerable elderly patients (ACOVE) or a pharmacist role in ICU patients to prevent medication-related harm. Also, multiple studies are executed to determine the type of medications with a high risk for patient harm. These medications can be used as targets for medication safety strategies.

Surgical patients are at risk for medication-related harm as well. Their type of medication used, their multiple transfers along the surgical pathway and the surgical procedure itself might play an important role considering medication safety. Surgical patients using medication for comorbidities unrelated to the surgical procedure have an increased risk for post-operative complications compared to patients not taking any medication. Due to these factors, most surgeons are in need of multidisciplinary cooperation with, for example, a hospital pharmacist for their specific knowledge about medication and medication processes to enhance the surgical patients’ quality of pharmaceutical care around the procedure.

Quality assessment of pharmaceutical care is essential to monitor whether certain medication safety strategies are indeed effective. In general, several types of measures can be used to assess the quality of care, e.g., structure, process, or outcome measures. This thesis focuses on the assessment of the quality of pharmaceutical care in surgical patients using developed process and outcome tools for measurement. Also, the improvement of this care was assessed by measuring the effectiveness of a medication safety strategy with a focus on ward-based interventions by a hospital pharmacy team. The fundament of this thesis is described in the SUREPILL (Surgery & Pharmacy In Liaison) study protocol.

To investigate the extent in which surgical patients experience medication-related harm, besides surgery-related harm, we performed a systematic review of international literature on the occurrence and preventability of ADEs in surgical patients. Only six studies described the occurrence of ADEs in surgical patients amongst others, with unfortunately various outcome measures. A large range from 2.0 to 27.7 ADEs per 100 admissions, 4.7 to 8.9 ADEs per 1,000 patient days, or ADEs involved in 8.9% of the patients was found. Two studies described proportions of 18% and 54%.
INTRODUCTION

Assessing and improving the quality of pharmaceutical care is a major issue in hospitals nowadays. Medication safety strategies are being developed and widely introduced in hospitals to reduce medication-related harm. In general, medication safety strategies are based upon processes, patients or pills or a combination of these three “P’s”: a so-called multifaceted approach. Considering the medication process, an example of a hospital wide strategy to reduce prescribing errors is the introduction of CPOE systems with or without CDS or the use of bar-code technology to reduce medication administration errors. For transfer errors, medication reconciliation at discharge of the patient from the hospital can be introduced. The patient specific strategies are mostly aimed at high-risk populations such as the elderly, ICU patients, or pediatric patients. For example, the introduction of a QI set to assess the care of vulnerable elderly patients (ACOVE) or a pharmacist role in ICU patients to prevent medication related harm. Also, multiple studies are executed to determine the type of medications with a high risk for patient harm. These medications can be used as targets for medication safety strategies.

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PART I DEVELOPMENT – Adverse drug events in surgical patients

To investigate the extent in which surgical patients experience medication-related harm, besides surgery related harm, we performed a systematic review of international literature on the occurrence and preventability of ADEs in surgical patients. Only six studies described the occurrence of ADEs in surgical patients amongst others, with unfortunately various outcome measures. A large range from 2.0 to 27.7 ADEs per 100 admissions, 4.7 to 8.9 ADEs per 1,000 patient days, or ADEs involved in 8.9% of the patients was found. Two studies described proportions of 18% and 54%
preventability of ADEs. In five studies a comparison was made with the occurrence of ADEs in the nonsurgical population, it appears that the nonsurgical population experience significantly more ADEs compare to the surgical population. From clinical perspective, it is likely that surgical patients are less ill than nonsurgical patients overall. First, the admission for surgery is usually planned, in contrast to admission of medical patients. Second, the key reason for admission of the surgical patient is the surgical procedure itself, whereas the nonsurgical admissions usually require multiple medication interventions to improve their clinical course of disease.

The variety of outcome measures used in the systematic review to report ADEs indicates that a clear definition of ADE is not present. Also, a gold standard to measure ADEs as an outcome measure is lacking. This is one of the most problematic issues in medication safety research concerning ADE measurements. First of all, these measurements are solely retrospective and depend on registered data in medical records. Second, a widely used method is the IHI trigger tool to select events based on predefined triggers. This method is not specified to certain populations and adjustments are generally necessary. Furthermore, after selecting events the most crucial step is to find a causal relationship with medication. Several methods of causality assessment have been described. These methods can be divided into three categories: expert judgment, algorithms and probabilistic methods. Ideally a combination of these different methods would make the causality assessment method more reliable. Furthermore, we believed that standardization of the assessment method would also improve reproducibility and reliability.

For these reasons, we developed and tested a standardized assessment method for ADEs (chapter 4) for specifically the surgical population. With this method we also aimed to gain more knowledge about the incidence and nature of ADEs in surgical patients and to assess future necessary improvements in pharmaceutical care. This method comprises a surgical trigger tool of 51 triggers and causality assessment method with expert judgment based on algorithms and probabilistic methods to assess causality, preventability, severity, and also medication responsible for the ADEs. The inter- and intra-rater calculations showed substantial to almost perfect levels of agreement (kappa range 0.71–0.83) to apply the trigger tool. Fair to substantial levels of agreement were calculated for causality, severity and preventability assessments (kappa range 0.38–0.79). Although these kinds of retrospective detection methods are liable to subjectivity, the reliability data of this assessment method were comparable to other studies. Compared to an existing trigger tool method for ADEs, we found 20% more ADEs in a test population.

This method was concluded to be a useful alternative to existing trigger tool methods with causality assessment, in particular to assess quality of pharmaceutical care in surgical patients.

**PART II  ASSESSMENT – Adverse drug events and quality indicators**

Chapter 5 describes the results of our ADE assessment method when applied in surgical patients of three Dutch hospitals, an academic hospital, a tertiary hospital and a community hospital. All hospitals use CPOE systems with CDS. We included 567 surgical patients and we found an incidence of 27.5 ADEs and 4.2 (15.3%) preventable ADEs per 100 admissions. A quarter of the preventable ADEs were
severe or life threatening. Prescribing errors were the most frequent cause of preventable ADEs (87.5%). Opioids and anti-coagulation medication played a major role in the occurrence of ADEs and preventable ADEs respectively. Univariable analysis revealed an ASA classification of III or more as a risk factor for ADEs. Patients older than 65 years (IRR 2.77 (1.14–6.72)), with cardiovascular comorbidity (IRR 2.87 (1.13–7.28)), or undergoing vascular surgery (IRR 2.32 (1.01–5.32)) were at risk for preventable ADEs. Patients experiencing an ADE had a significant longer duration of admission than patients without an ADE (9 resp. 6 days, p=0.000).

In this study, we solely used a chart review method to collect ADEs. No data of voluntary reporting, direct observation or computerized monitoring was used. As described in chapter 2, Morimoto et al. assessed a comparable incidence of 27.7 ADEs per 100 admissions in surgical patients using three different assessment methods, namely chart review, voluntary reporting and direct observation. We conclude that our method of ADE assessment is therefore more sensitive and more efficient compared to the methods already described in literature.

If we compare our data to an elder (>65 years) Dutch population (n=250) of a university teaching hospital, a regional teaching hospital and tertiary teaching hospital, their incidence of ADEs and preventable ADEs was much higher, i.e. 47.2 ADEs and 33.2 pADEs (71%) per 100 hospitalizations. They also used an extensive chart review method, but their definition of an ADE was broader; also worsened and sustained harm or delayed recovery as well as omissions of medication were defined as ADEs. Furthermore, the included internal medicine patients used five or more medications at admission and were over 65 years old with multiple morbidities. Therefore, their risk in experiencing an ADE during admission was higher compared to our complete surgical population.

The definition of ADE and the type of method used in a medication safety studies determine the results of the studies performed. Therefore, additional methods to assess pharmaceutical care are necessary to give insight in the extensiveness of the medication safety problems.

We developed and tested 27 QIs to provide insight in the quality of the processes of pharmaceutical care in surgical wards (chapter 6). The inter-rater agreements of applying these QIs on a surgical population were almost perfect (kappa 0.92) for eligibility, and substantial (kappa 0.74) for pass rate assessments. Compared to the elderly population (>65 years) of the internal medicine department in the same academic hospital, Wierenga et al. found an overall pass rate, assessed with 87 validated medication-related quality indicators, of only 43%. Improving the quality of pharmaceutical care is necessary to prevent harm in both populations. With the surgical QIs explicit targets for quality improvements are exposed. Also, they can be used prospectively in the medication process and prevent errors and harm. QIs are therefore a valuable addition to the ADE assessments in improving the quality of pharmaceutical care. Overall, the quality of pharmaceutical care in 252 surgical patients of an academic medical centre can be improved for more than 50%. Especially processes related to medication to prevent thrombosis and gastrointestinal problems need attention. Our surgical population is not only at risk for (preventable) ADEs, the quality of the in-hospital medication processes is to be desired.
The conclusion of this part of the thesis is that surgical patients are at considerable risk for experiencing medication related harm during their admission, also in Dutch hospitals, despite the use of CPOE systems with CDS. Intensified monitoring may be needed in patients with a higher than average risk for medication related harm. Therefore, based on our data of our ADE assessment and QI assessment, a risk profile of the surgical patient for medication related harm could be extracted as displayed in table 1. Specific risk items are defined for the type of patient, type of medication (pills) and type of process. In addition, types of common events are specified. This means that surgical patients with one or more of these events/disorders in their history or present during their admission are defined as high-risk patients.

| TABLE 1. RISK PROFILE OF SURGICAL PATIENTS FOR MEDICATION-RELATED HARM |
|-----------------------------------|---------------------|---------------------------------|
| **BASED ON (P) ADEs** | **BASED ON QIs** |
| **TYPE OF PATIENT** | **TYPE OF PROCESS** |
| ASA* classification ≥ III | Prevention of pain |
| Age > 65 years | Prevention of thrombosis |
| Cardiovascular comorbidity | Prevention of opioid-induced obstipation |
| Vascular surgery | Documentation of medication on admission |
| Admission > 6 days | Documentation of medication in different resources |
| **TYPE OF MEDICATION** | Sending discharge letter to outpatients’ physician |
| ATC Nervous system: opioids |
| ATC blood & blood forming organs: anti-coagulants |
| **TYPE OF EVENT** |
| Hematologic disorder |
| Cardiovascular event |
| Renal function / electrolyte disorder |

*With a pass rate of less than 50% with more than 50% eligible patients. *ASA: American Society of Anesthesiologists; classification for fitness of patients prior to surgery. >III: severe to life-threatening systemic disease

**PART III IMPROVEMENT – Ward-based pharmacy interventions**

Improvement of pharmaceutical care in surgical patients can be measured by reduction of the incidence of (preventable) ADEs and/or increment of the quality of medication related processes. In chapter 2 we described our study protocol to evaluate effectiveness of an intervention strategy. In chapter 7 we described this developed intervention strategy in detail. Our aim was to develop a broad multidisciplinary intervention strategy based on different phases of the surgical pathway, and to evaluate its effect on the incidence of (p)ADEs and outcomes (chapter 8).

Overall, the intervention strategy includes medication reconciliation on admission and discharge, and medication reviews by pharmacists of patients admitted at the randomised
intervention wards in three participating hospitals. Pharmacy technicians / practitioners performed medication reconciliation in consultation with the patient using standardized questionnaires and pre-registration of medication in the CPOE system for the physician. During admission, the (hospital) pharmacist performed medication reviews using a checklist with common surgical problems related to medication and a standardized registration form to register the executed interventions with help of an acronym TREATRAFID (Type of medication-related event; Reason for the event; Evaluation of the medication-related event; Action of the pharmacist; Type of action; Reaction on the action by the ward doctor; Acceptance by the ward doctor; Follow-up; Intervening hospital pharmacist and Date) (chapter 7).

In total, 547 patients were included in the ward-based pharmacy team intervention wards and 547 patients in the control wards. Eighty nine per cent of intervention patients had their medications reconciled on admission as well as received at least one medication review by the pharmacist during their stay. The median number of medication reviews per patient during admission was three (IQR 2-5). The total average time for the pharmacist to perform a medication review was six minutes per patient. The pharmacist performed 880 specific interventions to improve pharmacotherapy in 309 patients mostly stopping, starting or altering medications. Approximately one third of the pharmacists’ interventions were not or only partially accepted by the ward doctor.

Overall, we found 316 ADEs with our ADE assessment tool in the included 1094 surgical patients. These ADEs were seen in 265 patients. A minority of ADEs (36 ADEs in 35 patients; 11.4%) was judged preventable by the expert panels. The overall incidence was 3.3 pADEs per 100 admissions. A non-significant crude reduction of 28.6% preventable ADEs was seen after intervention on the intervention wards when compared to the control wards (2.74 vs 3.84 pADEs per 100 admissions; incidence rate ratio 0.714, (95% CI: 0.366-1.393); p=0.324). Adjusting for differences in treatment groups and for potential confounding resulted in a remaining non-significant incidence rate ratio of 0.819 (95% CI: 0.39-1.721; p=0.598). No differences were seen for other outcomes, such as length of hospital stay, number of complications and quality of life (chapter 8).

A reduction of 60% of pADEs was hypothesized based on two previous studies28,29. Our controlled study with randomisation at ward-level could not replicate these published results in a surgical population. Based on our results, we have to ascertain so far that general surgical patients will not benefit from this broad intervention strategy. Some hesitation still remains.

A cross-over study design might have given a more precise point estimate of the intervention effect, as by this design baseline differences between wards are less important30. In addition, we chose a broad intervention strategy instead of a strategy targeted on high-risk surgical patients (as described in table 1). Medication reviews were not performed daily by the pharmacists. Finally, almost one third of the interventions were not or partially accepted by the ward doctor.

All these above mentioned factors could have negatively influenced potential effect on preventable ADEs in surgical patients.
Chapter 9

**Future perspectives**

In The Netherlands, pharmaceutical care is mainly provided from a central pharmacy: in approximately 25% of the hospital pharmacies, pharmacists visit the ward daily, and only 10% of the hospital pharmacies have pharmacists spending at least half of their time on the ward. In 85% of the hospital pharmacies in the UK, the pharmacists visit the wards daily and in almost half the pharmacies, the pharmacists spend at least 50% of their time on the ward. Although pharmaceutical care in the Netherlands might still seem centralized and product focused, we do move more and more toward a patient focus and clinical pharmacy service since we realize this is the future of our ambition. In addition, since 2007 a Dutch law describes that (hospital) pharmacists are responsible for a patients’ therapeutic medical plan besides the medical specialist. It is therefore inevitable that the role of the hospital pharmacist is moving towards clinical practice and multidisciplinary teamwork. This movement is also supported by the Dutch minister of health care.

This thesis is an example of this movement and can be used by hospital pharmacies to improve their clinical pharmaceutical care services taking our experiences into account.

In Dutch hospitals, CPOE with CDS systems are used for a decade now. These systems alert for interactions or overdoses etc. and can reduce the number of medication errors and in addition adverse drug events. Integrating third generation medication alert systems, such as clinical rules or quality indicators, might even reduce the number of medication errors even more. Due to these systems and the alert fatigue as a logical consequence, the medication errors mostly found nowadays are prescribing errors. Although these systems are used, ADEs still occur as we concluded in this thesis. Therefore, these systems are inadequate to use as a sole solution to prevent medication related harm and multifaceted intervention strategies are necessary.

First, adequate methods or tools are necessary to assess outcome measures as well as a clear definition of the outcome measure since a gold standard is still lacking. The definition and the type(s) of method used to assess the outcome measure are unquestionably determining the outcome results of your studies. At the moment, studies are difficult to compare and a clear insight in the problems and/or solutions in medication safety is absent. In this thesis we present an efficient and practical method to assess ADEs in surgical patients specifically. One might decide to exclude some triggers that were not scored in our surgical population, but the trigger tool and causality assessment method as proposed, should be used as a whole. We suggest that future studies about this subject should therefore use the same method and definitions for accurate comparison of the results found in different studies. For other types of populations, different triggers can be chosen and experts should be chosen in concordance with the type of population. Validation of the new composition is however inevitable. Our suggestion is also underlined by a recent systematic review. It states that existing instruments in assessing preventable ADEs should be further studied and developed, and the validity and reliability of the instruments should be established.

Furthermore, multifaceted intervention strategies are needed to reduce the number of ADEs and medication errors. Many local and national medication safety initiatives are executed in the Netherlands, such as clinical rules, drug rules or quality indicators, satellite pharmacies for...
medication preparation, or participation in multidisciplinary teams. Although, these strategies seem beneficial in practice, actual evidence-based data on clinical outcomes about these clinical pharmacy interventions is lacking in literature as yet. Preferably a strategy to reduce errors prior to prescription of the medication by the physicians should be initiated. Prospective clinical or ward-based pharmacy interventions are therefore necessary. Due to translational reasons to other hospitals, as one of a few other reasons, we developed a broad and general applicable ward-based intervention strategy with the aim to reduce medication errors and preventable ADEs in surgical patients. Since we could not find a significant reduction in preventable ADEs in the surgical population with this intervention strategy, we suggest future research to focus on pre-selected high-risk patients. For surgical patients, the risk profile as described in the summary can be used. Risk patients, risk processes and risk pills (three P’s) are described, as well as common events. For an effective intervention strategy we suggest to include this risk profile for surgical patients to successfully prevent medication related harm.

Until now, only four published studies\textsuperscript{10,28,29,40} and one unpublished study\textsuperscript{7} showed an effect of clinical pharmacy interventions on ADEs in hospitals. In literature, multiple studies have assessed the effect of pharmacist interventions in hospitals on medication safety issues. For example, medication reconciliation on admission and at discharge reducing medication related problems in internal medicine patients\textsuperscript{9}, in-hospital medication reviews reducing drug related problems in elder patients\textsuperscript{41}, comprehensive medication review in older patients reducing overall number of scheduled medications\textsuperscript{42}, or post-surgical care by pharmacist performing interventions with high probability in preventing ADEs\textsuperscript{43}. These examples of recent studies, all suggest a positive effect on related outcomes such as adverse drug events, but none of these studies were genuine outcome studies. Furthermore, studies that show an effect of clinical pharmacy interventions on ADE outcomes\textsuperscript{10,28,29,40} have not used a randomized controlled setting, or have used a controlled setting but without a large number of patients. Literature lacks evidence on the actual outcome effect of clinical or ward-based pharmacy interventions in hospitalised patients. This statement is also subscribed by a recent Cochrane review\textsuperscript{44} about medication review in hospitalised patients to reduce morbidity and mortality. Our study adds relevant data about the effectiveness of clinical or ward-based pharmacy services in surgical patients in a randomized controlled setting. When ward-based pharmacy was evaluated in this prospective and comparative way no effect was found. Only one other study\textsuperscript{45} described no effect of clinical pharmacist interventions on ADEs in patients after discharged from the hospital.

Economic evaluations on the subject have an important role. Several economic evaluation studies are executed as described in a recent systematic review on clinical pharmacy services\textsuperscript{46}. Although the evaluation of the economic impact of the interventions are very relevant for implementing in clinical practice (as we also describe in our study protocol in chapter 1), most studies show cost avoidance by for example calculating a price per (probable) reduced ADE\textsuperscript{43,47,48}. None of these studies calculated direct cost reductions. This type of research is indeed difficult to perform (also due to the lack of a gold standard). But, as already described by De Rijdt\textsuperscript{49}, more economic research with high quality study design is necessary. Since our study showed no effect of ward-based pharmacy interventions on preventable ADEs, cost-effectiveness analyses were not relevant. Using the results and experiences of the study design in this thesis (mainly described in chapter 7), future
research projects focussing on clinical pharmacy services with outcome measurements should take these into account. Hereafter, clear economic evaluations can be executed.

Although hospital pharmacists move more and more towards clinical pharmaceutical care, it is still not clear which approach is the most effective and efficient. Considering the results in this thesis, with no broad effect on ADEs of the ward-based pharmacy approach, hospital pharmacy teams should at least focus on the transfer moments of the patient during the complete surgical pathway which are at high risk of losing information. On each transfer moment, in particular on admission and at discharge but also at transfer from ICU to the ward, clarification of the actual medication use of the patient with specification of reasons for starting and stopping medication, is desirable to optimize the pharmaceutical care. Pharmacy technicians or practitioners are perfectly capable of performing such reconciliations. Also, a focus on the high-risk surgical patients by ward-based surveillance of medication during hospital stay is advisable. This part can be performed by a hospital pharmacist considering his clinical role.

Looking forward, integrated pharmaceutical care should follow all care paths regardless of any boarders in the health care system. This is especially the case in surgical patients, because nowadays they are discharged from the hospital as soon as possible after their surgical procedure. Necessary prolonged care is provided in the primary care setting. Multidisciplinary teamwork with outpatient pharmacists and physicians to enhance the patients’ safe transfer to the primary care is inevitable. The overall major question is how we can effectively improve the complete patients’ pharmaceutical care pathway from primary care, to the hospital (including multiple inhospital transfers due to the surgical procedure), to possibly tertiary care and vice versa? Also, which part of this pharmaceutical care can be the responsibility of the patient himself to improve its overall quality of pharmaceutical care?

Future research remains necessary to provide effective and efficient multifaceted approaches to optimize the pharmaceutical care in surgical patients by hospital pharmacy teams in close cooperation with surgeons.
References


32. Dutch Association for Hospital Pharmacists (NVZA). Visiondocument Specialized Pharmacy (Blauwdruk Specialistische Farmacie). 2012.


