School of Pharmacy

Pharmacists' Interventions in Minimising Medication Misadventure in Children with Cancer

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Declaration

To the best of my knowledge and belief this thesis contains no material previously published by any other person except where due acknowledgment has been made.

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university.

Signature: 

Date: 27-02-2015

Abstract

Medication misadventure has been extensively studied in adults, but has not been well characterised in children – in particular vulnerable children with cancer. To date, little is known about medication misadventure in paediatrics and the role of pharmacists' interventions in minimising the misadventure in this area. This study consists of four parts, aiming to evaluate the role of pharmacists' interventions in minimising the occurrence of medication misadventure in children including those with cancer, the clinical significance of pharmacists' active interventions (i.e. interventions leading to changes in drug therapy) and the involvement of medication misadventure detected through the active interventions, and contributing factors and preventive strategies relating to medication misadventure, particularly medication error, in this population.

The study was undertaken in a children's hospital in Perth, Australia. Part One was a prospective study to document ward-based pharmacists' interventions through direct observation by principal researcher on five study wards (General Medical Ward for Infants, General Medical Ward for Young Children, General Medical Ward for Adolescents, General Surgical Ward and the Haematology-Oncology Ward) representing three clinical units (general medicine, general surgery, haematology-oncology). Pharmacists' interventions during dispensing in the Haematology-Oncology Pharmacy were also observed by the principal researcher and documented over 33 days. Part One was conducted from September 2011 through August 2012. The predictors for physicians' acceptance of ward-based pharmacists' active interventions were identified using multivariate logistic regression. A total of 982 interventions were documented, related to the 16,700 medication orders reviewed on the five wards in the three clinical units over 35-37 non-consecutive days on each ward. Taking medication histories and/or patient counselling were the most common pharmacists' interventions in the general settings, (n=453/787, 57.6% of all interventions). In contrast, on the Haematology-Oncology Ward, the data revealed drug therapy changes as the most common interventions (n=73/195, 37.4% of all interventions). Active interventions constituted less than one-quarter of all interventions on the general medical and surgical wards, compared to nearly half on the specialty Haematology-Oncology Ward. Dose adjustment was the most frequent active interventions in the general settings, whilst drug addition constituted the most

common active interventions on the Hematology-Oncology Ward. The degree of acceptance of pharmacists' active interventions by physicians was high (n=223/244, 91.4%). With respect to interventions during dispensing, a total of 359 interventions were performed from the 1791 medication orders reviewed and dispensed by the pharmacists. The rates of intervention were 21.29 per 100 medication orders reviewed, and 35.18 per 100 patients. Amongst these interventions, less than 10% were classified as 'active' interventions, but all of the active interventions were accepted by the physicians. Drug information-related consultation by pharmacists was the most common intervention, constituting more than three-quarters of all interventions. With regard to the predictors of physicians' acceptance of ward-based pharmacists' active interventions, three significant variables were identified: patients' age (OR = 0.89; 95%CI 0.81, 0.98), non-high-risk medication category (OR = 2.80; 95% CI 1.09, 7.17), and pharmacists' experience (OR = 1.11; 95%CI 1.03, 1.20). This body of research supports the role of pharmacists in optimising patient care in a range of paediatric settings, through their active interventions either during pharmacy rounds or dispensing. Direct observation offers the alternative approach for measuring the rate and pattern of pharmacists' interventions.

Part Two of the study involved expert panel assessment of a sample of randomly-selected pharmacists' active interventions data from Part One to determine the clinical significance of the interventions; to identify and categorise medication misadventure; and to classify medication misadventure involving medication error according to the type of error and the severity of their consequences. A random sample of 42 cases (15.8%) was selected from 266 pharmacists' active interventions (244 interventions during pharmacy ward rounds on the five study wards, supplemented by 22 interventions documented during dispensing in the Haematology-Oncology Pharmacy). Panel 1 consisted of two researchers and three independent panellists (hospital pharmacist, academic pharmacist, clinical nurse), and its assessment was undertaken in March-June 2013. Panel 2 consisted of the two researchers and two independent panellists (medication safety pharmacist, paediatric oncology pharmacist) and was set up in July 2014 as Panel 1 could not reach consensus. For the clinical significance assessment, the rating system modified by Dooley *et al.* was used, whilst the assessment of the type and severity of medication error were conducted using the National Coordinating Council for Medication Error

Reporting and Prevention Taxonomy. The most common clinical significance rating of the active interventions assessed by Panel 1 was 'moderate'. Meanwhile, the majority (n=37/42, 88.1%) of the active interventions were deemed by Panel 2 to be clinically significant; although no intervention was classified as life-saving. The strength of agreement between all reviewers of Panel 1 was "fair" (α =0.321) regarding the presence of medication misadventure, and "fair" (α =0.222) regarding the category of medication misadventure. "Fair" agreement (α =0.351) was also noted when classifying the type of medication error, with "slight" agreement (α =0.154) for the error severity. Part Two of this study provided data supporting the clinical significance of the interventions documented in Part One. "Fair" agreement between interdisciplinary reviewers regarding the assessment of medication misadventure is consistent with published literature; as such, this indicates support by other healthcare professionals for the contribution of clinical pharmacists in reducing medication misadventure.

Part Three was a retrospective study to analyse data from pharmacist interventions from short-term ('snapshot') 2009-2010 self-reports in the study hospital. Intervention data were compared with interventions documented during direct observation (Part One) to examine the pattern and representativeness of short-term documentation as opposed to continuous documentation using observation. Subsequently, a focus group discussion involving eight hospital pharmacists was conducted in July 2013 to gather pharmacists' opinions on the utility of the alternative documentation methods. A total of 398 interventions were documented by pharmacists during three snapshot reporting periods, with 'clarification of medication orders' being the commonest type of intervention. The overall rate of pharmacists' interventions documented during direct observation was not significantly different to that of the snapshots (p=0.054). However, the rate of active interventions was significantly higher (p=0.002) during direct observation. During the focus group discussion, participants reported that the snapshot reports were an inadequate representation of pharmacists' clinical activities. 'Snapshot' data may underestimate the impact of pharmacists' interventions in minimising medication misadventure amongst paediatric inpatients.

Part Four applied root cause analysis to five simulated clinical case scenarios involving medication errors in children. The root cause analysis was undertaken via a self-administered questionnaire disseminated to doctors, nurses and pharmacists at the study hospital in order to determine the clinical significance of the medication errors, the responsible health care professionals, the contributing factors and the preventive strategies. In addition, general estimating equation analysis was conducted to develop an agreement model between the participants and the principal researcher regarding the contributing factors. Of 111 questionnaires administered during the study period (August-October 2014), 25 (22.5%) were returned and analysed. The majority of the participants rated the medication errors involved in the five cases ranged from 'moderate' to 'life-threatening'. In relation to the factors contributing to the errors, the participants' perceptions varied across the five cases. However, the majority of the participants identified two major contributing factors in all cases: dismissal of policies/procedures or guidelines and human resources issues. The most frequently cited strategies in this study included improved availability and accessibility of hospital policies/procedures or clinical guidelines for medication use, adequate staffing and supervision, adequate staff education and training, and improved communication either between staff or between staff and patient/family. There were varied agreement patterns across the contributing factors. This analysis confirmed the findings of the previous studies regarding the contributing factors and strategies to prevent medication error. Pharmacists, through their clinical services, were again central to prevention of medication error.

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"To err is human; to fail to learn is inexcusable"

(Susan Sheridan, Vice President, Consumers Advancing patient Safety, 2004)

Presentations and Publications

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Glossary

ACE	Angiotensin-Converting Enzyme
ADE	Adverse Drug Event
ADR	Adverse Drug Reaction
ALL	Acute lymphoblastic Leukaemia
AMH	Australian Medicines Handbook
AUC	Area Under curve
BD	*Bis In Die* (Latin: two times per day)
BSA	Body Surface Area
CAST	Commercial Aviation Safety Team
CDS	Clinical Decision Support
CIVAS	Centralised Intravenous Admixture Service
CI	Confidence Interval
CPOE	Computerised Physician order Entry
DRP	Drug-Related Problem
ED	Emergency Department
FGD	Focus Group Discussion
g	Gram
GEE	General Estimating Equation
HFE	Human Factor Engineering
HITH	Hospital in the Home
HIV	Human Immunodeficiency Virus
h	Hour
ICCC	The International Classification of Childhood Cancer
ICU	Intensive Care Unit
Inh	Inhaler
IV	Intravenous
IR	Immediate Release
IT	Information Technology
kg	Kilogram
L	Litre
LOS	Length of Stay
Mane	Morning (Latin)

MAR	Medication Administration Record
mcg	Microgram
ME	Medication Error
mg	Miligram
mL	Mililitre
NCCMERP	The National Coordinating Council for Medication Error Reporting and Prevention
Neb	Nebuliser
NG	Nasogastric
N/S	Normal Saline
Nocte	Night (Latin)
OD	Once Daily
PCA	Patient-Controlled Analgesia
PEG	Percutaneous Endoscopic Gastrostomy
PI	Pharmacists' Intervention
PL	Professional Level
PRN	*Pro Re Nata* (Latin: as required)
RCA	Root Cause Analysis
QID	*Quater In Die* (Latin: four times per day)
SC	Subcutaneous
SD	Standard Deviation
SL	Sublingual
SR	Sustained Release
Susp	Suspension
TDS	*Ter die Sumendus* (Latin: three times per day)
UK	The United Kingdom
USA	The United States of America
US	The United States
WHO	The World Health Organization

Chapter 1

BACKGROUND

In this chapter information is provided on pharmacists' interventions to minimise medication misadventure in children with cancer. The discussion is supported by an in-depth literature review on medication safety terms; the incidence and consequences of medication misadventure; the causes of medication misadventure; the risk factors of misadventure in children; pharmacists' interventions in minimising medication misadventure ; and the clinical significance and economic implications of pharmacists' interventions. Also discussed is the role of root-cause analysis (RCA) as a comprehensive and systematic approach to identify systems failure.

Healthcare delivery involves a sequence of steps, which starts with diagnosing a patient's condition through to monitoring treatment. To minimise the occurrence of medication misadventure during treatment, these steps need to be conducted in an effective, safe and timely manner. It is common for patients admitted to hospital to receive multiple medications; each medication administered carries the risk of misadventure or error.(1) According to a report from the Institute of Medicine in the USA, errors occurring during healthcare delivery are the major causes of morbidity and mortality.(2) An estimated 44,000 to 98,000 deaths in the USA were attributed to these errors and medication-related errors were a significant proportion. This has significant implications on healthcare expenditure.(2) The report also highlighted that patient safety should be at the forefront of medication use. In Australia, medication misadventure is a significant burden on the health system and accounts for 2.4% to 3.6% of all hospital admissions in general patients. Up to 69% of these medication-related admissions are potentially preventable.(3) As a consequence, medication misadventure may impact on community confidence in the health system and increase healthcare costs.(3, 4)

To date, most investigations of adverse events related to medication use have been undertaken in adults. Despite the evidence that such events may be more common in children, there is a dearth of data on error-related events in this population.(5) The epidemiological characteristics of medication errors (MEs) may be different between children and adults.(6) Children have a unique physiology and an immature ability to

metabolise drugs.(7, 8) The consequences of MEs have significant ramifications in children with complicated medical conditions such as cancer.(9-11) Children with cancer receive diagnosis-specific antineoplastic drugs with narrow therapeutic indexes that require complex administration regimens.(7, 8) The risks associated with medication misadventures in paediatric oncology warrant further research.

Besides inadequate and inconclusive information on medication misadventure in the paediatric population, there has been concern about the lack of strategies to minimise errors and maximise care in the ambulatory and inpatient settings.(12) Multiple studies have analysed error-prevention strategies utilising clinical pharmacists.(13-15) Several reports have shown that ward-based clinical pharmacists reduce MEs.(15-17) The largest studies of clinical pharmacists' interventions in acute care in Australia have demonstrated that interventions initiated and undertaken by clinical pharmacists have a significant positive impact on patient outcomes and hospital costs.(3, 18) However, the impact of clinical pharmacists in minimising medication misadventures in paediatric oncology has yet to be justified.

Another concern that health services continue to face is the lack of utility of the medication misadventure data to support system improvement. To promote safer health services, systems need to identify and learn from previous incidents of medication misadventure.(12) The most effective way of system improvement is to ascertain the underlying causes of the misadventures through a well-structured investigation utilising RCA.(19) RCA has been implemented in many high-risk environments such as aviation. When applied to health systems, it is used to investigate retrospectively all the subsets of medication misadventures, e.g. adverse drug events (ADEs), adverse drug reactions (ADRs) and 'near misses'.(19) A key feature of RCA is its comprehensive and systematic examination of multi-level factors that lead to the negative outcome of interest, e.g. medication misadventure. RCA has been designed to produce strategies to improve the system, not individual performance, and to prevent recurrence of the events.(20, 21)

1.1 Medication Safety Terms

Many countries have made medication safety a priority.(22-25) The terminology/definition used to describe medication-related events and/or medication-related harm continue to be debated and create confusion among health professionals

and researchers.(26, 27) As patient safety initiatives are strengthened and reporting systems are embedded into practice, a universal definition of what constitutes medication-related events is imperative.(10) A universal terminology/definition for medication safety would: encourage research; allow comparison of medication-related events; prevent medication misadventure; and improve patient safety.(10, 28)

According to Manasse(29) medication misadventure is: 'any iatrogenic hazard or incident associated with drug therapy'. Manasse(29) also specifies the criteria for a hazard or incident, i.e. events: 'created through either omission or commission by the administration of a drug or drugs during which a patient is harmed, with effects ranging from mild discomfort to fatality; events attributable to error, immunologic response, or idiosyncratic response; and events where the outcome may or may not be independent of the pre-existing pathology or disease process'. The American Society of Health-System Pharmacists and researchers have adopted this definition of medication safety.(4, 11, 27, 30) Under the broad definition of medication misadventure there are three subtypes of medication safety: ADE, ADR and ME.(28) ADE and ME are overlapping subsets of medication misadventure. The relationship between these three subsets of medication misadventure is illustrated in Figure 1.1.

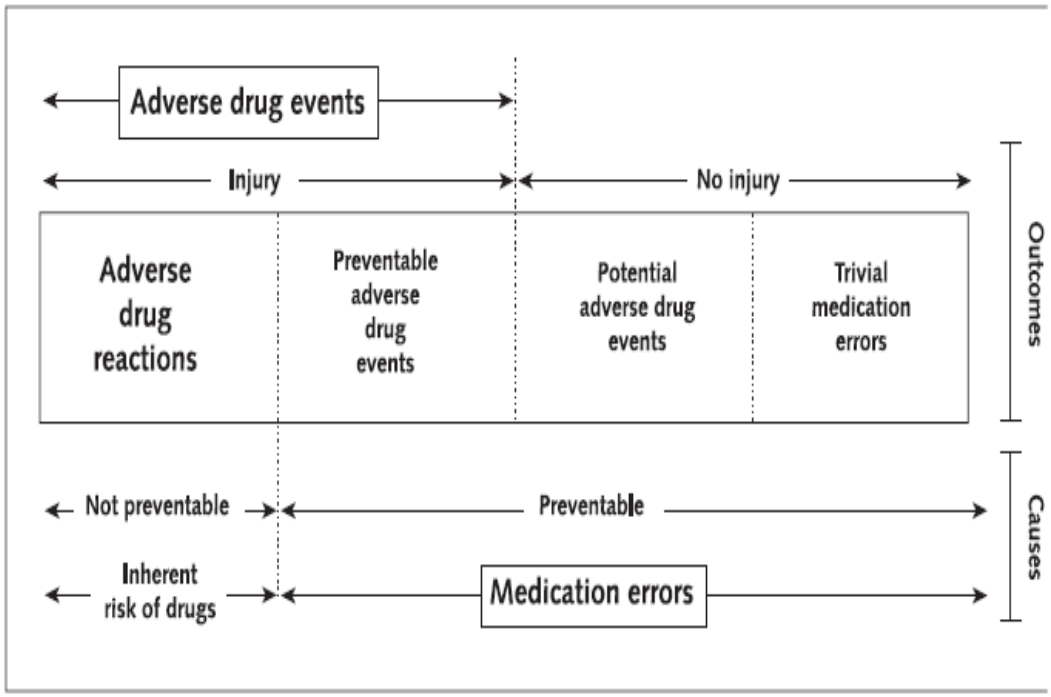


Figure 1.1 Relationship between adverse drug event, adverse drug reaction and medication error(28) (Reproduced with permission.)

ADE accounts for the largest category of adverse events in patient safety.(31) An ADE is: ‘an injury resulting from a medication or lack of an intended medication’.(27, 32) For example, if an event resulted in patient injury it would be classified an ADE, which can be further subclassified based on its preventability (preventable and non-preventable).(28, 33) An ADE may or may not result from MEs (error versus non-error). ADEs that do not result from MEs are considered non-preventable ADEs or ADRs. An example of an ADR is when a patient without a known history of allergy to penicillin develops an anaphylactic reaction immediately after receiving Timentin (ticarcillin + clavulanic acid). According to Bates *et al*.(34), the majority of ADEs due to MEs are predictable and preventable. Some instances of preventable ADEs due to MEs include administration of the wrong drug to the right patient, the right drug to the wrong patient, or the wrong route of administration. Bates *et al*.(32) have proposed a practical and straightforward definition of an ADE: ‘an injury occurring due to medical intervention associated with medication use. The adverse event could include injury resulting from MEs and ADRs that happen without involving any errors’.(32)

According to the National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP) an ME is: ‘any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health professional, patient or consumer’.(35) The Institute of Medicine defines MEs as: ‘particular types of errors in which the occurrence of events can be prevented and is likely to happen at any stage of medication use process’.(27)

MEs are not merely the result of less competent individuals but due to failure in: drug distribution; systems mismanagement; communication breakdown; inadequacy and/or unavailability of standardisation in pharmaceutical packaging, labelling and nomenclature; and limited availability of information about patients.(36) Hence, it is crucial to detect MEs in order to uncover failures during the treatment process that may lead to harm if not intercepted.

MEs range in severity from trivial errors, such as incomplete medication orders requiring clarification from prescribers, to life-threatening errors, such as a child receiving a 10-fold dose of a drug with a narrow therapeutic index.(34) Most MEs can be considered minor if the errors are associated with little or no potential for

harm, e.g. missing the dose for a non-critical medication. If an ME has potential to harm but does not actually cause harm/injury, the error is considered a potential ADE ('near miss').(32) That is, the harm/injury is not attributed to specific circumstances, chance, the patient's ability to tolerate the error, or if the error was intercepted and corrected. If an ME results in harm/injury, it is considered an ADE.(33) MEs occur more frequently than ADEs and a miniscule percentage of MEs result in injury.(9) Further investigation of potential ADEs could help identify where the system is failing (i.e. the error), as well as the success of the system *in situ*.(37) An example of a potential ADE that does not lead to harm is a patient prescribed digoxin in a dose that could cause toxicities that is intercepted by the pharmacist before administration.

According to the American Society of Health-System Pharmacists, an ADR is: 'any unexpected, unintended, undesired, or excessive response to a drug, with or without an injury'.(27) The WHO has defined an ADR as: 'a response to a drug that is noxious and unintended, and occurs at doses normally used in man for prophylaxis, diagnosis or therapy of a disease, or for modification of physiologic function'.(38) According to the WHO, an ADR does not include treatment failures, drug misuse, errors during administering the medicine, noncompliance with right directions for taking the medicine, or intentional and accidental poisonings. Therefore, all ADRs lead to injury, whether temporary or permanent. Allergic and idiosyncratic reactions are also considered ADRs.(10, 39)

ADRs occur due to intrinsic pharmacological properties of the medicine, when taken alone or in combination with other medicines.(40, 41) ADRs can be prevented by minimising patients' exposure to suspected medications, switching to less hazardous alternatives and developing new medicines.(42) MEs are considered preventable and associated with inappropriate medication use. If an error leads to patient injury, it should be considered a preventable ADE.(28) For example, cough resulting from the use of an angiotensin converting enzyme inhibitor (ACEI) in a patient without a history of ACEI-induced cough is not an ME but an ADR. It is an ME if a patient with a history of ACEI-induced cough is prescribed the medicine.(28)

However, some ADRs may result from MEs.(10) Nebekker *et al*.(42) is opposed to the feature of preventability to exclude events related to errors from the definition of ADR. They state that harm due to a drug is always caused in part by the drug's

intrinsic properties, regardless of whether an error is judged to be present. They add that not all errors are preventable, given the intrinsic limitations of human designed systems and behaviours Their assumptions have been depicted in Figure 1.2.(42) There is still no universally accepted definition of an ADR. The WHO definition, clearly states that ADRs do not include events due to errors during medication use. This conservative and widely used definition could underestimate ADR incidence by only including the events due to medications properly prescribed and administered.(38) The WHO definition is supported by the Institute of Medicine, which defines ADRs as: 'non-preventable reactions to medications related to inherent pharmacologic properties of the medications themselves instead of the result of human mistakes or system flaws'.(2)

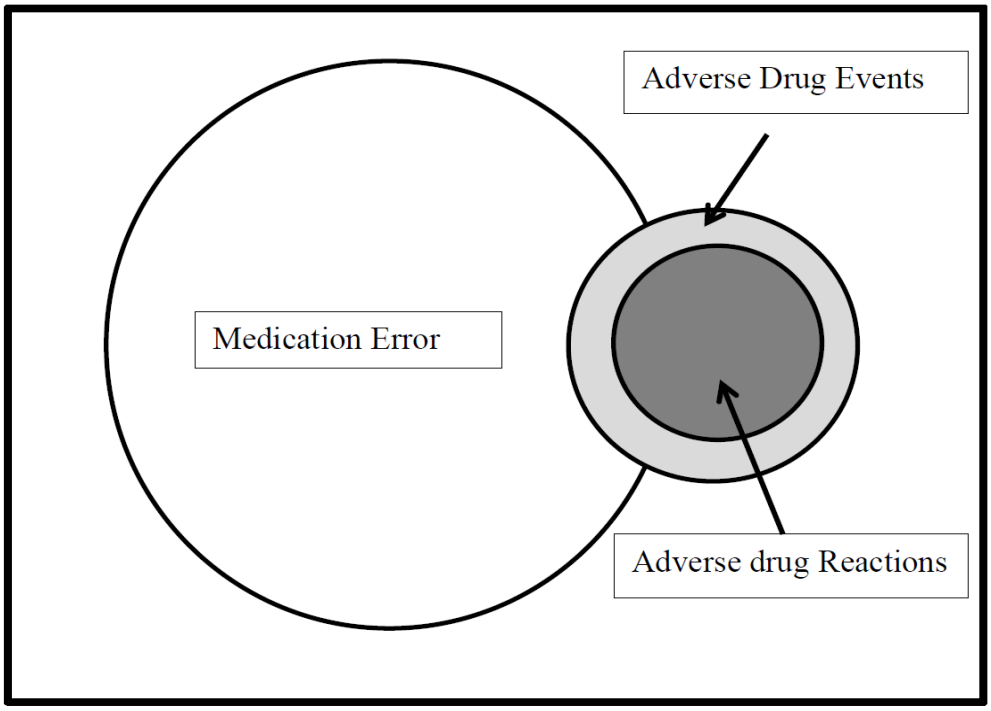


Figure 1.2 Relationship between adverse drug event, medication error and adverse drug reaction (some adverse drug reactions are due to medication errors)(42) (Adapted)

1.2 Incidence and Consequences of Medication Misadventure

Medication misadventure is common and a significant contributor to patient morbidity and mortality in general practice.(43) Medication misadventure also negatively impacts on patients treated in hospitals and may prolong hospitalisation or lead to death.(44) In the USA, ADEs occur in 3.7% to 30% of hospital admissions

and is a significant public health concern; an estimated 28% of identified ADEs are preventable.(32) One study reported that the rate of ADEs was 6.5 per 100 hospital admissions; approximately 1% were fatal and 12% were life-threatening.(34) The UK Department of Health reported that adverse events associated with medication use in 2007 were responsible for around 10% of hospital admissions.(45) In Australia, ADEs are associated with 2.4% to 3.6% of hospital admissions and an estimated 80,000 people are hospitalised every year as a result of drug-related problems (DRPs).(46) Preventable errors during healthcare delivery in hospitals account for one-quarter of adverse events in Australia.(47) The comprehensive Quality in Australian Health Care Study identified that 1.8% of all admissions to hospitals were associated with severe complications leading to disability.(47)

The 1999 Institute of Medicine report stated that medical errors were directly responsible for up to 98,000 patient deaths annually in the USA, making it the fourth highest cause of death. MEs accounted for the majority of all medical errors.(48) In 2007, the UK National Patient Safety Agency reported over 86,000 incidents of ME. A review of hospital inpatients found MEs were involved in 7% of medication orders, 2% of patient-days and 50% of hospital admissions.(45) A multi-site study of MEs in paediatric inpatients in the UK reported that prescribing errors occurred in 13.2% of medication orders.(49) In a study of medication misadventures in paediatric and adult inpatients based on concurrent medication orders and chart review, and errors reported by doctors, nurses and pharmacists, Kaushal *et al*.(50) reported an ADE rate of 2.3 per 100 admissions or 6.6 per 1000 patient-days. They identified 616 MEs among 10,788 medication orders reviewed; an error rate of 5.7% of all orders. They ascertained that one-fifth of these errors were near-misses (potential ADEs) and 1% resulted in patient harm. They also highlighted that potential ADEs occurred three times more often among paediatric patients than adults.

Other studies have reported that MEs are common during paediatric hospitalisations and occur in nearly 6% of all medication orders.(9, 50) A comprehensive study on MEs in paediatric oncology patients, reported that 13% of errors reached patients and 2% resulted in temporary patient harm, requiring medical intervention. The study also reported that errors during prescribing were responsible for over 70% of the incidents, while errors during administration and dispensing accounted for 13% and

9% of the incidents, respectively.(51) However, the study of MEs in paediatric patients remains in its infancy due to lack of consensus on the medications of most concern and the children at greatest risk.(52, 53)

In the era of heightened fiscal constraints, the cost burden of compromised patient safety has received attention. The implications of medication misadventure in health systems are significant. Medication misadventure imposes a threat to patient safety and a high financial burden on the health system. Medication misadventure is costly with regard to human, economic and societal perspectives. From the human perspective, patients may experience discomfort, complications, prolonged hospital stay, disability or death and health professionals often experience emotional distress. The economic impact of the misadventure affects individuals, healthcare organisations, third-party payers and society.(54)

The economic burden for all areas of health care from drug misadventure in the USA exceeds USD100 billion annually.(54) In addition, time spent by healthcare providers in researching errors can impact on time for direct patient care. In a study of medical liability suits over a 16-year period, the Physician Insurers Association of America found MEs to be the fifth most common misadventure for paediatricians. More than 30% of the ME cases resulted in a paid claim, with a total indemnity of USD14.7 million.(55) The national projections of total healthcare costs with respect to MEs in in USA hospitals have ranged from USD2 to 4 billion annually.(11, 44) Most studies have only considered costs during hospitalisation, and ignored the outpatient treatment of the complications of MEs, the costs of disability and lost work time, family implications of caregiving burden and premature death. The financial implications of MEs may be significantly underestimated.(11, 56)

The consequences of the occurrence of one ADE was associated with an average increased length of hospital stay of 1.91 days, based on a study by Classen *et al.*(44) and 2.2 days in a study by Bates e*t al*.(32) In another study around 2 in 100 patients experienced preventable ADEs during hospitalisation.(57) The researchers estimated that extra costs due to preventable ADEs were USD4700 per admission or USD2.8 million annually for a 700-bed teaching hospital. If these findings are extrapolated to hospitals across the USA, the hospital costs for inpatients due to preventable ADEs would approach USD43 billion.(57) In the UK, more than 800,000 adverse events

occur annually in national health system hospitals, accounting for £2 billion in direct costs for additional hospital days; half of these events were avoidable.(58) Medication misadventure can also result in significant healthcare costs.(58)

The Australian Institute of Health and Welfare data suggest that the annual healthcare costs associated with medication misadventures in Australian public hospitals in 2002 was as high as AUD380 million.(59) Based on annual data of hospital admissions from 2006-2007, of the 7.7 million admissions recorded, around 190,000 were due to medication misadventure; with an associated cost of AUD660 million.(3) Medication safety is a major challenge in the Australian health system.(3)

The consequences of MEs have ramifications in oncology patients already burdened by multimodal treatment. Antineoplastic drugs are distinguished by their toxicity profiles. The consequences of the MEs result in prolonged hospitalisation, readmissions to hospital, increased cost and premature death.(44, 57) It is evident that reducing the occurrence of such misadventure will lead to better outcomes for patients, and reduce the financial burden.(59)

There may also be great personal costs to those involved and may result in time away from work, low patient satisfaction and decreased public trust toward health care.(6, 32) Staff may experience shame, guilt and depression after making a mistake, with litigation and complaints imposing an additional burden. Doctors and nurses whose confidence has been impaired will work less effectively and efficiently; at worst they may abandon their career.(60)

1.3 Causes of Medication Misadventure

Medication misadventure can occur at any step of the medication management process: prescribing, transcribing, dispensing, administration and monitoring. The American Society of Health-System Pharmacists acknowledges the myriad of factors and the multidisciplinary team as sources of errors in medication use.(61) Errors cannot be resolved without correcting underlying causes.(62) Any individual in a healthcare team (physicians, pharmacists, nurses and supportive staff) could commit errors.(61) Studies have emphasised that the two leading causes of medication misadventure are lack of knowledge and breakdown in communication.(34, 63-66)

The other causes are attributed to performance lapses and failure of hospital authorities to optimise the availability of data for system improvement.(67-69)

The medication management process requires intellectual activity in combination with the physical act of preparing and administering medications. A study investigating the preparation of intravenous medications in two UK hospitals revealed that around 265 MEs were observed during preparation of 483 medications.(84) The errors ranged from insignificant slips or mistakes to major violations. The authors concluded that 79% of the errors were caused by lack of knowledge and experience dealing with medications and equipments. This study highlighted the need for specific training because the staff who frequently made mistakes in selecting medications were unfamiliar with medication names.(64)

A system analysis in the USA identified lack of drug knowledge as the major cause of dosing errors.(32) This finding was confirmed by Lesar *et al*.(65), who identified that the most common variables associated with errors were related to deficient knowledge, such as the application of knowledge about specific drug therapies (i.e. expected toxicities, usual route, correct drug) and the synthesis of knowledge relating to patient factors that influence drug therapy outcomes (i.e. allergy, physiological status alterations).(65) Inappropriate prescribing is possibly the most common cause of avoidable events and account for over half of all preventable hospital MEs.(70) Prescribing is associated with errors, due to its complexity and challenging nature that requires diagnostic skills, knowledge of medicines, awareness of risks and experience. It is an anomaly that hospital doctors who have the least experience are expected to prescribe most often.(66) The consequence of this anomaly is that junior doctors are implicated in approximately 90% of serious hospital MEs related to incorrect dose.(70)

Another common source of error is the lack of knowledge in dose calculation, especially among nurses.(71) The two skills that are critical in accurate drug calculations are basic mathematics and the ability to conceptualise the clinical information presented and extract the relevant information.(71) This is of special significance in paediatrics where medication dosing is often based on weight and body surface area (BSA).(72)

The other major cause of medication misadventure is communication breakdown between healthcare providers and their patients and/or caregivers. However, there is little evidence that improved communication between health professionals and paediatric patients will prevent MEs in this population. An analysis of medication-related incidents has postulated that improvement in communication between healthcare providers and patients could minimise MEs in children.(73) Other contributors to medication misadventure in the post-discharge period include: inadequate communication to patients and/or caregivers about medication-related changes that have occurred in hospital; errors in prescribing or transcribing at discharge; and unclear health professionals' expectations of how patients should use their medications.(74) This situation has been associated with poor or unavailable written communication that can result in errors.(75) Another concern is establishing and maintaining communication that deals with functional health literacy of patients and/or their caregivers. Successful communication relies on the quality and quantity of information that can be absorbed by patients.(76) Functional health literacy is the ability to understand and apply both written and oral health-related information.(69) Communication in paediatric patients is complex as it may often involve three- or four-way conversations with patients, parents, clinicians and others (e.g. social workers, interpreters).(73) Information transfer is also affected by a myriad of other barriers. Some studies have emphasised the correlation between the ability to recall information and improvement in adherence and relapse reduction.(73, 77, 78) There is some evidence that the effect of communication goes beyond this by improving patients' health status.(73, 79) Effective communication with caregivers is one of the six patient safety goals included in the accreditation standards of the Joint Commission on Accreditation of Healthcare Organization.(80)

Communication is a crucial strategy to reduce the occurrence of errors when working in a team. Well-established and well-maintained communication and interactions between healthcare providers could minimise the occurrence of MEs.(14) Effective communication is important during critical situations such as patient transfer between care settings/institutions, e.g. post-discharge. Poor continuity of care after discharge and lack of communication between the hospital and community settings increase the chance of patients experiencing medication misadventure.(4, 74, 81) Kripani *et al*.(79) investigated communication and information transfer during and

after hospital discharge and reported that direct communication between hospital authorities and general practitioners occurred infrequently, and could contribute to misadventure.

There are also problems with communication between hospitals. For a study undertaken in a regional hospital in Queensland (Australia) medical records were reviewed of patients referred to the hospital's oncology unit.(82) These patients had been prescribed chemotherapy at another hospital. Around 72% of the referral medical records had been associated with one or more potential errors with respect to patients' medicines, such as inadequate documentation to confirm the doses, poorly handwritten or illegible medication orders, and lack of sufficient information on the length of time between cycles of chemotherapy.(82)

Another factor cited as a major cause of errors in the medication management process is related to performance lapses.(67) Performance lapses or deficits are defined as: 'slips and/or mistakes that generally take place when there is any impairment of a professional's attention that may divert human cognitive functions'.(83) These lapses may result in inadvertent errors. Performance lapses are not related to knowledge and are mainly associated with intrinsic factors, such as health status and ability to manage stress and focus, and extrinsic factors, such as non-conducive working environments, (83) e.g. excessive workload, distractions.(84) For critical tasks, such as preparing intravenous additives and calculating medication doses, distractions may have harmful consequences for patients.(83)

Another cause of medication misadventure is the failure of hospital authorities to utilise their data to prioritise and support system improvements. The first step would involve identifying the nature and occurrence of errors, analysing and reporting their pattern of occurrence within delivery systems to reduce the likelihood of adverse events.(12) Systems should be designed and modified based on actual and potential errors. The American Academy of Pediatrics has included identifying and learning from errors as one of its three principles of patient safety.(85) Error-learning systems should be transparent, promote discussion of errors without blame and punitive actions and provide contextual and robust data about the errors.(2)

1.4 Risk Factors associated with Medication Misadventure in Children

An understanding of the risk factors associated with MEs would enable improved monitoring of patients and medications associated with increased risk of serious errors.(86) Paediatric patients are at risk of DRPs for a variety of reasons, such as physiological factors and healthcare settings unable to accomodate the safe use of medications in paediatrics.(87, 88) Psychological factors pertaining to communication are another risk factor for the likelihood of medication misadventure in this population.(89) In those diagnosed with cancer, the complexity of chemotherapy regimens increases their risk of experiencing medication misadventure.(6, 11, 90)

Children are not 'mini adults'. They vary in size from early infancy to adolescence, along with profound alterations to their physiology. Weight and BSA also vary greatly and range from less than 500 g to over 100 kg in body weight and 0.1 to over 2 m^2 in BSA between premature neonates and adolescents. The relationship of body size with age and other clinical characteristics may impact on drug absorption, distribution, metabolism and excretion, especially, in neonates and infants.(91) These variations may lead to difficulties in clinical practice, most notably in drug dosing and administration. Paediatric pharmacokinetic parameters are frequently scaled based on body weight. This scaling approach has the advantage of being easy to calculate and apply to dosing of the medicines.

Many physiological functions that affect drug clearance (i.e. renal function, cardiac output, hepatic blood flow) do not scale proportionally to weight. Therefore, estimated BSA is an alternative approach to determine drug clearance. Empirically, BSA correlates more closely with the clearance of drugs than weight.(92) Volume of distribution may not correlate as well with BSA as it does with weight. BSA calculation requires height measurement that can complicate the dose calculation.(93)

Substantial changes in body proportions, organ systems and composition accompany growth and development in children. This dynamic process of growth, differentiation and maturation differs from adults with respect to physiological and pharmacological changes. The variability in organ system maturation complicates the determination of medication dosages for children.(88, 93) Pharmacokinetic parameters, such as

volume of distribution, half-life and clearance also alter during development.(92, 93) Many drugs doses need to be adjusted for increased body mass and compensate for increased clearance and short half-life due to development of hepatic and renal functions.(88, 92) Besides specific dosage requirements such as weight-based dosages, medication delivery for children is complex because of the limited availability of liquid oral medication formulations in different concentrations.(6, 90) Simplified dose administration approaches are not adequate for individualising drug dosages in childhood.(94) For potent drugs, when small fractions of the adult dose are required for children, risks of 10-fold dosing errors increase, leading to under dosing or overdosing.(6, 14, 90, 95) Some incidents may be fatal.(87, 96)

Another risk factor contributing to the possibility of medication misadventure is healthcare settings unable to accomodate the safe use of medications in paediatrics.(87) Most healthcare settings are primarily built around the needs of adults. Data related to efficacy, tolerability of drugs, and ADR in children are often lacking, partly because drug regulation authorities and the pharmaceutical industry have ignored routine drug evaluation in this population.(97) Many settings lack trained staff with expertise in paediatric care protocols and safeguards, and current and readily accessible reference materials for medications used in paediatrics.(87, 98) Few drugs are commercially available in ready-to-administer unit doses or dose forms appropriate for children.(99) Errors in dosing could result from the inability to deal with complex calculations and additional procedures to dilute and reformulate medications from adult formulations.(100-103) These manipulations may involve splitting or grinding tablets or dispersing or mixing drugs with food or drink. This practice creates opportunities for dosing errors, as the bioavailability of the drugs following such manipulations is often unknown and unpredictable.(104)

Around 75% of medications prescribed for children have not been adequately studied in this population.(105) Current trial and error prescribing practices (off-label use) may be associated with therapeutic failure and increased risk of adverse events. Conversely, without such precribing, effective therapy would be denied to many children. Information or labelling on dosing, safety, efficacy and clinical use in paediatrics is either not available or is insufficient and off-label use occurs. Many drugs used in children are either not registered (unlicensed) or outside the terms of

their licence (off-label indications).(102, 103) Off-label prescribing is: 'lawfully prescribing a drug or biologic agent for treatment regimens not specified in the approved labelling or package insert'.(106) The common reason for off-label prescribing in children is that the drug is prescribed at a different dose, for a different indication, through a different route of administration or for an age group for which the drug is not licensed.(107) A study in the USA found that off-label use accounted for 21% of all prescriptions for 160 common drugs.(108) Conroy *et al.*(107) reported that two-thirds of 600 children admitted to five European hospitals were prescribed unlicensed and/or off-label drugs during their hospitalisation. While some off-label uses are accepted as standard care, e.g. beta-blockers for congestive heart failure, many lack evidence of clinical efficacy.(108) There is little guidance to differentiate between off-label uses that are supported by evidence and those that are not.(106)

Communication issues may also complicate treatment in children. Children often lack communication and/or cognitive capabilities to express their feelings and report adverse effects.(109) Young children cannot provide sufficient feedback on potential adverse effects or mistakes in administration.(73) Patient monitoring can also be challenging for health professionals when caring for children. Many children cannot reliably communicate complaints or effectively understand the questions from health professionals. They simply feel that they are not well.(6, 110, 111)

Another risk factor, particularly for children with cancer, is associated with the characteristics of antineoplastic drugs. Antineoplastic drugs are among the most potent medications given to children, and have narrow therapeutic windows with high potential for toxicity. Administration of chemotherapy is error prone and even small errors can cause serious harm.(11, 112, 113) Analysis in the USA revealed that cytostatic drugs are the second most common reason for fatal MEs.(114) Protocols used for cancer treatment are complex and involve many medications. Chemotherapy dosage is unique and specific, in that dosing should be individualised and non-standardised. Doses are prescribed on the basis of body size (e.g. weight, BSA) in addition to factors, such as renal and liver function, blood cell count and substance-specific parameters, such as neurotoxicity (e.g. vincristine).(115) The dosing process requires patient-specific calculations, which should be reviewed regularly, since such factors can change during therapy and the dose should be adjusted accordingly.(96)

Some antineoplastic drugs are administered via different routes in variable doses over various periods of time (e.g. bolus, continuous infusion). Some antineoplastic drugs can be given safely by one route but not by another. Vincristine, for example, can be potentially life-threatening if administered intrathecally.(116) Most antineoplastic drugs require reconstitution and preparation, with several available in multi-dose vials in varying concentrations. Dosages are often extemporaneously compounded to meet the need for small doses in these patients.(96)

Several chemotherapy and supportive drugs have sound-alike and look-alike names. Oral orders involving sound-alike medications may be misinterpreted or misunderstood, e.g. carboplatin and cisplatin, docetaxel and paclitaxel, vincristine and vinblastine. Doxorubicin has been confused with the antibiotic dicloxacillin and methotrexate has been confused with methohexital.(117) Chemotherapy protocols stated as acronyms (e.g. CHOP) can also cause confusion. Referring to chemotherapy drugs by their nickname (e.g. 'donna' for duanorubicin, 'epi' for epirubicin) has also caused errors.(117) Similarities in labelling and packaging of chemotherapy drugs also increase the risk of MEs. On labels, names of medicines may be in small print that is easily misread, and many medicine labels have similar designs and layouts.(117, 118) Some chemotherapy drugs from the same manufacture are packaged using similar colours and designs. Vials may appear similar in size and shape but contain vastly different medications.(117)

The process from prescribing to monitoring chemotherapy involves individuals from multiple disciplines whose efforts must be coordinated to minimise risks.(119) All of the above mentioned factors have implications on clinical decision making for paediatric patients, and each of the stages of dose calculation, preparation and administration of chemotherapy has potential for error.(120) Children receiving chemotherapy are identified as high-risk in terms of their likelihood to suffer the consequences of an untoward event associated with medication misadventure.

1.5 Pharmacists' Interventions in Minimising Medication Misadventure

Clinical pharmacy services aim to ensure optimal outcomes for patients. The main focus of clinical pharmacy practice, as stated by the Society of Hospital Pharmacists of Australia, is: 'for ensuring the correct patient receives the optimum dose of the most appropriate medication for a specific condition via a rational dosage form and

regimen, over an appropriate time period'.(121) This definition also identifies the role of clinical pharmacists to improve patient safety and minimise any harm related to medication use through identification, management and prevention of ADEs and drug interactions. Clinical pharmacy practice is prevalent in hospital settings across Australia, albeit variable in the nature and extent of the service. One of the major outcomes of a clinical pharmacy service is to prevent or reduce drug-related harm and enhance the efficacy of drug treatment.(122) Clinical services that may lead to pharmacists' interventions cover all aspects of patient care and include: provision of drug information resources and education for health professionals; development of treatment protocols; patient education and counselling; analysis and performance improvement; medication reconciliation; and other services consistent with pharmaceutical care.(123, 124)

A pharmacist's intervention is: 'any reactive activity in response to an erroneous medication order and suggestion with regard to the medication order where the activity may involve contacting the prescriber'.(125) The Indian Health Service Pharmacy's definition of pharmacist's intervention is: 'any action undertaken by a pharmacist during the prescription screening and dispensing process when recognising a drug-related problem in order to solve the problem'.(126) A UK study has defined a clinical intervention as: 'any recommendation made by pharmacy staff with the purpose of changing drug treatment or its monitoring'.(127) Although the precise definition is still debated, in Australia, there is general consensus that a clinical pharmacy intervention is: 'any action by a pharmacist that directly results in a change in patient management or therapy'.(128) This definition acknowledges that clinical pharmacy interventions occur if they have been discussed with prescribers, nurses and patients, i.e. no intervention can occur if the pharmacist has not been able to influence their behaviour.(128)

Besides intervening to resolve/prevent actual/potential DRPs, clinical pharmacists perform a number of other functions that might not result in recommendations or direct changes in medication management. These include (but are not limited to) clarifying medication orders, drug use evaluations, providing education for medical and nursing staff, therapeutic drug monitoring and counselling patients and/or parents/caregivers. All of these non recommendation generating activities are

important in minimising drug-related harm and could be considered clinical pharmacy interventions.(129)

For the purpose of this study, the term pharmacist's intervention was adopted from the Society of Hospital Pharmacists of Australia and refers to any action by a clinical pharmacist related to patients' management or therapy. The interventions were classified as either resulting in drug changes (active interventions) or not resulting in drug changes (passive intervention). Passive interventions are care-centred activities performed by clinical pharmacists in relation to interactions with doctors, nurses, other pharmacists, and patients. The term 'clinical intervention' incorporates a wide range of activities performed by pharmacists to promote patient safety and protect patients from drug-related harm.

Pharmacists are best positioned to ensure that medications are used rationally and safely, increase awareness of MEs and prevent medication misadventure. The traditional role of pharmacists particularly in hospitals (e.g. compounding, dispensing and supply of medicines) has expanded to include clinical activities. This transition has increased the contribution of pharmacists as part of healthcare teams in minimising DRPs and optimising patient outcomes.(130) Pharmacists are crucial for successful medication misadventure reporting and are critical in error-prevention interventions, especially when participating in ward rounds.(131) Many critical units, such as neonatal critical care and oncology, have relied on pharmacists' participation during ward rounds to resolve ADRs, drug interactions and MEs associated with complex medical conditions and medication regimens.(14, 15) Substantial savings can be made by maximising the competencies of pharmacists and implementing pharmaceutical care.(56) The economic implications of pharmacists' interventions are expanded in Section 1.6.

One type of passive intervention involves provision of drug information and education to other healthcare providers. Pharmacists should ensure the availability of current evidence-based references on the appropriate use of drugs for all those involved in the medication use process.(123, 132) Pharmacists need to be well informed in order to be able to provide medication-related information to other healthcare providers. This information may include: drug-specific precautionary warnings and adverse effects, particularly dose- and schedule-limiting effects;

potential interactions with other drugs, disease states, and foods; administration methods, including drug admixture stability and compatibility with other drugs and additives; dose calculation; dose recommendations for single- and multiple-treatment courses; medication and dose adjustment for persons with concurrent diseases and organ impairment, e.g. renal failure; and dosing based on pharmacokinetic parameters and monitoring guidelines.(133) Pharmacists should provide current discipline-specific educational materials about medication use to those who prescribe, prepare and administer medications. Pharmacists should consider both the sources of the materials and effective ways to deliver information so that it is easily interpreted and understood. When new medications are introduced, pharmacists' contribution in developing educational materials on medication regimens and treatment protocols are paramount.(123, 132)

Through these interventions pharmacists can ensure that the treatment protocol has been described clearly by using standardised language, abbreviations, content and units of measurement.(133) In clinical units where treatment regimens are used intensively (e.g. paediatric oncology), pharmacists can initiate the development of protocols to assist with quality and accurate prescribing, minimise misinterpretation, and facilitate effective and safe practices. Pharmacists should also lead initiatives to standardise all procedures related to drug preparation, e.g. reconstitution, dilution, and drug admixture. This intervention is imperative in paediatric oncology where treatment protocols are complex and specific to cancer type.(134) Kohler *et al*.(135) have developed explicit guidelines for outlining chemotherapy dosage schedules, templates to describe chemotherapy drug regimens in a clear, uniform and consistent manner, and standardised labels for dispensed medications.

Pharmacists have professional responsibilities to ensure patients use their medications appropriately.(136) Studies conducted at the Albany Medical Center (New York) demonstrated that most patients did not have a clear understanding or possessed limited knowledge about their medications.(137) In another study, discrepancies between the medications prescribed and the medications taken by patients were reported in 76% of cases.(138) Failure to educate patients about their medications has also been the subject of litigation. The duty of pharmacists to educate and warn patients of potential problems and/or hazards related to medication

use has been tested in the courts in the USA and Australia; failure to perform this duty has had legal consequences for pharmacists.(1) The Institute of Medicine's, *To Err is Human: Building a Safer Health System*, has heightened awareness on the necessity to increase a patient's role in effective and safe medication use. Pharmacists are critical to facilitating this process through educating and counselling patients about their medical conditions and medications.(2)

Medication reconciliation may trigger pharmacists' interventions. Medication reconciliation is: 'a process to consciously continue, discontinue or modify medication orders'.(139) This is thorough process is used to collate a complete and accurate list of patients' current medications.(140) It ensures that patients receive all intended medications during hospitalisation. Discrepancies are discussed with the prescriber and reasons for changes to therapy are documented. The medication list should include all prescription and non-prescription medications, including dietary supplements and over-the-counter medicines. Medication reconciliation should be performed for each patient being transferred within the same institution or to other institutions.(141) Medication orders can be incomplete, particularly when patients are transferred to other units in the same hospital or to another hospital, or discharged from hospital.(142) Medication accuracy at transitions of care is one of five patient safety priorities nominated by the World Health Alliance on Patient Safety, which can be achieved through medication reconciliation.(140) The effectiveness of medication reconciliation in error reduction is well established. Around 40% of MEs are due to inadequate reconciliation during hospital admission, transfer and discharge.(143) Medication reconciliation by pharmacists could decrease MEs by 70% to 80% and ADEs by more than 15%.(144)

1.6 Clinical Significance and Economic Implications of Pharmacists' Interventions

Numerous studies have highlighted clinical pharmacists' roles in ensuring safe and optimal medication management in the continuum of care in critical settings, specifically emergency departments (EDs) (145) and intensive care units (ICUs).(15, 17, 146) A study in a metropolitan teaching hospital in Australia examined the impact of an ED clinical pharmacist on prescribing errors. The rate of prescription errors detected was 1.6 errors per patient during the control period, which decreased

to 0.5 errors per patient during the intervention period, when the ED clinical pharmacist participated in the healthcare team.(145)

Leape *et al*.(15) justified the contribution of clinical pharmacists in reducing the rate of ADEs in an ICU. They reported a decrease in preventable ADEs in adult patients by 66% after the implementation of clinical pharmacy services. There were 10.4 ADEs per 1000 patient-days before the intervention and 3.5 ADEs per 1000 patient-days after the intervention, with no change in the control ICU. The introduction of clinical services including pharmacists' interventions in a 30-bed medical ICU in a tertiary teaching hospital in Korea were considered essential by other members of the healthcare team. This one-year study also highlighted the highest need for pharmacists' interventions was for severely ill patients with renal impairment and long length of stay.(146)

Studies investigating the incidence of ADEs in paediatric patients are lacking. A prospective epidemiological study in two university hospitals found that the ADE rate in children was similar to adult patients. This study also highlighted that the potential ADE rate was three-fold higher in children.(50) A pharmacist in a paediatric ICU was shown to intercept MEs, as well as recognise ongoing problems related to medication use.(17) Clinical pharmacists in the ICU, in adult or paediatric settings, could also be the main source of knowledge for medical and nursing staff in relation to the pharmacology of medications.(17, 144, 145)

To measure the clinical significance of pharmacists' interventions, it is beneficial to establish a specific scale of measurement. Dodds *et al*.(147) classified pharmacists' interventions as minor, moderate and major impact. Analysis of the clinical significance of pharmacists' interventions revealed five distinct scales that have been used for rating pharmacists' interventions. The scale by Folli *et al*.(148) has been widely used and rates the interventions into five levels: extremely significant, very significant, significant, somewhat significant and no significance. Hatoum *et al*.(149) published a ranking system that highlighted the value of clinical pharmacy services by assessing the potential impact of the interventions with regard to patient care. An Australian study reported the clinical significance of pharmacists' interventions into five scales: no clinical significance, minor, moderate, major and life-saving.(18)

Pharmacists' interventions can be classified and analysed further based on the DRPs addressed. Classifying DRPs is an essential component of pharmaceutical practice and research.(150, 151) A systematic review of DRP classification systems identified 20 different of classification systems. As evaluation of pharmaceutical care of a wide range of studies requires a universal DRP classification system, the review highlights the need for consensus.(152)

Many studies have evaluated the economic implications resulting from pharmacists' interventions in hospitals (Table 1.1).(17, 18, 153-158) There is a wide variety of study settings, study duration, definition of interventions and method of cost assessment. A review of the economic effects of clinical pharmacy interventions revealed that the majority of studies were undertaken in adult patients.(159)

1.7 Root Cause Analysis

A common issue faced by hospitals is that medication misadventure, particularly MEs, does not neatly fall into defined categories. For instance, when a patient receives another patient's medications, it may be assumed that this error is the result of inadequate patient identification. Although a reasonable assumption, this approach does not identify the cause(s) of the error. Possible causes in this case may be an incorrect patient identification wristband or a mistake during medication order entry. The same errors may be repeated because incident reporting systems fail to identify root causes. It is important, therefore, to ensure that incident reporting systems and data are used to fuel RCA which results in corrective action in the systems.(1)

The concept of RCA is detailed in Section 1.7.1 and its application in health systems is explored in Section 1.7.2. Another major issue relating to error-reporting systems is misleading assumptions among pharmacists who consider errors do not need to be reported if they can be corrected. For example, pharmacists may not report prescribing errors if the errors can be corrected in the pharmacy department. They assume their actions are interventions instead of MEs. This leads to an under estimation of MEs for the organisation and a lost opportunity to learn from potential errors.(160) If errors and the results of RCA are only reported and disseminated locally, the lessons cannot be learned by other departments/institutions.(60)

Table 1.1 Characteristics of pharmacist intervention studies and cost assessment

Year	Authors	Setting	Interventions	Parameters	Key findings
August 1998	Dooley *et al.* (18)	8 major public hospitals (361-395 beds) in Australia	Actions that directly resulted in a change to patient therapy or management. Each hospital collected 200 interventions.	Cost saving related to length of stay (LOS), readmission, drugs, medical procedure and laboratory monitoring.	Estimated annual cost saving was AUD4.4 million. One dollar spent on the change recommended by a pharmacist could save AUD23.
April 1998 to April 1999	Lee *et al.* (154)	Veteran Affairs medical centre in the USA: 362-bed teaching hospital, 120-bed nursing home and clinics	When a provider applied the pharmacist's knowledge to a patient or physician order. The first 600 pharmacist recommendations recorded in the electronic documentation system.	Average cost avoidance was calculated if the recommendations prevented/caused harm.	Overall mean cost avoidance per recommendation was USD700 and the mean total cost was USD420,155.
Not stated. Results published in 2001	Bond *et al. (155)*	Data from the 1992 National Clinical Pharmacy Services in the USA for 14 clinical pharmacy services and pharmacist staffing	14 clinical pharmacy services, e.g. drug use evaluation, in-service education, drug counselling, admission drug history and medical rounds	Relationship between some variables (mortality rates, drug costs, total costs of care and LOS).	Clinical pharmacist staffing increase was associated with 43% decrease in hospital deaths. This translated into USD320 of pharmacy salary cost/death averted.
1 September to 31 December 2003	Lada *et al.* (156)	100-bed ED at a 340-bed teaching hospital for adult patients in the USA	Categories such as provision of drug information, dose adjustment, initiation/ discontinuation of drug therapy.	Average cost, probability of harm and potential cost avoidance	2150 pharmacists' interventions were documented; cost avoidance was USD1,029,776.

February 2000	Van den Bemt *et al.* (158)	600-bed teaching hospital and 300-bed non-teaching hospital in the Netherlands	Over 5 consecutive days, all medication orders were screened for prescribing errors by pharmacy staff.	Cost-benefit analysis based on direct medical costs. Benefit-to-cost-ratio was calculated by considering the net time spent by pharmacy staff to prevent the error and the possible consequences of the error.	9.9% of screened medication orders contained prescribing errors. Time investment of the pharmacy staff had net cost of EUR285 and estimated investment-related benefits were EUR9867.
September to November 2001	Olson *et al.* (157)	360-bed teaching hospital in Canada	Interventions that prevented ADEs (described as very serious and serious by the self-reporting pharmacists).	Cost savings attained by shortening a planned course of drug therapy and cost avoidance achieved by avoiding ADEs.	Total cost avoidance of the 33 preventable ADEs was USD84,631. USD1.20 was saved for each USD1 spent on pharmacist's salary.
19 November 1996 to 6 May 1997	Krupicka *et al.* (17)	Ten-bed paediatric ICU in a 124-bed university-affiliated children's hospital in the USA	Every intervention performed and documented by a paediatric clinical pharmacist during rounds and private discussion with the physicians.	Drug acquisition costs were used to calculate drug cost savings. Drug acquisition costs were multiplied by 2.4 (average LOS). Labour, supplies and any other indirect costs were not included.	Total cost savings for the 24-week study period was USD1977. Extrapolated direct cost savings per year was USD9135.

1.7.1 Improvement of System Analysis to Overcome Organisational Failure

Patient safety is one of the most crucial issues facing health systems across the globe.(161, 162) The initial step in the process of creating a safe health system is to promote a culture of safety within an organisation. A culture of safety is an environment where individuals receive adequate support to report any deviant incident.(163) As the blame is usually with organisational system failure, the system and not the individual should be evaluated.(163, 164) Systems that receive incident reports without investigating, analysing and acting on these reports are inadequate. These flawed systems also discourage frontline staff from reporting incidents, as the effort and time invested in reporting these incidents are undermined.(165) On the grounds that humans make mistakes, the goal of system analysis is to invent a system that will minimise and prevent errors from occurring.(164)

Reason(166) has developed a systematic perspective on organisational failure by introducing the concepts of active and latent failures to describe the multi-level nature of incident causation. Active failure is associated with the errors and rule violations of front-line staff that have an immediate and apparent impact on the system. Latent failure implicates individuals more distant from the incident, i.e. individuals at the upper levels of the system (e.g. policy maker, manager) and may be left untouched indefinitely. Reason created the 'Swiss cheese' model (Figure 1.3) to illustrate how organisations are built with multiple layers of safeguards against error (active failure), yet with holes at each layer indicating weaknesses and gaps that can lead to latent failure. Incidents occur if the holes in all defensive layers line up perfectly in a constant flux to create the pathway for incidents to happen.(167)

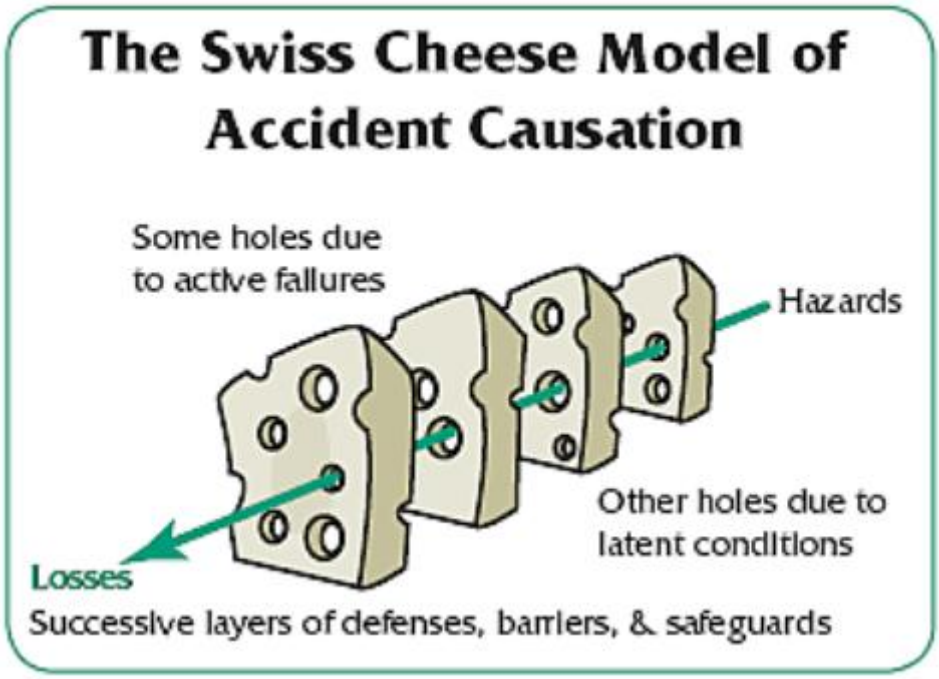


Figure 1.3 James Reason's Swiss cheese model(179) (Reproduced with permission.)

A similar perspective is shared by the National Patient Safety Agency who proposed that the system is analogous to a blade, i.e. it is divided into two parts: sharp and blunt ends (Figure 1.4).(162) The sharp end represents the direct/immediate point during provision of service to customers (i.e. patients in the health system) whereas the blunt end encompasses a wide range of factors such as organisational policies, staffing, information technology systems and the physical structure of the workplace.

In order to resolve why incidents occur at the sharp end of the system, RCA is necessary to examine and analyse the contributing factors at the blunt end.(168) Thorough examination and analysis of incidents (actual and near misses) followed by adequate and well-designed recommendations are key to improving patient safety and reliability of the system.(169)

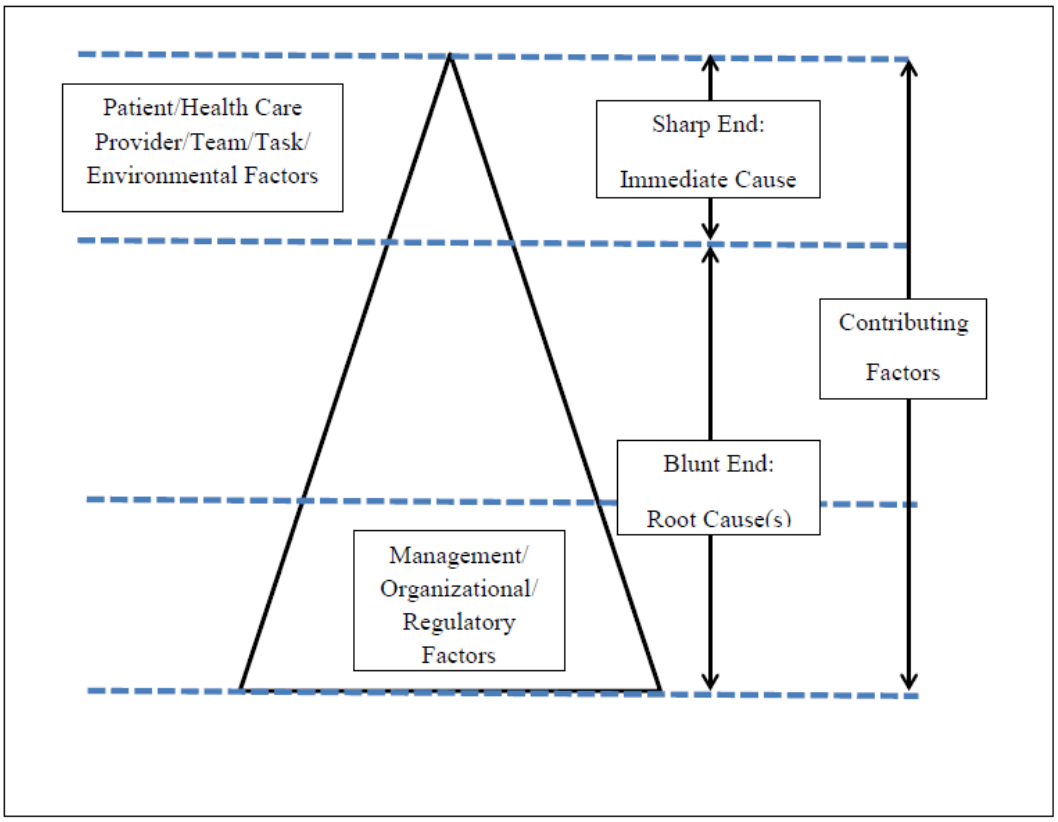


Figure 1.4 Sharp and blunt ends of the system as enablers of incidents(162) (adapted)

1.7.2 Root Cause Analysis for Improving Patient Safety in Organisations

The RCA that follows an incident investigation identifies weaknesses and failures in the system, thereby preventing the likelihood of the recurrence of similar incidents. RCA encompasses the methods for the retrospective and structured investigation of adverse incidents, near misses and sentinel events (Section 1.7.1).(169) RCA can also be used to evaluate undesirable patterns or trends whenever there is a performance deviation from recognised standards.(170) RCA has been applied successfully to uncover latent errors that underlie incidents in high-risk industries such as aviation.(20) RCA was developed to analyse major industrial incidents and has been taken up by health systems in the USA, Australia, Canada and the UK.(20, 162) Health service provision occurs in a complex and high-risk environment with even simple procedures requiring multiple steps and providers. The probabilities of incidents occurring in health services are high, and safety tools such as RCA are essential to prevent the recurrence of similar incidents.(162) In the USA, the Joint Commission on Accreditation of Hospitals has mandated that all hospitals use RCA to investigate cases associated with patient incidents or sentinel events.(170)

RCA is the most important development in the transformation of error management in healthcare delivery.(171) To effectively minimise errors, system weaknesses that lead to errors must be identified and the system changed to improve its performance.(172) RCA designed as a quality improvement tool must be able to help organisations determine the contributing factors and root causes resulting in an incident. Striving to identify and address the root or underlying causes of critical incidents will lead to a greater understanding of hazards/problems in the system.

RCA is widely adopted by hospitals and healthcare organisations, and has helped to identify many problems and solutions.(162, 171, 173) It has become the system analysis tool to investigate mistakes in healthcare delivery and provides strategies for developing effective recommendations and action plans for system improvement.(20) There are many benefits in conducting RCA, e.g. building collaborative and professional relationships among physicians, pharmacists, nurses and other healthcare providers, and providing an excellent learning opportunity for those involved in the RCA process. The main advantage is correcting system flaws in order to prevent the recurrence of similar incidents in the future.(174)

1.7.3 Conducting Root Cause Analysis

RCA is designed to answer three questions: What happened? Why did it happen? What can be done to prevent it from happening again?.(168) RCA is founded on the principles that patients, direct healthcare providers, senior management, board members and representatives of key external organisations play significant roles in improving the system.(20, 162) For RCA to work, it requires: a non-punitive and confidential method for reporting adverse events; collaboration of health professionals; an understanding of relevant legislation and human factor engineering (HFE); identification of problems in the system; and strategies to improve the system.(161, 162, 171) There must also be timely and relevant feedback to reporters of events.(171)

Contributing factors and root causes identified are either of the HFE or non-HFE types. HFE is ‘the scientific discipline concerned with the understanding of interactions among humans and other elements in a system in order to optimise human wellbeing and overall system performance’.(172) HFE builds on the premise that human performance and subsequent occurrence of errors are influenced by

system factors. HFE-type factors and root causes refer to interactions between humans and their environment, and may include policies, procedures, communication, training, workload, equipment and the physical environment/workplace. Non-HFE-type factors and root causes include patient behaviour and course of disease, which are more difficult, if not impossible, to modify with recommendations resulting from an RCA. Consequently, when patient behaviour or course of disease is identified as the primary root cause, this finding significantly lowers the possibility that any effective recommendations from RCA can be identified and implemented to prevent the event from recurring.(175)

There is broad consensus that RCA represents a variety of approaches instead of a single method. Woloshynowych *et al*.(176) have described more than 40 RCA techniques, such as brainstorming, cause-effect charts, 'five whys' diagrams and fault trees, which provide different options of RCA analysis techniques. Although variations exist, the RCA process is usually organised in sequential steps. According to Rooney *et al*.(19), RCA is a four-step process involving data collection, causal factor charting, root cause identification, and recommendation generation and implementation as follows:

1. In Step 1 information related to the incident is collected. This step is crucial because without a complete dataset and an understanding of the incident, the causal/contributing factors and root causes associated with the incident cannot be comprehensively identified. Inevitably, a great deal of time invested in analysing the incident is spent in gathering the data.

2. Step 2, causal factor charting, can be initiated immediately. This step provides a structure and visual guide for investigators to organise and analyse the information gathered during the investigation, and to identify gaps and deficiencies in knowledge as the investigation progresses.(19) This step can be considered the review process to brainstorm why the incident happened and the possible causes that resulted in the incident. Causal factor charting is a sequence diagram that describes the incidents and the conditions surrounding these incidents, and drives the data collection process by identifying the need for gathering more data. Data collection continues until the investigators are satisfied with the thoroughness of the investigation. When the entire occurrence has been charted, along with the complete dataset, the investigators are in

a confident position to uncover the major contributing/causal factors to the incident. Causal factors, if eliminated, would have either prevented the occurrence of an incident or reduced its severity. The focus is on identifying all issues/flaws in the system and all possible causes that may have contributed to the adverse incident.

3. After all the causal factors have been identified, Step 3 involves organising and analysing the causal factors by category in order to identify the root causes of each causal factor. A key aspect of this step is to understand how the causal factors relate to each other and ensure that the RCA has progressed far enough into the blunt end of the system so that root causes can be clearly defined. A root cause map can assist in better visualising these inter-relationships, ensure thorough review, clarify understanding and shift the focus away from individual performance/sharp end towards system performance/blunt end. Options include the Ishikawa/fishbone and tree diagrams.(162)

4. Step 4 is recommendation generation and implementation. After recognising the root causes for each causal factor, achievable recommendations for preventing recurrence of the incident are generated. The recommendations should directly address the root causes identified from the previous step. This step also includes the specific timelines for fixing the problems. The final step also includes the development of ongoing monitoring strategies to evaluate the improvements.(170)

1.7.4 Limitations of Root Cause Analysis

Conducting an RCA or another retrospective investigation presents an opportunity to learn valuable lessons about how to redesign health systems and prevent recurrence of the incident/error. Nevertheless, the RCA process is not without problems. Many RCAs are performed incorrectly or incompletely, and therefore, cannot produce appropriate and usable results. In many organisations RCA is used erroneously to uncover the fundamental and apparent causal factor of the incident instead of ‘the root causes for all possible causal factors.(20) As the determination of causal factors is dependent on the training and experience of the analyst, the decisions on the causes are inherently subjective and inconclusive. The danger of drawing conclusions from inadequate sample sizes (i.e. incidents with remote possibilities) should also be recognised. If events are common across hospitals, remedial action should be designed at the health system rather than individual hospitals.(20, 177)

Another shortcoming relates to the level at which to terminate the analysis; a sensible stopping point is required for each RCA process.(177) While recognising the limitations of RCA, significant benefits can be derived with adequate and exhaustive processes for each step, followed by thoughtful implementation.(162)

Chapter 2

AIMS

The aims of the study were to evaluate the role of clinical pharmacists' interventions in minimising medication misadventure in children with cancer; to investigate the clinical significance and identification of medication misadventure through these interventions; and to apply RCA to examine the factors contributing to medication misadventure.

The study was divided into four parts.

Part One: Clinical Pharmacists' Interventions in a Children's Hospital

The objectives were to:

- observe and document pharmacists' interventions from three clinical units - general medicine, general surgery and haematology-oncology - in a children's hospital
- compare the rate and pattern of pharmacists' interventions and pharmacists' active interventions between the clinical units
- observe and document pharmacists' interventions during dispensing in the Haematology-Oncology Pharmacy
- identify the predictors for physicians' acceptance of pharmacists' active interventions.

Part Two: Clinical Significance of Pharmacists' Active Interventions and Identification of Medication Misadventure through Pharmacists' Active Interventions Using an Expert Panel

The objectives were to:

- determine the clinical significance of a sample of pharmacists' active interventions
- identify whether these interventions involved medication misadventure, to categorise medication misadventure into three subsets - ADE, ADR and ME -

and to classify medication misadventure involving ME according to the type of error and its severity.

Part Three: Comparison of Documentation Methods used for Pharmacists' Interventions

The objectives were to:

- analyse pharmacists' interventions based on snapshot self-reports of interventions
- examine the representativeness of the snapshot self-reports versus continuous documentation using direct observation
- ascertain pharmacists' perceptions on the interventions documented through snapshot self-reports versus direct observation
- identify barriers perceived by pharmacists to documenting their interventions during snapshot periods and to seek suggestions on how to improve the documentation of pharmacists' interventions.

Part Four: Medication Errors in Children: Root Cause Analysis Using Simulated Case Scenarios

The objectives were to:

- apply RCA in a sample of simulated cases to determine the clinical significance of MEs and the responsible health professional(s)
- investigate the contributing factors for the MEs and preventive strategies to reduce the occurrence of MEs in children.

Chapter 3

METHOD

The entire study was conducted in three clinical units (haematology-oncology, general medical, general surgical) at the Princess Margaret Hospital for Children (Perth, Western Australia). This 220-bed public paediatric hospital has approximately 250,000 patient visits (inpatient and outpatient) annually. The haematology-oncology unit consisted of the Haematology-Oncology Ward (inpatient) and the Haematology-Oncology Pharmacy (inpatient and outpatient).

For Part One clinical ward pharmacists' interventions were prospectively documented across the three clinical units and the Haematology-Oncology Pharmacy. The non-disguised principal researcher observed the pharmacists and documented their interventions.

For Part Two randomly selected pharmacists' active interventions from Part One were analysed. Two of the four researchers and three independent panellists (Panel 1) analysed the interventions for clinical significance and identified medication misadventures and classified them as an ADE, ADR or ME. If the intervention involved an ME, the type of error and its severity were examined. As the rating of the clinical significance of the interventions could not be resolved through consensus, a second panel (researchers and two independent panellists) was set up.

For Part Three pharmacist's interventions from self-reports of three snapshot periods were analysed retrospectively. The interventions from the self-reports were compared with the interventions documented during direct observation in Part One to examine the pattern and representativeness of short-term documentation versus continuous documentation by an independent observer. A focus group discussion followed with pharmacists from the hospital to ascertain their perceptions on the *in situ* intervention documentation process and their suggestions to improve the process.

For Part Four an RCA was conducted of five simulated clinical cases involving MEs in children. For the RCA self-administered questionnaires were disseminated to doctors, nurses and pharmacists at the study hospital.

3.1 Part One: Clinical Pharmacists Interventions in a Children's Hospital

3.1.1 Description of Study Settings

Data were collected using prospective non-disguised observation from September 2011 to August 2012 in three clinical units (general medicine, general surgery and haematology-oncology). There were three wards in the General Medical Unit - General Medical Ward for Infants, General Medical Ward for Young Children and General Medical Ward for Adolescents – one General Surgical Ward and one Haematology-Oncology Ward; a total of five study wards. The general medical wards admitted patients under general paediatrics and a range of non-oncology medical specialties, while the general surgical ward admitted patients under general surgery, opthalmology and otolaryngology.

Ward-based clinical pharmacy services were provided Monday to Friday 0830 to 1700 and from 0900 to 1600 during weekends/public holidays (for intravenous admixture services and urgent drug supplies only). Outside these hours an on-call pharmacist was available for urgent drug inquiries. Ward pharmacists undertook the pharmacy round/full ward visit once a day during weekdays, either in the morning or afternoon. After that, pharmacist could be contacted via pager. During pharmacy rounds, they reviewed patients' medication orders prescribed on the inpatient medication charts and reconciled the medications by comparing the recent medication orders with previous orders in patients' medical records and double-checking with patients and/or parents and carers. Pharmacists also took patient medication histories, including allergy and ADR histories. If there were any discrepancies, pharmacists contacted the doctor to resolve the problem.

Ward pharmacists provided drug information to medical and nursing staff and education and counselling to patients and/or their parents. They also monitored the medications stocked on the ward ('imprest'). The imprest medications were stored in a drug room on each ward and organised alphabetically, based on their dose forms. If there were 'non-imprest' medication orders requiring intravenous admixture, e.g. intravenous antibiotics, the ward pharmacists supplied these medications to the ward. Nurses were responsible for preparing imprest medications, i.e. selecting the medications from the imprest cupboard and placing them in the patient's drug tray.

There was no supervision by the pharmacist to ensure that the medications in the drug trays corresponded with the medication chart. Discharge medications were organised by pharmacists in the main pharmacy mainly in the mornings.

The hospital has three pharmacies - main pharmacy and two satellite pharmacies (cardiology and neurology, and haematology-oncology). Besides their ward-based clinical activities, the haematology-oncology pharmacists dispensed medications, including cytotoxic chemotherapy and fluid therapy. For outpatients, the non-parenteral cytotoxic chemotherapy medications and supportive care medications (i.e. antiemetics, prophylactic antifungals and prophylactic antibacterials) were dispensed from the Haematology-Oncology Pharmacy. For inpatients, nurses prepared these medications from the imprest. Medication orders requiring centralised intravenous admixture service (CIVAS), e.g. intravenous antibiotics, were prepared and dispensed by the pharmacists. The Haematology-Oncology Pharmacy services were provided Monday to Friday 0830 to 1700 and during weekends/public holidays from 0900 to 1600 (for intravenous cytotoxic orders and urgent drug supplies only). Outside these hours an on-call pharmacist was available for urgent drug inquiries.

Three to four pharmacists and one technician were on duty each weekday in the Haematology-Oncology Pharmacy. Although most of the pharmacists worked part-time in this satellite pharmacy, they were permanently assigned to the facility so they were familiar with the workflow and patients' chemotherapy protocols. The workflow in the Haematology-Oncology Pharmacy usually involved six steps:

1. Reviewing the patients' chemotherapy protocols and transferring the information onto a parenteral cytotoxic sheet (yellow sheet) and fluid therapy order sheet (white sheet).
2. Creating the labels for medications to be formulated and dispensed.
3. Setting up the chemotherapy medications and hydration fluids prior to formulating in the Laminar Airflow Hood.
4. Formulating the chemotherapy medications and fluid therapy in the Vertical Laminar Airflow Cytotoxic Drug Safety Cabinet.
5. Dispensing the parenteral cytotoxic medications to the nurses for administration.

6. Dispensing the non-parenteral medications and providing counselling to Haematology-Oncology Clinic patients and/or carers.

Two pharmacists were usually responsible for Steps 1 and 2; one to two pharmacists set up the fluid therapy and parenteral cytotoxic medications, and dispensed the medications to nurses and non-parenteral medications to outpatients; and one pharmacist formulated the parenteral cytotoxic medications and fluid therapy in the Vertical Laminar Airflow Cytotoxic Drug Safety Cabinet. A technician processed outpatient prescriptions under the pharmacist's supervision, checked the stock and ordered the low-stock medications from the main pharmacy. The background information of pharmacists' clinical activities during ward rounds and dispensing was provided as to establish the study protocol.

3.1.2 Direct Observation for Documentation of Pharmacists' Interventions

Pharmacists working on the study wards and in the Haematology-Oncology Pharmacy were invited to participate in the study. The principal researcher described the direct observation method and the ethics requirements (Section 3.1.3) of the study. The rationale for the direct observation approach was to ensure that the data collected was comprehensive and not subjected to reporting bias. Although direct observation has the potential to interfere in the activities of those being observed due to the presence of an observer (Hawthorne effect) the evidence suggests that the observation method has little effect on the behaviour of those being observed.(178) Direct observation has been used to detect MEs and ADEs, few studies have utilised this approach to document pharmacists' interventions.(37, 179-182) The majority of studies in a range of healthcare settings have relied on self-reporting methods to document pharmacists' interventions.(129, 147, 183-185) Self-reporting of pharmacists' interventions are used in the study hospital. Comparison of the self-reporting method with direct observation is described in Section 3.3.

Twelve pharmacists agreed to participate in the study. The ward pharmacists worked on the General Medical Ward for Young Children, General Medical Ward for Adolescents and the Haematology-Oncology Ward permanently and were senior pharmacists with more than 10 years experience. The General Medical Ward for Infants and the General Surgical Ward were staffed by junior pharmacists on a

temporary rotation. The ward pharmacists on the general medical and general surgical wards reviewed medication orders and patients on more than one ward each weekday. The characteristics of pharmacists assigned to the Haematology-Oncology Pharmacy are described in Section 3.1.1.

3.1.2.1 Ward-based Pharmacists' Interventions

The principal researcher (observer) shadowed pharmacists during their ward rounds and documented their interventions on the five study wards for a total of 35 to 37 non-consecutive days. The observer followed one ward pharmacist for each weekday and collected the pharmacist's interventions for that ward. On the following day, the observer went to another ward and documented another pharmacist's interventions. This protocol was used to minimise fatigue in the pharmacist under observation. If, during direct observation, an intervention or the omission of an intervention could result in substantial patient discomfort or harm, the observer notified the senior pharmacist immediately after the ward round. For example, if an antibiotic order was written for a patient with a known allergy and the pharmacist did not detect the errant order, the observer could notify the senior pharmacist. Data collected during direct observation was annotated on the intervention documentation form (Appendix 1).

For the data collected during direct observation (Table 3.1), the diagnosis on admission was classified using the *International Statistical Classification of Diseases and Related Health Problems*(186) for the general medical and general surgical wards, and the *International Classification of Childhood Cancer*(187) with slight modifications for the haematology-oncology patients. The medications involved in the interventions were categorised using the *Australian Medicines Handbook* (AMH).(188). The medications were also categorised based on their dose form and risk category.(189) The description of interventions were categorised into major type with further sub-categorisation as described by Condren *et al.*(190) with slight modifications to include 'clarification of medication order' as an additional category of the intervention. The intervention categories are outlined in Table 3.2. The rates of interventions were defined as the number of interventions per 100 medication orders reviewed. A medication order could have more than one intervention. The principal researcher divided the interventions into 'active' and 'passive', as defined previously.

3.1.2.2 Pharmacists' Interventions during Dispensing

The observer shadowed pharmacists in the Haematology-Oncology Pharmacy for a total of 33 days. Observations were conducted during weekday trading hours. In order to minimise fatigue of those under observation pharmacists were not observed continuously (Section 3.1.2.1). Data collected during direct observation was written on the intervention documentation form (Appendix 1). Details of the data are described in Table 3.1. A medication order reviewed could have more than one intervention. The principal researcher divided the interventions into 'active' and 'passive', as defined previously.

Table 3.1 Data collected by the observer during direct observation

Variables	Source	Response options
Patient demographics - Age - Gender - Admitted ward - Length of hospitalisation	 Medical record Medical record Observation Medical record	 Free text (years) Male/female Free text Free text (days)
Admission and discharge dates	Medical record	Free text
Diagnosis on admission	Medical record	Free text
Medical history	Medical record	Free text
Medication history	Medical record	Free text
ADR and/or allergy history	Medical record	Free text
Current medication(s)	Medication chart	Free text
Description of intervention	Observation	Free text
Medication(s) involved in intervention	Observation and medication chart	Free text
Cause of intervention	Observation	Prescribing/ dispensing/ administration/ monitoring
Trigger of intervention	Observation	Doctor / nurse /other pharmacist inquiry/ patient request/ ward meeting/ medication chart review/ laboratory result/ medication history taking
Intervened health personnel	Observation	Doctor/ nurse/ pharmacist
Acceptance of intervention	Observation	Accepted/declined
Characteristics of intervening pharmacist - Gender - Year of experience - Highest qualification - Employment status	Intervening pharmacist	 Male/Female Free text (years) Free text Full-time/part-time and permanent/temporary post
Time to complete ward round	Observation	Free text (minutes)

3.1.3 Ethics

The study protocol was approved by the Princess Margaret Hospital Institutional Review Board No: 2923 (Appendix 2) and the Curtin University Human Ethics Committee No: PH-14-11 (Appendix 3). Pharmacists working on the study wards and in the Haematology-Oncology Pharmacy received the Participant Information Sheet (Appendix 4) prior to consenting to participate (Appendix 5). The method used was one that minimised observer effects. Coding of data from patients' medical records maintained patient confidentiality. Data files are being stored on a password-

protected computer and archived securely for at least five years. The same procedure for handling of data files applied to other data collected in other parts of the study.

3.1.4 Data Management and Analysis

Data collected during direct observation were transcribed onto Excel spread sheets. The data were checked several times to ensure there were no missing variables. The variables of date of discharge and length of hospitalisation were incomplete in some patients. These missing variables were retrieved using iSoft Clinical Manager via the hospital intranet. Demographic variables and pharmacists' intervention-related data were summarised using descriptive statistics (mean ± standard deviation or median [range] for variables measured on a continuous scale, and frequencies and percentages for categorical variables). Several pharmacists' intervention-related parameters were compared using the Kruskal-Wallis test. The rates of pharmacists' interventions were reported as the number of interventions per 100 medication orders reviewed and treated as continuous variables to enable comparison to the published literature. The rates of all pharmacists' interventions and active interventions on the five wards were compared using Poisson regression analysis. Poisson regression analysis was also used to determine the influence of pharmacists' level of employment and the duration of pharmacy ward round on the rates of all pharmacists' interventions and the active interventions. All data were analysed using SPSS version 22.0.

The univariate and multivariate logistic regression for predictors of physician-acceptance of pharmacists' active interventions were based on a backward likelihood ratio method using SPSS version 22.0. The first step of logistic regression is selecting dependent and independent variables. 'Acceptance' of each intervention, as a binary variable, was used as the dependent variable in a logistic regression model. Selection of independent variables/predictors, either continuous or categorical, was guided by published research and the direct observation data (Table 3.1). The independent variables were grouped into:

- Patient characteristics: age, gender, diagnosis on admission, clinical area during hospital stay, length of stay, number of medications prescribed
- Drug characteristics: therapeutic class(188), dose form, high-risk category(189)

- Types of active interventions (Table 3.2)
- Pharmacists' characteristics: gender, years of experience, highest academic qualification, work pattern (full-time/part-time), work post (permanent/temporary).

A contingency table of dependent variables (degree of acceptance) versus categorical independent variables was used to ensure that no cell had a zero cell count and that not fewer than 20% of cells had a frequency count of fewer than five, in accordance with best practice (Step 2). After regrouping as necessary, univariate logistic regression analysis was conducted for each variable selected for inclusion in the model (continuous and categorical) (Step 3). As the traditional p-value (0.05) often fails to identify variables deemed to be important,(191) any variable demonstrating an association with the outcome with $p<0.25$ was initially included in the multivariate regression model (Step 4). The multivariate logistic regression applied backward elimination (the least significant variable was progressively deleted until all variables remaining in the model were statistically significant at $p<0.05$) to produce Model 1. Next, all possible two-way interactions of the significant independent variables from Model 1 were examined (Step 5). Each interaction was tested in a full regression model including all significant independent variables from Model 1. An interaction that was not significantly associated with the outcome was deleted. However, every interaction term with a significant contribution ($p<0.05$) was included in the next model. For the final step, the logistic regression was repeated to include all significant independent variables and significant interaction variables as the predictors. The odds ratios, their significance levels and 95% confidence intervals (95%CI) were calculated for each variable. Significant variables ($p<0.05$) in the final model were considered to be the predictors of the outcome (physician-acceptance of pharmacists' active intervention).

Table 3.2 Pharmacist intervention categories developed by Condren *et al*.(184) with slight modification

Intervention categories	Intervention subcategories
ADE or ME occurrence	Dose missing Illegible order Inappropriate rate/dilution Incompatibility Incorrect/missing route Known patient allergy Label incorrect MAR error Missing/wrong weight Overdose Scheduling error Under dose Wrong drug Wrong patient Wrong/missing direction Wrong/missing strength
Drug information provision	Consulted for drug information in-service Provided administration information Provided compatibility information Provided without consult
Drug interaction	Disease Drug Food Herb Laboratory test Vitamin
Drug therapy change	Antibiotic change Decreased dose Decreased dosing interval Dose form change/strength change Dose adjustment for renal/hepatic impairment Drug added Drug deleted – no indication Drug deleted – therapeutic duplication Drug deleted – impaired renal/hepatic function Duration of therapy change Increased dose Increased dosing interval Intravenous to per oral change or vice versa Non-formulary to formulary change Regular to if required or vice versa
Laboratory monitoring	Recommended deletion Scheduling error

Medication history/patient counselling	Allergy/ADR clarification Discharge counselling Medication history and/or medication reconciliation Patient and/or parent education
ADE or ME prevented	Dose missing Illegible order Inappropriate rate/dilution Incompatibility Incorrect/missing route Label incorrect MAR error Missing/wrong weight Overdose Patient allergy/ADR history Scheduling error Under-dose Wrong drug Wrong patient Wrong/missing strength Wrong/missing frequency Wrong/missing duration
Clarification of medication order on medication chart	
Other	Add patient identification on medication chart Monitor the possibility of adverse effect Clarify the diagnosis/drug indication Cost saving

ADE = adverse drug event, ADR = adverse drug reaction, MAR = medication administration record

3.2 Part Two: Clinical Significance of Pharmacists' Active Interventions and Identification of Medication Misadventure through Pharmacists' Active Interventions Using an Expert Panel

3.2.1 Clinical Significance of Pharmacists' Active Interventions

The principal researcher de-identified all of the pharmacists' active interventions collected during the ward round and dispensing from Part One. Forty-two active interventions were randomly selected from a total of 266 active interventions (approximately 16% of active interventions) using a random number generator. The selected active interventions were presented as vignettes describing the patient-related information (demographics, medical history, medication history, allergy/ADR history, presenting complaints, diagnosis on admission, current medications), medication-related issues and pharmacists' interventions to solve the issues (Appendix 6). The two researchers (YP, JH) with clinical pharmacy experience and

no involvement in data collection, reviewed the clinical significance of the selected cases and reached consensus. Three independent panellists (hospital pharmacist, academic pharmacist, clinical nurse) also reviewed the cases in their own time. As consensus could not be reached between the researchers and the three independent panellists (Panel 1), a second panel was set up. Panel 2 involved the researchers (YP, , JH) and two independent panellists from the study hospital (medication safety pharmacist, paediatric oncology pharmacist). The two panellists reviewed the cases in their own time. For the clinical significance assessment, the rating system described by Dooley *et al*.(19) was used with modification to include an 'unsure' option (Table 3.3). A meeting was organised between the researcher (YP) and the two independent panellists in order to reach consensus.

3.2.2 Identification and Assessment of Medication Misadventure

The two researchers (YP, JH) and Panel 1 also assessed the 42 vignettes to ascertain whether the cases involved medication misadventure (Section 3.2.1). If the cases involved medication misadventure, the researchers and the panellists determined the type of medication misadventure (ADE, ADR, ME). If medication misadventure involved an ME, the researchers and panellists classified the type of ME and rated the severity of the consequences using the National Coordinating Council for Medication Error Reporting and Prevention Taxonomy (NCCMERP).(35) The researchers and Panel 1 could not reach consensus. Inter-rater reliability analysis for the assessment of medication misadventure detected through pharmacists' active interventions were determined based on Krippendorff's alpha values calculated using SAS version 9.2. The Krippendorff's alpha was the extension of Cohen's Kappa which was used for inter-reliability assessment for multiple raters.

The interpretation of the Krippendorff's alpha values (192) was as follows:

- 0.00: poor agreement
- 0.01-0.20: slight agreement
- 0.21-0.40: fair agreement
- 0.41-0.60: moderate agreement
- 0.61-0.80: substantial agreement
- 0.81-1.00: almost perfect agreement.

Table 3.3 Clinical significance rating of pharmacists' interventions

Clinical significance	Definition
Life-saving	Related to a potential life- and death situation
Major	Expected to prevent or address a 'very serious' drug-related problem defined as >20% chance of noticed effect or >5% chance of harmful effect
Moderate	Expected to enhance the effectiveness of drug therapy, producing minor reductions in patient morbidity or a <20% chance of noticed effect
Minor	Adjustment and optimisation of therapy, not expected to significantly alter hospital stay or clinical outcome
No clinical significance	Information only

3.3 Part Three: Comparison of Documentation Methods for Pharmacists' Interventions

3.3.1 Documentation of Pharmacists' Interventions during Snapshot Periods

In addition to the prospective direct observation of pharmacists' interventions (Part One), pharmacists' interventions documented through self-reports were also analysed. Snapshot intervention documentation is used by the study hospital during certain periods to document pharmacists' interventions. Snapshot periods occurred twice yearly during March to May and September to October and were of five days duration. These periods were selected to enable rotational medical staff to settle into their new areas before monitoring their practices. During the snapshot periods, the interventions were documented by pharmacists in the main pharmacy, the two satellite pharmacies (cardiology and neurology, and haematology-oncology), centralised intravenous admixture services unit and all wards. Pharmacists documented the interventions on a standardised form (Appendix 7) and recorded the patient identification number, ward location, brief description of the intervention and medication(s). The number of medication charts reviewed, the number of patients seen and other clinical activities, i.e. review of treatment protocols, teaching and presentations to peers were also recorded. An administrative staff member transferred the completed intervention forms onto Excel spread sheets (snapshot intervention database).

The principal researcher retrospectively analysed the documentation form of pharmacists' interventions from the five study wards for three snapshot periods -

September 2010 (period I), April 2011 (period II), and May 2012 (period III) - to determine the number and type of interventions. The snapshot documentation form was used instead of retrieval data from the snapshot intervention database as it was incomplete. The type of intervention was categorised as described by Condren *et al.*(184) with slight modification (Table 3.2). The interventions were further classified into 'active' and 'passive' as defined previously. The rates of intervention were defined as the number of interventions per 100 medication charts reviewed. Each medication chart reviewed could have one or more interventions. Demographic variables and pharmacists' intervention data were summarised using descriptive statistics. The rates of pharmacists' interventions per 100 medication charts reviewed documented through snapshot periods and during direct observation for each ward (Part One) were compared using Poisson regression analysis. Data were analysed using SPSS version 19.0 (Chicago, USA). This study was covered by the ethics as described in Section 3.1.3. The data extraction from snapshot reports maintained patients and pharmacists confidentiality by using coding system.

3.3.2 Focus Group Discussion

A focus group discussion (FGD) was conducted at the study hospital. Participants were invited via official electronic mail by the preceptor pharmacist to all pharmacists in the Pharmacy Department. A Study Information Sheet (Appendix 8) and Consent Form (Appendix 9) were attached to the invitation; consent included participants' approval for the session to be audio recorded. The study was approved by Princess Margaret Hospital institutional review board and Curtin University Human Ethics Committee No: PH-11-13 (Appendix 10). The principal researcher presented the pharmacists' interventions documented from snapshot reports and the direct observations. This was followed by a discussion conducted by an independent facilitator. The principal researcher took notes during the discussion for crosschecking. The FGD was audio recorded and transcribed verbatim for thematic analysis. Transcripts of the discussion were entered into qualitative data management software program (QSR NVivo10). Within this software the partial transcripts were then coded and emergent themes were linked.

The research questions addressed during the FGD were:

- Pharmacists' interventions documented during snapshots versus observation were different. Are the results from observation more reflective? Why do you think so?
- How important is the documentation of pharmacists' interventions?
- How valuable are your clinical interventions?
- Are there any problems in documenting your interventions? Why do you think so?
- Are there problems with the way data are used? Why do you think so?
- What are the benefits and limitations of the snapshot documentation?
- Would you like to see modifications made to your current intervention documentation method? What are your suggestions to improve the existing documentation method?

3.4 Part Four: Medication Errors in Children: Root Cause Analysis Using Simulated Case Scenarios

3.4.1 Development of Simulated Case Studies and Survey Instrument

The principal researcher developed five simulated case studies involving paediatric patients. Each case study represented the patient characteristic of the five study wards (Part One) and was associated with one ME with a different type of error - inappropriate dose, dispensing error, drug omission, transcribing error and monitoring error. Each case study was reviewed by the other researchers (YP and JH) for accuracy of the clinical information and its relevance with the treatment policy and procedure at the study hospital. The questionnaire was divided into two sections. Section one contained questions related to participants' demographics (age, gender, type of health professional, current position, years of experience as a health professional, and years of experience in paediatrics). Section two presented five simulated case studies in children followed by questions on ME and RCA. ME-related questions required rating of clinical significance of the error and identification of the health professional(s) responsible for the error.

The RCA questions were used to identify the potential contributing factors to the error in each case. The RCA questions were adapted from the *Clinical Incident Management Toolkit*(193) and included only those with relevance to the case studies.

The adapted RCA questions consisted of seven items. Participants were asked to determine the potential contributing factors by selecting the options provided for each question and describing why the factor(s) selected contributed to the error. The RCA questions included:

- specific patient issues
- dismissal of policies/procedures/guidelines (sub-factors: patient misidentification, error/omission in medication reconciliation, clinical guidelines, coordination of care, medical record documentation, level and frequency of monitoring of patient)
- human resources-related issues (sub-factors: staff workload and inadequate staffing, recruitment, staff training and supervision, staff supervision)
- communication-related issues (sub-factors: miscommunication between staff, miscommunication between staff and patient and/or family)
- physical environment of the health service (sub-factors: noise, lighting, space)
- control/provision of medication (sub-factors: medication storage, labelling, documentation of administration, internal transfer of medication).

Participants could tick the 'unsure' option if in doubt about selecting the contributing factors. Participants could also list under the 'other' category any extra factors that contributed to the errors. After all potential contributing factors were identified and evaluated participants were asked to give their suggestions on strategies to prevent the recurrence of the error in the future.

3.4.2 Face Validity Test

A pilot study involving three academic pharmacists (including one of the researchers, LE) was conducted to determine the face validity of the questionnaire. Participants were asked to assess the clarity of the questionnaire including the instructions, case studies and questions. Participants were also asked to evaluate the questionnaire design and layout, and to estimate the time needed to complete the questionnaire. Participants' comments were used to refine the final questionnaire.

3.4.3 Participants and Questionnaire Administration

A total of 111 coded self-administered questionnaires (Appendix 11) were distributed to potential participants from mid-July 2014 to mid-August 2014.

Potential participants included all pharmacists (n=37) and randomly selected (20%) doctors (n=31, around 5-6 doctors/ward) and nurses (n=43, around 8-9 nurses/ward) from the five study wards in the hospital (Part One). A Participant Information Sheet (Appendix 12) containing information about the study aims, confirmation that collected information would remain confidential and researchers' contact details was attached to the questionnaire. A consent form (Appendix 13) and reply-paid envelope were also provided along with the questionnaire and the Participant Information Sheet. This study was covered by the ethics as described in Section 3.1.3. The principal researcher handed the questionnaires directly to the pharmacists. The questionnaires for doctors and nurses were disseminated either directly by the principal researcher under the supervision of the ward pharmacists or by the ward pharmacists using convenience sampling until the number of doctors/nurses recruited reached the predefined sample size. Participants were allowed to complete the questionnaires in their own time. They were asked to return the questionnaires by the predefined time in the envelope provided. The overall expected response rate was around 40%. Participation was voluntary and no incentives were offered. The first reminder for returning the questionnaire was sent via email to all pharmacists at the end of August 2014. The ward pharmacists undertook the reminders for doctors and nurses during ward rounds and via staff electronic mail. The second reminder was sent at the end of September 2014.

3.4.4 Data Analysis

Demographic data of the participants, and their rating of clinical significance of the error, identification of the responsible health professional(s) and the contributing factors for each case were entered into SPSS version 22.0. Data were randomly checked for accuracy and descriptive statistical analysis was conducted. The principal researcher assigned the pre-determined answers for the questions related to contributing factors of MEs for each case. A General Estimating Equation (GEE) analysis was adopted to develop an agreement model between the participants' responses on the contributing factors for each case and the principal researcher's pre-determined answers. If the agreement model using GEE was not able to be fitted (e.g. due to complete agreement in some or all cases), the results was summarised more appropriately using descriptive statistics. Participants' statements on the description of the contributing factors and their suggestions on the prevention of the error in each

case were entered into the qualitative data management software (QSR Nvivo version 10.0) for thematic analysis. Participants' statements were coded for any emergent themes. This study was covered by the ethics as described in Section 3.1.3. Data extraction from the questionnaire maintained the participants' confidentiality by using coding system.

Chapter 4

PART ONE: RESULTS AND DISCUSSION

4.1 Direct Observation and Documentation of Ward Pharmacists' Interventions

4.1.1 Observation and Documentation in the General Medical Unit

There were three wards in the General Medical Unit - General Medical Ward for Infants, General Medical Ward for Young Children and General Medical Ward for Adolescents. The characteristics of patients admitted to these three wards during the study period (September 2011-August 2012) are summarised in Table 4.1. Patients ranged in age from newborn to 19 years, and females accounted for nearly two-thirds of the patients in the adolescent ward. There were differences in length of stay and number of medications across the three wards. The five most common reasons for admission to each ward are presented in Figure 4.1. Diseases of the respiratory system were the prevalent reason for admission in the wards for infants and young children, while mental and behavioural disorders were prevalent in the adolescent ward.

Table 4.1 Characteristics of patients on the three general medical wards

Parameters	Infants	Young Children	Adolescents
Age (years), median (range)	0.35 (0.02-2.42)	5.83 (2.00-13.00)	15.00 (4.33-19.00)
Gender (%)			
-Male	320 (56.7%)	361 (55.5%)	258 (35.8%)
-Female	244 (43.3%)	290 (44.5%)	463 (64.2%)
Median length of stay (days) (range)	6.00 (1-95)	9.00 (1-73)	14.00 (1-91)
No. of medications prescribed per patient			
-Oral medications, median (range)	1.00 (0-8)	2.00 (0-18)	4.00 (0-22)
-Non-oral medications, median (range)	1.00 (0-11)	2.00 (0-30)	1.00 (0-19)

The 35-day observation data of pharmacists' interventions (passive and active) and active interventions are shown in Table 4.2 and Table 4.3, respectively. The duration of pharmacy rounds ranged from 15 to 137 minutes (Table 4.2). Ward pharmacists made 4 to 6 interventions per day, and the rates of interventions ranged from 4.38 to 7.83 interventions per 100 medication orders reviewed on the general medical wards.

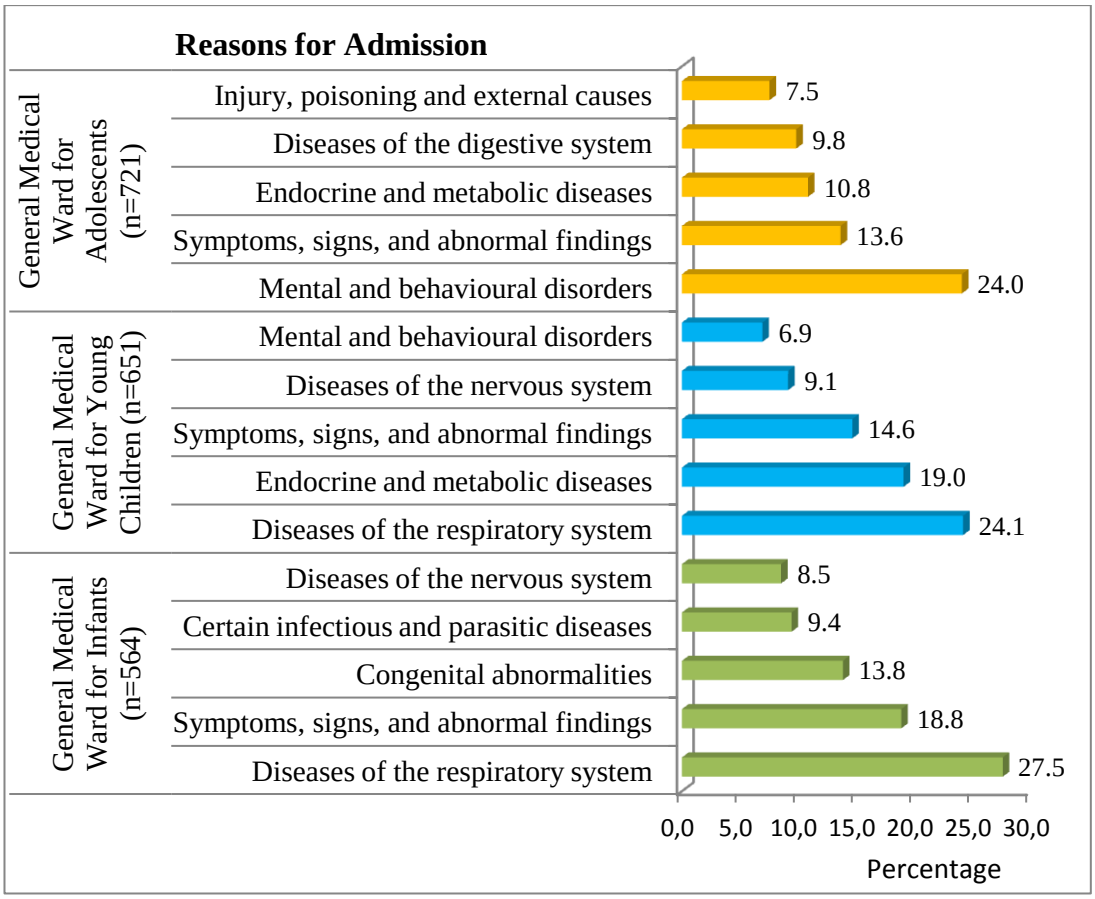


Figure 4.1 Top five reasons for admission to the general medical wards

Table 4.2 Pharmacists' interventions on the three general medical wards (direct observation 35 days)

Parameters	Infants	Young Children	Adolescents
Duration of pharmacy round (minutes), mean ± SD (range)	35.14 ± 14.21 (15-70)	57.60 ± 24.39 (20-110)	58.69 ± 22.34 (32-137)
No. of Pis	145	153	218
No. of medication orders reviewed	1903	3778	4813
No. of medication charts reviewed	468	500	528
No. of patients	564	651	721
Rate of PIs per 100 medication orders reviewed, mean ± SD	7.83 ± 6.84	4.38 ± 4.17	4.77 ± 3.07
Rate of PIs per 100 medication charts reviewed, mean ± SD	32.72 ± 29.45	33.79 ± 32.49	53.62 ± 48.94
Rate of PIs per 100 patients, mean ± SD	25.75 ± 21.63	24.32 ± 22.35	30.82 ± 18.89
Rate of PIs per day, mean ± SD	4.14 ± 3.53	4.49 ± 3.93	6.23 ± 3.71

PIs = pharmacist's interventions

Pharmacists' active interventions constituted less than one-quarter of interventions in the general medical wards. Physician acceptance of the interventions was high; 90% or more in the wards for infants and young children. The rates of active interventions ranged from 0.81 to 1.15 per 100 medication orders reviewed across the medical wards (Table 4.3).

Table 4.3 Pharmacists' active interventions on the three general medical wards (direct observation 35 days)

Parameters	Infants	Young Children	Adolescents
No. of active PIs (%)*	16 (11.0%)	28 (18.3%)	51 (23.4%)
Physician acceptance of active PIs (%)			
- Yes	15 (93.8%)	26 (92.9%)	40 (78.4%)
- No	1 (6.3%)	2 (7.1%)	11 (21.6%)
Rate of active PIs per 100 medication orders reviewed, mean ± SD	0.85 ± 1.35	0.81 ± 1.24	1.15 ± 1.19
Rate of active PIs per 100 medication charts reviewed, mean ± SD	3.97 ± 6.88	5.72 ± 8.31	17.34 ± 30.16
Rate of active PIs per 100 patients, mean ± SD	2.89 ± 4.76	4.35 ± 6.17	7.40 ± 7.77
Rate of active PIs per day, mean ± SD	0.46 ± 0.74	0.80 ± 1.13	1.46 ± 1.42

*Percentage of active interventions of all pharmacists' interventions (i.e. passive and active).
PI = pharmacists' interventions

The most common interventions by clinical pharmacists on the general medical wards were medication histories and/or patient counselling (Figures 4.2, 4.3 and 4.4). These activities constituted more than half of all interventions. The proportion of interventions relating to drug therapy change gradually increased from younger to older patients on the general medical wards. On the ward for infants (Figure 4.2), provision of drug information to other healthcare providers was the second most common intervention; just over 10% of interventions. Activities associated with drug therapy changes constituted the second most common intervention on the ward for young children (Figure 4.3).

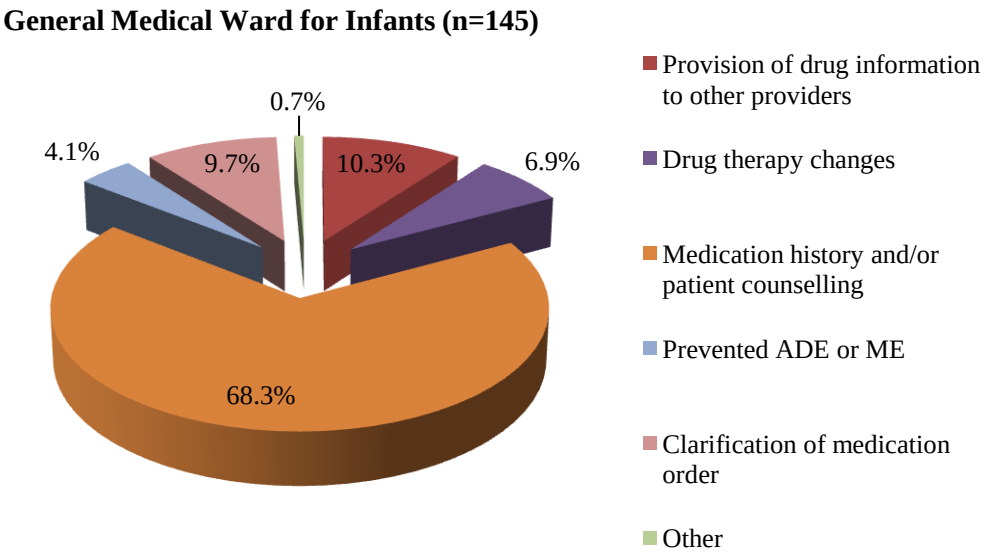


Figure 4.2 Pharmacists' interventions on the general medical ward for infants

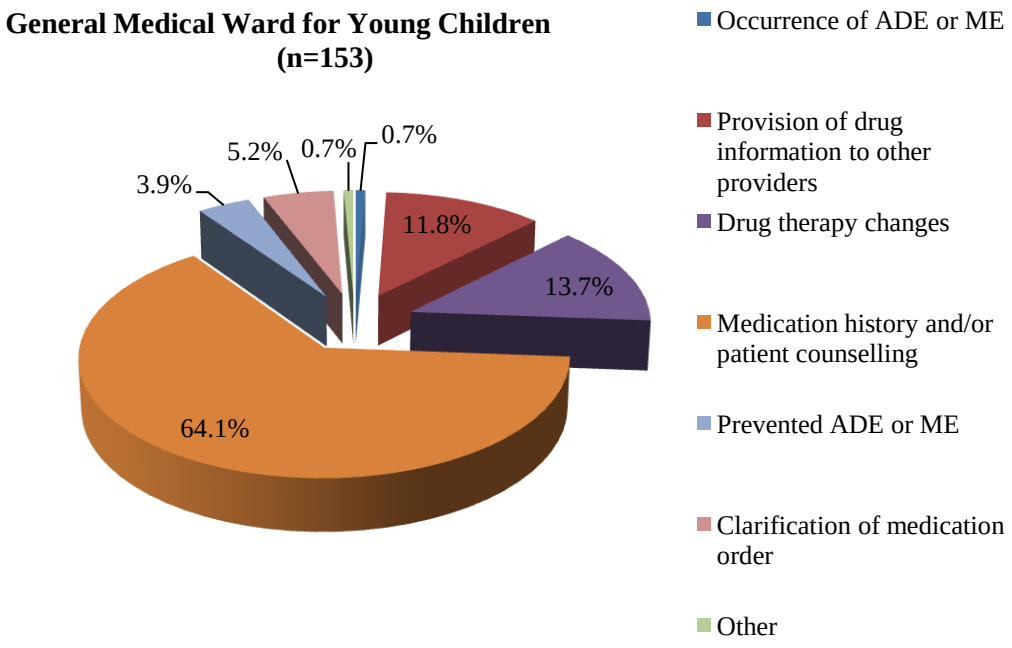


Figure 4.3 Pharmacists' interventions on the general medical ward for young children

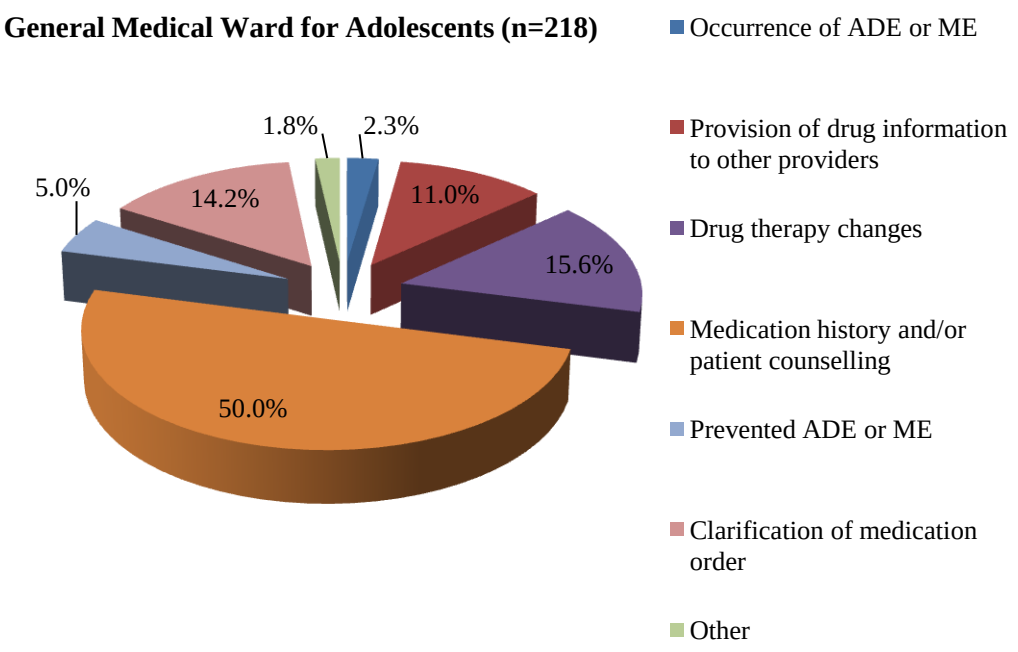


Figure 4.4 Pharmacists' interventions on the general medical ward for adolescents

The subcategory of medication history and/or medication reconciliation dominated the interventions (Table 4.4). The proportion of other categories and subcategories of the interventions varied widely across the three medical wards.

Table 4.4 Categories of pharmacists' interventions on the three general medical wards

Categories and subcategories of pharmacists' interventions	Infants (n=145), n (%)	Young Children (n=153), n (%)	Adolescents (n=218), n (%)
Occurrence of ADE or ME	0 (0.0)	1 (0.7)	4 (2.3)
- Known patient allergy		0 (0.0)	2 (0.9)
- Overdose		0 (0.0)	0 (0.0)
- Scheduling error		0 (0.0)	2 (1.4)
- Under dose		1 (0.7)	0 (0.0)
Provision of drug information	15 (10.3)	18 (11.8)	24 (11.0)
- Consulted for in-service	2 (1.4)	10 (6.5)	9 (4.1)
- Provided administration information	7 (4.8)	5 (3.3)	8 (3.7)
- Provided compatibility information	0 (0.0)	2 (1.3)	0 (0.0)
- Provided without consult	6 (4.1)	1 (0.7)	7 (3.2)
Medication history and/or patient counselling	99 (68.3)	98 (64.1)	110 (50.5)
- Allergy/ADR clarification	32 (22.1)	14 (9.2)	13 (6.0)
- Medication history and/or medication reconciliation	66 (45.5)	66 (43.1)	82 (37.6)
- Patient and/or parent education	1 (0.7)	18 (11.8)	15 (6.9)
Clarification of medication order	14 (9.7)	8 (5.2)	30 (13.8)
Drug therapy changes	10 (6.9)	21 (13.7)	34 (15.6)
- Antibiotic change	0 (0.0)	0 (0.0)	2 (0.9)
- Decreased dose	2 (1.4)	2 (1.3)	2 (0.9)
- Decreased dosing interval	0 (0.0)	1 (0.7)	2 (0.9)
- Dose form change/strength change	2 (1.4)	2 (1.3)	0 (0.0)
- Dose adjustment for renal/hepatic function	0 (0.0)	0 (0.0)	1 (0.5)
- Drug added	1 (0.7)	1 (0.7)	8 (3.7)
- Drug deleted - no indication	0 (0.0)	0 (0.0)	1 (0.5)
- Drug deleted - therapeutic duplication or drug interaction	1 (0.7)	4 (2.6)	4 (1.8)
- Duration of therapy change	0 (0.0)	1 (0.7)	0 (0.0)
- Increased dose	4 (2.8)	7 (4.6)	7 (3.2)
- Increased dosing interval	0 (0.0)	3 (2.0)	3 (1.4)
- Drug deleted - impaired renal/hepatic function	0 (0.0)	0 (0.0)	3 (1.4)
- Regular to if required or *vice versa*	0 (0.0)	0 (0.0)	1 (0.5)
ADE or ME prevented	6 (4.1)	6 (3.9)	11 (5.0)
- Dose missing	3 (2.1)	2 (1.3)	0 (0.0)
- Illegible order	0 (0.0)	1 (0.7)	0 (0.0)
- Incorrect/missing route	0 (0.0)	0 (0.0)	2 (0.9)
- MAR error	0 (0.0)	0 (0.0)	1 (0.5)
- Overdose	0 (0.0)	0 (0.0)	1 (0.5)
- Scheduling error	0 (0.0)	0 (0.0)	1 (0.5)
- Under dose	0 (0.0)	0 (0.0)	1 (0.5)
- Wrong patient	1 (0.7)	0 (0.0)	0 (0.0)
- Wrong/missing strength	0 (0.0)	0 (0.0)	2 (0.9)
- Wrong/missing frequency	2 (1.4)	3 (2.0)	4 (1.8)
Other	1 (0.7)	1 (0.7)	4 (1.9)

ADE = adverse drug event, ADR = adverse drug reaction, MAR = medication administration record, ME = medication error

Drug classes implicated in active interventions are listed in Table 4.5. Unadjusted for prescription volume, anti-infectives were the drugs most often associated with active interventions, followed by analgesics and gastrointestinal drugs.

Table 4.5 Drug classes associated with active interventions (n=95) on the three general medical wards

Drug classes	Infants	Young Children	Adolescents	Frequency* (%)
Anti-infectives	3	16	13	32 (33.7)
Analgesics	5	4	18	27 (28.4)
Gastrointestinal	3	1	4	8 (8.4)
Neurological	1	0	4	5 (5.3)
Respiratory	0	4	0	4 (4.2)
Blood and electrolytes	2	0	2	4 (4.2)
Endocrine	1	0	2	3 (3.2)
Anaesthetics	0	1	1	2 (2.1)
Cardiovascular	1	1	0	2 (2.1)
Immunomodulators/ antineoplastics	0	0	2	2 (2.1)
Obstetric/gynaecological	0	0	2	2 (2.1)
Allergy/anaphylaxis	0	1	0	1 (1.1)
Ear, nose, and throat	0	0	1	1 (1.1)
Psychotropic	0	0	1	1 (1.1)
Vaccines	0	0	1	1 (1.1)

*Total number of medications implicated in the active interventions, not adjusted for the prescribing volume of medications.

Unadjusted for prescribing volume, antibacterials were the predominant anti-infectives involved in the interventions (just over 90% of anti-infectives related active interventions, n=29); the remaining involved antifungals. The most common antibacterials involved were aminoglycosides, vancomycin and penicillins. Dose adjustment (n=18) was responsible for the majority of interventions; accounting for more than half of interventions in this class. Another common intervention outcome was dose interval/frequency adjustment (n=6); nearly 19% of interventions.

Non-opioid analgesics (n=20) were the major contributor to active interventions on the general medical wards; almost three-quarters of analgesics-associated active interventions. The interventions were documented most frequently in adolescents (n=18). Pharmacists performed two-thirds of the analgesics-related interventions in this patient population. The three major subcategories of active interventions in this class were: dose adjustment, dose interval/frequency adjustment, and drug deletion.

The most frequent trigger for pharmacists' interventions was medication chart review (Table 4.6).

Table 4.6 Triggers for pharmacists' interventions

Trigger for interventions	Infants, n (%)	Young Children, n (%)	Adolescents, n (%)
Medication chart review	135 (93.1)	114 (74.5)	180 (82.6)
Doctor inquiry	1 (0.7)	8 (5.2)	5 (2.3)
Patient and/or parent inquiry	1 (0.7)	7 (4.6)	11 (5.0)
Nurse inquiry	7 (4.8)	9 (5.9)	10 (4.6)
Laboratory result	1 (0.7)	4 (2.6)	10 (4.6)
Medication history taking	0 (0.0)	11 (7.2)	2 (0.9)

4.1.2 Observation and Documentation in the General Surgical Unit

There was one ward within the general surgical unit in the study hospital. The characteristics of patients admitted to the general surgical ward during the study period (September 2011-August 2012) are summarised in Table 4.7. Patients ranged in age from newborn to 17 years, and there were considerably more male patients. The top five reasons for admission to this ward are presented in Figure 4.5. Diseases of the digestive system were the most common reason for admission; more than one-quarter of all admissions in this ward.

Table 4.7 Characteristics of patients on the general surgical ward

Patient characteristics	Value
Age, median years (range)	6.17 (0.06-17.00)
Gender (%) - Male - Female	 311 (60.5%) 203 (39.5%)
Length of stay, median days (range)	5.00 (1-71)
No. of medications prescribed per patient - Oral medications, median (range) - Non-oral medications, median (range)	 3.00 (0-10) 2.00 (0-13)

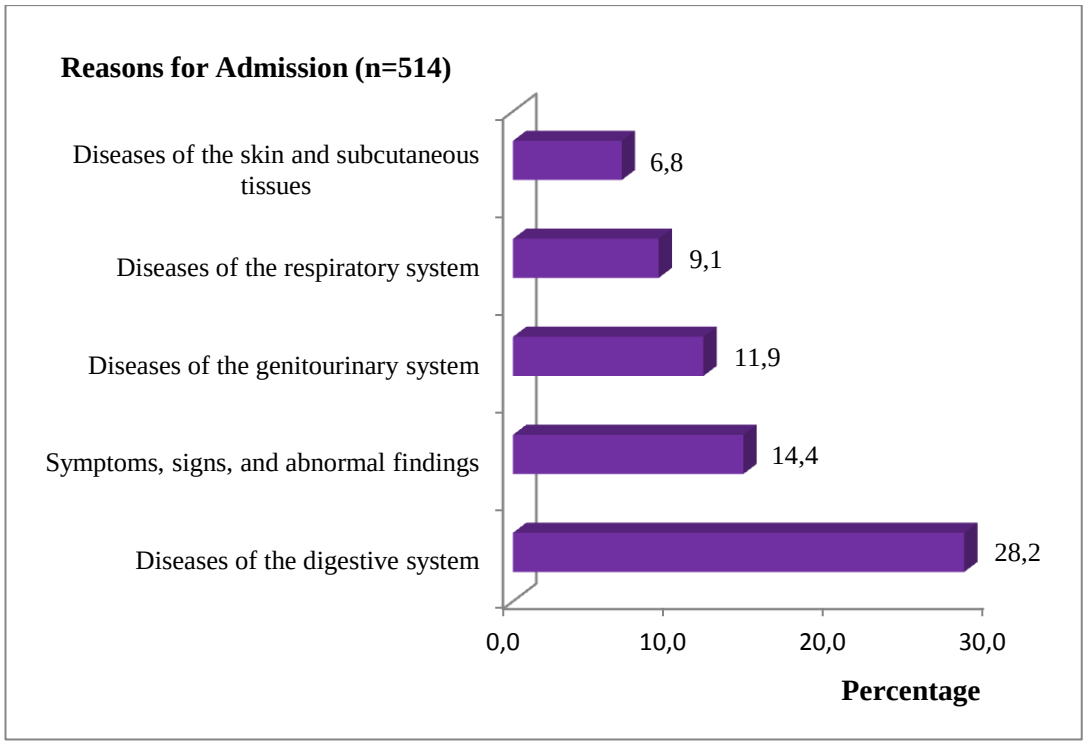


Figure 4.5 Top five reasons for admission to the general surgical ward

Ward pharmacists spent on average 50 minutes per day to complete their ward round (Table 4.8). They made around seven interventions per day; 10.48 interventions per 100 medication orders reviewed and 76.83 interventions per 100 medication charts reviewed. Active interventions accounted for just over 20% of pharmacists' interventions, with high physician acceptance (Table 4.9).

Table 4.8 Pharmacists' interventions on the general surgical ward (direct observation 37 days)

Parameters	Value
Duration of pharmacy round in minutes per day, mean ± SD	50.70 ± 18.99
No. of PIs	271
No. of medication orders reviewed	2700
No. of medication charts reviewed	422
No. of patients	514
No. of patients receiving PIs (%)	155 (30.2%)
Rate of PIs per 100 medication orders reviewed, mean ± SD	10.48 ± 6.59
Rate of PIs per 100 medication charts reviewed, mean ± SD	76.83 ± 80.31
Rate of PIs per 100 patients, mean ± SD	54.01 ± 31.31
Rate of PIs per day, mean ± SD	7.41 ± 4.62

PIs = pharmacist's interventions

Table 4.9 Pharmacists' active interventions on the general surgical ward (direct observation 37 days)

Parameters	Value
No. of active PIs (% of all interventions)	59 (21.8%)
Physician acceptance of active PIs (%) - Yes - No	 50 (84.7%) 9 (15.3%)
Rate of active PIs per 100 medication orders reviewed, mean ± SD	2.34 ± 2.23
Rate of active PIs per 100 medication charts reviewed, mean ± SD	24.54 ± 64.76
Rate of active PIs per 100 patients, mean ± SD	12.39 ± 11.71
Rate of active PIs per day, mean ± SD	1.59 ± 1.36

PIs = pharmacist's interventions

Taking a medication history and/or patient counselling was the most common intervention in the surgical ward (Table 4.10).

Table 4.10 Categories of pharmacists' interventions on the general surgical ward (n=271)

Categories and subcategories of pharmacists' interventions	No. of cases (%)
Occurrence of ADE or ME	0 (0.0)
Provision of drug information to other providers	27 (10.0)
- Consulted for drug information in-service	8 (3.0)
- Provided administration information	7 (2.6)
- Provided without consultation	12 (4.4)
Drug interaction	1 (0.4)
- Drug-drug	1 (0.4)
Laboratory monitoring	1 (0.4)
- Recommended/deletion	1 (0.4)
Medication history and/or patient counselling	146 (53.9)
- Allergy/ADR clarification	19 (7.0)
- Discharge counselling	1 (0.4)
- Medication history and/or medication reconciliation	104 (38.5)
- Patient and/or parent education	22 (8.1)
Clarification of medication order	35 (12.9)
Drug therapy changes	50 (18.5)
- Antibiotic change	2 (0.7)
- Decreased dose	8 (3.0)
- Decreased dosing interval	2 (0.7)
- Dose form change/strength change	3 (1.1)
- Drug added	8 (3.0)
- Drug deleted - no indication	2 (0.7)
- Drug deleted - therapeutic duplication or drug interaction	2 (0.7)
- Increased dose	12 (4.4)
- Increased dosing interval	2 (0.7)
- Non formulary to formulary change	3 (1.1)
- Regular to if required or *vice versa*	6 (2.2)
Prevention of ADE or ME	8 (3.0)
- Illegible order	1 (0.4)
- Overdose	1 (0.4)
- Patient allergy/ADR history	2 (0.7)
- Wrong/missing strength	1 (0.4)
- Wrong/missing frequency	3 (1.1)
Other	3 (1.1)

ADE = adverse drug event, ADR = adverse drug reaction, ME = medication error

Drug classes associated with pharmacists' active interventions are outlined in Table 4.11. Anti-infectives were the drugs most frequently associated with active interventions, followed by analgesics and gastrointestinal drugs.

Table 4.11 Drug classes associated with pharmacists' active interventions (n=59) on the general surgical ward

Drug classes	No. of active interventions (%)*
Anti-infectives	30 (50.8)
Analgesics	12 (20.3)
Gastrointestinal	9 (15.3)
Respiratory	2 (3.4)
Ophthalmic	1 (1.7)
Genitourinary	1 (1.7)
Immunomodulators/antineoplastics	1 (1.7)
Neurological	1 (1.7)
Psychotropic	1 (1.7)
Other	1 (1.7)

*Total number of medications implicated in the active interventions, not adjusted for the prescribing volume of medications.

Antibiotics accounted for all cases of anti-infectives associated interventions. Dose adjustment was responsible for 50% of the interventions in this class, mainly to increase the dose (n=9). Antibiotics involved in the interventions, unadjusted for prescribing volume, were aminoglycosides, vancomycin and penicillins; nearly half of the interventions on this ward.

Triggers to initiate interventions (passive and active) on the general surgical ward are listed in Table 4.12. Medication chart review was the predominant trigger of the interventions; more than 80%.

Table 4.12 Triggers for pharmacists interventions on the general surgical ward (n=271)

Trigger for intervention	No. of cases (%)
Medication chart review	234 (86.3)
Patient and/or parent inquiry	12 (4.4)
Nurse inquiry	9 (3.3)
Laboratory result	8 (3.0)
Medication history taking	7 (2.6)
Other pharmacist inquiry	1 (0.4)

4.1.3 Observation and Documentation on the Haematology-Oncology Ward

There was one ward in the haematology-oncology unit in the study hospital during the study period (September 2011-August 2012). Patients ranged from infants to adolescents, and male patients constitued more than 60% of patients (Table 4.13). There was notable variation in the length of hospital stay and the number of medications prescribed per patient in this specialty ward.

Table 4.13 Characteristics of patients on the Haematology-Oncology Ward

Patient characteristics	Value
Age in years, median (range)	6.83 (0.35-17.00)
Gender (%) - Male - Female	 279 (63.3%) 162 (36.7%)
Median length of stay (days) (range)	7.00 (1-82)
No. of medications for each patient - Oral medications, median (range) - Non-oral medications, median (range)	 4.00 (0-21) 3.00 (0-14)

Leukaemias, myeloproliferative diseases and malignant bone tumors were the three major diagnoses; nearly three-quarters of admissions in this ward (Figure 4.6).

Data representing pharmacists' interventions (passive and active) and active interventions are outlined in Table 4.14 and Table 4.15, respectively. Clinical pharmacists spent on average, 42 minutes undertaking their ward round, with up to six interventions per day (Table 4.14). Active interventions constituted nearly half of pharmacists' interventions, and acceptance was common, with almost all active interventions accepted by physicians (Table 4.15).

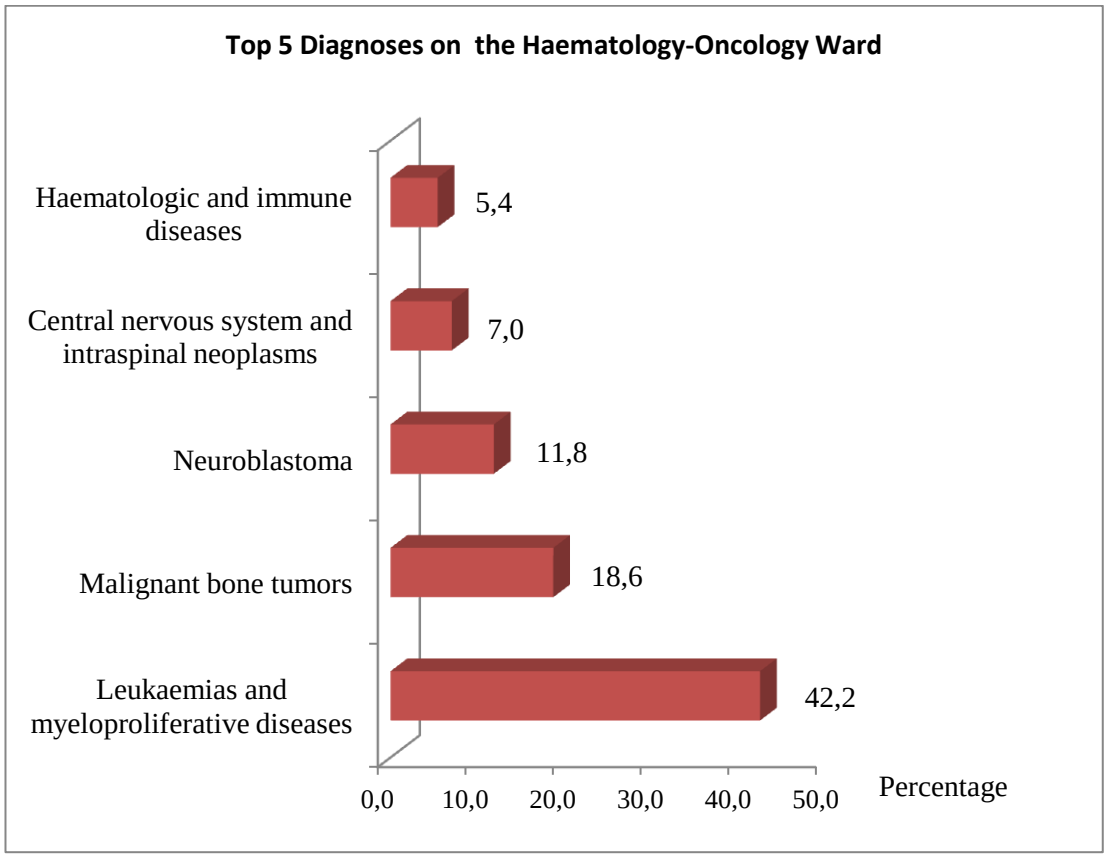


Figure 4.6 Top five diagnoses of patients (n=441) admitted to the Haematology-Oncology Ward during the 35-day study period

Table 4.14 Pharmacists' interventions on the Haematology-Oncology Ward (direct observation 35 days)

Parameters	Value
Duration of pharmacy round in minutes per day, mean ± SD	41.71 ± 20.06
No. of Pis	195
No. of medication orders reviewed	3506
No. of medication charts reviewed	357
No. of patients	441
No. of patients receiving PIs (%)	123 (27.9%)
Rate of PIs per 100 medication orders reviewed, mean ± SD	5.63 ± 3.36
Rate of PIs per 100 medication charts reviewed, mean ± SD	54.53 ± 28.17
Rate of PIs per 100 patients, mean ± SD	42.99 ± 23.53
Rate of PIs per day, mean ± SD	5.57 ± 3.42

PIs = pharmacists' interventions

Table 4.15 Pharmacists' active interventions on the Haematology-Oncology Ward (direct observation 35 days)

Parameters	Value
No. of active PIs (%)*	90 (46.2%)
Physician acceptance of active PIs (%) - Yes - No	 88 (97.8%) 2 (2.2%)
Rate of active PIs per 100 medication orders reviewed, mean ± SD	2.43 ± 1.84
Rate of active PIs per 100 medication charts reviewed, mean ± SD	23.25 ± 17.19
Rate of active PIs per 100 patients, mean ± SD	19.08 ± 14.06
Rate of active PIs per day, mean ± SD	2.57 ± 2.10

*Percentage of active interventions per pharmacists's intervention (i.e. passive and active).
PIs = pharmacists' interventions

Drug therapy changes were the most common interventions, representing over one-third of interventions in this specialty ward (Table 4.16). Provision of drug information to other healthcare providers, and medication history and/or patient counselling were the next major interventions with both intervention types, contributing to just over half of the interventions.

Table 4.16 Categories of pharmacists' interventions (n=195) on the Haematology-Oncology Ward

Categories and subcategories of pharmacists' interventions	No. of cases (%)
Occurrence of ADE or ME	1 (0.5)
- Overdose	1 (0.5)
Provision of drug information to other providers	52 (26.7)
- Consulted for drug information in-service	41 (21.1)
- Provided administration information	7 (3.6)
- Provided compatibility information	2 (1.0)
- Provided without consultation	2 (1.0)
Medication history and/or patient counselling	48 (24.6)
- Allergy/ADR clarification	1 (0.5)
- Medication history and/or medication reconciliation	26 (13.4)
- Patient and/or parent education	21 (10.8)
Clarification of medication order	3 (1.5)
Drug therapy changes	73 (37.4)
- Decreased dose	8 (4.1)
- Decreased dosing interval	1 (0.5)
- Dose form change/strength change	1 (0.5)
- Drug added	36 (18.6)
- Drug deleted - therapeutic duplication or drug interaction	5 (2.6)
- Duration of therapy change	6 (3.1)
- Increased dose	12 (6.2)
- Intravenous to per-oral change	1 (0.5)
- Regular to if-required or *vice versa*	3 (1.5)
ADE or ME prevented	16 (8.2)
- Dose missing	2 (1.0)
- Medication administration record error	4 (2.1)
- Overdose	1 (0.5)
- Scheduling error	3 (1.5)
- Wrong drug	1 (0.5)
- Wrong/missing frequency	5 (2.6)
Other	2 (1.0)

ADE = adverse drug event, ADR = adverse drug reaction, ME = medication error

Drug classes implicated in active interventions are presented in Table 4.17. Anti-infectives were the drugs most often associated with active interventions, followed by gastrointestinal drugs, immunomodulators/antineoplastics and analgesics.

Table 4.17 Drug classes associated with pharmacists' active interventions (n=90) on the Haematology-Oncology Ward

Drug class	No. of active interventions (%)*
Anti-infectives	38 (42.2)
Gastrointestinal	19 (21.1)
Immunomodulators/antineoplastics	18 (20.0)
Analgesics	7 (7.8)
Endocrine	2 (2.2)
Neurological	2 (2.2)
Cardiovascular	1 (1.1)
Ear, nose and throat	1 (1.1)
Ophthalmic	1 (1.1)
Psychotropic	1 (1.1)

*Actual number of medications implicated in active interventions; not adjusted for the prescribing volume of medications.

Antibacterials (n=33) were the predominant anti-infectives involved in the anti-infectives related active interventions and the remaining due to antifungals. Dose adjustment (n=15) accounted for the most common interventions in relation to the use of anti-infectives, followed by drug addition (n=11). Antibacterials associated with active interventions were trimethoprim-sulfamethoxazole (n=14), vancomycin (n=9) and aminoglycosides (n=5). With respect to antifungals, the majority of active interventions were related to the azoles (e.g. fluconazole, posaconazole).

The second major drug class involved in active interventions was for the gastrointestinal system. When categorised according to subclasses, antiemetics constituted almost 80% (n=15/19) of the interventions followed by drugs for dyspepsia. Drug addition was the most common intervention in this drug class (n=12), predominantly to add antiemetics as regular medications for patients on emetogenic chemotherapy. With regard to immunomodulators/antineoplastics, the majority of interventions were related to immunosuppressants (n=13), with the remaining involving antineoplastics. Drug addition (n=9) was the most common active intervention in this class.

The most common trigger for interventions in the Haematology-Oncology Ward was medication chart review; more than half of all triggers (Table 4.18).

Table 4.18 Triggers for interventions (n=195) on the Haematology-Oncology Ward

Triggers of interventions	No. of cases (%)
Medication chart review	116 (59.5)
Doctor inquiry	30 (15.4)
Patient and/or parent inquiry	22 (11.3)
Nurse inquiry	11 (5.6)
Laboratory result	10 (5.1)
Ward meeting	3 (1.5)
Other pharmacist inquiry	2 (1.0)
Medication history taking	4.1 (0.5)

4.1.4 Rates and Patterns of Pharmacists' Interventions on the Five Study Wards

During the six months of the study, eleven clinical pharmacists on the five study wards reviewed 2891 patients. Six pharmacists were categorised as Professional Level 1 (PL1), two as Professional Level 2 (PL2) and three as Professional Level 3 (PL3) (Table 4.19). Nearly half of the pharmacists had postgraduate qualifications, and three-quarters worked full-time. A total of 982 interventions were observed and documented by the principal researcher, which arose from the 16,700 medication orders reviewed.

Table 4.19 Characteristics of pharmacists (n=11) by level of employment*

Pharmacist level	Number	No. with postgraduate qualification	No. working full-time	No. assigned in permanent post
Level 1	6	2	5	1
Level 2	2	0	1	1
Level 3	3	3	2	2

**Employment of clinical pharmacists in Australia* starts with the pre-registration training year, followed by Professional Level 1 (must work under supervision), Professional Level 2 (often rotate among sections of the pharmacy), and Professional Level 3 (responsible to the Director of Pharmacy for the management and efficient performance of a specific unit or function of the hospital pharmacy).(194)

Intervention rates ranged from 4.38 to 10.48 per 100 medication orders across the five wards (Table 4.20). Poisson regression modelling identified significant differences in intervention rates between the five wards ($p<0.001$). The highest rate of interventions was documented on the General Surgical Ward, followed by the General Medical Ward for Infants, the Haematology-Oncology Ward, the General Medical Ward for Adolescents, and the General Medical Ward for Young Children. There was no significant difference in the intervention rate between the general medical wards for Young Children and Adolescents. The rates of interventions were

significantly different across the employment level of the observed pharmacists ($p<0.01$). The PL2 pharmacists had the highest rates (8.13 interventions/100 medication orders, SD 6.93), followed by PL1 (8.04, SD 5.82) and PL3 (4.58, SD 3.82), respectively. No significant difference was observed in the rates of interventions between PL1 and PL2 pharmacists, but PL3 pharmacists were associated with significantly lower rates than PL1 ($p<0.05$) and PL2 pharmacists ($p<0.01$).

Table 4.20 Rates of pharmacists' interventions per 100 medication order reviews on the five study wards

Parameters	Infants (Ward A)	Young Children (Ward B)	Adolescents (Ward C)	Surgical (Ward D)	Haematology-Oncology (Ward E)
Mean±SD	7.83±6.84	4.38±4.17	4.77±3.07	10.48±6.59	5.63±3.36
95% Confidence interval for mean	5.48-10.18	2.95-5.81	3.71-5.82	8.28-12.68	4.48-6.78
Overall p-value	p<0.0001				

A = General Medical Ward for Infants, B = General Medical Ward for Young Children, C = General Medical Ward for Adolescents, D = General surgical Ward, E = Haematology-Oncology Ward

Pharmacists on average spent 49 minutes (SD 22.01) on ward rounds each day. Longer time spent on the ward was associated with a higher rate of interventions ($p<0.001$). Pharmacists spending more than 60 minutes on rounds made 8.09 interventions/100 medication orders (SD 6.00), while those spending 30 to 60 minutes and less than 30 minutes made 6.42 interventions/100 medication orders (SD 5.41) and 5.68 intervention/100 medication orders (SD 5.24), respectively.

Rates of pharmacists' active interventions per 100 medication orders are summarised in Table 4.21. The Haematology-Oncology Ward had the highest rate of active interventions, followed by the General Surgical Ward and the General Medical Ward for Adolescents. The general medical wards for Young Children and Infants had the lowest active intervention rates. The pair-wise differences of active intervention rates were not significantly different between the three general medical wards. The rate of active interventions on the Haematology-Oncology Ward was significantly different to those in general medical settings ($p<0.001$) but not the general surgical ward.

Rates of active interventions were not significantly associated with pharmacists' employment level ($p<0.4$). PL1 pharmacists had the highest rate of active

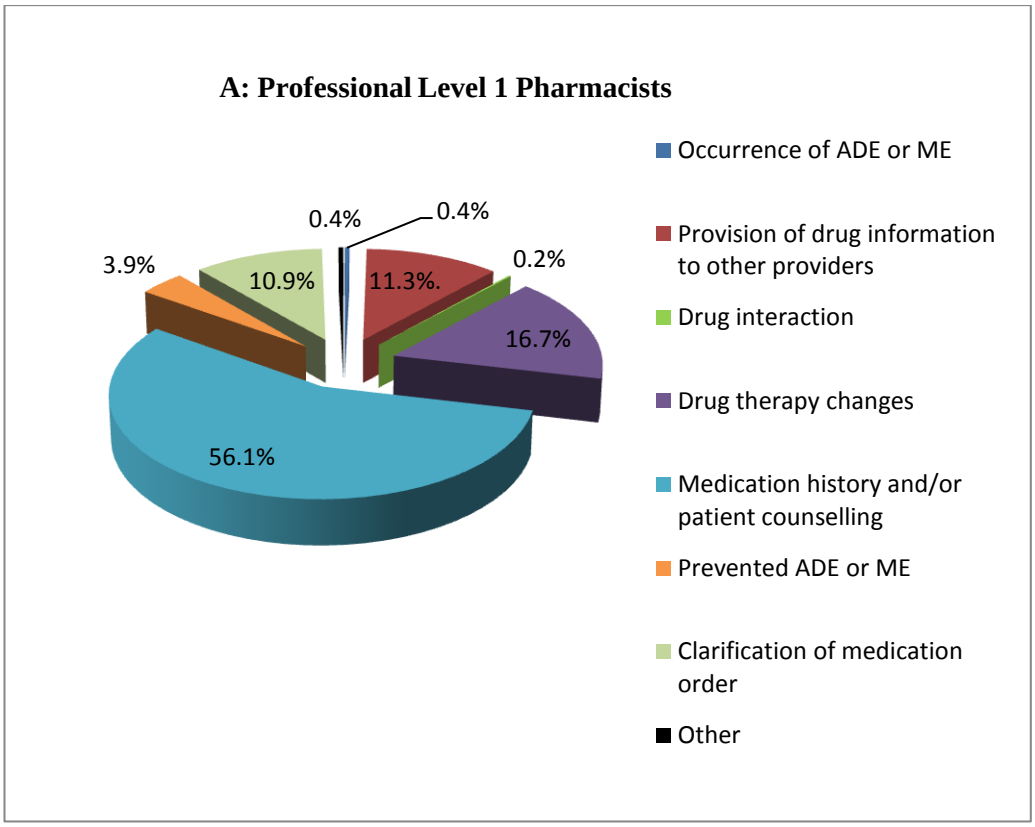
interventions (1.69 active interventions/100 medication orders, SD 1.99), followed by PL3 (1.43, SD 1.59) and PL2 (1.24, SD 1.38) pharmacists, respectively. The rates of active interventions were not significantly associated with the time spent on the ward ($p<0.2$).

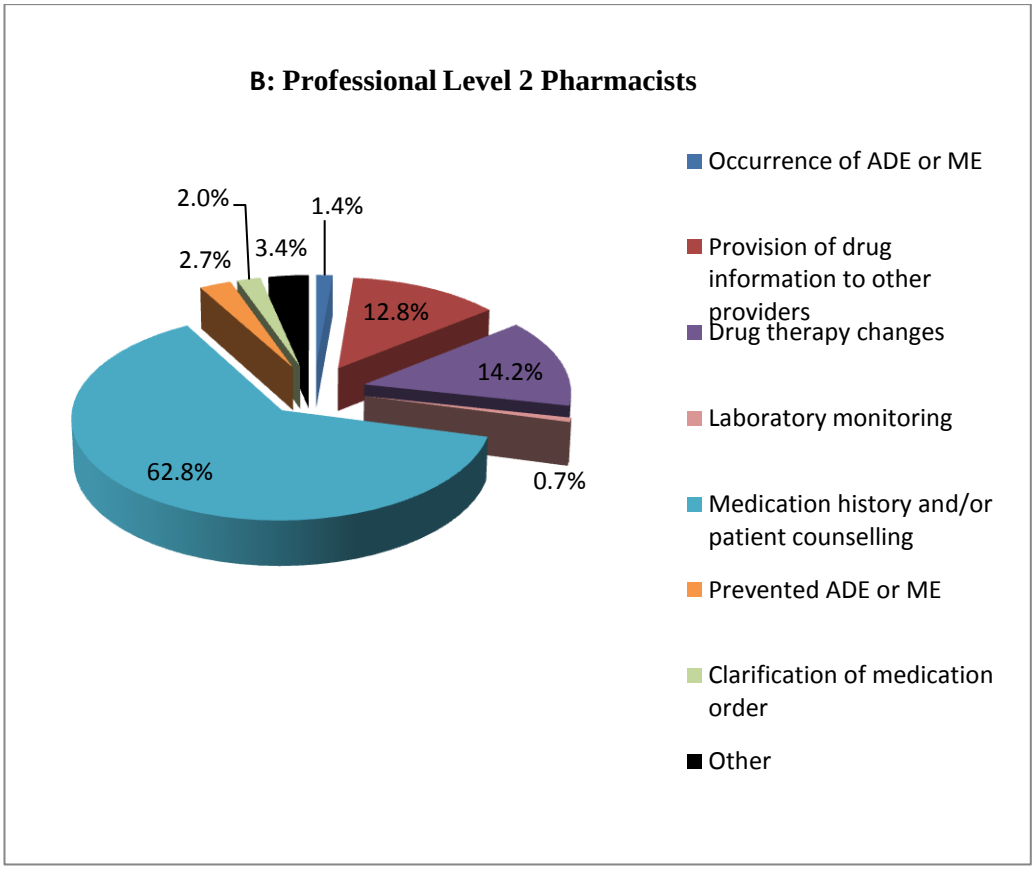
Table 4.21 Pharmacists' active interventions per 100 medication orders reviewed on the five study wards

Parameters	Infants (Ward A)	Young Children (Ward B)	Adolescents (Ward C)	Surgical (Ward D)	Haematology -Oncology (Ward E)
Mean±SD	0.85±1.35	0.81±1.24	1.15±1.19	2.34±2.23	2.43±1.84
95% Confidence interval for mean	0.39 – 1.31	0.38 – 1.23	0.74 – 1.55	1.60 – 3.09	1.79 – 3.06
Overall p-value	p<0.001				

A = General Medical Ward for Infants, B = General Medical Ward for Young Children, C = General Medical Ward for Adolescents, D = General surgical Ward, E = Haematology-Oncology Ward

The pattern of pharmacists' interventions across the five study wards based on the level of pharmacists' employment is detailed in Figure 4.7. The three most common interventions for pharmacists at all levels of employment were medication history and/or patient counselling, drug therapy changes and provision of drug information to other health professionals. However, PLI and PL2 pharmacists had a greater proportion of interventions related to taking medication history and/or patient counselling compared to PL3 pharmacists, but both had a lower proportion of drug therapy change-associated interventions.


A: Professional Level 1 Pharmacists
0.4%
0.4%
3.9%
10.9%
11.3%.
0.2%
16.7%
56.1%
Occurrence of ADE or ME
Provision of drug information to other providers
Drug interaction
Drug therapy changes
Medication history and/or patient counselling
Prevented ADE or ME
Clarification of medication order
Other


B: Professional Level 2 Pharmacists
2.0%
1.4%
2.7%
3.4%
12.8%
14.2%
62.8%
0.7%
Occurrence of ADE or ME
Provision of drug information to other providers
Drug therapy changes
Laboratory monitoring
Medication history and/or patient counselling
Prevented ADE or ME
Clarification of medication order
Other

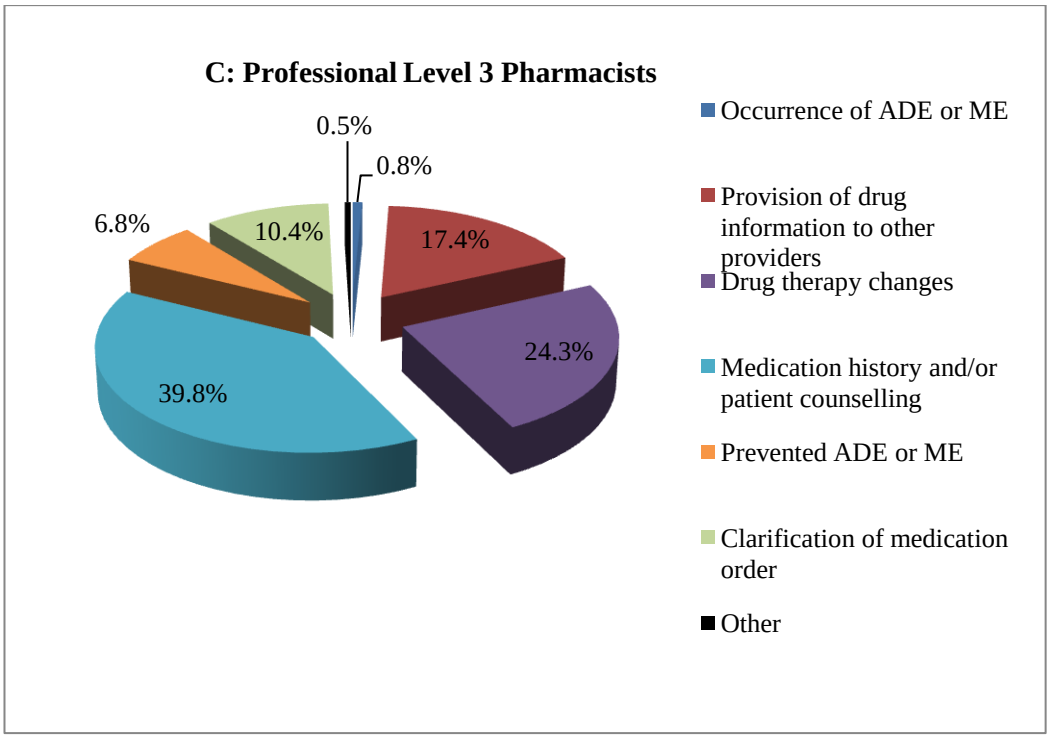


Figure 4.7 Types of pharmacists' interventions by pharmacists' level of employment across the five study wards

Active interventions constituted less than one-quarter of all interventions on the general medical and surgical wards, compared to 46.2% ($p<0.001$) on the Haematology-Oncology Ward. Table 4.22 shows the distribution of 244 active interventions by type. For all active interventions, acceptance by physicians was common, at around 90% (n=223/244), and ranged from 78.4% on the General Medical Ward for Adolescents to 97.8% on the Haematology-Oncology Ward ($p<0.05$).

Dose adjustment was the most frequent active intervention on the general medical and surgical wards. In the general medical wards, adjusting the dose accounted for more than half of all active interventions in the infant population. The majority of dose adjustments related to pharmacists' interventions to increase suboptimal doses of the correct medication. Other common sources of interventions were wrong/missing dosing interval, therapeutic duplication requiring deletion, wrong/missing dose form/strength, and untreated indication requiring regular medication. A different trend was found on the Haematology-Oncology Ward, where interventions to prescribe medications regularly constituted the most common active interventions (40.0%), followed by dose adjustment (26.7%); approximately two-

thirds of all the active interventions in this unit. Other common active interventions on the Haematology-Oncology Ward were related to improper dosage frequency/interval, drug deletion, and adjustment of treatment duration.

Table 4.22 Types of pharmacists' active interventions on the five study wards

Types of active interventions	No. of active interventions (%)				
	Ward A (n=16)	Ward B (n=28)	Ward C (n=51)	Ward D (n=59)	Ward E (n=90)
Wrong/missing dose	9 (56.3)	12 (42.9)	15 (29.4)	21 (35.6)	24 (26.7)
Wrong/missing dosage interval/frequency	2 (12.5)	7 (25.0)	9 (17.6)	7 (11.9)	6 (6.7)
Drug added	1 (6.3)	1 (3.6)	8 (15.7)	8 (13.6)	36 (40.0)
Drug deleted	1 (6.3)	4 (14.3)	10 (19.6)	6 (10.2)	5 (5.6)
Antibiotic change	0 (0.0)	0 (0.0)	2 (3.9)	2 (3.4)	0 (0.0)
Wrong/missing duration of therapy	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)	6 (6.7)
Wrong/missing dose form or strength	2 (12.5)	2 (7.1)	2 (3.9)	4 (6.8)	1 (1.1)
Wrong/missing route	0 (0.0)	0 (0.0)	2 (3.9)	0 (0.0)	0 (0.0)
Wrong drug	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)
Scheduling error	0 (0.0)	0 (0.0)	1 (1.9)	0 (0.0)	3 (3.3)
Non formulary to formulary change	0 (0.0)	0 (0.0)	0 (0.0)	3 (5.1)	0 (0.0)
Regular to if required or vice versa	0 (0.0)	0 (0.0)	1 (1.9)	6 (10.2)	3 (3.3)
Intravenous to per-oral change	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)
Wrong patient	1 (6.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Illegible order	0 (0.0)	1 (3.6)	0 (0.0)	1 (1.7)	0 (0.0)
Medication administration record error	0 (0.0)	0 (0.0)	1 (1.9)	0 (0.0)	4 (4.4)
Drug interaction	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)

A = General Medical Ward for Infants, B = General Medical Ward for Young Children, C = General Medical Ward for Adolescents, D = General surgical Ward, E = Haematology-Oncology Ward

Drug classes implicated in active interventions on the five study wards are presented in Table 4.23. Anti-infectives were most often associated with active interventions (n=100), followed by analgesics (n=46), gastrointestinal drugs (n=36), and immunomodulators/ antineoplastics (n=21).

Table 4.23 Drug classes associated with active pharmacists' interventions on the five study wards (n=244)

Drug classes	No. of active interventions (% medication orders*)				
	Ward A	**Ward B**	**Ward C**	**Ward D**	**Ward E**
Anti-infectives	3(24.2)	16 (38.5)	13 (20.8)	30 (41.4)	38 (41.1)
Analgesics	5 (16.7)	4 (9.2)	18 (29.2)	12 (27.7)	7 (5.9)
Gastrointestinal	3 (22.8)	1 (1.8)	4 (6.5)	9 (10.3)	19 (15.7)
Immunomodulators/ antineoplastics	0 (0.0)	0 (0.1)	2 (1.4)	1 (0.1)	18 (23.2)
Neurological	1 (4.6)	0 (6.4)	4 (5.4)	1 (4.6)	2 (2.2)
Respiratory	0 (4.5)	4 (11.9)	0 (4.2)	2 (4.0)	0 (0.4)
Endocrine	1 (4.6)	0 (4.6)	2 (4.8)	0 (0.7)	2 (1.6)
Blood, electrolytes	2 (10.6)	0 (9.2)	2 (6.5)	0 (1.1)	0 (4.9)
Cardiovascular	1 (4.6)	1 (6.4)	0 (0.9)	0 (0.6)	1 (2.8)
Psychotropic	0 (0.0)	0 (0.0)	1 (11.6)	1 (0.1)	1 (1.1)
Anaesthetics	0 (0.0)	1 (0.9)	1 (0.6)	0 (0.0)	0 (0.0)
Ear, nose, and throat	0 (0.0)	0 (3.7)	1 (3.3)	0 (4.1)	1 (0.5)
Ophthalmic	0 (0.0)	0 (2.8)	0 (0.0)	1 (2.2)	1 (0.5)
Obstetric, Gynaecological	0 (0.0)	0 (0.0)	2 (2.9)	0 (0.0)	0 (0.0)
Allergy and anaphylaxis	0 (1.5)	1 (1.9)	0 (1.2)	0 (0)	0 (0.0)
Genitourinary	0 (1.5)	0 (0.0)	0 (0.0)	1 (2.8)	0 (0.0)
Vaccines	0 (1.4)	0 (0.9)	1 (0.6)	0 (0.0)	0 (0.0)
Others	0 (0.0)	0 (0.1)	0 (2.4)	1 (0.1)	0 (0.0)

A = General Medical Ward for Infants, B = General Medical Ward for Young Children, C = General Medical Ward for Adolescents, D = General Surgical Ward, E = Haematology-Oncology Ward
*Percentage of medication orders for each class during the study period.

The top four drug classes accounted for the major classes of medications prescribed across all study wards. More than one-third of the anti-infectives related interventions took place on the Haematology-Oncology Ward, while 30% of the cases were from the General Surgical Ward. The percentages of active interventions associated with anti-infectives were similar in the general medical wards for Young Children and Adolescents, with the lowest percentage in the youngest patient cohort on the General Medical Ward for Infants. Antibacterials were the predominant anti-infectives involved in the interventions (92% of anti-infectives related active interventions), with the remainder involving antifungals. Antibacterials associated with anti-infective related interventions were trimethoprim-sulfamethoxazole (n=20), vancomycin (n=17), aminoglycosides (n=15), penicillins (n=13) and metronidazole (8). Dose adjustment (n=48) accounted for the most common interventions in relation to the use of anti-infectives, followed by drug addition (n=15) and dose interval/frequency adjustment (n=15).

Active interventions related to non-opioid analgesics were observed in general medical and surgical settings, while interventions related to opioid analgesics were predominant in the haematology-oncology setting. Almost 60% of analgesics-related interventions (n=27) occurred on general medical wards, predominantly involving adolescent patients, and more than one-quarter of the interventions were documented on the surgical ward (n=12). Drug deletion (n=11) was the most common active interventions associated with this class of medication. The next most common analgesics-related interventions were adjustment of dosage interval/frequency (n=10) and dose adjustment (n=9).

The third major drug class involved in active interventions involved the gastrointestinal system. More than half of the gastrointestinal medication related active interventions (n=19) were observed in the haematology-oncology setting. When categorised according to drug subclasses, antiemetics were involved in around 64% of interventions (n=23), while drugs for dyspepsia accounted for 22.2% of the interventions (n=8). Interventions to add medications accounted for the majority of active interventions related to gastrointestinal drugs (n=15), and almost three-quarters were related to suggestions to chart antiemetics for haematology-oncology patients. The second major active intervention category in relation to gastrointestinal drugs was to change the medications from regular to if required or vice versa (n=7). With regard to immunomodulators/antineoplastics, more than 80% of the interventions (n=18) were recorded on the Haematology-Oncology Ward. When categorised by subclasses of medications, immunosuppresants (n=15) accounted for approximately 71% of the interventions, with the remainder involving antineoplastics. Drug addition (n=12) was the most frequent intervention, accounting for more than half of all active interventions related to this drug class.

4.2 Direct Observation and Documentation of Pharmacists' Interventions in the Haematology-Oncology Pharmacy

The characteristics of patients in the Haematology-Oncology Unit admitted to the clinic (outpatients) or to the ward (inpatients) during the 33-day data-capture period (September 2011-August 2012) are summarised in Table 4.24. Patients ranged in age from newborn to 18 years, and more male patients were admitted than females. Just over half of the medications dispensed in the Haematology-Oncology Pharmacy were non-oral chemotherapy orders. The top five patients' cancer diagnoses are

outlined in Figure 4.8. Leukaemias and myeloproliferative diseases were the most frequent diagnoses seen in this specialty unit.

Table 4.24 Characteristics of patients in the Haematology-Oncology Unit

Patients' characteristics	Value
Total number of patients	1028
Source of patients - Inpatients - Outpatients	 430 (41.8%) 598 (58.2%)
Age in years, median (range)	6.25 (0.35-18.00)
Gender (%) - Male - Female	 635 (61.8%) 393 (38.2%)
Total no. of medication orders dispensed by pharmacists - Oral non-chemotherapy orders - Non-oral non-chemotherapy orders - Oral chemotherapy orders - Non-oral chemotherapy orders	1791 241 (13.5%) 367 (20.5%) 280 (15.6%) 903 (50.4%)

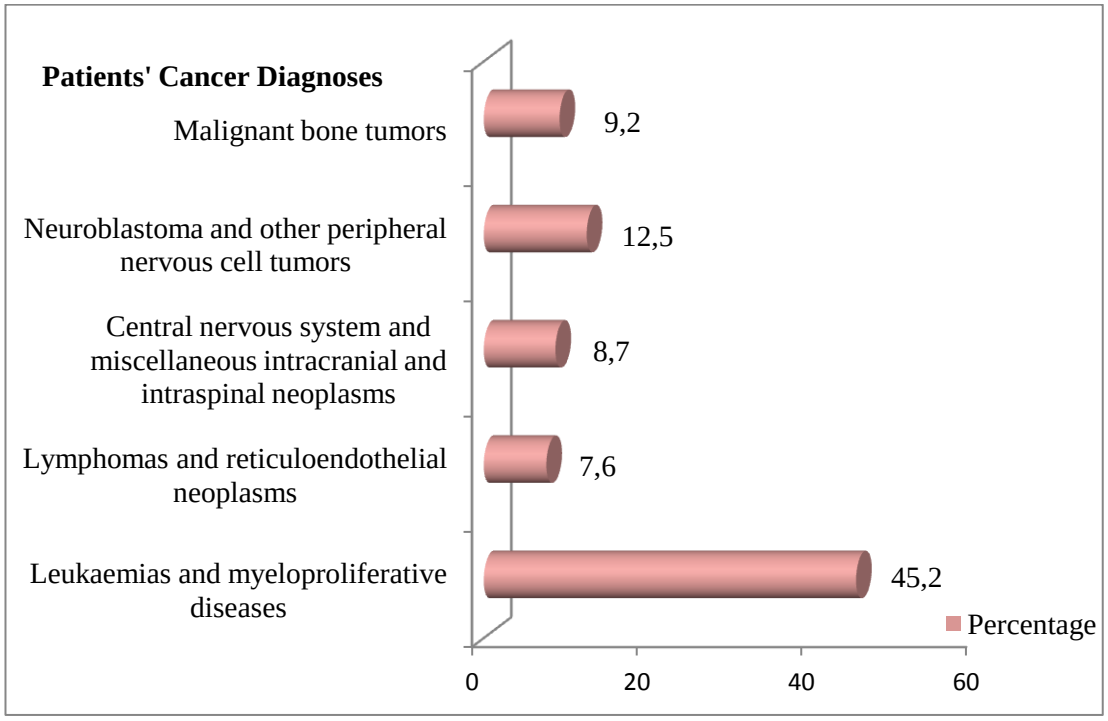


Figure 4.8 Top five cancer diagnoses (n=1028 patients) on the Haematology-Oncology Ward

Data on pharmacists' interventions (passive, active) and active interventions during the 33-day study period are shown in Tables 4.25 and 4.26, respectively. Pharmacists

made approximately eleven interventions per day and around 16% of patients received the interventions (Table 4.25). Less than 10% of pharmacists' interventions were classified as active interventions. Physicians accepted all of the active interventions (Table 4.26).

Table 4.25 Haematology-Oncology pharmacists' interventions (direct observation 33 days)

Parameters	Value
No. of patients	1028
No. of medication orders	1791
No. of PIs	359
Rate of PIs per 100 medication orders reviewed, mean ± SD	21.29 ± 9.95
Rate of PIs per 100 patients, mean ± SD	35.18 ± 17.53
Rate of PIs per day, mean ± SD	10.88 ± 4.73

PIs = pharmacists' interventions

Table 4.26 Haematology-Oncology pharmacists' active interventions (direct observation 33 days)

Parameters	Value
No. of active PIs (%)*	22 (6.1%)
Physician acceptance of active PIs (%) • Yes • No	 22 (100.0%) 0 (0.0%)
No. of medication orders	1791
No. of patients	1028
Rate of active PIs per 100 medication orders, mean ± SD	1.22 ± 1.91
Rate of active PIs per 100 patients, mean ± SD	2.20 ± 3.84
Rate of active PIs per day, mean ± SD	0.67 ± 1.08

*Percentage of active interventions of all pharmacists' interventions (passive and active).
PIs = pharmacist's interventions

Provision of drug information to other healthcare providers accounted for the majority of interventions (Figure 4.9).

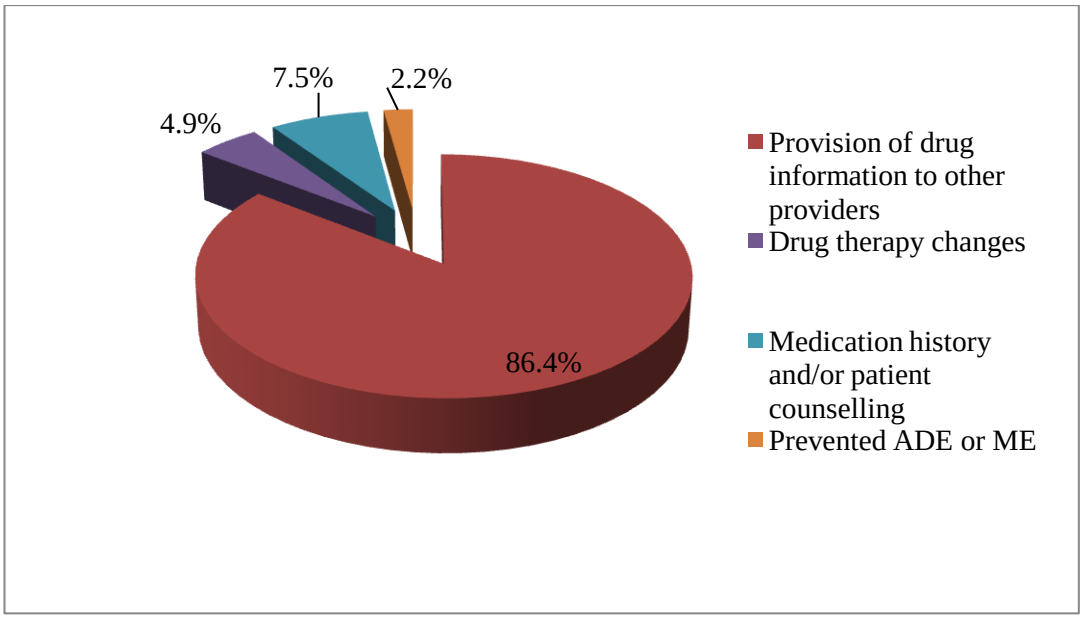


Figure 4.9 Classification of Haematology-Oncology pharmacists' interventions (n=359)

Consultations provided by pharmacists for drug information service constituted almost three-quarters of the interventions (Table 4.27). In relation to prevented ADE or ME, interventions for correcting the medication label were seen most frequently during dispensing in this specialty pharmacy.

Table 4.27 Categories of Haematology-Oncology pharmacists' interventions

Categories and subcategories of pharmacists' interventions	**No. of cases (%)**
Provision of drug information	310 (86.4)
- Consulted for drug information in-service	365 (73.8)
- Provided administration information	15 (4.2)
- Provided compatibility information	6 (1.7)
- Provided without consult	24 (6.7)
Medication history and/or patient counselling	27 (7.5)
- Discharge counselling	2 (0.6)
- Medication history and/or medication reconciliation	4 (1.1)
- Patient and/or parent education	21 (5.8)
Drug therapy changes	14 (3.9)
- Decreased dose	6 (1.7)
- Dose form change/strength change	1 (0.3)
- Drug added	6 (1.7)
- Increased dose	1 (0.3)
Prevented ADE or ME	8 (2.2)
- Incorrect label	6 (1.7)
- Scheduling error	1 (0.3)
- Wrong/missing frequency	1 (0.3)

ADE = adverse drug event, ME = medication error

Immunomodulators/antineoplastics accounted for the majority of medications associated with active interventions (n=18/22, 81.8%) followed by drugs for the gastrointestinal system (n=3) and anti-infectives (n=1).

With respect to immunomodulators/antineoplastics, antineoplastics predominated the active interventions, where these medications were responsible for more than three-quarters (n=14) of the interventions in this class and the remaining cases were due to drugs used with antineoplastics (n=2), non-cytotoxic antineoplastics (n=1) and immunosuppresants (n=1). Dosing adjustment (n=7) was the commonest intervention pertinent to the use of immunomodulators and antineoplastics, followed by incorrect label (n=6), drug addition (n=3), dose form change (n=1) and scheduling error (n=1). The second drug class involved in active interventions was drugs for the gastrointestinal system (n=3); antiemetics accounted for all interventions in this class. Interventions to add antiemetics for patients prior to/during treatment with emetogenic chemotherapy comprised all of the interventions in this class.

Triggers to initiate interventions during the dispensing process are listed in Table 4.28. The most common trigger was questions from other pharmacists, followed by questions from medical staff.

Table 4.28 Triggers for pharmacists' interventions (n=359) during dispensing

Trigger of interventions	No. of cases (%)
Other pharmacist inquiry	160 (44.6)
Doctor inquiry	83 (23.1)
Medication order review	62 (17.3)
Nurse inquiry	33 (9.2)
Patient and/ parent inquiry	13 (3.6)
Laboratory result	6 (1.7)
Ward meeting	2 (0.6)

4.3 Predictors of Physician-Accepted Pharmacists' Active Interventions

There were 244 pharmacists' active interventions identified during direct observation on the five study wards. According to Miles and Shevlin(195) a sample size of 200 with up to 20 predictors can identify a medium effect with a high level of power (i.e. 80%). The outcome of the interventions (accepted/not accepted) was used as the dependent variable for multivariate logistic regression analysis. The significant

predictors of the outcome were determined by independent variable selection, and model building and interaction testing.

4.3.1 Independent Variable Selection

The logistic regression analysis began with selection of independent variables (predictors). Based on literature research and the data collected during direct observation, the following 15 independent variables were selected for initial inclusion: patients' age and gender; study ward during hospitalisation; diagnosis on admission; length of stay; number of medications prescribed; therapeutic drug class; dose form; high-risk category of medication; type of active interventions; and pharmacists' gender, experience, academic qualification, work pattern (full-time/part-time) and term of employment (permanent post/temporary). A contingency table of the dependent variable (physician acceptance of pharmacists' active interventions) versus each independent variable was used to ensure that no cell had a zero cell count and that not fewer than 20% of the cells had a frequency count of less than five. Five independent variables did not meet these criteria: study ward, diagnosis on admission, therapeutic drug class, dose form and type of active interventions. For the purposes of this analysis, the variable 'study ward' was collapsed from five categories to three: general medicine, general surgery and haematology-oncology (Table 4.29).

Table 4.29 Contingency table of clinical units versus physicians' acceptance of pharmacists' active interventions

	Physician acceptance of pharmacists' active interventions		
Clinical units	**Yes, n (%)**	**No, n (%)**	**Total, n (%)**
General Medicine	81 (33.2)	14 (5.7)	95 (38.9)
General Surgery	50 (20.5)	9 (3.7)	59 (24.2)
Haematology-Oncology	88 (36.1)	2 (0.8)	90 (36.9)
Total	219 (89.8)	25 (10.2)	244 (100.0)

The variable 'diagnosis on admission' was collapsed from 21 to two categories: neoplasms and others (Table 4.30).

Table 4.30 Contingency table of diagnosis on admission versus physicians' acceptance of pharmacists' active interventions

Diagnosis on admission	Physician acceptance of pharmacists' active interventions		Total, n (%)
	Yes, n (%)	No, n (%)	
Neoplasms	91 (37.3)	1 (0.4)	92 (37.7)
Others	128 (52.5)	24 (9.8)	152 (62.3)
Total	219 (89.8)	25 (10.2)	244 (100.0)

The variable 'therapeutic drug class' involved in the active interventions was collapsed from 20 to three categories: anti-infectives, analgesics, and others (Table 4.31).

Table 4.31 Contingency table of therapeutic drug class versus physicians' acceptance of pharmacists' active interventions

Therapeutic drug class	Physician acceptance of pharmacists' active interventions		Total, n (%)
	Yes, n (%)	No, n (%)	
Anti-infectives	90 (36.9)	10 (4.1)	98 (41.0)
Analgesics	37 (15.2)	9 (3.7)	46 (18.9)
Others	92 (37.7)	6 (2.5)	100 (40.2)
Total	219 (89.8)	25 (10.2)	244 (100.0)

The 'dose form' variable was collapsed from three categories (oral, parenteral, others) to two categories (oral, non-oral) (Table 4.32).

Table 4.32 Contingency table of dose form of medication versus physicians' acceptance of pharmacists' active interventions

Dose form of medication	Physician acceptance of pharmacists' active interventions		Total, n (%)
	Yes, n (%)	No, n (%)	
Oral	140 (57.4)	17 (7.0)	157 (64.3)
Non-oral	79 (32.4)	8 (3.3)	87 (35.7)
Total	219 (89.8)	25 (10.2)	244 (100.0)

The variable 'type of active interventions' was collapsed from 17 (Table 4.21) to five categories: dose adjustment, drug addition, drug deletion, adjustment of dosage interval/frequency, and others (Table 4.33).

Table 4.33 Contingency table of type of active interventions versus physicians' acceptance of the active interventions

Type of intervention	Physician acceptance of pharmacists' active interventions		Total, n (%)
	Yes, n (%)	No, n (%)	
Dose adjustment	76 (31.1)	7 (2.9)	83 (34.0)
Drug addition	52 (21.3)	2 (0.8)	54 (22.0)
Drug deletion	17 (7.0)	5 (2.0)	22 (9.0)
Adjustment of dosage interval/frequency	28 (11.5)	4 (1.6)	32 (13.1)
Others	46 (18.9)	7 (2.9)	53 (21.7)
Total	219 (89.8)	25 (10.2)	244 (100.0)

Univariate logistic regression was undertaken for each independent variable (Table 4.34). All variables met the criteria for inclusion ($p<0.25$) except patients' gender, length of stay, number of medications prescribed, and dose form of medication. These four variables were not retained for the subsequent analysis.

Table 4.34 Univariate logistic regression coefficients of candidate variables

Variables	SE	P-value	OR	95% CI for OR	
				Lower	Upper
Patient age	0.041	0.027	0.913	0.842	0.990
Patient gender (1)	0.450	0.279	0.614	0.254	1.484
Clinical units		0.024			
- General medicine (1)	0.771	0.009	0.131	0.029	0.596
- General surgery (1)	0.802	0.010	0.126	0.026	0.608
- Haematology-Oncology (ref)					
- Diagnosis on admission (1)	1.030	0.006	0.059	0.008	0.441
Length of stay	0.009	0.733	0.997	0.980	1.015
No. of medications	0.046	0.622	0.977	0.893	1.070
Therapeutic class		0.057			
- Anti-infectives (ref)					
- Analgesics (1)	0.499	0.117	0.457	0.172	1.215
- Others (1)	0.537	0.321	1.704	0.594	4.883
High-risk medication (1)	0.425	0.085	2.080	0.904	4.783
Dose form (1)	0.451	0.687	1.199	0.495	2.904
Type of active intervention		.173			
- Dose adjustment (1)	0.566	0.375	1.652	0.545	5.012
- Drug addition (1)	0.827	0.096	3.957	0.782	20.008
- Drug deletion (1)	0.651	0.311	0.517	0.145	1.852
- Adjustment of dose interval/frequency (1)	0.671	0.925	1.065	0.286	3.969
- Others (ref)					
Pharmacist gender (1)	1.035	0.105	5.363	0.705	40.816
Pharmacist experience	0.032	0.058	1.062	0.998	1.130
Pharmacist qualification (1)	0.636	0.194	2.283	0.657	7.936
Pharmacist work pattern (1)	0.752	0.031	0.197	0.045	0.861
Pharmacist work post (1)	0.631	0.009	5.214	1.515	17.941

Variables were coded as follows: variables with two items, the categories of interest were coded as 1; gender (1) for male, diagnosis on admission (1) for others, high-risk medication (1) for non-high-risk, dose form (1) for non-oral, pharmacists' gender (1) for male, pharmacists' qualification (1) for undergraduate with postgraduate as reference, pharmacists' work pattern (1) for full-time, pharmacists' work post (1) for permanent post.

For variables with more than two categorical variables, the category (ref) was set as reference group, and category (1) indicated the group of interest.

SE = standard error, OR = odds ratio, 95% CI for OR = 95% confidence interval for odds ratio.

4.3.2 Model Building and Interaction Test

All variables selected from the univariate logistic regression were included for testing in multivariate logistic regression Model 1. The regression analysis used the backward likelihood ratio (LR) method using SPSS version 22. Some variables

demonstrated extremely large odds ratios and standard errors, namely clinical units, diagnosis on admission, pharmacists' gender, pharmacists' work pattern, and pharmacists' post (Table 4.35). The regression analysis failed to reach conclusion to calculate odds ratios after maximum iterations (20 iterations) had been reached, shown by the odds ratios of offending variables of zero. This situation indicated that a problem existed presumably due to the model overfitting with small samples or combination of discrete variables with few cases in one outcome. The offending variables of pharmacists' gender, work pattern, and post were dichotomous variables. Collapsing the categories of these variables was not possible, so the variables were removed. With regard to variables of clinical unit and diagnosis on admission, the categories were modified as per Tables 4.29 and 4.30 in order to identify whether the specialty haematology-oncology unit and patients with complicated conditions (e.g. cancer) had an impact on the acceptance of the active interventions. Therefore, both variables were deleted, leaving six independent variables for testing in logistic regression Model 2 (Table 4.36).

Table 4.35 Multivariate logistic regression coefficients of variables in Model 1

Variables	SE	p-value	OR	95% CI for OR	
				Lower	Upper
Patients' age	0.050	0.031	0.899	0.816	0.991
Clinical units		0.841			
-General medicine (1)	14.933	0.762	92.370	0.000	4.753E+14
-General surgery (1)	14.947	0.764	126.872	0.000	6.705E+14
Diagnosis on admission (1)	2.751	0.002	0.000	0.000	0.048
Therapeutic class		0.077			
-Analgesics (1)	0.608	0.034	0.275	0.084	0.907
-Others (1)	0.656	0.807	0.852	0.236	3.081
High-risk/non high-risk (1)	0.532	0.035	3.075	1.085	8.720
Type of active intervention		0.514			
-Dose adjustment (1)	0.721	0.377	1.893	0.460	7.782
-Drug addition (1)	0.993	0.687	1.493	0.213	10.461
-Drug deletion (1)	0.797	0.288	0.429	0.090	2.046
-Adjustment of dosage interval/frequency (1)	0.797	0.931	0.934	0.196	4.453
Pharmacist gender (1)	3.321	0.002	35.425E+3	52.773	237.799E+5
Pharmacist experience	0.171	0.010	0.645	0.462	0.902
Pharmacists' qualification (1)	0.701	0.387	1.834	0.464	7.251
Pharmacis pattern (1)	37.186E+3	1.000	0.676	0.000	-
Pharmacist post (1)	49.375E+2	.998	0.000	0.000	-

Variables were coded as follows: variables with two items, the categories of interest were coded as 1; diagnosis on admission (1) for others, high-risk medication (1) for non-high-risk, pharmacists' gender (1) for male, pharmacists' qualification (1) for undergraduate with postgraduate as reference, pharmacists' work pattern (1) for full-time, pharmacists' work post (1) for permanent post.

For variables with more than two categorical variables, the category (ref) was set as reference group, and category (1) indicated the group of interest; clinical units (ref) for haematology-oncology, therapeutic class of medication (ref) for anti-infectives, type of active intervention (ref) for others.

SE = standard error, OR = odds ratio, 95% CI for OR = 95% confidence interval for odds ratio.

Table 4.36 Multivariate logistic regression Model 2 with significant independent variables (predictors)

Variables	SE	p-value	OR	95% CI for OR	
				Lower	Upper
Patient age	0.048	0.018	0.893	0.813	0.981
Medication		0.032			
- Non high-risk	0.480		2.801	1.094	7.169
- High-risk			1 (ref)		
Pharmacist experience	0.038	0.005	1.114	1.033	1.200
Constant	0.764	0.318	2.145		

SE = standard error, OR = odds ratio, 95% CI for OR = 95% confidence interval for odds ratio. R^2 = 0.103 (Cox & Snell), 0.214 (Nagelkerke).

Testing of Model 2 revealed that three variables significantly predicted the physician-accepted pharmacists' active interventions: patients' age, high-risk medication and pharmacists' experience. Removing these variables produced a significant difference in the log likelihood value and would have a significant effect on the predictive ability of the model. A test of the full model with all three predictors against a constant-only model was statistically significant, $\chi 2$ (3, N=244) = 26.6, p=0.002, indicating that the predictors, as a set, significantly distinguished between accepted and non-accepted pharmacists' active interventions by physicians. The classification was impressive, with 99.5% of the accepted and 4.0% of the non-accepted interventions correctly predicted for an overall success rate of 89.8% (Table 4.37). This demonstrated that the overall predicted percentage of the physician-acceptance of pharmacists' active intervention was 90.2% accurate.

The interaction test was run for these three variables, resulting in three pairs of possible interaction variables. Multivariate logistic regression was conducted to identify significant interaction variables. The regression was performed by testing one interaction variable at a time along with those three significant independent variables from Model 2. The significance levels of all possible interaction variables are detailed in Table 4.38.

Table 4.37 Classification table of logistic regression Model 2

Observed physician acceptance of pharmacists' active interventions		**Predicted physician acceptance of pharmacists' active interventions***		
		Degree of acceptance		**Percentage correct**
Degree of acceptance		Yes	No	
	Yes	218	1	99.5
	No	24	1	4.0
Overall percentage				89.8

*Probability of physician acceptance of pharmacists' active interventions ranges from 0 to 1. Cut-off value is 0.500.

Table 4.38 Significance levels of interaction variables

Interaction variables	**p-value**	**Note**
Patient age - high risk medication	0.580	Excluded
Patient age - pharmacist experience	0.417	Excluded
High risk medication - pharmacist experience	0.903	Excluded

There were no significant interactions identified between variables (Table 4.38). Therefore, logistic regression Model 2 with three predictors (Table 4.36) is presented as the final model.

The final model revealed that patients' age significantly predicted the physicians' acceptance of active interventions. The odds ratio for patients' age when holding all other variables constant, for a one-year increment of patients' age, corresponded with a decrease in acceptance of the intervention of 0.893. Inverting the odds ratio revealed that for every one year of decreasing age, the odds of the intervention being accepted was 1.1 times higher. In addition, the medication category (high-risk versus non-high-risk) significantly predicted physician acceptance of active interventions, with the interventions involving non-high-risk medications being nearly three times more likely to be accepted by the physician than those associated with high-risk medications. The results also uncovered that for every extra year of experience of pharmacists, the acceptance by physicians increased (odds ratio 1.114).

4.4 Discussion

4.4.1 Direct Observation and Documentation of Ward Pharmacists' Interventions

The prevalence of pharmacists' interventions per 100 medication orders in this study ranged from 4.38 to 7.83 on the General Medical Wards to 10.48 on the General Surgical Ward, and 5.63 on the Haematology-Oncology Ward. The intervention rate on the General Surgical Ward was the highest compared to the other two clinical units ($p<0.05$), although the surgical unit is considered less complex pharmacologically than general medical, intensive care or specialty areas.(196) A self-reported study by Chan *et al.*(94) involving paediatric general and specialty inpatients uncovered a similar rate of active intervention (0.75 interventions per 100 medication orders) as those documented on the general medical wards for Infants and Young Children in our study. However, in comparison to the rates recorded in general settings in our study, a higher active intervention rate (2.4/100 medication orders) was reported from a study assessing the impact of interventions performed by clinical pharmacists in reducing prescribing errors in children hospitalised in a maternity and children's hospital in Spain.(197) The rate of active interventions on the Haematology-Oncology Ward in our study was similar to the Spanish study. The Spanish study did not provide further information on the nature of patients' medical

conditions; presumably, active intervention rates are influenced by the complexity of patients' medication regimens. This may account for the higher incidence of active interventions among haematology-oncology patients compared to patients in other settings who may have less complex conditions requiring less medication.

Besides the number of medications prescribed, other factors need to be considered as predictors for pharmacists' intervention rates. A study in ICUs involving children and adults found that the rate of interventions was significantly higher in patients with long hospital stay.(146) However, in our study lower intervention rates were observed in the general medical wards for Young Children and Adolescents where patients stayed longer than in other wards. Consistent with our study, a large pharmacists' interventions study in the UK, which included paediatric and adult patients, found the time spent during ward round significantly predicted the rates of the interventions.(127)

With respect to the pattern of pharmacists' interventions, activities related to taking medication histories and/or patient counselling were the most frequent interventions in general wards, while drug therapy changes were responsible for the most frequent interventions in the haematology-oncology ward. The subcategories of taking medication histories and medication reconciliation activities constituted the most common interventions performed by clinical pharmacists on general wards. This is not surprising, as taking medication history and medication reconciliation are the initial steps in reviewing patients and assessing the appropriateness of their medications orders. Medication reconciliation and medication history have been justified as effective strategies to reduce MEs in children and adults.(139, 144, 198) However, these activities occurred less frequently on the Haematology-Oncology Ward than the general medical wards. The lower percentage might be explained by the availability, completeness and the ease of access to patients' medical and medication history on this specialty ward. As the haematology and oncology patients were admitted regularly to hospital for treatment and monitoring, the healthcare providers (including pharmacists) were apparently familiar with the patients and their treatment protocols, so the pharmacists often examined the patients' records instead of interviewing the patients and/or the parents.

The reduced incidence of this type of intervention on the general medical wards with patients' increasing age may have been due to a delay between the patients' admission and day of clinical pharmacist observation on the adolescent ward compared to the wards catering for younger children. Drug therapy change-associated interventions on the general medical wards increased with the patients' age. The larger number of medications prescribed for older children might have attributed to the higher incidence of this type of intervention in adolescent patients as compared to their younger counterparts. A paediatric study documenting pharmacists' interventions associated with electronic prescription review found the youngest patients (under 2 years old) were associated with more interventions than older children.(199)

There are limited published studies on pharmacists' interventions in different paediatric settings than adult patients. Condren *et al.*(184) conducted a study in a paediatric population including general and intensive care inpatients, and ambulatory patients. They reported interventions performed by an academic paediatric pharmacy team including pharmacy students, using similar intervention categories to the present study. There were 4605 interventions performed for 3978 patients in a year. The study reported 1.15 interventions per patient, the most frequent intervention categories being drug therapy change, medication history and/or patient counselling, and providing drug information to other health professionals.(184) Under the drug therapy change category, drug addition and drug deletion accounted for the most common recommendations. Our study uncovered a different pattern of recommendations; dose adjustment, drug addition and adjustment of dosage interval/ frequency accounted for the majority of recommendations. The most common category of active intervention found by Condren *et al.*(184) was consistent with the pattern of active interventions in the haematology-oncology unit in our study.

A Dutch study conducted in a range of settings, including the haematology unit in a paediatric hospital, implementing electronic prescribing, revealed that pharmacists performed 1557 interventions for 138,449 prescriptions (1.1%) over 46 months.(15) This study reported that interventions leading to drug changes were most frequently performed in the haematology unit (31.1%), similar to our study (90/244, 36.8%). In keeping with our study, that study also found dosing adjustment was the most

frequent intervention, and antibacterials were the most commonly implicated medications.(199)

In a four-week study in 16 paediatric wards (nine specialist, seven general) in the UK, interventions to resolve improper dosing, incomplete prescriptions and wrong frequency were the most common interventions by pharmacists.(200) Dosing issues were also identified as the main concern requiring pharmacist intervention in hospitalised children in a Spanish study.(197) Likewise, a retrospective analysis of four-year self-reported pharmacists' interventions conducted by Chan *et al.*(94) involving paediatric patients in general and specialty areas (including haematology-oncology) also detected dosing issues as the major source of problems. Studies incorporating general and specialty settings have consistently shown that dosing-associated issues were the main problem in paediatric patients.(94, 184, 197, 199, 200) However, those studies did not provide further information on the breakdown of interventions, as intervention data are generally aggregated for the purpose of analysis rather than presented by clinical setting. Accordingly, the pattern and rate of interventions among different settings, in particular general versus specialty settings, in the child patient populations cannot be compared and analysed comprehensively.

Maat *et al.*(199) report in a study associated with electronic prescription review that interventions were most frequently conducted in the specialty units of immunology/haematology and neurology compared to other units such as internal medicine. Kaushal *et al.*(201) in their study of serious MEs before and after the introduction of unit-based clinical pharmacists in three units (ICU, general surgery, general medicine) in an American paediatric hospital reported that clinical pharmacists' interventions substantially decreased the rate of MEs in the ICU, while there was no reduction in the general settings. The investigators pointed out that the setting influenced the rates of ME-intercepting interventions by pharmacists, in particular, between general and non-general settings such as ICU.(201)

When involving adult patients, a large study of pharmacists' interventions in the UK involving a range of settings in 27 acute care hospitals also found dosing-associated interventions as the major type of intervention, and highlighted that ward type was significantly associated with the rate of pharmacists' interventions ($p<0.001$). The highest intervention rates were reported from ICU wards, followed by paediatrics

and special wards (e.g. haematology, oncology, organ transplant, AIDS), and other type of wards (e.g. medical, surgical, geriatrics, psychiatric and obstetrics).(127)

A multicentre study of ward pharmacists' interventions in six French hospitals documented an intervention rate of 4.66 interventions per 100 medication orders in a range of practice settings, with dose adjustment the most common intervention type.(202) Details of interventions in each setting from the British and French studies are lacking, and it is unclear whether the inclusion of adult patients influenced the pattern of interventions. When comparing the interventions among specialist areas, a prospective study involving seven specialties (three ICUs, cardiosurgery, haematology, nephrology and psychiatry) in an Austrian hospital uncovered provision of information to other healthcare providers as the most common intervention type. However, it appears that there was no comparable pattern when evaluating the next most frequent intervention types among the specialties.(203)

With respect to medications implicated in the active interventions, it is understandable that larger numbers of interventions were documented from antibiotics and analgesics, as these medications accounted for the major drug classes prescribed.(199) The majority of medications implicated in the active interventions were used for treating acute medical conditions with the exception of immunomodulators and antineoplastics on the Haematology-Oncology Ward.

The acceptance rate of pharmacists' active interventions was high across all settings in our study. This acceptance rate is similar to those found in other paediatric studies.(197, 199, 204, 205) This strengthens the established evidence supporting the confidence of other healthcare providers in the significant contribution of pharmacists to improve the quality of patient paediatric.(17, 184, 201, 206)

To the best of our knowledge, this is the first study that compared pharmacists' interventions in a range of settings in paediatrics in terms of frequency, type, degree of acceptance and medications implicated. Most of the early studies on pharmacists' interventions were conducted using self-report by pharmacists. Self-report has been associated with bias and underestimation of the intervention rates due to time constraints and omission of interventions that the pharmacists regarded as insignificant or non-favourable.(207) The prospective observational approach used in

the current study allowed the observer to obtain actual number of interventions performed by the ward pharmacists to overcome aforementioned issues with self-reporting.(183, 208)

4.4.2 Direct Observation and Documentation of Pharmacists' Interventions during Dispensing in a Haematology-Oncology Pharmacy

During the data collection period, pharmacists' interventions rates documented during dispensing in the Haematology-Oncology Pharmacy were 21.29 per 100 medication orders and 35.18 per 100 patients. Based on these data, pharmacists undertook approximately 11 interventions each weekday. Provision of drug information to physicians, nurses and other pharmacists (86.4%) constituted the majority of the interventions followed by medication histories and/or patient counselling, drug therapy changes, and prevented ADE and ME. More than three-quarters of the interventions in our study related to chemotherapy medications. Waddell *et al.*(206) also analysed the interventions performed by oncology pharmacy staff within inpatient and outpatient settings. During that study, pharmacists self-documented 503 interventions over eight months, which meant that pharmacy staff performed around two interventions each day, a much lower rate than our study. Corresponding well with our study, the majority of the interventions documented were the provision of drug information/consultation to other healthcare providers.

An intervention study by Wong *et al.*(209) in haematology-oncology clinics in Virginia, providing ambulatory cancer services for adults and children, demonstrated lower numbers of interventions per day, half as many as our study. Wong *et al.*(209) found patient counselling and therapeutic recommendations (i.e. cessation of drugs without clear indications, dose recommendation, drug selection) as the leading categories of interventions. While our study revealed that more than 80% of interventions were non-chemotherapy related. The disparate rate and pattern of the interventions between the two studies may be explained by the complexity of the disease states of the patients in the study by Wong *et al.*(209), given that the studies did not specifically focus on paediatric oncology patients.

By contrast, a retrospective study by Ruder *et al.*(208) analysed interventions by oncology pharmacists over two years in an ambulatory oncology clinic for adults

reported a higher rate of interventions than our study. Ruder *et al*.(208) demonstrated 583 clinical intervention for 199 patients, with approximately three interventions performed for each patient, and the most frequent interventions related to patient education. A similar pattern relating to intervention type has been found in American and Jordanian studies involving adult(28) and paediatric patients with cancer.(29) Both studies reported patient counselling as the most common intervention, accounting for more than one-quarter of all interventions.

With regard to interventions leading to changes to patient medication management (active interventions), our study documented 22 active interventions (6.1% of total interventions), with rates of 1.2 per 100 medication orders and 2.1 per 100 patients. Our finding is consistent with studies undertaken in general patient settings, demonstrating rates of active interventions per 100 medication orders from 0.7% to 8.5%.(18, 94, 126, 197, 210) In relation to haematology-oncology intervention studies, Shah *et al.*(211) retrospectively analysed clinical pharmacy activities in a haematology-oncology outpatient practice. Pharmacists documented their clinical activities into personal digital assistants. During the 12-month study, 308 drug-specific interventions were performed for 423 patients (0.73 interventions for each outpatient). This is a much higher intervention rate than our study. Their study reported that supportive care issues were responsible for half of the interventions, predominantly for anaemia, pain, constipation/diarrhoea and nausea/vomiting. Their top three interventions were drug addition, drug discontinuation and dose adjustment. The pattern of interventions was similar to our findings, where the predominant active interventions resulted in interventions to add medications and adjust the dose (in particular, reduce the dose) of medications.(211)

All active interventions during dispensing in the Haematology-Oncology Pharmacy were accepted by doctors, nurses or other pharmacists. High rates of acceptance of pharmacists' interventions in this high-risk area have also been reported in other studies.(206, 208, 209, 212) The high acceptance rate is a positive indicator that pharmacists are well accepted and considered reliable sources of information by other healthcare providers.

4.4.3 Predictors of Physician-Accepted Pharmacists' Active Interventions

This study included an analysis of determinants of physicians' acceptance of pharmacists' active interventions. Pharmacists' recommendations are meaningless if there is no acknowledgement and uptake by physicians. Some studies have reported that acceptance of the interventions strongly predicted the desired clinical outcome.(204, 213-215) It is essential to identify the determinants or factors affecting the acceptance of pharmacists' interventions. Physicians' acceptance of interventions may be influenced by factors such as patients' characteristics (age, co-medications), type of interventions, physicians' characteristics (specialty, perception on the importance of the intervention), level of interaction between pharmacists and physicians and the clinical setting.(216-218) However, this has not, as yet, been validated, and well-designed studies are required for justification.

This appears to be the first study to determine the factors that impact on physicians' acceptance of the interventions across different clinical settings (general medicine, general surgery, haematology-oncology) in a paediatric hospital using multivariate modelling. The multivariate approach benefited this study, as the data comprised multiple observations for each pharmacist. Pharmacists subjected to more observations were represented in the data to a greater degree than those with fewer observations. Multivariate analysis can eliminate misleading confounding factors from univariate analysis by accounting for all independent variables concurrently and different number of observations from each variables.(127, 219) In the present study, three factors significantly and positively predicted intervention acceptance by physicians: patients' younger age, non-high-risk medications and pharmacists' experience. Experienced pharmacists are more likely to make confident and strong evidence-based interventions given their longstanding professional experience and knowledge to convince precribers.(127) Patient's age and pharmacists' years of experience were not strong predictors. While interventions related to non-high-risk medications were three times more likely to be accepted than interventions associated with high-risk medications.

Little is known about the factors that influence prescribers to accept or decline pharmacists' recommendations particularly in paediatrics.(199) Comparison of the results of the present study with similar studies is challenging for several reasons,

such as the differences in study settings, methods and the predictors evaluated. Consistent with our study, a study examining the determinants of pharmacists' interventions in electronic prescriptions in a paediatric hospital in the Netherlands reported patients' age as a determinant of the interventions. Younger patients were significanly more likely to receive interventions than older patients. Other significant determinants associated with an increased rate of interventions were electronic prescriptions (without clinical decision support) and oral dose forms.(199) However, that study focussed on factors associated with interventions rather than the acceptance of the interventions. A study in Denmark undertaken in an ED for adults revealed that physicians accepted 59% of pharmacists' recommendations. The Danish study uncovered the determinants of accepted recommendations as patients admitted with medical problems (more frequently than surgical patients) and the recommendation category of 'untreated indication'.(216) However, another study conducted in the UK demonstrated no difference in the acceptance rate between physicians working in medical and surgical wards.(127) Consistent with the UK study, the present research determined lack of association between the clinical setting and acceptance of the intervention.

Multivariate analysis from a palliative care study revealed that none of the variables assessed (patient and pharmacist characteristics, type of intervention) were associated with physicians' decisions to accept or decline pharmacists' interventions.(220) A study of 27 hospitals in the UK assessed the factors predicting the rate of physician acceptance of interventions by pharmacists using a mixed-model Poisson regression technique. That study identified three significant predictors: ward type, pharmacist grade and time spent on the ward. The ICU and specialty wards, including paediatrics, were associated with a higher acceptance rate than other wards. In addition, pharmacists employed at grade C and above (specialist pharmacists and pharmacy managers) and more time spent on the ward predicted the increased acceptance rate.(127) Consistent with our study, the British study did not find significant contribution from other pharmacists' characteristics (academic qualification, work pattern, post). Nonetheless, the univariate approach in the UK study showed that interventions by more experienced pharmacists had a lower acceptance rate in comparison to the less experienced ones, which was not confirmed by our study, although this predictor failed to contribute in the final model.

A different result was also reported in a Swiss study analysing the factors impacting on neurologist acceptance of pharmacists' interventions in collaboration with clinical pharmacologists when addressing the DRPs detected in a university hospital neurology unit.(42) That study evaluated four factors: type of prescription, type of DRP, cause of DRP and type of intervention, without taking into account the factors related to patients and intervening pharmacists. The authors reported that prescribing a regular medication (instead of 'as required' medications) was the sole determinant of acceptance of interventions.(221)

A community-based study using written communication by fax to convey pharmacists' interventions to the prescribers demonstrated a higher acceptance rate with cost-saving implications, compared to interventions for compliance with guidelines directed to primary care physicians compared to those directed to specialists.(222)

Our study and a study by Barber *et al.*(127) did not observe a significant effect of pharmacists' academic qualification as a factor in acceptance of interventions. It is premature to conclude that this factor has no effect, and that additional education is not effective. Barber *et al.*(127) presumed that pharmacists without postgraduate qualification tend to be assigned to wards for younger patients who are therapeutically less complex. The impact of pharmacists' academic qualification should be evaluated further by conducting controlled studies.

4.5 Limitations and Recommendations

A number of limitations need to be acknowledged in this direct observational study. The rate of interventions directly observed during ward rounds may have been underestimated and the pattern of the interventions might not be reflective of broader practice, as the principal researcher only documented the interventions performed by clinical ward pharmacists during their ward rounds. Additional interventions may have been performed by telephone or pager at other times. This study mainly documented interventions associated with drug prescribing and monitoring. As ward pharmacists have limited time to undertake their rounds on each ward they do not check the medications prior to their administration to each patient. Data were collected on non-consecutive days to avoid pharmacist observation fatigue, which may have influenced the pattern of the interventions. Future studies might consider

employing a combination of intervention documentation methods over a period of time, i.e. direct observation and self-reporting.

This study was conducted in one paediatric hospital, which diminishes the ability to generalise the findings. It is recommended future studies involve multiple paediatric institutions, i.e. other paediatric hospitals and/or paediatric wards in general hospitals. Also of note are difficulties in drawing accurate comparison with other intervention studies due to variations in settings, design, duration, size, method and definitions of intervention used.

Although the results of this study are informative with respect to the analysis of predictors of physician-accepted active interventions, there are several limitations. Firstly, in line with the existing literature assessing the factors affecting physician acceptance of pharmacists'interventions, this study did not include the physicians' characteristics as predictors.(127, 199, 220, 221) It was not feasible for a non-staff researcher to collect these data. The theory of physicians' reactance, highlighted by De Almeida Neto *et al.*(223) might clarify physicians' psychological disposition during decision making about recommendations proposed by pharmacists. Reactance is: 'a reaction to a recommendation to take a certain course of action which is affected by a motivational state compelling a response in which freedom of choice is maintained'.(223) The perceptions of physicians on those recommendations addressing the significant clinical relevance issues are likely to affect reactance. It has also been suggested that pharmacists frame their recommendation with options from which physicians can choose. In this way, the physicians still hold their sense of freedom of choice.(223, 224)

Secondly, evaluating the association between acceptance of the recommendations and impact on patient outcome was beyond the scope of the present study. It would be interesting to explore this issue in future studies, in order to evaluate pharmacists' recommendations to patient care. Previous studies have shown that implementation of accepted recommendations contributed to improved patients' clinical outcome.(146, 204, 214, 215, 220)

Thirdly, other factors (predictors) were not associated with significant contributions to the accepted interventions in the final model, even though they were demonstrated

as significant predictors during univariate analysis. This may be due to the sample size having insufficient power to detect the effects related to those predictors. Thus, escalating the sample size in future research may increase the likelihood of detecting other influential predictors. A follow-up study to assess the pharmacists' attitudes toward interventions is warranted, as some pharmacists may intervene only on major issues, while others may do so for any issue. Regardless of these limitations, this study presents important findings to improve our understanding of the determinants influencing physicians' acceptance of pharmacists' active interventions in a range of paediatric settings.

4.6 Conclusion

Pharmacists can optimise patient care in a range of paediatric settings through their active interventions either during pharmacy rounds or dispensing. The rate and nature of pharmacists' interventions appear to be influenced by the clinical setting. Specialty units, such as the haematology-oncology, had a higher active intervention rate where most interventions were related to drug therapy changes compared to the general medical and surgical units. The interventions are of value if acknowledged, accepted and implemented by physicians. This study found that interventions were more likely to be accepted by physicians for younger patients, non-high-risk medications, and those raised by more experienced pharmacists.

Chapter 5

PART TWO: RESULTS AND DISCUSSION

5.1 Clinical Significance of Pharmacists' Active Interventions

The most common significance rating following the first review of the interventions undertaken in March-June 2013 was 'moderate' (Table 5.1). The strength of agreement between all reviewers (α=0.265, 95%CI 0.125-0.400) was 'fair', and marginally stronger when the significance categories were collapsed into 'significant' versus 'not significant' (α=0.394, 95%CI 0.022-0.694).

Table 5.1 Panel 1: Clinical significance of pharmacists' active interventions (n=42)

Clinical significance	Frequency, n (%)			
	Reviewer 1	Reviewer 2	Reviewer 3	Reviewer 4
Not significant	2 (4.8)	2 (4.8)	6 (14.3)	5 (11.9)
Minor	15 (35.7)	11 (26.2)	16 (38.1)	12 (28.6)
Moderate	21 (50.0)	18 (42.9)	16 (38.1)	13 (31.0)
Major	2 (4.8)	10 (23.8)	4 (9.5)	12 (28.6)
Life-saving	2 (4.8)	1 (2.4)	0 (0.0)	0 (0.0)

Reviewer 1 = clinical nurse, Reviewer 2 = hospital pharmacist, Reviewer 3 = independent academic pharmacist, Reviewer 4 = consensus between two researchers

Agreement between pairs of reviewers revealed the best agreement for discrete significance categories between Reviewers 3 and 4 (α=0.314) (Table 5.2). With respect to categories collapsed to 'significant' versus 'not significant', the highest level of agreement was evident between Reviewers 1 and 4. Reviewers 1 and 2 demonstrated the lowest level of agreement.

Table 5.2 Panel 1: Agreement for discrete and collapsed significance ratings

Reviewer pairs	Agreement for discrete categories (Krippendorff's α)	Agreement for combined categories (Krippendorff's α)
Reviewer 1 vs 2	0.121	0.475
Reviewer 1 vs 3	0.173	0.462
Reviewer 1 vs 4	0.211	0.540
Reviewer 2 vs 3	0.260	0.192
Reviewer 2 vs 4	0.106	0.234
Reviewer 3 vs 4	0.314	0.478

Reviewer 1 = clinical nurse, Reviewer 2 = hospital pharmacist, Reviewer 3 = independent academic pharmacist, Reviewer 4 = consensus between two researchers

As Panel 1 could not reach consensus, Panel 2 (medication safety pharmacist, paediatric oncology pharmacist) was set up (Section 3.2.1) in July 2014. Review of a

random sample of data by Panel 2 determined that the majority (n=37/42, 88.1%) of active interventions were clinically significant; no intervention was considered life-saving (Table 5.3).

Table 5.3 Panel 2: Clinical significance of pharmacists' active interventions (n=42)

Clinical significance	No. per category, n (%)
Not significant	5 (11.9)
Minor	18 (42.9)
Moderate	11 (26.2)
Major	8 (19.0)
Life-saving	0 (0.0)

5.2 Identification and Assessment of Medication Misadventure

Panel 1 assessed a random sample of the active interventions to determine whether medication misadventure was implicated; a yes/no decision. The entire Panel 1 indicated that the majority of active interventions addressed medication misadventure (Table 5.4). The strength of agreement between the reviewers was 'fair' (α=0.321, 95%CI 0.113-0.544).

Table 5.4 Panel 1: Inter-rater reliability of medication misadventure detected by pharmacists' active interventions (n=42)

Medication misadventure?	Frequency, n (%)			
	Reviewer 1	Reviewer 2	Reviewer 3	Reviewer 4
Yes	31 (73.8)	35 (83.3)	26 (61.9)	31 (73.8)
No	11 (26.2)	7 (16.7)	16 (38.1)	11 (26.2)

Reviewer 1 = clinical nurse, Reviewer 2 = hospital pharmacist, Reviewer 3 = independent academic pharmacist, Reviewer 4 = consensus between two researchers

When the reviewers assigned each case into three categories of medication misadventure (ADE, ADR, ME), they noted 'fair' agreement (α=0.222, 95%CI 0.096-0.341) (Table 5.5). Reviewers 2, 3 and 4 most commonly rated the medication misadventures as ME.

Table 5.5 Panel 1: Inter-rater reliability of type of medication misadventure detected by pharmacists' active interventions (n=42)

Type of medication misadventure	Frequency, n (%)			
	Reviewer 1	Reviewer 2	Reviewer 3	Reviewer 4
Medication error	10 (23.8)	34 (81.0)	26 (61.9)	29 (69.0)
Adverse drug event	20 (47.6)	1 (2.4)	1 (2.4)	0 (0.0)
Adverse drug reaction	1 (2.4)	1 (2.4)	0 (0.0)	3 (7.1)
Not applicable	11 (26.2)	6 (14.3)	15 (35.7)	10 (23.8)

Reviewer 1 = clinical nurse, Reviewer 2 = hospital pharmacist, Reviewer 3 = independent academic pharmacist, Reviewer 4 = consensus between two researchers

The reviewers further classified the MEs using the NCC MERP taxonomy.(225) The strength of agreement between all reviewers was 'fair' (α=0.351, 95%CI 0.207-0.487) (Table 5.6). There were some similarities in the ratings by Reviewers 1 and 4, while Reviewers 2 and 3 demonstrated disparate ratings.

Table 5.6 Panel 1: Inter-rater reliability of medication error type detected by pharmacists' active interventions (n=42)

Type of medication error	Frequency, n (%)			
	Reviewer 1	Reviewer 2	Reviewer 3	Reviewer 4
Improper dose	16 (38.1)	9 (21.4)	8 (19.0)	16 (38.1)
Other	4 (9.5)	15 (35.7)	8 (19.0)	4 (9.5)
Drug omission	2 (4.8)	2 (4.8)	5 (11.9)	7 (16.7)
Monitoring error	5 (11.9)	2 (4.8)	0 (0.0)	0 (0.0)
Wrong rate	0 (0.0)	7 (16.7)	0 (0.0)	0 (0.0)
Wrong administration route	1 (2.4)	1 (2.4)	2 (4.8)	1 (2.4)
Dose omission	1 (2.4)	1 (2.4)	1 (2.4)	1 (2.4)
Wrong patient	1 (2.4)	1 (2.4)	0 (0.0)	1 (2.4)
Wrong strength/ concentration	0 (0.0)	2 (4.8)	0 (0.0)	1 (2.4)
Wrong duration	0 (0.0)	0 (0.0)	2 (4.8)	0 (0.0)
Wrong drug	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)
Wrong dose form	1 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)
Not applicable	11 (26.2)	2 (4.8)	16 (38.1)	10 (23.8)

Reviewer 1 = clinical nurse, Reviewer 2 = hospital pharmacist, Reviewer 3 = independent academic pharmacist, Reviewer 4 = consensus between two researchers

The reviewers used the severity rating of the NCC MERP index(225) to judge the severity of the MEs addressed through pharmacists' active interventions. The level of agreement for severity between the reviewers was 'slight' (α=0.154, 95%CI 0.024-0.274) (Table 5.7).

Table 5.7 Panel 1: Severity of MEs detected by pharmacists' active interventions (n=42)

	Reviewer 1	Reviewer 2	Reviewer 3	Reviewer 4
A: Circumstances or events that have the capacity to cause error	7 (16.7)	15 (35.7)	22 (52.4)	3 (7.1)
B: An error occurred but the error did not reach the patient	9 (21.4)	18 (42.9)	1 (2.4)	13 (31.0)
C: An error occurred that reached the patient but did not cause patient harm	13 (31.0)	5 (11.9)	0 (0.0)	6 (14.3)
D: An error occurred that reached the patient and required monitoring to confirm that it resulted in no harm to the patient and/or required intervention to preclude harm	2 (4.8)	2 (4.8)	1 (2.4)	1 (2.4)
E: An error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention	0 (0.0)	1 (2.4)	0 (0.0)	9 (21.4)
F: An error occurred that may have contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalisation	0 (0.0)	1 (2.4)	1 (2.4)	0 (0.0)
Not applicable	11 (25.6)	0 (0.0)	17 (40.5)	10 (23.8)

Reviewer 1 = clinical nurse, Reviewer 2 = hospital pharmacist, Reviewer 3 = independent academic pharmacist, Reviewer 4 = consensus between two researchers

There was a notable decrease in the Krippendorff's alpha value to 0.086 (95%CI 0.045-0.216) when reported using collapsed categories of severity (Table 5.8). Reviewer 3 tended to rate the severity of the errors lower than the other reviewers.

Table 5.8 Panel 1: Assessment of the severity of MEs (combined severity categories)

Combined category of ME severity	Frequency, n (%)			
	Reviewer 1	Reviewer 2	Reviewer 3	Reviewer 4
No error (category A)	18 (41.9)	15 (35.7)	39 (92.9)	13 (31.0)
Error, no harm (B-D)	24 (57.1)	25 (59.5)	2 (4.8)	20 (47.6)
Error, harm (E-H)	0 (0.0)	2 (4.8)	1 (2.4)	9 (21.4)

Reviewer 1 = clinical nurse, Reviewer 2 = hospital pharmacist, Reviewer 3 = independent academic pharmacist, Reviewer 4 = consensus between two researchers

Category A: Circumstances or events that have the capacity to cause error.

Category B: An error occurred but the error did not reach the patient.

Category C: An error occurred that reached the patient but did not cause patient harm.

Category D: An error occurred that reached the patient and required monitoring to confirm that it resulted in no harm to the patient and/or required intervention to preclude harm.

Category E: An error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention.

Category F: An error occurred that may have contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalisation.

Catgeory G: An error occurred that may have contributed to or resulted in permanent patient harm.

Category H: An error occurred that required intervention necessary to sustain .

5.3 Discussion

5.3.1 Clinical Significance of Pharmacists' Active Interventions

Published studies on pharmacists' clinical interventions have used different methods. To date, there are no validated methods or standardised rating scales to assign clinical significance to pharmacists' interventions, making it difficult to compare our findings. Significance assessment was initially performed by a panel comprising three independent experts (hospital pharmacist, academic pharmacist, clinical nurse) and consensus between two researchers (counted as a single reviewer). The pattern of agreement between the reviewers could have been different if physicians had participated. Studies have demonstrated that physicians tended to rate the impact of pharmaceutical care interventions lower than pharmacists.(226-228)

The present study uncovered little agreement between the raters for the clinical significance of pharmacists' active interventions, evidenced by low Krippendorff's alpha values, α=0.265 and α=0.394 for discrete rating scales and collapsed scales, respectively. In accordance with our finding, low level of agreement ($\varkappa$=0.35) was reported in a reliability study assessing the clinical significance of pharmacists' interventions in a tertiary care hospital that included a paediatric unit. The assessment was conducted between the intervening pharmacists and an independent clinical pharmacist using six-point significance rating scale. There was no face-to-face training in significance assessment provided to the evaluators.(203)

A low level of agreement was also reported by Fernandez-Llamazares *et al.*(197) They evaluated the impact of pharmacists' interventions to reduce prescribing errors in paediatric wards. They used a six-point rating scale (harmful, insignificant, somewhat significant, significant, very significant, extremely significant). The intervening pharmacists and an independent clinical pharmacist carried out the assessment.

An American study in an integrated healthcare centre for adults found 'slight' agreement ($\varkappa$=0.18) for the impact of pharmacists' recommendations between two independent evaluators (physician, pharmacist).(154) A similar level of agreement ($\varkappa$=0.20) was also reported by Bosma *et al.*(226) in a gastroenterology unit in a Dutch general hospital. A Danish study noted modest agreement ($\varkappa$=0.25) between two raters (internal medicine specialist, clinical pharmacologist) for the significance

of pharmacists' interventions in a clinical unit for adult patients. They employed a four-level significance assessment (minimal importance, moderate, significant, vital).(216) Better agreement was reported by Overhage *et al*.(227) at an American general hospital involving the intervening pharmacists and four independent reviewers (two physicians, two pharmacists).

A meeting organised for Panel 2 (researchers and two independent panellists) to resolve the rating differences and reach consensus identified that the majority of the interventions were rated significant (45.2% moderate or major significance), leaving less than 12% as non-significant. An analysis of clinical pharmacists' interventions by self-assessment in an Austrian hospital with a Department of Paediatric and Adolescence Medicine demonstrated that around three-quarters of the interventions were judged to be significant.(203) These findings were in accordance with a study by Virani *et al*.(204) undertaken in a Canadian paediatric mental health unit where 86% of pharmacist-initiated recommendations had a potential positive impact on patient care ranging from 'minor' to 'markedly significant'. However, nearly 10% of the recommendations had a potentially detrimental effect, compared to none in our study. Comparable results were also reported by a Spanish study, where more than three-quarters of pharmacists' interventions rectifying prescribing errors had a significant impact.(197) The clinical significance of interventions documented in a range of paediatric healthcare settings in the USA reported more than half of the interventions as 'somewhat significant' and nearly 40% as 'significant'.(184) A study conducted in a children's hospital in the USA claimed that almost two-thirds of pharmacists' interventions during medication reconcilliation were self-rated by the pharmacists as contributing a 'moderate' impact to patient care, 7% as 'life-saving' and the remaining 27% as 'minimal impact'.(139)

A large Australian study involving eight hospitals assessed the impact of pharmacists' interventions on patients' clinical outcomes judged by the intervening pharmacist and then referred to the independent panel for final assessment. Despite using the same significance rating scale as our study, the authors reported more than one-quarter of the interventions were of 'major significance', while 'moderate' and 'minor' categories accounted for around 30% each.(18)

A different method was reported by Mogensen *et al.*(216) who evaluated the significance of interventions in an ED. They applied the highest rating from either of the two independent specialists as the final rating and did not seek consensus. They argued that the expertise of the specialists would be more relevant for the final assessment than consensus. They deemed around 47% of interventions to be of 'vital importance', with the remainder of 'minor-moderate importance'.

Sircar-Ramsewak *et al.*(229) retrospectively evaluated the potential impact of pharmacists' interventions on addressing DRPs over one year in a general hospital in Trinidad. There was no clear explanation about the assessment process. More than two-thirds of the interventions were of 'moderate impact' on patient care, while around 30% had a 'major impact' and a small proportion 'minor impact'. Although Sircar-Ramsewak *et al.*(229) used different terms to classify the value of pharmacists' interventions, there were no distinct differences in defining the value. This means that the term 'impact', describing the value of the assessment, can be replaced by the term 'significance'. Sircar-Ramsewak *et al.*(229) reported greater significance of pharmacists' interventions than our study.

A retrospective study of pharmacists' interventions to resolve MEs during dispensing was conducted in a general hospital in Oman. Some challenges to the method were noted. Pharmacists based the intervention data on legible annotations on the prescriptions. The researchers did not describe their assessment processes for the interventions. The study revealed slightly better findings than our study, where the majority (72.3%) of the interventions were of 'minor significance', while nearly 20% and 7.5% were of 'moderate significance' and 'major significance', respectively.(230)

Different findings were also noted in a study evaluating the impact of Doctor of Pharmacy students' interventions during an internal medicine clerkship. The significance of the interventions were assessed by panels of two faculty members and 10 independent pharmacists using a three-level scale (low, moderate, high). The differences among the panellists was resolved by a vote. Around 50% of the interventions were categorised as having 'low-level significance'.(231)

It is evident from these studies that methods for assessing the clinical significance of interventions are variable. The subjectivity of the reviewers, characteristics of the rating scales and the accuracy of their predictions compromise all of the methods. Studies involving self-assessment by the intervening pharmacists may also be subject to bias.

Applying actual clinical outcomes of pharmacists' interventions would circumvent the subjectivity involved in theoretical estimation of significance and impact. This approach was attempted by McLennan *et al.*(232) in an assessment of pharmacists' interventions in an Australian tertiary referral centre for cancer. They employed three classifications of patient outomes to assess the interventions (beneficial, detrimental, no change). The assessment was undertaken by an independent pharmacist who reviewed patients' clinical status in their medical histories following the intervention episode until discharge, or for a maximum of seven days. McLennan *et al.*(232) claimed approximately 90% of the interventions benefitted the patient. As the study was conducted in a specialty setting, familiarity with the patients' medical conditions may have facilitated this approach. Assessment of outcomes is expected to be more complex in general medical settings.

5.3.2 Identification and Assessment of Medication Misadventure

Analysis of medication-related events, particularly the frequency, type and severity, is essential to improve the quality of healthcare delivery.(233, 234) Therefore, reliability in the classification is vital. However, variation in judgement between raters may contribute to errors in reliability analysis. Variability is expected as a result of the raters' clinical specialties, their awareness of best-practice management across a range of conditions, and their experience and familiarity with the classification process.(233)

The level of agreement within Panel 1 was 'fair' for judgements on involvement of medication misadventure. Reviewers relied on concise explanations of the categories, without examples. Consequently, there was disagreement between the reviewers as to what constituted an error. Different perceptions were also noted when determining the presence of harm. Although the NCC MERP has created an algorithm to facilitate the assignment of severity to ME-related events and to minimise variability,(225) its utility has been questioned.(235)

It is challenging to compare our findings with other studies, despite widespread application of the NCC MERP index, for which inter-rater reliability has been established by a small number of studies. Forrey *et al.*(235) evaluated the reliability of the NCC MERP index among MedMARx ADE data repository users using 27 actual ME scenarios. They reported the NCC MERP index was accurate and reliable, with some ability to generalise findings. However, Forrey *et al.*(235) proposed that collapsing categories E, F and H into one category, and categories C and D into another category, would minimise ambiguity. The present study collapsed the categories into four (no error, error - no harm, error - harm, error - death), as indicated in the NCC MERP index; paradoxically this generated a lower level of agreement as opposed to discrete categories.

Little research has investigated inter-rater reliability associated with medication misadventure in paediatrics. Variations in definitions and categories of terms such as ADE, ADR and ME complicate the comparison of published research. Consistent with our findings, Kunac *et al.*(233) determined the reliability in assessment of paediatric inpatient medication-related events. They found low agreement ranging from 'slight' to 'fair' on the type and the seriousness of the event. Kunac *et al.*(233) used simulated test cases and guidelines consisting of the definitions and examples of the event categories to aid reviewers during the judgement process.

Previous paediatric studies have revealed high levels of agreement for the classification of event type.(236, 237) 'Substantial' agreement was reported by King *et al.*(236); 20 randomly selected incident reports were judged by two independent physicians. Potts *et al.*(237) found 'almost perfect' agreement between two independent reviewers (physician, clinical pharmacist) who assessed a random sample (10%) of data relating to paediatric patients in a critical care unit. With respect to the severity of ME, comparison of our findings with the existing literature was challenged by the majority of studies evaluating the severity of all medication-related events, not necessarily MEs. The studies also used a variety of rating scales resulting in distinct interpretations of the event severity. For example, two paediatric studies reported 'substantial' agreement between two independent raters for the severity of the event (ADEs, potential ADEs, MEs) using a four-point Likert-type scale.(50, 238)

Some differences in this concept are notable when comparing paediatric and adult population studies. Snyder *et al.*(239) modified the NCC MERP index by replacing the word 'error' in each severity category with the word 'event', combining categories B-D (error - no harm) and E-H (error - harm), and excluding categories A and I. They found that the level of agreement for classification of medication safety events ranged from 'substantial' to 'almost perfect'. They also reported that the level of agreement for event severity among the reviewers for original discrete categories was substantial, and slight improvement in agreement was noted when using the combined categories.(239) Abdel-Qader *et al.*(210) conducted a study in a UK teaching hospital to determine the reliability of the severity of prescribing errors rectified by pharmacists. They found substantial agreement between intervening pharmacists and an independent senior pharmacist. By contrast, poor agreement was reported between two independent raters (hospital pharmacist, clinical pharmacologist) on the severity of MEs intercepted by pharmacists' interventions in a specialty unit in the Netherlands.(226)

Over three-quarters of the selected sample of pharmacists' active interventions in our study addressed medication misadventure, of which over 90% involved MEs and the rest were due to ADRs. In line with paediatric studies,(17, 50, 99, 148, 238, 240, 241) the researchers' assessment demonstrated that overall, the most common type of MEs addressed in the active interventions during pharmacy rounds on the five wards and during dispensing in the Haematology-Oncology Pharmacy was related to inappropriate doses. A situation compounded by the limited availability of drug formulations for children.(242) However, the pattern of MEs on the Haematology-Oncology Ward was slightly different, with drug omission comprising around 46% of the MEs. Inappropriate doses of the correct drugs were the second most frequent errors, contributing to 23% of the errors in this specialty unit. Half of the sampled MEs were not intercepted, and resulted in additional monitoring or temporary patient harm. A two-month study in an American paediatric teaching hospital reported a negligible proportion of the errors reaching patients.(243)

Chan and Kotzin(94) described a distinct way of assessing the severity of MEs detected by pharmacists' interventions. They evaluated four years of data from interventions in paediatric patients and found that more than half of the errors were

'moderate' in severity and just over one-fifth were 'severe', while the remaining errors were 'minor' and 'unknown' in comparable proportions. A systematic review of MEs in paediatric patients revealed that, MEs were moderate in severity and very few incidents resulted in fatal outcomes.(244) When focusing on paediatric chemotherapy MEs, Rinke *et al*.(10) assessed the five-year voluntary report of the *US Pharmacopeia MedMARx* database and found that 85% of the errors reached patients and 15.6% of non-intercepted errors resulted in patient monitoring or therapeutic interventions. The differences might be due to the researchers' focus on chemotherapy instead of all medications used in oncology. Furthermore, errors submitted to the MedMARx ADE data repository might from all stages of medication-use process, which was not the case in the present study.

5.4 Limitations and Recommendations

There are some limitations in the study design and the results of this study. For convenience, only randomly selected cases of pharmacists' active interventions were included in the analysis. Despite this, the findings provide some insight into medication misadventure in paediatrics.

The samples used to assess the classification agreement were from a single children's hospital, which might limit the generalisability of the findings. Data were gleaned from observations during ward rounds and dispensing. The lack of continuous monitoring could mean less opportunity to detect MEs during drug administration. Kaushal(245) has claimed that each method of error measurement detects only certain types of errors. The most common medication-related events, including MEs, occur during prescribing and administration.(3, 37, 50, 52, 179)

The independent panellists were selected for convenience. In the selection process, it was deemed that the independent panellists had appropriate clinical knowledge and professional experience. Low levels of agreement among reviewers might be due to their inadequate experience in using the clinical significance rating and the NCC MERP index.

Limited information provided for each case could have influenced the agreement. There was no formal training using simulated scenarios prior to the assessment, and no examples were provided for each component of assessment. The findings might

be different if more detailed information had been provided, along with training for the panellists.

Our findings highlight that more research is needed to elucidate the rate and pattern of medication-related events identified through pharmacists' active interventions in paediatrics. Future studies should assess all pharmacists' active interventions documented within a time frame in a range of paediatric settings, and in multiple institutions and with actual clinical patient outcomes. Future research could also address the issue of selection of the independent expert panel via random selection of a broad group of eligible experts - doctors, nurses and pharmacists. The resulting data would provide a broader picture of pharmacists' interventions in relation to their capacity to identify and resolve medication misadventure, and a better understanding of the nature of medication misadventure in children.

5.5 Conclusion

Most of the selected active interventions were rated as clinically significant and reliability of reviewers' rating was 'slight' for severity of ME. Meanwhile, 'fair' agreement was achieved for the presence of medication misadventure, classification of medication misadventure and classification of ME. It is beneficial to implement approaches to improve the reliability of the assessment and generalisability of the findings. This study highlighted the clinical significance of pharmacists' active interventions and justified the role of clinical pharmacists through their active interventions in paediatric settings by identifying and resolving medication misadventure related events, in particular ME. The medication misadventures detected and corrected by pharmacists provide valuable data on the pattern of the misadventure and subsequent direction to improve the medication use process.

Chapter 6

PART THREE: RESULTS AND DISCUSSION

This chapter comprises a published paper reproduced with permission from the journal:

Hesty U Ramadaniati, Ya P Lee, Jeffery D Hughes. Snapshot versus continuous documentation of pharmacists' interventions: are snapshots worthwhile? *Journal of Pharmacy Practice and Research* 2014; 44: 205-12. DOI: 10.1002/jppr.1029.

The headings, page number, tables, figures and references have been reformatted in line with the thesis structure. This chapter also presents qualitative data from the FGD that had not been included in the paper.

6.1 Introduction

Clinical pharmacy services play an important role in ensuring optimal drug outcomes for patients.(121) Pharmacists' interventions have been considered in some developed countries as one of the main parameters in evaluating the importance of clinical pharmacy services for improving safety and efficacy of medication use.(185, 210, 246) Hence, the documentation of pharmacists' clinical interventions and activities are of paramount importance in providing evidence that clinical pharmacists play an integral role in preventing medication misadventure, improving overall patient care and justifying their value within the healthcare system.(247, 248)

A national survey was conducted in Australia to evaluate the extent of clinical services provision and their level of documentation. The survey indicated that clinical pharmacy services are common in hospital settings across Australia and that the level of documentation varied amongst institutions.(248) Likewise, a national survey by the American Society of Hospital Pharmacy demonstrated that most hospital pharmacists documented their interventions.(249) Nonetheless, there have been limited studies specifically evaluating the different approaches in documenting interventions, particularly in the paediatric population.(89, 184, 201) Paediatric patients are particularly at risk of medication misadventure for many reasons, including unique physiologic characteristics, inadequate healthcare settings to accommodate safe use of medication in paediatrics and psychological factors

specifically related to communication issues.(87) Thus, this study aimed to evaluate the nature of pharmacists' interventions documented through self-reporting during snapshot periods in comparison to interventions documented during direct observation. Further, it sought to gather pharmacists' opinions on the utility of the different documentation methods.

6.2 Method

6.2.1 Documentation of Pharmacists' Interventions during Snapshot Periods

This study was conducted in a 220-bed paediatric teaching hospital in Perth, Western Australia. This hospital has an in-house method for documenting pharmacists' interventions during snapshot periods. Snapshot periods occur twice a year around March to May and September to October and are of five days' duration. The interventions are self-reported manually by all pharmacists using a specific form (Appendix 7). The principal researcher retrospectively analysed ward-based pharmacists' interventions from the five study wards (General Medical Ward for Infants, General Medical Ward for Young Children, General Medical Ward for Adolescents, General Surgical Ward and Haematology-Oncology Ward) for three snapshot periods, namely September 2010, April 2011 and May 2012. The snapshot reports from the study periods were evaluated to determine the number and type of the interventions. The type of intervention was categorised as described by Condren *et al.*(184) with slight modification. In addition, the interventions were divided into active and passive interventions. An active intervention was defined as any activity by a pharmacist that directly leads to a change in a patient's drug management or therapy.(121) All other care-centred activities not resulting in medication changes were considered as passive interventions. The medications involved in the interventions were categorised using the AMH.(188) The results of the snapshot reports were then compared to interventions documented during direct observation.

6.2.2 Documentation of Pharmacists' Interventions during Direct Observation

The principal researcher shadowed pharmacists during their ward rounds and documented all interventions undertaken by the pharmacists in the five study wards. This observation was made between 35 and 37 non-consecutive days per ward. The

type of data collected during direct observation can be seen in the data collection form (Appendix 1).

6.2.3 Focus Group Discussion

The principal researcher presented the results of pharmacists' intervention documentation from direct observation and snapshot reports to the pharmacy staff. A focus group discussion was conducted after the presentation by an independent facilitator to gather the pharmacists' perceptions and comments on the results. The barriers to effective documentation of pharmacists' interventions and their suggestions to improve the established intervention documentation system were also sought. The discussion was audio recorded and transcribed *verbatim* for thematic analysis.

6.2.4 Data Analysis

Demographic variables and pharmacists' intervention data were summarised using descriptive statistics. Data were analysed using SPSS version 19.0 (Chicago, IL, USA). The rates of pharmacists' interventions per 100 medication charts reviewed, documented through direct observation and during snapshot periods for each ward, were compared using Poisson regression using SAS version 9.2 (SAS Institute Inc., Cary, NC, USA). Transcripts of the discussion were entered into a qualitative analysis software program (QSR NVivo 10) to code and link emergent themes.

6.3 Results

6.3.1 Pharmacists' Interventions Documented during Snapshot *versus* Observation Periods

A total of 398 interventions were documented and 1022 medication charts were reviewed by pharmacists during three snapshot periods in 2009 and 2010 (I, II, III). Complete snapshot reports from the five study wards were available for snapshot period II, while only reports from three wards were submitted during periods I and III. Of all interventions, approximately 18% (n=70/398) were considered active interventions. The characteristics and rates of all interventions and the active interventions documented by pharmacists during snapshot periods are shown in Table 6.1, and the types of interventions during snapshot periods are described in Figure 6.1. The highest rates of intervention per 100 medication charts reviewed was recorded in the General Surgical Ward, followed by the General Medical Ward for

Infants and the Haematology-Oncology Ward, respectively (Table 6.1). However, the analysis of active interventions revealed a different trend with the Haematology-Oncology Ward showing the highest rate followed by the General Surgical Ward and the General Medical Ward for Adolescents, respectively. A total of 982 pharmacists' interventions were observed and documented, and 2275 medication charts were reviewed in the five study wards during the direct observation. The characteristics and rates of pharmacists' interventions from each ward are summarised in Table 6.2 and the types of interventions performed by ward-based pharmacists in the study wards are described in Figure 6.2. As detailed in Table 6.2, the General Surgical Ward had the highest intervention rate per 100 medication charts reviewed. It was followed by the Haematology-Oncology Ward and the General Medical Ward for Adolescents. In terms of active interventions, the Haematology-Oncology Ward ranked first, followed by the General Surgical Ward and the General Medical Ward for Adolescents. It is interesting to note that the pattern of active interventions during observation was similar to that of the snapshots.

Comparison of the rates of interventions during the snapshot periods and direct observation were undertaken using a Poisson regression model. This model showed no significant difference in the interventions rates of the two documentation methods; snapshot 37.4 (95%CI 27.4–47.4) per 100 medication charts reviewed *versus* observation 50.6 (95%CI 43.1–58.1) per 100 medication charts reviewed, p = 0.054. A similar statistical analysis was undertaken to compare the rates of active interventions between snapshot and observation periods. The analysis revealed that the rate of documentation of active interventions during the direct observation period was significantly higher compared to that of the snapshots (snapshot 6.7 [95%CI 4.3–9.2] per 100 medication charts reviewed *versus* observation 15.1 [95%CI 10.0–20.2] per 100 medication charts reviewed, p = 0.002).

Table 6.1 Characteristics and rates of pharmacists' interventions (PIs) on the five study wards during snapshot periods

Parameters	Medical Ward for Infants	Medical Ward for Young Children	Medical Ward for Adolescents	Surgical Ward	Haematology-Oncology Ward
Duration of data collection (days)	15	10	10	9	10
No. of PIs	141	11	42	150	54
No. of active PIs (%)*	9 (6.4)	4 (36.4)	19 (45.2)	17 (11.3)	21 (38.9)
No. of medication charts reviewed	278	179	219	194	152
Rate of PIs per 100 medication charts reviewed	50.72	6.15	19.18	77.32	35.52
Rate of active PIs per 100 medication charts reviewed	3.24	2.23	8.68	8.76	13.82

*Percentage of active interventions per number of interventions on each ward.

Table 6.2 Characteristics and rates of pharmacists' interventions (PIs) on the five study wards during direct observation

Parameters	Medical Ward for Infants	Medical Ward for Young Children	Medical Ward for Adolescents	Surgical Ward	Haematology-Oncology Ward
Duration of data collection (days)	35	35	35	37	35
No. of PIs	145	153	218	271	195
No. of active PIs (%)*	16 (11.0)	28 (18.3)	51 (23.4)	59 (21.8)	90 (46.2)
No. of medication charts reviewed	468	500	528	422	357
Rate of PIs per 100 medication charts reviewed	30.98	30.60	41.29	64.22	54.62
Rate of active PIs per 100 medication charts reviewed	3.42	5.60	9.66	13.98	25.21

*Percentage of active interventions per number of interventions on each ward.

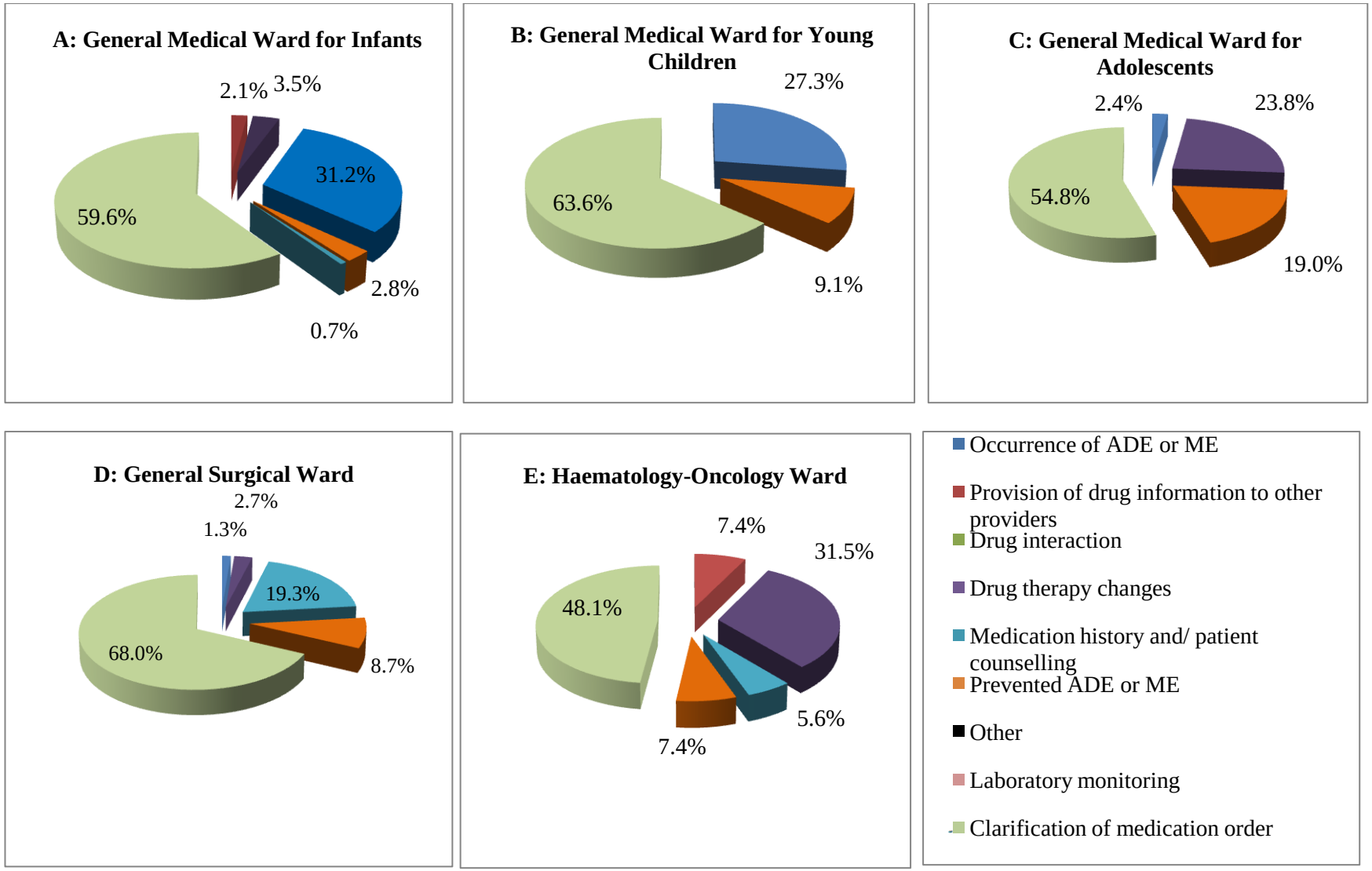


Figure 6.1 Types of pharmacists' interventions performed and documented by clinical pharmacists on the five study wards during snapshot

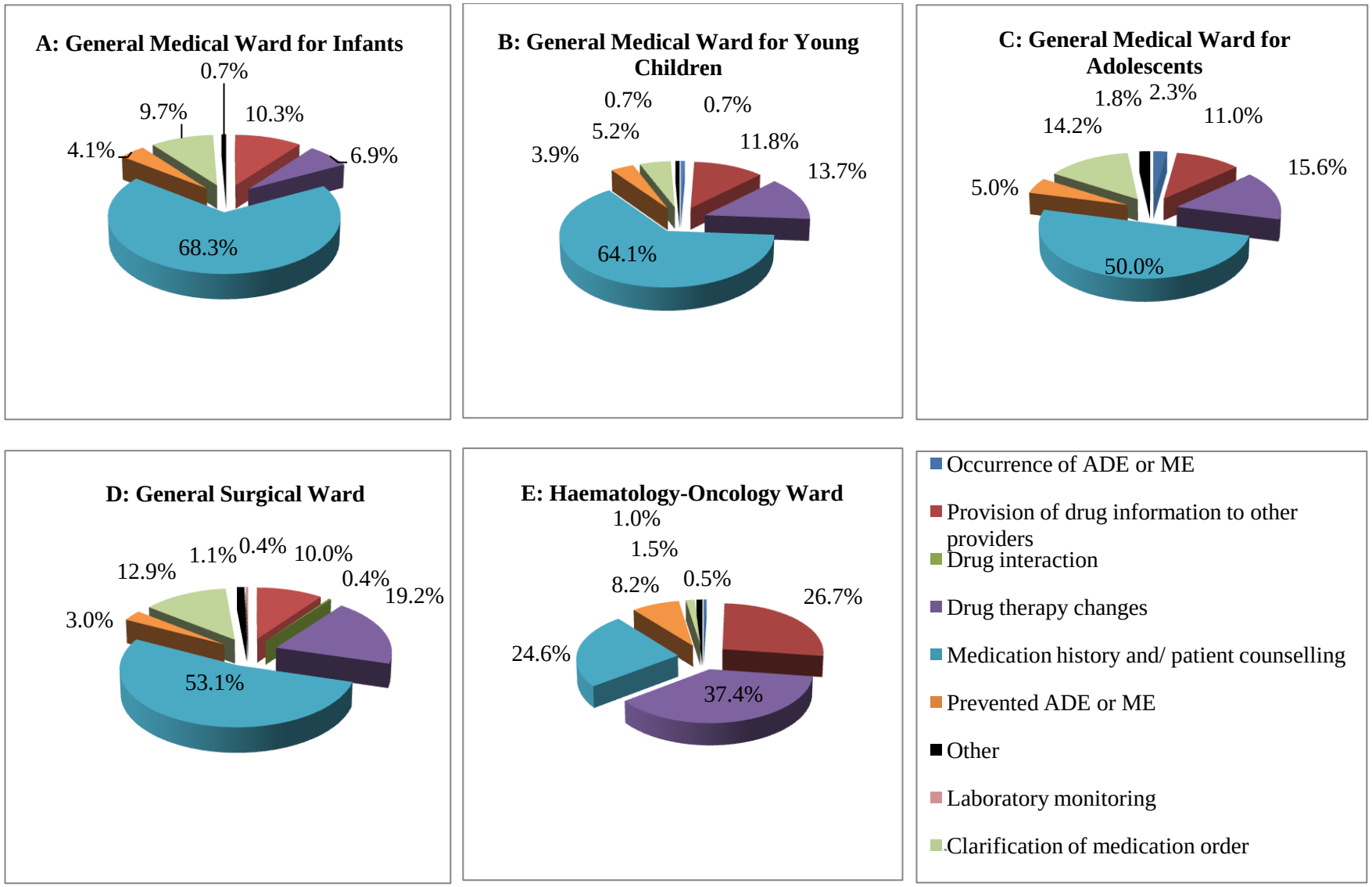


Figure 6.2 Types of pharmacists' interventions performed by clinical pharmacists and documented by observation on the five study wards

In terms of the types of interventions, clarification of medication orders (Figure 6.1) was the commonest type of intervention documented by pharmacists during snapshots across all settings. Clarification of medication orders arose as a result of activities performed by the pharmacists in annotating additional information for specific medications on the medication charts. As shown in Figure 6.2, taking medication histories and/or patient counselling were responsible for the most common interventions performed by clinical pharmacists in the general medical and surgical settings during the direct observation period. These types of interventions accounted for 50% or more of all interventions recorded in these settings. However, a different pattern was seen in the Haematology-Oncology Ward, where drug therapy changes constituted the most common intervention type. When comparing the pattern of all interventions during the direct observation period with that of snapshot reports, it can be clearly seen that the interventions across the study wards were not comparable.

6.3.2 Characteristics of Pharmacists' Active Interventions and Implicated Medications during Snapshot *versus* Observation Periods

In terms of active interventions self-reported (n=70) by pharmacists across the five study wards during the snapshot periods, the highest proportion of active interventions was found in the Haematology-Oncology Ward, followed by the General Surgical Ward and the General Medical Ward for Adolescents, respectively. Interestingly, the proportion of active interventions increased as the patients' age went up in the general medical setting. In all General Medical Wards, except the Ward for Infants, dosing associated interventions were the most common active intervention type. Similarly, dose adjustment accounted for the most common active interventions in Haematology-Oncology. Meanwhile, the General Medical Ward for Infants and the General Surgical Ward shared the same pattern of most frequent active intervention, namely recommendation to clarify wrong/missing dosing interval/frequency of medication orders.

Active interventions (n=244) contributed less than a quarter of all interventions in each General Ward during the direct observation. However, the Haematology-Oncology Ward revealed a different pattern with a considerably higher proportion of active interventions (46.2%). Adjusting the dose was the most frequent active interventions in general settings; however, in the Haematology-Oncology Ward,

recommendations to prescribe regular medications constituted the most common active interventions and dosing adjustment ranked second, which differed from the snapshot reports. When compared with snapshot reports, active interventions during direct observation showed a different pattern. Nonetheless, dosing-associated interventions during snapshot periods and direct observation were the most common active interventions in almost all general medical wards. Drug addition and dosing-associated recommendations in the Haematology-Oncology Ward accounted for two thirds of active interventions.

With respect to the classes of medications implicated in active interventions during snapshot periods, analgesics (n=25, 35.7%) were the most common drug class implicated. It was found that almost half of analgesics-associated recommendations occurred in the General Medical Ward for Adolescents. Dosage interval/frequency adjustment (n=12, 48.0%) accounted for the most frequent recommendations in relation to the use of analgesics. Anti-infectives (n=20, 28.6%) were the second major class of medications associated with active interventions. Sixty-five percent of anti-infectives-related interventions were reported in the Haematology-Oncology Ward. Dosing adjustment (n=10) constituted exactly half of the interventions in this class. Antibacterials (n=17/20) were implicated in the majority of the active interventions related to anti-infectives. Drugs for the gastrointestinal system (n=12, 17.1%) were the third major class of medications associated with active interventions. Half of the interventions related to this class were documented in the General Surgical Ward. When categorised according to subclasses of medications, 50% of recommendations in this class were related to the use of antiemetics. The most frequent active intervention in this class of medication was dose adjustment.

Meanwhile, anti-infectives were the drugs most often associated with active interventions (n=100, 41.0%), followed by analgesics (n=46, 18.9%), gastrointestinal drugs (n=36, 14.8%) and immunomodulators and antineoplastics (n=21, 8.6%), respectively, during the observation study. Antibacterials were the predominant anti-infectives associated with active recommendations. In terms of the use of analgesics, almost 40% of analgesic-related recommendations occurred in general medical wards. Drug deletion (n=11/46, 23.9%) was the most common active interventions in this class of medications. The third major class of medications involved in active

interventions was drugs for the gastrointestinal system. More than half of the recommendations related to this medication class occurred in the haematology-oncology setting. When categorised according to subclasses of medications, antiemetics were involved in around 63% of interventions associated with this class. Recommendations to add medications accounted for the major active interventions involving gastrointestinal drugs (n=15/36; 41.7%). With regard to immunomodulators and antineoplastics, not surprisingly, more than 80% of the recommendations were recorded in the Haematology-Oncology Ward. Drug addition was the most frequent recommendation accounting for more than half of all active interventions associated with this class of medications.

6.3.3 Some Examples of Pharmacists' Active Interventions

A five-month-old female patient with a brain tumor was admitted to the oncology ward. During medication history taking, the parents told the ward pharmacist that the patient took 2.5 mL (0.1 mg) of clonazepam twice daily. When reviewing the medication chart, the pharmacist found clonazepam was prescribed 2.5 mg twice daily. The doctor confused 'microlitre' and 'microgram', and the patient almost received the dose that was 25 times higher than intended. The doctor reduced the dose to 2.5 mL twice daily on the pharmacist's recommendation.

A 17-year old female patient was hospitalised due to congenital right leg oedema. During hospitalisation, the patient was prescribed pregabalin 25 mg twice daily. The order written on the medication chart was slightly illegible. The '25 mg bd' looked like '250 mg bd' so the nurse assumed the dose was 250 mg and administered the wrong dose. The patient received 10-fold higher dose in the morning and she felt very drowsy afterwards. In the afternoon, the pharmacist noticed the error and asked the doctor to rewrite the medication order more clearly.

6.3.4 Barriers in Documenting Pharmacists' Interventions and Suggestions in Improving the Documentation

The pharmacists who participated in the focus group discussion conducted in July 2013 identified a number of barriers to documenting their interventions continuously including time constraints, fatigue, heavy workload and staffing deficiencies. The quotations below illustrate many of these issues:

"...And the reason that we moved from that [continuous recording] to snapshot recording, was because of the sort of things that we're hearing now, about recording fatigue, about it taking up so much time that you've spent an enormous amount of time collecting data, and that is then impacting on how much time you had to actually do your work..." PA3

"...And many other tertiary and hospital pharmacists are routinely documenting in the patient's inpatient progress notes, but because of those particular staffing or resourcing differences between our hospital and other tertiary hospitals, we mightn't necessarily have time to individually document a swag of interventions..." PA5

The majority of pharmacists thought that the snapshot report was inadequate to reflect their actual contribution to patient care and their workload. They suggested that modification of the timing of snapshot so it was undertaken during a busy period rather than a downtime as usual would be worthwhile (see quotations below).

"Because we do try and do it during quiet periods, even if you do, like, rather than doing a week of snapshot, do a day during a busy period, and you'll get some data and it'll be more reflective of what your day-to-day life is going to be like..." PA6

The pharmacists also proposed a hybrid system with continuous recording of interventions during certain periods of time by an independent observer in addition to existing snapshot documentation (see quotations below).

"...that another model that we could use would be rather than the ward pharmacist doing the documentation, you could have, as I said, we have a medication safety pharmacist starting soon. One of the roles, perhaps, of the medication safety pharmacist could be to do a, once or twice a year for every ward pharmacist, to actually go around and shadow them..." PA3

6.4 Discussion

It is the evident that the majority of previous studies in a range of healthcare settings relied on self-reporting methods to document pharmacists' interventions.(178, 183, 247) This method may lead to bias and under-reported findings, since documentation is influenced by pharmacists' perceptions and preferences on whether or not to report their interventions. The direct observation approach, in combination with

retrospective analysis of self-reporting documentation, allows this study to determine the actual rate of pharmacists' interventions as a reflection of the pharmacists' daily workload. The direct observation approach is expected to be effective in resolving the issue of potential under-reporting associated with self-documenting intervention studies.(178) When comparing pharmacists' interventions across the study wards between both documentation approaches, direct observation uncovered higher rates of active interventions than the snapshot method. Furthermore, the pattern of interventions reported during the snapshots did not mirror that documented during direct observation. However, it is not feasible to adopt direct observation as a routine practice since this method is time and labour intensive. Nonetheless, this study raised questions about the value of documenting pharmacists' interventions during certain periods using only self-reporting methods. Routine self-documentation of pharmacists' interventions is common amongst hospitals in the USA, Australia, and New Zealand (196, 246, 250); however, our study raises questions about the worth of this practice.

An appropriate documentation system should accurately reflect the nature of the activities provided, must be able to provide information on the factors that influence the pattern of interventions and showcase the value of pharmacists' contribution.(247) Although the interventions occur every day, it is not feasible to accurately quantify their impact on patient care if there is no adequate documentation on a day-to-day basis.(18, 246) Our findings indicated that the information recorded on the intervention form during snapshots was not sufficient to provide meaningful description of the interventions, particularly to assess the clinical significance of the interventions. Furthermore, there was no standardised definition and classification of pharmacists' interventions to guide the pharmacists when documenting their interventions.(248, 250) Dooley *et al.*(251) suggested a national standard for the documentation of clinical pharmacy practices to provide new opportunity to quantify clinical pharmacists' contribution to patient care and benchmark clinical services.

The benefits of pharmacists' intervention documentation have been justified in a number of studies,(131, 197, 252, 253) where these activities promote medication safety and ensure optimal outcomes for patients. In line with other studies, limited time, limited staff and heavy workload have been identified by pharmacists in our

study as the main barriers to documenting their interventions.(247, 251) This under-reporting of interventions leads to an underestimation of pharmacists' clinical contribution and loss of opportunities to improve clinical services and patient care. This underlines the necessity to improve the documentation process of pharmacists' interventions by employing innovative tools (e.g. applications on smartphones or tablets).(121, 253-255) Additionally, staff motivation is crucial to improving documentation. This may be enhanced by providing incentives to pharmacists and/or by making intervention documentation compulsory.(247, 253) It has been reported that an improved utilisation of intervention reports can considerably motivate pharmacists to document their interventions.(246, 248, 250)

In summary, the self-reported pharmacists' interventions during snapshot periods was not representative of the interventions documented during direct observation. This raises the question of the value of this documentation method, and suggests the need for efficient means by which pharmacists document their interventions as part of day-to-day practice.

6.5 Acknowledgements

The authors thank all ward-based clinical pharmacists at Princess Margaret Hospital for Children for participating in this study. The authors also thank Dr Richard Parsons for his help with the statistical analysis.

6.6 Additional Qualitative Results

For brevity, the following data were not reported in the published paper. These data represented the participants' comments on the other questions posed during FDG, but not reported in the paper.

6.6.1 Pharmacists' comments on the results of pharmacist's interventions documented during observation vs snapshot reports

Participants were given the opportunity to comment on the differences between pharmacists' interventions documented in snapshot reports and those documented during observation. Even though some participants did not expect these differences, they thought the interventions documented during observation were valid and more reflective than snapshot reports to describe their routine practice (see quotations below).

"...the difference in snapshot versus observation stuff is, we are really bad, we do not record when we do our snapshot...So, I know when we do snapshot, we're supposed to record what comes into the office, but we're very poor at doing it." PA3

"...although it's different to what I expected to see, I still think it's valid, it's not like the data is incorrect ... I think the 3B [Haematology-Oncology] stuff's pretty true." PA4

"Oh, absolutely, yes. Especially for the long time periods ... you were very thorough in recording what we actually did." PA4

6.6.2 How important is the documentation of pharmacists' interventions?

Participants in the focus group were asked to provide their opinion on the importance of documentation of pharmacists' interventions. Their responses supported documentation as a data source for justification of staffing, medical and legal reasons, and pharmacy practice improvement. These issues are reflected in following quotations from participants:

"That, in itself, is also very, something that is, perhaps, is staffing to justify extra staff." PA3

"And also for medical and legal reasons too, to cover your self in the future if something, you know is shown to have gone wrong." PA4

"...some of the ... preliminary data showed how good potentially a satellite pharmacy is, and 3B [Haematology-Oncology] is a satellite pharmacy, our only satellite pharmacy in the hospital ... it could provide, I guess, cases for satellite pharmacies in new children's hospital." PA5

In addition, they perceived that the documentation of pharmacists' interventions was important for quantification of pharmacists' contribution to patient care, identification of problems during the healthcare process in hospital, and quality assurance (see quotations below).

"You need to be able to, you know, show what we do, to quantify what we do." PA2

"...then looking at common occurrences throughout the ward, because everyone's covering different places, and to see and go, oh PA7 picked up an interaction, oh PA5 has done that same thing. Oh, look PA2 done that there, as well. Wow! That must be a real issue in the hospital..." PA7

"...just with the focus on health and safety … hospitals also need to be reassured that the right things are done." PA3

6.6.3 How valuable do you think are your clinical interventions?

When the participants were asked to assess the value of their interventions, they agreed that their interventions were valuable, but varied perspectives were evident in defining the value. They argued that the interventions can be considered valuable because the interventions can minimise patient harm. Further, they perceived that the values were dependent of the nature and/or the timeframe of the interventions after identifying the harm-related problems. These themes are reflected in the following quotations.

"I think there's a full scale of it. You comment on with the things that have minimal value, such as writing, with food on ibuprofen at normal doses, right up to identifying a medication error and taking it further. So there's a range of how valuable they might be." PA1

"But then if you've got the minimal intervention things that are picked up early, you pick that up when they first started in hospital, but then if they continue for the next six months to take that ibuprofen without food, it becomes more and more valuable that you've picked it up early …"PA6

In addition, the participants mentioned the value of pharmacists' interventions for hospital accreditation and staff compliance during clinical trial (see quotations below).

"Yes. It's valuable toward process in the hospital. If it doesn't, if it assists us in getting accredited as a hospital, that's massively valuable in the whole health system, because you want all your hospitals to be accredited." PA6

"I think it's also valuable with the clinical trial stuff to pick it up and document it as well … [it] helps staff compliance, where you do really well when you get audited on that..." PA4

6.6.4 Do you think there are problems with the way data are used? Why do you think so?

In terms of the use of intervention documentation during snapshots, participants revealed some issues, including inaccesibility of snapshot data, lack of feedback for reporting pharmacists, and underutilisation of the reports. The following quotations reflect these issues.

"…our continuous intervention system we had before was, [the data] were pretty well inaccesible, you know, we handed in the sheets to [administrator]. She entered them in a database, but … in the six or seven years it was running while I was here, I never went back and looked at the database at anything. I'm not sure anyone actually did." PA4

"I've been here six and a half years. I've never seen any feedback." PA6

"Down here, we're doing it for higher up, basically, to keep them satisfied … we never see the results." PA4

6.7 Discussion of Additional Qualitative Results

The practice of pharmacy in hospital settings has transformed considerably, and the documentation of the clinical interventions of pharmacists has become increasingly important.(256) Understandably, professional and regulatory bodies in some countries have recommended that pharmacists record their interventions.(121, 250, 257, 258) The American Society of Health-System Pharmacists mandates pharmacists to document their recommendations.(257) The Joint Commission on Accreditation of Healthcare Organizations in the USA even stresses the importance of pharmacists' intervention documentation as the clinical indicators of medication-use system monitoring.(259) Meanwhile, the Society of Hospital Pharmacists of Australia strongly advises each pharmacy department to provide the policy for documentation of pharmacists' interventions.(121) The Royal Pharmaceutical Society of Great Britain has published guidelines on the recording of pharmacists' interventions.(258) As with other studies, the participants of the FGD claimed that

the documentation of the clinical interventions performed by pharmacists is important and they argued that the documentation can be used for a range of purposes, including justification of staffing, identification of DRPs, quantification of pharmacists' contribution, evidence of pharmacy practice improvement, source of information for quality assurance, clinical trial protocol compliance and medico-legal issues.

It has been acknowledged in numerous studies that the documentation of pharmacists' interventions can provide a great deal of information that can be used for assessing task workload and justifying staffing levels.(18, 184, 226, 260) Catania et al.(261) used documentation of clinical interventions performed by pharmacists to justify the cost of hiring additional hospital pharmacists. Similarly, Davydov(185) found that intervention data can be used to evaluate the cost-effectiveness of hiring additional pharmacists. In line with other pharmacists' intervention studies, this study also revealed that the documentation was beneficial for identication of DRPs. In addition, the analysis of the intervention involving DRPs from time to time can identify the trends of the problems during healthcare process. These trends can be monitored to evaluate the appropriateness of the solutions to correct the perceived problems.(147, 185) The documentation can also be employed to monitor incidents or near misses during the care process.(258) Furthermore, some studies proposed that the analysis of incident-related intervention data can be used in drug bulletin articles and presentations during clinical meetings to educate medical officers, pharmacists and other healthcare professionals.(185, 196, 226)

As with our study, improved documentation of pharmacist interventions has been highlighted as the crucial component of clinical pharmacy services to quantify pharmacists' contribution to patient care, and as a rich source of information for clarifying DRPs with prescribers.(185) Likewise, pharmacy managers participating in a New Zealand survey perceived that the collection of pharmacists' intervention data can identify pharmacists' impact on patient's treatment management.(250) Corresponding with other studies, the pharmacists in our study have pointed out the importance of intervention records from a medico-legal perspective. The retrieved records can be the strong evidence when the decisions during care delivery are challenged.(257, 258) The records can also be used for quality assurance to evaluate

the pharmacists' competency and ensure the quality and continuity of patient care.(258)

In relation to the value of pharmacists' clinical interventions, the participants generally thought that the interventions were valuable. However, the focus group revealed varied perspectives in defining the value of the interventions, and participants highlighted three points related to the value of pharmacists' interventions, namely, minimisation of patient harm, hospital accreditation, and increased staff compliance to clinical trial protocols. Consistent with our finding, other studies have described the positive impact of clinical intervention of pharmacists on patient safety. These interventions may prevent ADEs, reduce mortality rates and even improve health-related quality of life.(37, 262-264) In addition, the recorded interventions could provide evidence of benefit to hospital administrators (e.g. the institutional drug and therapeutics committee), and subsequently for institutional accreditation, which corresponds with the responses of our participants.(121)

Aside from the concerns surrounding the circumstances in documenting pharmacists' interventions, there is another critical issue to be resolved: how intervention reporting should be taken forward to educate healthcare personnel, and subsequently improve patient care. During the FGD, the predominant themes emerging from the data related to the shortcomings of the snapshot documentation method, including underutilisation of the resulting reports and lack of feedback for reporting pharmacists. Accepting that identification of parmacists' intervention relies on documentation, the valuable documented data are frequently underutilised.(265) In a New Zealand study, some pharmacy managers felt intervention data were not used optimally, i.e. for educational purposes.(250) On the contrary, an American study reported the use of intervention data by quality assurance personnel, pharmacy directors and/or hospital administrators in healthcare institutions.(246) Similarly to suggestions in our study, intervention data have been used for peer review and feedback.(196, 266) With respect to the accessibility of the intervention data, Nurgat et al.(267) demonstrated the improved accesibility of the intervention documentation after implementation of web-based tool.

6.8 Overall Limitations and Recommendations

There are some limitations to be acknowledged in this study. Firstly, this study involved pharmacists' intervention reports collected during three snapshot periods only from the five study wards in a children's hospital. A greater number of reporting periods would increase the opportunities to reveal the pattern of the interventions more representatively. Although the three snapshot periods were identified with the most complete set of intervention reports, the reports were largely incomplete. The manually-completed forms completed during snapshot documentation periods were not validated using patients' medical records. Furthermore, it is recommended to data collection within multiple paediatric institutions for greater generalisability. It is possible to expand this study to include adult settings.

FGD was chosen as the method to identify barriers and improvements regarding documentation of interventions. Even with skilled facilitation, this method may not adequately extract dissenting opinions from participants. Nonetheless, this method was deemed suitable for the small group of participants to collect qualitative data on this topic of interest.(268, 269) The method enables the investigators to understand issues in depth,(270) is highly flexible, and allows researchers to assess views and opinions directly and efficiently.(268) Future studies might consider undertaking further FGD research or employing other method (e.g. in-depth interview) to increase the likelihood of more pharmacists participating, and to obtain more insights from each pharmacist.

6.9 Overall Conclusions

To summarise, self-report by pharmacists of their interventions during snapshot recording periods was not representative of the interventions documented during direct observation. This raises the question of the value of self-documentation, and suggests the need for an efficient means by which pharmacists can document their interventions in routine practice. Meanwhile, the findings from the FGD confirmed previous studies regarding the barriers to documentation of pharmacists' interventions, which included time constraints, limited staffing, workload and lack of standardisation of the documentation. The pharmacists also raised concerns around underutilisation of the intervention reports and lack of feedback from their employer. The focus group data offered clear directions for improving the existing intervention

documentation. The suggestions may include standardisation of intervention documentation, improvement in the utilisation of collated intervention data, and implementation of a hybrid system combining snapshot and observational reporting.

Chapter 7

PART FOUR: RESULTS AND DISCUSSION

Few studies have been conducted on medication misadventure including MEs in paediatrics compared to adult patients. There are lacks of strategies to prevent MEs. As established in Section 1.7.2, RCA was applied to identify the contributors to MEs and preventive strategies. An RCA was conducted using a questionnaire depicting five simulated case scenarios with a cohort of health professionals (doctors, nurses, pharmacists) at the study hospital.

7.1 Results

Of the 111 RCA questionnaires administered to doctors, nurses and pharmacists during the study period (August-October 2014), six (19.4%), 11 (25.6%) and eight (21.6%) were returned, respectively. All of the returned questionnaires were included in the analysis. The overall response rate was 22.5%. Most participants were aged 31 to 40 years, and the majority were female (Table 7.1). Three of the doctors were registrars and three were consultants/specialists. Six participants were registered nurses/midwives, four were clinical nurses/clinical midwives/clinical development nurses and one was a clinical nurse/midwife consultant. Four of the pharmacists were not assigned a clinical pharmacist position; two were junior clinical pharmacists; one was a senior clinical pharmacist; and one was in a senior leadership position (Pharmacy Director/Deputy Director). With regard to overall years of experience as health professionals, each group showed a similar pattern, with most participants having worked for more than 10 years.

Table 7.1 Demographics of participants returning the RCA questionnaire

Characteristics	Number (%)		
	Doctors (n=6)	**Nurses (n=11)**	**Pharmacists (n=8)**
Age (years)			
21-30	1 (16.7)	3 (27.3)	0 (0.0)
31-40	4 (66.7)	4 (36.4)	5 (62.5)
41-50	0 (0.0)	2 (18.2)	1 (12.5)
>50	1 (16.7)	2 (18.2)	2 (25.0)
Gender			
Male	2 (33.3)	1 (9.1)	1 (12.5)
Female	4 (66.7)	10 (90.9)	7 (87.5)
Overall experience (years)			
<5	0 (0.0)	2 (18.2)	0 (0.0)
5-10	2 (33.3)	2 (18.2)	2 (25.0)
11-20	3 (50.0)	4 (36.4)	3 (37.5)
>20	1 (16.7)	3 (27.3)	3 (37.5)
Paediatric experience (years)			
<5	0 (0.0)	2 (18.2)	2 (25.0)
5-10	2 (33.3)	4 (36.4)	4 (50.0)
11-20	3 (50.0)	4 (36.4)	2 (25.0)
>20	1 (16.7)	1 (9.1)	0 (0.0)

As explained in Section 3.4.1, the participants were presented with five simulated case studies followed by two ME-related questions and seven RCA questions for identifying the contributing factor of ME in each case. The participants were also asked to give their suggestions for preventing the MEs. The results comprised six sections, the first five sections related to the simulated case studies, and the last section described the RCA assessment on the contributing factors of each case and the agreement of the participants' responses.

7.1.1 Case Study 1 (Inappropriate Dose)

The first case was designed to highlight a prescribing error involving the high-risk drug digoxin in a six-month-old baby (Appendix 11). The physician wrote the digoxin dose inappropriately (not including a leading zero before the full stop), resulting in the patient receiving a 100-fold higher dose. The patient died after receiving the digoxin overdose.

All participants except one pharmacist rated the error as life threatening. All doctors and pharmacists perceived all three health professionals (doctor, nurse, pharmacist)

accountable for the error. Nine of the 11 nurses agreed, with the remaining two nurses pointed to their own profession as responsible for the error.

The majority of doctors and pharmacists thought patient-specific issues contributed to the error (Table 7.2).

Two main themes emerged on patient-specific issues. Participants viewed the complexity of the patient's medical condition in part as a contributing factor.

'Unwell, pneumonia, underlying cardiac condition.' (Doctor 59)
'Had open heart surgery so dosage should have been checked – cardiac abnormalities.' (Nurse 98)

In addition, some participants noted the patient's young age as the issue in this case:

'Young age.' (doctor 60)
'Young age with severe consequence of overdose of a drug...' (Pharmacist 39)

Table 7.2 Participants' perceptions on the factors contributing to the ME (Case 1)

Contributing factors and sub-factors	Number (%)		
	Doctors (n=6)	Nurses (n=11)	Pharmacists (n=8)
Patient specific issues	4 (66.7)	3 (37.3)	6 (75.0)
Dismissal of policies/ procedures or guidelines	6 (100.0)	11 (100.0)	7 (87.5)
- Error/omission in medication reconciliation	3 (50.0)	5 (45.5)	0 (0.0)
- Clinical guidelines	2 (33.3)	8 (72.7)	5 (62.5)
- Coordination of care	1 (16.7)	5 (45.5)	3 (37.5)
- Medical record documentation	3 (50.0)	6 (54.5)	6 (75.0)
- Level and frequency of monitoring of patient	0 (0.0)	5 (45.5)	2 (25.0)
Human resources issues	5 (83.3)	10 (90.9)	7 (87.5)
- Staff workload and inadequate staffing	2 (33.3)	3 (27.3)	5 (62.5)
- Staff training and competencies	5 (83.3)	8 (72.7)	7 (87.5)
- Staff supervision	4 (66.7)	4 (36.4)	6 (75.0)
Miscommunication	5 (83.3)	5 (45.5)	3 (37.5)
- Miscommunication between staff	5 (83.3)	5 (45.5)	3 (37.5)
- Miscommunication between staff and patient and/or family	0 (0.0)	2 (18.2)	0 (0.0)
Physical environment of the health service	0 (0.0)	1 (9.1)	0 (0.0)
Control/provision of medication	4 (66.7)	4 (36.4)	3 (37.5)
- Medication storage	1 (16.7)	0 (0.0)	0 (0.0)
- Labelling	1 (16.7)	0 (0.0)	0 (0.0)
- Documentation of administration	2 (33.3)	1 (9.1)	2 (25.0)
- Internal transfer of medication	0 (0.0)	2 (18.2)	1 (12.5)
'Other'	2 (33.3)	4 (36.4)	3 (37.5)

Participants proposed how the subsets of dismissal of policies/procedures or guidelines could have contributed to the error. Four themes were identified from the analysis of participants' descriptions: dismissal of clinical guidelines or hospital policy/protocol, no/inadequate coordination of care, no/inadequate medical/medication record documentation and no/inadequate patient monitoring.

Dismissal of clinical guidelines or hospital policy/protocol and no/inadequate coordination of care are exemplified by the following:

'Dose wasn't written correctly, mg instead of micogram, used decimal with no 0.' (Doctor 36)
'Nurse did not double check prior to giving cardiac meds [medications]. Should be checked by two nurses.' (Nurse 94)
'Resident should have contacted child registrar or consultant.' (Nurse 95)

No/inadequate medical/medication record documentation and no/inadequate patient monitoring is supported by:

'The dose in mg/kg has not been entered on the chart and therefore not easily checked by nurse and pharmacist.' (Pharmacist 19)
'Pulse and rate/minute should be checked before giving it.' (Nurse 95)
' No evidence of pt [patient] monitoring.' (Nurse 103)

With regard to human resources issues as the contributing factors, comments highlighted problems surrounding staff training and competencies. Some participants argued that the error could be associated with staff workload and inadequate staffing, and deficiency in staff supervision:

'Resident just started and did not want to bother busy registrar.' (Pharmacist 9)
'Registrar was busy and did not have time to adequately supervise new resident.' (Pharmacist 19)

Participants also mentioned lack of staff training and competencies as an enabler of the error.

'First week in paediatrics, but unaware of seriousness of error consequence and guidelines.' (Pharmacist 17)
'Lack of training in correct documentation of medication.'(Doctor 61)

Miscommunication between staff comprised all but one of the comments; miscommunication between staff and patient and/or family was mentioned by only one participant.

'Lack of communication between resident and senior health staff assumption that every party had checked dosing. Nursing belief that dosing correct instead of checking.' (Doctor 61)

'The nurse thought dosage had been checked by pharmacist and doctor, but did not make sure.' (Nurse 96)

Regarding control/provision of medication as the contributing factors, participants identified documentation of administration and internal transfer of medication as relevant issues.

'Only one nurse signed, high-risk drug – not double checked and amount given not written. No mg/kg in dosing box for nurse or pharmacist to check.' (Pharmacist 17)
'Potentially no information given on strength digoxin given to ward to administer dose.' (Nurse 98)

With regards 'Other' as a contributing factor, two identified themes included the high-risk drug and fear of senior staff by the junior staff:

'Digoxin has a very low therapeutic window, and overdose can occur more readily than with other drugs.' (Pharmacist 31)
'Fear of RMO [Resident Medical Officer] letting registrar [check the medication order].' (Doctor 60)

The last RCA question asked participants to give their suggestions on how to prevent recurrence of the error. Four themes emerged: firstly, improved availability and accessibility of clinical guidelines and strict hospital policies/protocols for high-risk drugs. The guidelines and the policies/protocols should cover all stages of medication use from prescribing through to monitoring. Secondly, all staff should be aware of, and comply with, the guidelines and the policies/protocols.

'Clinical guidelines and clear protocol and easy access for prescribing staff and nursing and pharmacy staff.' (Pharmacist 17)
'Doctor, pharmacist and nurse should all check the prescribed dose is correct with AMH or other guidelines before administration and not assume correct.' (Doctor 59)
'Additional restriction on who can chart dangerous/high risk drug such as digoxin.' (Doctor 37)

Thirdly, the participants proposed adequate staff supervision would prevent the identified error.

'Close supervision of new residents and easy access to ask questions, especially when just starting out.' (Doctor 59)
'RMO [Resident Medical Officer] being adequately supported.' (Nurse 50)

Fourthly, participants suggested adequate staff education and training/competencies can improve practice and subsequently prevent MEs.

'Competency of all involved, knowledge of drug, dosage and paediatric dosage especially.' (Nurse 100)
'Ensure adequate education around high-risk drugs with prescribing, with dispensing, with administration.' (Pharmacist 10)

7.1.2 Case Study 2 (Dispensing Error)

Case study 2 (Appendix 11) illustrated a dispensing error where a locum pharmacist with poor vision and inadequate supervision filled the medication orders for seizure patient. The drugs in the dispensary were arranged alphabetically by generic name and the locum dispensed prednisolone instead of primidone.

All nurses and pharmacists rated the error in the range of major to life threatening (Table 7.3). The majority of the doctors offered similar assessment; one doctor rated the error as moderate in significance.

Table 7.3 Participants' ratings of the clinical significance of the ME (Case 2)

	Number (%)		
Clinical significance of ME	**Doctors (n=6)**	**Nurses (n=11)**	**Pharmacists (n=8)**
Life-threatening	1 (16.7)	5 (45.5)	4 (50.0)
Major	4 (66.7)	6 (54.5)	4 (50.0)
Moderate	1 (16.7)	0 (0.0)	0 (0.0)

The majority of the participants identified two health professionals as responsible: nurse and pharmacist (Table 7.4).

Table 7.4 Participants' responses on the responsible health professional(s) (Case 2)

Health professional(s)	Number (%)		
	Doctors (n=6)	Nurses (n=11)	Pharmacists (n=8)
Nurse	0 (0.0)	1 (9.1)	0 (0.0)
Pharmacist	0 (0.0)	0 (0.0)	2 (25.0)
Nurse and pharmacist	4 (66.7)	9 (81.8)	6 (75.0)
Doctor and nurse and pharmacist	2 (33.3)	1 (9.1)	0 (0.0)

Specific patient issues were identified by only one participant as a contributor, while the majority of responses pointed to dismissal of policies/procedures or guidelines (Table 7.5).

Three themes emerged in comments relating to the dismissal of policies/procedures or guidelines: omission/dismissal of medication reconciliation, dismissal of clinical guidelines or hospital policy/protocol, and no/inadequate coordination of care.

'Medication was not reconciled to chart.' (Nurse 96)

'Lack of medication reconciliation at discharge. Did patient have a list of current medications? If so, this may have helped the error to be noted.' (Pharmacist 9)

'Pharmacist not checking with another before dispensing as per guidelines.' (Nurse 98)

'If there was a discharge procedure requiring nurses to double check the medication prior to discharge, then it should have been followed. This process may have detected the dispensing error.' (Pharmacist 19)

'Pharmacy/nurse not coordinating discharge medications.' (Nurse 96)

Participants' responses on human resources issues uncovered three themes: staff workload and inadequate staffing, staff training and competencies, and staff supervision.

'Adequate cover for lunch time.' (Pharmacist 9)

'Locum pharmacist and adequacy of orientation.' (Doctor 37)

'Locum pharmacist in dispensary over lunch, not supported by experienced pharmacist in normal checking procedure.' (Pharmacist 31)

Table 7.5 Participants' perceptions on the factors contributing to the ME (Case 2)

Contributing factors and sub-factors	Number (%)		
	Doctors (n=6)	Nurses (n=11)	Pharmacists (n=8)
Patient specific issues	1 (16.7)	0 (0.0)	0 (0.0)
Dismissal of policies/ procedures or guidelines	6 (100.0)	11 (100.0)	8 (100.0)
- Error/omission in medication reconciliation	4 (66.7)	6 (54.5)	4 (50.0)
- Clinical guidelines	3 (50.0)	10 (90.9)	2 (25.0)
- Coordination of care	3 (50.0)	4 (36.4)	4 (50.0)
- Medical record documentation	0 (0.0)	1 (9.1)	0 (0.0)
Human resources issues	6 (100.0)	10 (90.9)	8 (100.0)
- Staff workload and inadequate staffing	5 (83.3)	7 (63.6)	7 (87.5)
- Recruitment	1 (16.7)	0 (0.0)	1 (12.5)
- Staff training and competencies	2 (33.3)	6 (54.5)	6 (75.0)
- Staff supervision	4 (66.7)	7 (63.6)	3 (37.5)
Miscommunication	2 (33.3)	4 (36.4)	2 (25.0)
- Miscommunication between staff	2 (33.3)	1 (9.1)	2 (25.0)
- Miscommunication between staff and patient and/or family	0 (0.0)	3 (27.3)	2 (25.0)
Physical environment of the health service	4 (66.7)	11 (100.0)	8 (100.0)
- Lighting	5 (83.3)	11 (100.0)	7 (87.5)
- Space	1 (16.7)	4 (36.4)	1 (12.5)
Control/provision of medication	5 (83.3)	9 (81.8)	6 (75.0)
- Medication storage	4 (66.7)	7 (63.6)	3 (37.5)
- Labelling	1 (16.7)	5 (45.5)	3 (37.5)
- Documentation of administration	1 (16.7)	0 (0.0)	0 (0.0)
- Internal transfer of medication	1 (16.7)	4 (36.4)	1 (12.5)
'Other'	3 (50.0)	7 (63.6)	4 (50.0)

Participants' comments on miscommunication revealed two themes: miscommunication between staff, and miscommunication between staff and patient and/or family.

'Miscommunication between requirements of dispensing discharge medications.' (Pharmacist 10)

'Nurses should have checked every medication with family prior to D/C [discharge].' (Nurse 87)

Participants' comments on the physical environment of the health service revealed two themes. The first related to poor lighting:

'Inadequate lighting in this case may have contributed to the selection of the wrong medication.' (Pharmacist 19)

One-quarter of participants highlighted space as the other contributor.

'Medication stocked closely together.' (Nurse 105)

Comments relating to control or provision of medicines identified medication storage, labelling and internal transfer of medication as concerns.

'Medication stored in alphabetical order so easier to confuse.' (Doctor 59)
'Label may have covered original package or drug may have been repacked making checking by nurse/parent difficult.' (Pharmacist 3)
'No check (second time) in Pharmacy and no check by nurse when reviewing.' (Pharmacist 17)

At least half of the participants in each group nominated 'other' factor(s); some were related to the factors listed above (Table 7.5). One new theme emerged from the participants' comments: staff health, in particular the pharmacist's impaired vision:

'Pharmacist's vision should have been corrected when noticed.' (Nurse 87)
'Locum pharmacist in dispensing should have proper glasses when he is working in a responsible role. He should have been able to read label on the bottle.' (Pharmacist 31)

Suggestions to prevent the recurrence of the error encompassed six themes. The participants thought a policy for checking discharge medications by at least two staff should exist and be followed by all staff providing patient care.

'Nurse to check medications dispensed against chart and prescription.' (Nurse 96)
'There is no harm in checking the correct dose is given to the correct patient. Every person that handles the medication between Pharmacy and the patient should check.' (Pharmacist 19)

Three further themes emerged related to improved staffing and supervision, adequate staff education, and adequate staff health requirement.

'Dispensing manager should ensure staffing is adequate, so full dispensing checking procedures are followed at all times.' (Pharmacist 31)

'Educating staff and consistently refreshing staff about current practices and protocols.' (Nurse 87)

'Supervisor noting cracked glasses and asking staff to attend to these before working.' (Doctor 59)

Adequate discharge counselling was also proposed by the participants to avoid the recurrence of the error.

'Parents could have been better informed about meds [medications] prior to discharge and have noted absence of anticonvulsants.' (Doctor 44)

'Ward pharmacist to counsel patients on discharge regarding medications.' (Pharmacist 9)

Lastly, the participants suggested improving the physical environment of the pharmacy.

'Lighting in a dispensary should be fixed.' (Pharmacist 31)

'Change the way meds [medications] are stored in Pharmacy so that similar sounding/looking drugs aren't adjacent.' (Doctor 37)

'Storage of meds [medications] by therapeutic class.' (Pharmacist 9)

7.1.3 Case Study 3 (Drug Omission)

Case study 3 described a patient with history of asthma and seizures who was admitted due to asthma exacerbation(Appendix 11). As one of the anticonvulsants (levetiracetam) was out of stock, the patient was not given levetiracetam for five doses, triggering a seizure.

All doctors and pharmacists rated the error as major, while just over half of the nurses shared the same view (Table 7.6).

Table 7.6 Participants' ratings of the clinical significance of the ME (Case 3)

	Number (%)		
Clinical significance of ME	**Doctors (n=6)**	**Nurses (n=11)**	**Pharmacists (n=8)**
Life-threatening	6 (100.0)	6 (54.5)	8 (100.0)
Major	0 (0.0)	4 (36.4)	0 (0.0)
Unsure	0 (0.0)	1 (9.1)	0 (0.0)

There was little consensus between the groups on the responsible health professional (Table 7.7). The majority of the doctors thought all health professionals (doctor, nurse, pharmacist) contributed to the error, while the majority of the pharmacists suggested both nurse and pharmacist were responsible for the error. In the case of nurses, nearly half blamed their own profession alone.

Table 7.7 Participants' responses on the responsible health professional(s) (Case 3)

Health professional(s)	Number (%)		
	Doctors (n=6)	Nurses (n=11)	Pharmacists (n=8)
Nurse	0 (0.0)	5 (45.5)	0 (0.0)
Nurse and pharmacist	2 (33.3)	5 (45.5)	7 (87.5)
Doctor and nurse and pharmacist	4 (66.7)	1 (16.7)	1 (12.5)

Not more than half of the participants in each group considered specific patient issues as contributing factors (Table 7.8).

Participants' comments on patient issues uncovered two themes: patient's medical condition and patient's lack of drug knowledge:

'Dual diagnosis i.e. management of acute illness [asthma] taking priority over chronic illness/epilepsy.' (Doctor 59)

'15-year-old patient could have reminded nurse about missing meds [medications], as at that age, would have some involvement in compliance.' (Pharmacist 3)

Table 7.8 Participants' perceptions on the factors contributing to the ME (Case 3)

Contributing factors and sub-factors	Number (%)		
	Doctors (n=6)	Nurses (n=11)	Pharmacists (n=8)
Patient specific issues	3 (50.0)	2 (18.2)	3 (37.5)
Dismissal of policies/ procedures or guidelines	5 (83.3)	11 (100.0)	7 (87.5)
- Error/omision in medication reconciliation	3 (50.0)	8 (72.7)	4 (50.0)
- Clinical guidelines	2 (33.3)	5 (45.5)	1 (12.5)
- Coordination of care	4 (66.7)	9 (81.8)	6 (75.0)
- Medical record documentation	0 (0.0)	1 (9.1)	1 (12.5)
- Level and frequency of monitoring of patient	1 (16.7)	2 (18.2)	1 (12.5)
Human resources issues	6 (100.0)	9 (81.8)	8 (100.0)
- Staff workload and inadequate staffing	4 (66.7)	7 (63.6)	4 (50.0)
- Recruitment	0 (0.0)	1 (9.1)	0 (0.0)
- Staff training and competencies	3 (50.0)	6 (54.5)	6 (75.0)
- Staff supervision	3 (50.0)	4 (36.4)	0 (0.0)
Miscommunication	6 (100.0)	10 (90.9)	6 (75.0)
- Miscommunication between staff	6 (100.0)	10 (90.9)	6 (75.0)
- Miscommunication between staff and patient and/or family	2 (33.3)	4 (36.4)	1 (12.5)
Control/provision of medication	4 (66.7)	11 (100.0)	6 (75.0)
- Medication storage	1 (16.7)	1 (9.1)	2 (25.0)
- Labelling	1 (16.7)	0 (0.0)	0 (0.0)
- Documentation of administration	2 (33.3)	1 (9.1)	0 (0.0)
- Internal transfer of medication	2 (33.3)	9 (81.8)	6 (75.0)
'Other'	1 (16.7)	4 (36.4)	1 (12.5)

Three emergent themes were associated with the participants' comments on the dismissal of policies/procedures or guidelines. The participants perceived the error happened due to dismissal of clinical guidelines or hospital policies/protocols for supply of imprest medications.

'Levetiracetam was written on drug chart and should have been given on 2/5 [2 May[and 3/5 [3 May]. Nurses and ward pharmacist should have taken more care and followed through on low stock.' (Pharmacist 31)

They also indicated inadequate coordination of care and inadequate level and frequency of patient monitoring.

'Lack of coordination between nursing staff and pharmacist to arrange stock of medication.' (Pharmacist 28)
'All three health professionals not reviewed or paid attention to missed dosing.' (Pharmacist 17)

There were two emergent themes in relation to human resources: staff workload and inadequate staffing, and inadequate staff training and competencies.

'Pharmacist too busy and forgot to tell assistant to restock.' (Doctor 59)
'Nursing staff should be made aware of which medications not be withheld (not given) without endangering the patient and what steps to take to obtain the medication or inform the doctor so that an alternative can be prescribed.' (Pharmacist 19)
'Staff did not follow necessary steps to prevent this error and should be re-trained on importance of all aspects of their job.' (Pharmacist 31)

Participants' comments on miscommunication indicated two themes: miscommunication between staff, and miscommunication between staff and patient and/or family.

'Pharmacist not informing pharmacist assistant, nurses not informing other staff of lack of meds [medication], doctors not being informed of medication not being given.' (Nurse 98)
'Patient not told of omission, may have had own supply available.' (Nurse 95)

The issue of control/provision of medication gave rise to one theme: poor internal transfer of medication.

'Better process not followed for supply of drug to patient from Pharmacy.' (Pharmacist 17)
'Not having medication being restock when low. Nursing not aware of how to obtain more stock.' (Nurse 98)

Participants' comments on 'other' factor(s) revealed no new themes. These were classified under the contributors of miscommunication and control/provision of medication.

Suggestions on how to prevent recurrence of the error mapped to seven themes. Firstly, the participants identified the need for a hospital policy on the use of imprest medications.

'Clear process and protocol to follow if medicine not available from Pharmacy.' (Pharmacist 17)
'Policy of an after-hours imprest list so nurse staff can source medications from other wards after-hours.' (Pharmacist 9)

The participants also indicated adequate staffing, and adequate staff education and training, as the other two ways to avoid recurrence of the error:

'Increase staffing to decrease workload.' (Doctor 61)
'Re-education regarding obtaining meds [medications] rather than annotating chart with N[1].' (Pharmacist 3)

Two further themes related to patient education and monitoring.

'Empower patients to be partners in their own health and medications.' (Pharmacist 10)
'Medical team checking medication chart daily.' (Doctors 59)

Some participants deemed the use of technologies to monitor the stock level of medications a promising solution.

'Pharmacist to have a reminder note, electronic paper so they can tick off jobs completed for day.' (Nurse 105)
'Computer alerts to restock meds [medications].' (Doctor 59)

Good communication between staff was also suggested by most of the participants as a preventive measure.

'Clear route communication between ward nurses and ward pharmacist.' (Doctor 37)
'Nurse to inform shift coordinator of missing medication so it can be sourced and given as soon as available.' (Nurse 105)
'Night nurse should have read drug chart and called on-call pharmacist on evening on 2/5 [2 May] and get more levetiracetam.' (Pharmacist 31)

[1]On the National Inpatient Medication Chart 'N' equated 'Not Available' in the study hospital.

7.1.4 Case Study 4 (Monitoring Error – Documented Allergy)

Case study 4 was developed to illustrate inadequate communication and documentation resulting in an anaphylactic reaction in a patient with history of penicillin allergy (Appendix 11). At least half of the participants across the three groups assessed the error in this case as life threatening (Table 7.9).

Table 7.9 Participants' ratings of the clinical significance of the ME (Case 4)

Clinical significance of ME	Number (%)		
	Doctors (n=6)	Nurses (n=11)	Pharmacists (n=8)
Life-threatening	4 (66.7)	6 (54.5)	7 (87.5)
Major	2 (33.3)	4 (36.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	1 (12.5)
Unsure	0 (0.0)	1 (9.1)	0 (0.0)

There were varied perspectives among the three groups in assigning responsibility for the error. The doctors perceived at least two health professionals should take responsibility, while the majority of pharmacists thought the doctor with another health professional(s) was responsible (nurse, pharmacist) (Table 7.10).

Table 7.10 Participants' responses on the responsible health professional(s) (Case 4)

Health professional(s)	Number (%)		
	Doctors (n=6)	Nurses (n=11)	Pharmacists (n=8)
Doctor	0 (0.0)	1 (9.1)	1 (12.5)
Nurse	0 (0.0)	1 (9.1)	0 (0.0)
Doctor and nurse	2 (33.3)	3 (27.3)	1 (12.5)
Doctor and pharmacist	1 (16.7)	0 (0.0)	3 (37.5)
Doctor and nurse and pharmacist	3 (50.0)	3 (27.3)	2 (25.0)
None of the above	0 (0.0)	3 (27.3)	1 (12.5)

The participants' perceptions about the contributing factors revealed patient-related factors and miscommunication as the key issues (Table 7.11).

Explanation of patient-related factors was associated with one theme, the patient's drug allergy.

'Patient has an allergy/anaphylaxis.' (Doctor 59)
'Patient allergic to penicillin.' (Pharmacist 3)

Comments relating to the language barrier were assigned to miscommunication rather than a patient-related issue.

Table 7.11 Participants' perceptions on the factors contributing to the ME (Case 4)

Contributing factors and sub-factors	Number (%)		
	Doctors (n=6)	Nurses (n=11)	Pharmacists (n=8)
Patient specific issues	6 (100.0)	8 (72.7)	8 (100.0)
Dismissal of policies/ procedures or guidelines	3 (50.0)	9 (81.8)	8 (100.0)
- Error/omission in medication reconciliation	1 (16.7)	2 (18.2)	1 (12.5)
- Coordination of care	2 (33.3)	5 (45.5)	5 (62.5)
- Medical record documentation	1 (16.7)	4 (36.4)	7 (87.5)
- Level and frequency of monitoring of patient	1 (16.7)	0 (0.0)	1 (12.5)
Human resources issues	3 (50.0)	8 (72.7)	5 (62.5)
- Staff workload and inadequate staffing	1 (16.7)	1 (9.1)	0 (0.0)
- Recruitment	0 (0.0)	1 (9.1)	0 (0.0)
- Staff training and competencies	3 (50.0)	5 (45.5)	4 (50.0)
- Staff supervision	1 (16.7)	0 (0.0)	0 (0.0)
Miscommunication	6 (100.0)	10 (90.9)	8 (100.0)
- Miscommunication between staff	3 (50.0)	7 (63.6)	5 (62.5)
- Miscommunication between staff and patient and/or family	5 (83.3)	8 (72.7)	7 (87.5)
Control/provision of medication	1 (16.7)	1 (9.1)	1 (12.5)
- Labeling	0 (0.0)	1 (9.1)	0 (0.0)
- Documentation of administration	0 (0.0)	0 (0.0)	1 (12.5)
'Other'	1 (16.7)	3 (27.3)	0 (0.0)

Dismissal of policies/procedures or guidelines revealed four themes. The first was dismissal of clinical guidelines or hospital policy/protocol.

'I presume hospital guidelines say no cephalosporins if likelihood of penicillin anaphylaxis exist. If so, they were not followed.' (Doctor 44)
'Pen [penicillin] with allergy policy not followed.' (Nurse 50)

Some participants also indicated error/omission in medication reconciliation and no/inadequate coordination of care as contributing factors.

'Medication reconciliation not complete for allergies.' (Pharmacist 10)

'Breakdown in communication between pharmacy and doctor.' (Nurse 50)

No/inadequate medical or medication record documentation was also identified.

'Ward pharmacist did not write that penicillin allergy severity was still to be checked.' (Pharmacist 31)
'The GP [general practitioner] should have also provided some specific information in the letter.' (Pharmacist 19)

Analysis of participants' comments uncovered two themes related to human resources: staff workload and inadequate staffing, and staff training and competencies.

'GP being busy and not returning pharmacist phone call.' (Nurse 98)
'Training what to prescribe in the event of anaphylactic penicillin allergy.' (Nurse 95)

Two themes emerged in association with miscommunication issues. Participants perceived the error could be avoided with better communication between staff. Participants also highlighted miscommunication between staff and the patient and/or family contributed to the error.

'Pharmacist didn't notify doctor/nurses that they were waiting for a phone call from the GP.' (Nurse 87)
'Hospital doctor assumed pharmacist had checked degree of allergy.' (Pharmacist 31)
'Unable to communicate effectively with the family due to language barrier.' (Pharmacist 10)

There was one emergent theme associated with control/provision of medication, i.e. inadequate documentation of allergy was responsible for the error.

'Degree of severity of penicillin allergy not noted on medication chart.' (Pharmacist 31)
'Inadequate documentation of allergy.' (Nurse 98)

Preventive strategies were described in three themes relating to the need for clnical guidelines and clear hospital policies for antibiotics particularly dealing with allergy issues, with compliance by all staff.

'Following hospital guidelines. TGA [Therapeutics Goods Administration] antibiotics for prescribing in context of peniciliin allergy.' (Doctor 59)
'Adhere or review policies/guidelines in regards to allergies.' (Nurse 87)

Participants also highlighted the importance of staff education and training to prevent such errors.

'Improve education of staff in allergies, and that cephalosporin can cause allergic reaction if allergic to penicillin.' (Nurse 98)
'Proper staff training including checking properly.' (Pharmacist 17)

Improved communication between staff, and between staff and the patient and/or family, was proposed as another solution:

'Ward pharmacist should have noted that the severity of the penicillin allergy had not been clarified, so prescriber could have tried again to call GP [general practitioner].' (Pharmacist 31)
'Nurse giving the cephalosporin should have checked by calling doctor or ward pharmacist to see why it had been prescribed when medication chart had an allergy sticker applied.' (Pharmacist 9)
'Use an interpreter to overcome language problems between this patient and staff.' (Nurse 100)

7.1.5 Case Study 5 (Transcribing Error)

The fifth case study was developed to highlight the consequences of a transcribing error, where an antifungal was not recharted for a newly diagnosed oncology patient (Appendix 11). A non-oncology nurse was deployed to this ward, and was unable to identify the error.

More than half of the nurses and the pharmacists rated the error as major in significance (Table 7.12).

Table 7.12 Participants' ratings of the clinical significance of the ME (Case 5)

Clinical significance of ME	Number (%)		
	Doctors (n=6)	Nurses (n=11)	Pharmacists (n=8)
Life-threatening	1 (16.7)	2 (18.2)	2 (25.0)
Major	2 (33.3)	6 (54.5)	5 (62.5)
Moderate	3 (50.0)	3 (27.3)	1 (12.5)

The majority of respondents felt that the doctor alone or in combination with other health professionals was responsible for the error (Table 7.13).

Table 7.13 Participants' responses on the responsible health professional(s) (Case 5)

Health professional(s)	Number (%)		
	Doctors (n=6)	Nurses (n=11)	Pharmacists (n=8)
Doctor	3 (50.0)	4 (36.4)	5 (62.5)
Doctor and nurse	0 (0.0)	4 (36.4)	1 (12.5)
Doctor and pharmacist	0 (0.0)	2 (18.2)	1 (12.5)
Doctor and nurse and pharmacist	3 (50.0)	1 (9.1)	1 (12.5)

With respect to contributing factors, half of the doctors and the pharmacists perceived a specific patient issue(s) had contributed to the error (Table 7.14).

Table 7.14 Participants' perceptions on the factors contributing to the ME (Case 5)

Contributing factors and sub-factors	Number (%)		
	Doctors (n=6)	Nurses (n=11)	Pharmacists (n=8)
Patient specific issues	3 (50.0)	4 (36.4)	4 (50.0)
Dismissal of policies/ procedures or guidelines	3 (50.0)	11 (100.0)	6 (75.0)
- Error/omission in medication reconciliation	2 (33.3)	8 (72.7)	5 (62.5)
- Clinical guidelines	1 (16.7)	2 (18.2)	0 (0.0)
- Coordination of care	1 (16.7)	1 (9.1)	1 (12.5)
- Medical record documentation	0 (0.0)	4 (36.4)	3 (37.5)
- Level and frequency of monitoring of patient	1 (16.7)	0 (0.0)	0 (0.0)
Human resources issues	5 (83.3)	11 (100.0)	8 (100.0)
- Staff workload and inadequate staffing	5 (83.3)	11 (100.0)	8 (100.0)
- Recruitment	1 (16.7)	1 (9.1)	2 (25.0)
- Staff training and competencies	2 (33.3)	4 (36.4)	3 (37.5)
- Staff supervision	1 (16.7)	4 (36.4)	1 (12.5)
Miscommunication	2 (33.3)	6 (54.5)	1 (12.5)
- Miscommunication between staff	2 (33.3)	5 (45.5)	1 (12.5)
- Miscommunication between staff and patient and/or family	1 (16.7)	5 (45.5)	0 (0.0)
Control/provision of medication	0 (0.0)	7 (63.6)	2 (25.0)
- Documentation of administration	0 (0.0)	7 (63.6)	2 (25.0)
'Other'	3 (50.0)	5 (45.5)	2 (25.0)

Analysis of the participants' comments on the specific patient issue(s) revealed two themes: new diagnosis and complex medical condition with multiple medications.

'Recent diagnoses – parent not aware of meds [medications] he would usually be on.' (Nurse 94)

'Complex medical condition and being on multiple medications.' (Doctor 30)

Four emergent themes were associated with the participants' comments on the dismissal of policies/procedures or guidelines. Firstly, the participants perceived that the error was associated, at least in part, with dismissal of clinical guidelines or hospital policies/protocols.

'Transcribing policy not followed.' (Nurse 50)

'Need to check protocol.' (Nurse 105)

Secondly, the participants highlighted an error/omission in medication reconciliation as contributing to the error.

'Medication reconciliation should be completed across charts throughout the admission.' (Pharmacist 10)
'Drug charts not reconciled.' (Doctor 37)

No/inadequate coordination of care and no/inadequate medical or medication record documentation were perceived by the participants as the other two contributing factors.

'Doctors omitted [medication order] but not picked up by nurse.' (Nurse 105)
'The doctors didn't transcribe 100% of the medication chart.' (Nurse 87)

Regarding human resources issues, staff workload and inadequate staffing were commonly highlighted.

'Doctor overworked, not enough doctors, nurses, pharmacists.' (Nurse 100)
'Fatigue, inadequate staffing over public holidays.' (Doctor 61)

Participants also indicated staff training and competencies, and staff supervision as the other two factors accounting for the error.

'A nurse familiar with the treatment may have noticed the error, but staffing necessitated fill-ins who couldn't provide the same level of care.' (Nurse 85)
'Oncology is highly specialised field, and all staff working in the area should be suitably trained. If locum staff are required, the close supervision is needed.' (Pharmacist 19)

Participants' comments on miscommunication issues indicated two themes: miscommunication between staff, and miscommunication between staff and the patient and/or family.

'Doctor intended to chart all medications but failed to do so - miscommunication with nurse.' (Doctor 44)
'Staff not clarifying orders when transcribing medications.' (Nurse 98)
'Staff not being familiar with the patient.' (Nurse 87)
'Family not being aware of regular medication child is taking.' (Nurse 105)

Analysis of the participants' comments on the control/provision of medication as a contributing factor uncovered one theme: documentation of administration.

'Medication not given as not documented.' (Nurse 96)
'Checking of administration times across charts.' (Pharmacist 10)

Comments relating to prevention of the error revealed four themes. Firstly, the need for hospital policy to ensure accuracy of transcribing of medication charts.

'Mandatory check new versus old medication charts with two staff members to ensure everything transcribed correctly and old medication orders ceased if appropriate.' (Doctor 37)
'A procedure should be implemented to ensure that medications are correctly transcribed when new charts are written, e.g. a nurse/pharmacist/doctor could double check the new chart against the old chart, deliberately cancel each item on the old chart when it has been written onto the new chart.' (Pharmacist 19)

Secondly, some participants also proposed electronic prescriptions to prevent transcribing errors.

'Computerised prescriptions would overcome the dilemma of fatigue rewriting medication charts, missed medications.' (Doctor 59)
'An electronic prescription system would avoid need for manual transcribing.' (Doctor 60)

Thirdly, the participants also underlined the need for adequate staffing of experienced staff particularly in the specialty area of oncology.

'Ensure wards are adequately staffed with experienced nurses in the particular specialty.' (Nurse 87)
'Oncology ward nurse manager should endeavour to have ward staffed by nurses trained in Oncology who may have noticed that an anti-fungal drug should be given.' (Pharmacist 31)

Lastly, the need for improved communication between staff and patient and/or family was suggested.

'Nurse checking bedside with family of drug and dose to be given.' (Nurse 105)

'Check with patient along with patient's own supply to prompt if a medication has accidentally not been charted.' (Pharmacist 9)

7.1.6 RCA of the Contributing Factors in the Simulated Cases: Interpretation by the Principal Researcher

The principal researcher perceived three factors as contributing to MEs in all five cases: dismissal of policies/procedures or guidelines, human resources, and miscommunication (Table 7.15).

Table 7.15 Principal researcher's interpretation of the factors contributing to the MEs

Contributing factors	Case 1	Case 2	Case 3	Case 4	Case 5
Patient specific issues	Y	N	Y	Y	Y
Dismissal of policies/procedures or guidelines	Y	Y	Y	Y	Y
Human resources	Y	Y	Y	Y	Y
Miscommunication	Y	Y	Y	Y	Y
Physical environment of the health service	N	Y	N	N	N
Control/provision of medication	Y	Y	Y	N	N
'Other'	N	N	N	N	N

Y = contributing factor, N = non-contributing factor.

Agreement between the principal researcher and the participants on each contributing factor in each case was presented using simple descriptive statistics. General Estimating Equation (GEE) analysis was applied to model the contributing factors.

Table 7.16 shows the agreement between the principal researcher and the participants regarding patient specific issues as the contributing factor. High agreement was identified in Cases 2 and 5, and across all participants' roles except the nurses (Table 7.16).

Table 7.16 Agreement between the principal researcher and participants on patient-specific issues as a contributing factor

Variables	Agreement between researcher and participant, n (%)	Disagreement between researcher and participant, n (%)
Case study (25 participants)		
Case 1	13 (52.0)	12 (48.0)
Case 2	24 (96.0)	1 (4.0)
Case 3	8 (32.0)	17 (68.0)
Case 4	22 (88.0)	3 (12.0)
Case 5	11 (44.0)	14 (56.0)
Participants' role		
Doctor (6 participants x 5 cases)	21 (70.0)	9 (30.0)
Nurse (11 participants x 5 cases)	29 (50.9)	27 (49.1)
Pharmacist (8 participants x 5 cases)	29 (72.5)	11 (27.5)

Table 7.17 outlines the agreement model of patient-specific issues as the contributing factors using GEE analysis. The dependent variable in the GEE model was disagreement that patient-specific issues contributed to the MEs. An odds ratio greater than one indicated greater disagreement than the reference, while a value less than one indicated greater agreement that patient-specific issues contributed to the MEs. In comparing the case vignettes, Case 5 was set as the reference. The analysis showed significantly greater agreement about the contribution of patient-specific issues for Cases 2 and 4 compared to Case 5. Similarly, with agreement between the principal researcher and the pharmacists set as a reference, the nurses showed significantly higher disagreement.

Table 7.17 Agreement model between the principal researcher and participants on patient-specific issues as a contributing factor using GEE analysis

Variables	Odds ratio	95% CI		P-value
		Lower	Upper	
Case study				
Case 1	0.702	0.305	1.616	0.406
Case 2	0.027	0.002	0.300	0.003
Case 3	1.748	0.516	5.917	0.369
Case 4	0.090	0.022	0.369	0.001
Case 5*	1			
Participants' role				
Doctor	1.114	0.318	3.902	0.865
Nurse	3.719	1.069	12.937	0.039
Pharmacist*	1			

*Set as a reference

Regarding dismissal of policies/procedures or guidelines as a contributing factor, agreement between the principal researcher and participants was high across all case studies, and across all participants' roles, with responses from at least three-quarters of each profession aligning with the principal researcher. Due to a convergence problem arising from complete agreement in Case 2 (Table 7.18), the GEE model could not be fitted. Thus, the agreement was presented using descriptive statistics.

Table 7.18 Agreement between the principal researcher and participants on dismissal of policies/procedures or guidelines as a contributing factor

Variables	Agreement between researcher and participant, n (%)	Disagreement between researcher and participant, n (%)
Case study (25 participants)		
Case 1	24 (96.0)	1 (4.0)
Case 2	25 (100.0)	0 (0.0)
Case 3	23 (92.0)	2 (8.0)
Case 4	20 (80.0)	5 (20.0)
Case 5	20 (80.0)	5 (20.0)
Participants' role		
Doctor (6 participants x 5 cases)	23 (76.7)	7 (23.3)
Nurse (11 participants x 5 cases)	53 (96.4)	2 (3.6)
Pharmacist (8 participants x 5 cases)	36 (90.0)	4 (10.0)

In relation to human resources issues as a contributing factor, more than 80% of participants' responses were in agreement with the researcher in all cases except Case 4 (Table 7.19).

Table 7.19 Agreement between the principal researcher and participants on human resources issues as a contributing factor

Variables	Agreement between researcher and participant, n (%)	Disagreement between researcher and participant, n (%)
Case study (25 participants)		
Case 1	22 (88.0)	3 (12.0)
Case 2	24 (96.0)	1 (4.0)
Case 3	23 (92.0)	2 (8.0)
Case 4	16 (64.0)	9 (36.0)
Case 5	24 (96.0)	1 (4.0)
Participants' role		
Doctor (6 participants x 5 cases)	25 (83.3)	5 (16.7)
Nurse (11 participants x 5 cases)	48 (87.3)	7 (12.7)
Pharmacist (8 participants x 5 cases)	36 (90.0)	4 (10.0)

Only Case 4 showed a higher incidence of disagreement than Case 5, while all other cases were similar to Case 5 (Table 7.20). There appeared to be no significant difference in the incidence of agreement between pharmacists and doctors or nurses.

Table 7.20 Agreement model between the principal researcher and participants on human resources issues as a contributing factor using GEE analysis

Variables	Odds ratio	95% CI		P-value
		Lower	Upper	
Case study				
Case 1	3.290	0.625	17.319	0.160
Case 2	1.000	0.055	18.150	1.000
Case 3	2.093	0.165	26.486	0.568
Case 4	13.744	2.098	90.019	0.006
Case 5*	1			
Participants' role				
Doctor	1.677	0.320	8.787	0.541
Nurse	1.044	0.237	4.603	0.954
Pharmacist*	1			

*Set as a reference

For miscommunication as a contributing factor, only Cases 3 and 4 had high agreement, while the doctors showed the highest agreement of all roles (Table 7.21).

Table 7.21 Agreement between the principal researcher and participants on miscommunication as a contributing factor

Variables	Agreement between researcher and participant, No.n (%)	Disagreement between researcher and participant, No. n (%)
Case study (25 participants)		
Case 1	13 (52.0)	12 (48.0)
Case 2	8 (32.0)	17 (68.0)
Case 3	22 (88.0)	3 (12.0)
Case 4	24 (96.0)	1 (4.0)
Case 5	9 (36.0)	16 (64.0)
Participants' role		
Doctor (6 participants x 5 cases)	21 (70.0)	9 (30.0)
Nurse (11 participants x 5 cases)	35 (63.6)	20 (36.4)
Pharmacist (8 participants x 5 cases)	20 (50.0)	20 (50.0)

After considering Case 5 as a reference, the likelihood of agreement was significantly higher for Case 3 (15 times) and Case 4 (50 times) (Table 7.22). Doctors were significantly more likely to answer consistently with the researcher than pharmacists, but agreement for nurses and pharmacists was similar.

Table 7.22 Agreement model between the principal researcher and participants on miscommunication as a contributing factor using GEE analysis

Variables	Odds ratio	95% CI		P-value
		Lower	Upper	
Case study				
Case 1	0.501	0.129	1.944	0.318
Case 2	1.205	0.359	4.051	0.763
Case 3	0.067	0.015	0.294	<0.001
Case 4	0.020	0.002	0.178	<0.001
Case 5*	1			
Participants' role				
Doctor	0.299	0.099	0.898	0.031
Nurse	0.402	0.125	1.289	0.125
Pharmacist*	1			

*Set as a reference

Considering physical environment of the health service as a contributing factor, the agreement model using GEE could not be fitted due to complete agreement in Cases 3, 4 and 5. The incidence of agreement was more than 90% across all cases (Table 7.23). Similarly, the agreement with the principal researcher was very high across all professions.

Table 7.23 Agreement between the principal researcher and participants on the physical environment of the health service as a contributing factor

Variables	Agreement between researcher and participant, n o.(%)	Disagreement between researcher and participant, no. (%)
Case study (25 participants)		
Case 1	24 (96.0)	1 (4.0)
Case 2	23 (92.0)	2 (8.0)
Case 3	25 (100.0)	0 (0.0)
Case 4	25 (100.0)	0 (0.0)
Case 5	25 (100.0)	0 (0.0)
Participants' role		
Doctor (6 participants x 5 cases)	28 (93.3)	2 (6.7)
Nurse (11 participants x 5 cases)	54 (98.2)	1 (1.8)
Pharmacist (8 participants x 5 cases)	40 (100.0)	0 (0.0)

With respect to control/provision of medication as the contributing factor, agreement between the principal researcher and the demonstrated three cases answered consistently at least 80% of the time, and the agreement was similar across all roles (Table 7.24).

Table 7.24 Agreement between the principal researcher and participants on the control/provision of medication as a contributing factor

Variables	Agreement between researcher and participant, n (%)	Disagreement between researcher and participant, n (%)
Case study (25 participants)		
Case 1	11 (44.0)	14 (56.0)
Case 2	20 (80.0)	5 (20.0)
Case 3	21 (84.0)	4 (16.0)
Case 4	22 (88.0)	3 (12.0)
Case 5	16 (64.0)	9 (36.0)
Participants' role		
Doctor (6 participants x 5 cases)	24 (80.0)	6 (20.0)
Nurse (11 participants x 5 cases)	38 (69.1)	17 (30.9)
Pharmacist (8 participants x 5 cases)	28 (70.0)	12 (30.0)

Regarding control/provision of medication as the contributing factor, the level of disagreement was significantly less for Case 4 than for Case 5 (Case 4 showed significantly greater agreement with the principal researcher) (Table 7.25). Other

cases showed agreement similar to Case 5. No significant difference in agreement appeared between pharmacists and the other professions.

Table 7.25 Agreement model between the principal researcher and participants on the control/provision of medication as a contributing factor using GEE analysis

Variables	Odds ratio	95% CI		P-value
		Lower	Upper	
Case study				
Case 1	2.299	0.660	8.006	0.191
Case 2	0.439	0.123	1.573	0.206
Case 3	0.334	0.080	1.391	0.132
Case 4	0.238	0.069	0.897	0.034
Case 5*	1			
Participants' role				
Doctor	0.522	0.121	2.247	0.382
Nurse	1.068	0.383	2.980	0.900
Pharmacist*	1			

*Set as a reference

Table 7.26 describes the agreement between the principal researcher and the participants related to 'other' contributing factors. A high incidence of agreement of more than 70% was seen in Cases 3 and 4 only.

Table 7.26 Agreement between the principal researcher and participants on 'other' contributing factors

Variables	Agreement between researcher and participant, n (%)	Disagreement between researcher and participant, n (%)
Case study (25 participants)		
Case 1	16 (64.0)	9 (36.0)
Case 2	11 (44.0)	14 (56.0)
Case 3	19 (76.0)	6 (24.0)
Case 4	21 (84.0)	4 (16.0)
Case 5	15 (60.0)	10 (40.0)
Participants' role		
Doctor (6 participants x 5 cases)	20 (66.7)	10 (33.3)
Nurse (11 participants x 5 cases)	32 (58.2)	23 (41.8)
Pharmacist (8 participants x 5 cases)	30 (75.0)	10 (25.0)

The agreement model using GEE analysis demonstrated that only Case 4 had a stronger agreement with the principal researcher than Case 5, with other cases

showing similar agreement to Case 5. No difference in agreement appeared between pharmacists and the other professions.

Table 7.27 Agreement model between the principal researcher and participants on 'other' contributing factors using GEE analysis

Variables	Odds ratio	95%CI		P-value
		Lower	Upper	
Case study				
Case 1	0.840	0.271	2.603	0.762
Case 2	1.947	0.635	5.970	0.244
Case 3	0.465	0.164	1.317	0.150
Case 4	0.278	0.077	1.005	0.051
Case 5*	1			
Participants' role				
Doctor	1.504	0.473	4.780	0.489
Nurse	2.217	0.845	5.819	0.106
Pharmacist*	1			

*Set as a reference

7.2 Discussion

The analysis of medication-related events, including MEs, is important for quality improvement in healthcare processes.(233, 234) In the present study frontline staff (doctors, nurses, pharmacists) assessed the MEs through simulated case studies. Overall, a similar perspective was revealed among the participants across the three roles on the clinical significance of MEs, with the majority of participants rating the MEs as major and life threatening, as intended in the design of the cases.

The present findings were not consistent with prior studies assessing medication-related events either in paediatric or adult patients. In those studies, doctors rated the severity of the consequences of the incidents lower than pharmacists.(226, 227, 233) Less variation in the assessment of this study might be due to the non-ambiguous statements on the consequences of the MEs to patients' outcomes used in the case studies. However, there were variations in the responses to the open-ended question asking which health professional(s) was responsible for the occurrence of each of the five MEs. It has been reported that differing judgement of medication-related incidents between health professionals is related to factors such as their clinical knowledge and understanding of the standard of patient care in varied settings.(233) The majority of participants in this study thought the MEs were the consequence of action/inaction of at least two health professionals (doctor and nurse; nurse and

pharmacist; doctor, nurse and pharmacist). This was in agreement with the intentions of the researcher when developing the cases. To some extent, the findings of this study confirmed those of previous studies highlighting the nature of the healthcare process as being 'tightly coupled' and 'interdependent', whereby deviations during the process were likely due to the results of interactions among the care providers rather than a single person.(2, 271)

In the present setting, the varied responses on the contributing factors indicated making such judgements is no easy task. Understandably, similar agreement between the principal researcher and participants were noted in three contributing factors only in the majority of the cases. However, two contributing factors were frequently identified by participants in all five cases: dismissal of policies/procedures or guidelines, and human resources. Miscommunication was mentioned as a contributing factor in three cases, while patient-specific issue(s) and control/provision of medication were contributing factors in two cases, and physical environment a contributing factor in one case. As with this study, RCA of 17 critical incidents in a children's hospital in the Netherlands found task and team factors were the most frequent contributing factors. The task factors were associated with awareness among the staff regarding the existence of clinical guidelines and/or hospital protocols, and the implementation of the guidelines/protocols. Team factors referred to issues that can be resolved through training of team-based human resources, i.e. supervision, communication and situational awareness. The authors identified an average of five factors contributing to each incident.(271)

A report on incident management (including medication-related incidents) in the New South Wales public health system during 2005-2006 was in accordance with this study's findings.(272) That study found issues related to policy and procedures as a major contributing factor to the incidents, and included failure of staff in following guidelines, standards and regulations, and inadequate policies for supporting the safety and quality of clinical care. Communication was also a major contributing factor to the incidents, particularly deficiencies in patient handover between teams and facilities in the same institution or between institutions.(272) Communication is also critical during patient admission and discharge, as transition of patient care is particularly hazardous for introducing MEs.(273) Other

contributing factors reported in the Australian study included issues related to staff knowledge, skills and competence; work environment and staff scheduling; equipment; safety mechanism; and patient factors.(272)

Consistent with this study, RCA reports on ADEs submitted to the Veteran Affairs National Center for Patient Safety in the USA in the fiscal year 2004 uncovered problems with policies or procedures, staff training and education, communication, and equipment as the common factors contributing to ADEs.(274) Meanwhile, analysis of ME reports submitted to MedMARx (US national medication error reporting program) revealed workplace distractions, staffing issues (e.g. shift changes and locum staff) and workload increases as the most fequently cited contributing factors related to MEs during hospitalisation.(275)

Interestingly, some RCA studies focused on the proximal causes only, without accounting for the contributing factors of medication-related incidents.(271, 272, 274) Memory lapses were the most frequent proximal causes of error (23.8%) across all stages, reaching nearly 50% during administration in an observational study to detect MEs and ADEs in a paediatric ICU.(276) The major leading system failures identified and responsible for MEs and ADEs in that study were drug knowledge, standardisation of procedures, dose and identity checking, and order transcription.(276) Likewise, a ME study in general medicine and specialty units in a major US hospital reported most MEs identified were detected during prescribing, and the root causes were related to deficits in pharmacotherapy knowledge (particularly about appropriate drug dosing and drug selection) or with failure to consider critical patient information (e.g. laboratory test results). Furthermore, MEs during dispensing and administration were mostly due to performance deficits (74%, e.g. accidental slips and lapses).(277) A brief analysis of clinical pharmacists' interventions addressing DRP in an Australian hospital found that deficiencies in knowledge accounted for less than 25% of all DRP cases.(129) In the oncology setting, the most common cause of chemotherapy-related MEs have been reported as performance deficits (41.3%), equipment and medication delivery devices (12.4%), communication (8.8%), knowledge deficit (6.8%) and written order errors (5.5%).(10) It is beneficial to note that before proceeding to RCA, the majority of ME studies relied on manual reports of ME incidents, which were under-

reported.(271, 272, 274, 277) A recent study promoted the use of an electronic system of ME reporting, along with automatically mining data from the system, to provide comprehensive data relating to ME.(278)

As the contributing factors of MEs are numerous, evidence underlines the need for multiple strategies for ME prevention.(279) Analysis of the common themes of strategies proposed by participants in this study identified the need for five strategies to prevent each ME. The most frequently cited strategies included improved availability and accessibility of hospital policies or clinical guidelines, adequate staffing and supervision, adequate staff education and training, and improved communication either between staff or between staff and patient/family. The less frequently cited strategies were the implementation of technology (e.g. electronic prescribing and drug stock alert), adequate patient counselling and improved physical environment (e.g. arranging the medications in the dispensary by therapeutic class and proper lighting). In line with this study, RCA of serious cases in the aforementioned Dutch paediatric hospital reported an average of five recommendations per analysis; most recommendations related to task factors (36%), and required providing and/or adjusting hospital protocols or guidelines. The other recommendations were associated with team-based staff training and technical adjustment to improve the work environment (e.g. quiet area for medication preparation unit).(271) In addition, the findings in the current study corresponded well with the strategies for ME prevention in paediatrics recommended by the American Academy of Pediatrics Committee on Drugs and the Committee on Hospital Care(280) and the Pediatric Pharmacy Advocacy Group.(281) The strategies cited in this study also confirmed those reported by Kruk *et al*.(272) Although their RCA evaluated the broad spectrum of health incidents, and not necessarily focusing on medication-related incidents.

Few participants in this study mentioned the use of information technology (IT) as the solution to prevent MEs. One of the most developed and widely disseminated IT products is computerised physician order entry (CPOE). A systematic review of MEs in paediatrics found that the most common type of MEs were dosing-related errors, which can be minimised by CPOE.(99) Some studies have justified the use of CPOE

to decrease MEs in paediatric patients.(53, 237, 282, 283) A similar efficacy of CPOE can also be seen in adult patients.(284, 285)

Despite success at reducing MEs, IT-based interventions require considerable financial investment, health professional training, and system maintenance.(284) Electronic prescribing system support can facilitate the introduction of new types of prescribing errors, especially during the initial stage of technology deployment and dissemination.(210, 286)

Clinical pharmacy services is an important adjunct to IT strategies, including in paediatric settings.(181, 197, 199) Unit-based pharmacists' active participation during ward rounds is able to provide real-time information needed by physicians, just as CPOE provides real-time computerised decision support.(197, 201, 287) In addition to their role in preventing MEs during prescribing, pharmacists can also intercept MEs by reviewing medication orders.(207) Their presence can also facilitate communication between healthcare staff and the pharmacy, assisting nurses in drug preparation, monitoring drug storage, organising education programs for other staff and developing drug therapy protocols.(50, 201) Unit-based clinical pharmacists are generally less costly than most IT-based patient safety interventions.(288) These pharmacists' roles were the premise for the observational and self-documentation pharmacists' interventions studies reported in Chapter 4 and Chapter 6, respectively.

As suggested by this study and other RCA, education for healthcare staff is an important component of ME reduction.(279, 289) According to some studies, staff with the least training made the most errors.(210, 243, 289) It has been strongly recommended that staff in paediatric settings, particularly new and junior staff, receive continuous education and adequate training in the use of paediatric medications. Regular testing of their knowledge and ability to handle peadiatric medications should be undertaken to enable review of the training.(242) Pharmacists with their knowledge and expertise in medication have been known for their role as educators for other health professionals and their educator role has been justified as effective ME prevention measures in a range of patient populations.(133, 280)

Modification of staff behaviour toward patient safety culture has been regarded as an essential predictor of safety performance.(290) Major investment in patient safety reform through education has been conducted in numerous countries. Despite this, little improvement has been reported. The authors cited a flawed assumption that knowledge of safety will cause staff to change their behaviour.(290, 291) Wakefield *et al.*(290) claimed that behaviour change strategies required influential clinical leaders to be assigned at unit levels as role models and teachers for implementing patient safety.

Aside from educating health professionals, it has been recognised that empowering the patient is a valuable strategy for ME prevention. Healthcare staff should educate patients to improve their health literacy regarding information on their medical conditions, medications and healthy lifestyles. Healthcare staff can also encourage patients to actively participate in their health care by asking questions and expressing concerns about their health, and review their level of understanding.(27) In the case of paediatric patients, the involvement of their parents/guardians is important.(73, 292) The participants in the current RCA also underlined the contribution of well-informed parents/guardians to minimise the occurrence of MEs in most case studies. The current study also underlined the contribution of pharmacists in educating the patients along with their parents/guardians about appropriate use of medicines.

Improved communication has also been identified as a valuable solution to minimise MEs.(271, 274, 293) It is important that all members of the healthcare team, including pharmacists, are effective communicators with other team members and in their contact with patients. With respect to supporting clear communication among health professionals, initiatives have been proposed through improved networking between hospitals and assignment of the medical position of 'hospitalist'. Hospitalists are qualified doctors with additional training to coordinate care for patients across different departments and manage the transfer of care to other institutions.(272) These initiatives are important given the critical nature of accurate patient handover within the same and/or different institutions.(198)

One common issue among healthcare staff is their lack of awareness of hospital policies and procedures. In the current RCA, it has been suggested that pharmacists are able to contribute not only to develop policies in medication use (e.g. high-risk

drugs, discharge medications), but also to communicate these policies to other staff. The current study also confirmed the findings of previous RCA studies that identified the necessity of adequate communication between staff and patients and their families. Some studies underlined common barriers experienced by the healthcare staff in communicating with their patients, e.g. language, medical problems and psychological issues.(79, 84, 294) These barriers in communication, particularly relating to language and the complexity of patients' medical conditions, were also raised by the majority of the RCA participants in the current study. The barriers should be identified and resolved by pharmacists and other frontline health professionals, as these barriers will impede the overall quality of patient care, including increasing the risk of MEs.(271)

7.3 Limitations and Recommendations

There are several limitations to this study. The response rate was low, possibly due to the perceived time requirement to complete the task, and the study involved a single institution. A larger number of participants and involvement of other institutions may reveal different trends in the data on the clinical significance of the MEs, the contributing factors and participants' suggestions for ME prevention. Additionally, the use of simulated case studies and presentation of pre-determined options could bias the results. The cases were not randomised, and each case was prepared with different amounts of information. In an authentic RCA, the participants would be able to obtain additional information to assist their analysis, but it was impossible to apply a similar process in this study. The assignment of pre-determined answers was influenced by the researcher's clinical knowledge and experience, and others may give different assessments.

Future research could trial a number of RCA approaches (e.g. in-depth interview, focus group discussion) with frontline staff and hospital managers in order to gather diverse perceptions about the contributing factors and 'strong' strategies to minimise ME.

Additionally, the RCA framework to prevent ME and improve patient safety should be validated by comparing it with other analysis tools such as the Commercial Aviation Safety Team (CAST) and Failure and Mode Effect Analysis.(295, 296) The

implementation of the CAST framework in particular will enable future research to prioritise the findings of the contributing factors.

7.4 Conclusions

Consistent with other RCA studies, the most common contributing factors perceived by participants were the dismissal of hospital policies/procedures/clinical guidelines and human resources-related issues. Meanwhile, strategies related to development of policy/procedures/guidelines, staff education/training, staffing and communication were the most commonly cited preventive actions, in line with the majority of other studies. Indeed, pharmacists through their clinical services are an important strategy for preventing the occurrence of ME.

Chapter 8

OVERALL DISCUSSION

This chapter comprises three sections. The major findings presented in Chapters 4, 5, 6 and 7 are summarised in Section 8.1, with a global discussion of the study in Section 8.2. The limitations of this study, along with recommendations for future research, are described in Section 8.3.

8.1 Synthesis of Major Findings

In Part One of the study, a total of 982 interventions were observed and documented by the principal researcher, which arose from the 16,700 medication orders reviewed by the clinical pharmacists on the five study wards. The intervention rates ranged from 4.38 to 10.48 interventions per 100 medication orders reviewed across the wards. The intervention rates in this study were higher than reported by other paediatric intervention studies conducted in a range of settings using self-documentation.(94, 184, 199, 201) Poisson regression modelling identified significant differences in intervention rates between the wards ($p<0.001$). The highest rate of interventions was documented on the General Surgical Ward, followed by the General Medical Ward for Infants, the Haematology-Oncology Ward, the General Medical Ward for Adolescents and the General Medical Ward for Young Children. The model also showed that the rates of interventions significantly differed according to the employment level of the observed pharmacists ($p<0.01$), and longer time spent on the ward was associated with a higher rate of interventions ($p<0.001$). Taking medication histories and/or patient counselling were the most common interventions performed by the clinical pharmacists on the general medical and surgical wards, with these activities constituting more than half of all interventions. While on the Haematology-Oncology Ward here, drug therapy changes were the most common interventions; around 37% of all interventions.

Active interventions were defined as interventions resulting in drug changes. The rate of active interventions on the Haematology-Oncology Ward was significantly higher than the general medical wards ($p<0.001$), but not the general surgical ward ($p=0.34$). Active interventions constituted less than one-quarter of all interventions on the general medical and surgical wards, compared to 46.2% ($p<0.001$) on the

Haematology-Oncology Ward. For all active interventions, the degree of acceptance was high, at around 90% (n=223/244). Rates of active interventions were not significantly associated with the pharmacists' employment level ($p<0.4$) or the time spent on the ward ($p<0.2$). Adjusting the dose was the most frequent active interventions on both the general medical and surgical wards. A slightly different pattern was found on the Haematology-Oncology Ward, where interventions to prescribe medications regularly in place of *prn* constituted the most common active interventions (40.0%), followed by dosing adjustment (26.7%).

As for the drug classes implicated in active interventions, anti-infectives were most commonly associated with active interventions (n=100, 41.0%), followed by analgesics (n=46, 18.9%), gastrointestinal drugs (n=36, 14.8%), and immunomodulators/antineoplastics (n=21, 8.6%). Three variables significantly predicted the acceptance of the intervention: patients' age (OR 0.89; 95%CI 0.81-0.98), non-high-risk medications (OR 2.80; 95%CI 1.09-7.17) and pharmacists' experience (OR 1.11; 95%CI 1.03-1.20).

Data collection in the Haematology-Oncology Pharmacy provided an interesting contrast between the nature of interventions during dispensing and during ward rounds. There were 359 interventions observed and documented by the principal researcher during the dispensing of 1791 medications in the Haematology-Oncology Pharmacy. The rates of interventions were 21.29 per 100 medication orders reviewed and 35.18 per 100 patients. Less than 10% of pharmacists' interventions were classified as active. All of the active interventions were accepted by the physicians. The rates of interventions during dispensing were higher than on the five study wards, presumably due to more time allocation and varied clinical services that can be provided during dispensing. Most commonly, the interventions involved pharmacists providing drug information to resolve DRPs; more than three-quarters of interventions. Immunomodulators/antineoplastics accounted for the majority of medications associated with active interventions (n=18/22, 81.8%). It is critical to ensure these potent drugs are prescribed and dispensed appropriately; accounted for the high percentage of these drugs involved in the interventions in this setting.

A random sample of 42 (15.8%) of the 266 pharmacists' active interventions (244 during pharmacy ward rounds on the five study wards and 22 during dispensing in a

Haematology-Oncology Pharmacy) from Part One were selected for expert panel assessment of clinical significance and contribution to medication misadventure in Part Two. Review of the sample interventions revealed the majority (n=37/42, 88.1%) of the active interventions were considered clinically significant, although no intervention was thought to be life saving. Panel assessment indicated that the majority of the active interventions were performed to address medication misadventure, and the strength of agreement was 'fair'(192) (α=0.321). 'Fair'(192) agreement was also noted when assigning each case medication misadventure category (i.e. ADE, ADR, ME) and classifying the types of ME. However, the strength of agreement was 'slight'(192) (α=0.154) when the panellists judged the severity of ME.

Part Three of the research stage involved comparison of two pharmacists' intervention documentation methods: direct observation (Part 1) and self-reports using a hard-copy form. A total of 398 interventions were self-reported from 1022 medication charts that were reviewed by pharmacists. Of all the interventions, around 18% (n=70/398) were considered active interventions. Comparison of the rates of interventions during the snapshot self-report periods (Part Three) and direct observation (Part One) showed no significant difference in the two methods. However, comparison of the active interventions between snapshot and observation periods revealed the rate of documentation of active interventions was significantly higher during direct observation than snapshots (snapshot 6.7 [95%CI 4.3–9.2] per 100 medication charts reviewed vs. observation 15.1 [95%CI 10.0–20.2] per 100 medication charts reviewed, p=0.002). In terms of the types of interventions, clarification of medication orders was the most common type of intervention self-reported by pharmacists. When the pattern of all interventions and active interventions during the direct observation period were compared with the self-reports, it was apparent that the interventions across the study wards were not comparable. This finding will be discussed in Section 8.2.

The reasons for differences in the nature of pharmacists' interventions between those documented during direct observation and the self-reports were explored using a FGD involving eight pharmacists. Pharmacists identified a number of barriers to routinely documenting their interventions, such as time constraints, fatigue, heavy

workload, and staffing deficiencies. However, the majority of pharmacists thought self-report documentation inadequately reflected their contribution to patient care and their workload. They postulated that switching the of snapshot self-report timings to busy periods instead of hospital downtimes (as was the case) would be worthwhile. The pharmacists also proposed a hybrid system of continuous documentation during certain periods by an independent observer, plus the existing snapshot self-report documentation.

An RCA was conducted in Part Four, with the distribution of 111 RCA questionnaires to a stratified sample of doctors, nurses and pharmacists. Each questionnaire comprised five simulated cases for review; responses were received from 22.5% of those surveyed. The simulated cases represented sentinel events based on authentic features of the study hospital's policies/procedures and represented a range of MEs. The majority of the participants rated the clinical significance of MEs as moderate to life threatening. Determination of the responsible health professional(s) varied in each case. Similarly, the participants' perceptions on contributing factors to the ME also varied across the five cases. Two common contributing factors emerged: dismissal of policies/procedures or guidelines, and human resources issues. Some common suggestions for preventive action across the five cases included: improving availability and accessibility of clinical guidelines; ; strict hospital policies/protocol for medication use during prescribing, transcribing, dispensing, administration and monitoring; adequate number of staff with appropriate education and training/competencies, along with adequate staff supervision; and improved communication between staff, and between staff and the patient and/or family.

An agreement model on the contributing factors, between the participants and the principal researcher on a case-by-case basis was developed using GEE analysis. This model determined if the participants' perceptions on the contributing factors conformed to the anticipated answer pre-determined by the researcher. The GEE analysis found that the same pattern of agreement was observed for human resources issues, control/provision of medication, and 'other' contributing factors. The participants and the principal researchers were in agreement for all of the cases except Case 4 (described monitoring error). Meanwhile, a different pattern of

agreement developed for patient-specific issues and miscommunication. While two contributing factors - dismissal of policies/procedures or guidelines and physical environment of the health service - were not able to be fitted with the model.

8.2 Overall Discussion

The role of clinical pharmacists in paediatric healthcare settings is well established,(17, 181, 197, 199, 204) and their interventions to address medication-related issues can avert misadventure.(17, 204, 254) A number of studies support the role of pharmacists to avert misadventure in paediatric patients.(94, 184, 197, 201, 207) Until the time of this study, interventions had not been researched in detail in this hospital, despite it being one of major referral children's hospitals in Australia and providing specialist services including haematology-oncology. The hospital had in situ snapshot self-report documentation of pharmacists' interventions. However, the interventions data had not been analysed, and no outcome and feedback had been provided to the reporting pharmacists.

The current study adds to the body of knowledge by confirming the significant role of pharmacists in undertaking clinical interventions, especially those leading to change in drug therapy (active interventions) to minimise the occurrence of medication misadventure in paediatrics. This was achieved through a series of stages involving direct observation of pharmacists' interventions during ward rounds and dispensing; panel assessment of clinical significance of pharmacists' active interventions and medication misadventure detected through the active interventions; comparison of two intervention documentation methods; and RCA of simulated cases of ME. Collectively, this approach enabled investigation of pharmacists' contribution to medication safety, especially through interventions leading to drug changes in a range of paediatric settings.

This study uniquely used direct observation to measure the rate and pattern of pharmacists' interventions in a range of paediatric settings. Previous studies used self-documentation, and recognised the limitations of this approach, such as bias and under-reporting. This is the first known study to analyse and compare the interventions between direct observation and snapshot self-documentation. The comparative data have been presented and discussed with the pharmacy staff and the Director of Pharmacy in the study hospital and has resulted in improved

documentation, with the medication safety pharmacist undertaking direct observation to validate intervention data from the existing snapshot self-documentation. In addition, pharmacy staff in the study hospital now organise regular meetings to discuss the collated intervention data from the snapshot periods.

Pharmacists' interventions studies have been conducted in a range of paediatric clinical settings.(94, 197, 199) However, the majority have combined and analysed the data without exploring the influence of the clinical setting on the nature of the interventions. The current study uncovered that the clinical settings impacted on the rate and pattern of the interventions between general and specialty units. The haematology-oncology unit produced a higher rate of active interventions than the general medical and surgical units. As with other paediatric studies(184, 197, 199) dosing-associated interventions were predominantly noted in the general units. A distinct pattern emerged in the haematology-oncology unit, where drug additions to resolve untreated indications accounted for the major active interventions. More active interventions and the different pattern of interventions were possibly related to the specialist pharmacists assigned to the haematology-oncology unit. The haematology-oncology pharmacists were appointed in this unit on a permanent basis. These specialist pharmacists were well informed about the patients' medical conditions and medication regimens, including their chemotherapy protocols and supportive medications (e.g. antiemetics, antifungals). Thus, the haematology-oncology pharmacists, when delivering the clinical services, were able to identify DRPs and intervene through drug therapy changes.

The assessment of the sample of pharmacists' active interventions revealed that the majority of the interventions were clinically significant and interceptive of medication misadventure. At the time of writing, as the study hospital had not implemented electronic prescribing, pharmacists engaging in clinical services (e.g. taking medication histories, medication reconciliation and review of medication charts) either during ward rounds or dispensing contributed even more to ensure medication safety for patients. As with the current study, studies have showed that the active interventions during ward rounds were effective in changing therapeutic decisions and intercepting MEs in paediatric patients.(139, 197, 201) A systematic review highlighted that pharmacists' review of medication charts is crucial to

identification of MEs; it is possibly the most effective method of improving drug safety in children.(207) This evidence can be applied to ward-based pharmacy practice and also during dispensing.

Pharmacists' interventions require appropriate and adequate documentation to substantiate their contribution to patient care and build a body of evidence that clinical pharmacists play substantial roles within the medication use process. The direct observation approach undertaken in the current study enabled gathering of the number and pattern of pharmacists' interventions during ward rounds and dispensing. Higher rates of active interventions were found when the ward pharmacists were directly observed than those self-reported during snapshot periods. The study hospital may consider modifying their existing intervention documentation method to optimise data collection.

System breakdown can be analysed and improved by implementing RCA. Health system breakdown can be manifested in MEs. Implementation of RCA can identify the causes and contributing factors of medication misadventure, along with solutions to prevent recurrence of the misadventure.(12) The current study may have benefitted if the RCA had utilised authentic cases instead of simulated cases of intercepted MEs. This was not feasible due to medico-legal and ethical reasons.

The RCA used in this study served to assess theoretically the clinical significance of MEs described in the simulated cases, and to explore the contribution of pharmacists in preventing MEs. Nearly all of the surveyed participants concurred that the MEs in the five cases were sentinel events. The majority of the participants also identified more than one profession being responsible for the MEs. This is consistent with published RCA studies demonstrating the need for shared responsibility among health professionals of different disciplines.(271, 272, 274) The RCA in this study did not require that participants convene a formal meeting to discuss the cases. Thus, the data can be considered independent, notwithstanding participants discussing and completing the cases with colleagues. Varied responses relating to the contributing factors and preventive strategies were noted among the RCA participants.

The current study also showed that frontline health professionals are able to undertake RCA. Participants in this study have become familiar with RCA as a tool

for system improvement. The RCA provided further evidence supporting the role of pharmacists in provision of clinical services, e.g. development and dissemination of drug therapy protocols, facilitated communication between healthcare staff and the pharmacy, education of other healthcare professionals, and provision of counselling to patients and parents/guardians. Occurrences of medication misadventure identified in routine clinical services can be intercepted and resolved by pharmacists through their interventions, highlighting their role in reducing medication misadventure.

8.3 Limitations and Recommendations

This is the first study to compare pharmacists' interventions in a range of settings in paediatrics in terms of frequency, type, degree of acceptance, clinical significance and causative medications. However, a number of limitations need to be acknowledged. This study was conducted in one paediatric hospital, which diminishes the generalisability of the findings. Another limitation is the difficulty in drawing accurate comparisonss with other studies due to considerable variations in settings, design, duration, size and method.

During direct observation, data were collected on non-consecutive days to avoid pharmacist observation fatigue influencing the pattern of interventions. In relation to assessment of clinical significance of samples of pharmacists' active interventions and identification of medication misadventure, the expert panellists were selected for convenience after considering their clinical knowledge and professional experience. Further to the limitation relating to the use of simulated RCA cases, the low response rate and non-randomisation of the cases may not ideally represent the responses on the clinical significance of MEs, the contributing factors and suggestions for ME prevention.

Future studies might consider employing consecutive observation of pharmacists' interventions, more clinical units and other children's hospitals to further confirm variations in rates and patterns of pharmacists' clinical interventions. It would also be beneficial for future studies to evaluate the association between acceptance of the interventions and their impact on patient outcome in order to justify the value of the interventions to patient care.

It is recommended that in future studies panellists randomly selected from eligible experts that represent doctors, nurses and pharmacists assess pharmacists' active interventions. Therefore, the tendency of the researcher to select experts with similar opinions or because of convenience will be reduced, with benefits for validity of the research. Furthermore, use of a larger number of active interventions would allow comprehensive understanding of the pattern of active interventions and medication misadventure in paediatrics. When conducting analysis of medication misadventure, future studies may also consider involving the hospital management, as well as frontline health professionals, and applying different RCA approaches and other system analysis tools as described earlier.

Chapter 9

CONCLUSIONS

This study aimed to evaluate the contribution of pharmacists' interventions to reduction of medication misadventure in children with cancer.

Documentation and evaluation of clinical interventions in this study provides evidence that pharmacists can play an important role in optimising patient care through their clinical services during ward rounds and dispensing in general and specialty haematology-oncology settings. Direct observation of pharmacists' interventions in this study offers a novel approach to recording the rate and pattern of the interventions witnessed by the researcher during defined periods, as an alternative to reliance on self-documentation by practitioners. The rate and types of pharmacists' active interventions, addressing Objectives 1 and 2 in Part 1 of this thesis, differed between clinical settings, being most frequent in the specialty haematology-oncology setting. Patients' age, type of medication (high risk/non-high risk) and pharmacists' experience were identified as predictors for physicians' acceptance of ward-based pharmacists' active interventions. Furthermore, this study achieved the two objectives of Part 2 by systematically assessing the clinical significance of pharmacists' active interventions, defined as interventions leading to changes in drug therapy, and the role of clinical pharmacists through their active interventions to identify and resolve medication misadventure-related events, in particular, ME. Identification of the nature of medication misadventure through pharmacists' active interventions can provide direction to improvements in the medication use process in this patient population.

To date, there has been a paucity of literature comparing self-report and observation for documentation of pharmacists' interventions in paediatrics. Part 3 of the current study compared the intervention documentation approaches (direct observation *versus* short-term self-report). The current study found self-report by pharmacists during snapshot recording periods was not representative of the interventions documented during direct observation by the researcher. This questions the value of self-documentation and proposes a need for improved methods of documentation. This study also provided insight into pharmacists' barriers to documenting their

interventions. Standardisation of intervention documentation, improved utilisation of the intervention data and modification of the existing self-documentation approach are suggested to improve the documentation of pharmacists' interventions.

The two objectives of Part 4 of this study related to exploration of the clinical significance, along with contributing factors and resolution, of medication-related errors, using five scenarios and the perspectives of three groups of health professionals: pharmacists, nurses and doctors. Involvement the frontline healthcare professionals, instead of a team of system analysis experts – as described in the majority of studies of RCA – to analyse the scenarios, adds value to this study. Through their interaction with patients during routine practice, frontline health professions provide insight into sectors of the healthcare system and processes that need to be improved to minimise ME in children.

Pharmacists, as the medication experts and part of frontline health care professionals, can participate in improving medication safety through delivery of clinical services, including (but not limited to) ensuring hospital policies/guidelines are followed to ensure appropriate medication use, and by providing drug information services for other frontline staff and educating patients/carers. At the same time, ongoing documentation, analysis and review of these clinical interventions remain critical.

References

1. Medication safety: The University of Michigan; 2002 [updated 22 March 2011]. Available from: http://www.med.umich.edu/patientsafetytoolkit/medication/chapter.pdf.
2. Donaldson MS, Kohn L, Corrigan JM, editors. *To err is human : building a safer health system*. Washington, DC: National Academic Press; 1999.
3. Semple SJ, Roughead EE. Medication safety in acute care in Australia : where are we now? Part 2: a review of strategies and activities for improving medication safety 2002-2008. Australian and New Zealand Health Policy. 2009;6:1-11.
4. Ajdukovic M, Crook M, Angley C, Stupans I, Soulsby N, Doecke C, et al. Pharmacist elicited medication histories in the Emergency Department: identifying patient groups at risk of medication misadventure. Pharmacy Practice. 2007;5:162-8.
5. Costello JL, Torowicz DL, Yeh TS. Effects of a pharmacist-led pediatrics medication safety team on medication-error reporting. American Journal of Health-System Pharmacy. 2007;64:1422-6.
6. Kaushal R, Bates DW, Landrigan C, et al. Medication errors and adverse drug events in pediatric inpatients. Journal of American Medical Association. 2001;285:2114-20.
7. Baranowicki P, O'Neill J, Dwyer J. Improving complex medication systems : an interdisciplinary approach. The Journal of Nursing Administration. 2003;33:199-200.
8. Robinson D, Heigham M, Clark J. Using failure mode and effect analysis for safe administration of chemotherapy to hospitalized children with cancer. Joint Commission Journal on Quality and Patient Safety. 2006;32:161-6.
9. Holdsworth MT, Fichtl RE, Behta M, Raisch DW, Mendez-Rico E, Adams A, et al. Incidence and impact of adverse drug events in pediatric inpatients. Archives of Pediatric and Adolescent Medicine. 2003;157:60-5.
10. Rinke ML, Shore AD, Morlock L. Characteristics of pediatric chemotherapy medication errors in a national reporting database. Cancer. 2007;110:186-95.
11. Boyle DA, Schulmeister L, Lajeunesse JD, Anderson RW. Medication misadventure in cancer care. Seminar in Oncology Nursing. 2002;18:109-20.
12. National Initiative for Children's Health Care Quality Project Advisory Committee. Principles of patient safety in pediatrics. Pediatrics. 2001;107:1473-5.
13. Ross LM, Wallace J, Paton JY. Medication errors in a paediatric teaching hospital in the UK: five years operational experience. Archives of Disease in Childhood. 2000;83:492-7.
14. Fortescue EB, Kaushal R, Landrigan CP, McKenna KJ, Clapp MD, Federico F, et al. Prioritizing strategies for preventing medication errors and adverse drug events in pediatric inpatients. Pediatrics. 2003;111:722-9.
15. Leape LL, Cullen DJ, Clapp MD, Burdick E, Demonaco HJ, Erickson JI, et al. Pharmacist participation on physician rounds and adverse drug events in the intensive care unit. Journal of American Medical Association. 1999;282:267-70.
16. Kane SL, Weber RJ, Dasta JF. The impact of critical care pharmacists on enhancing patient outcomes. Intensive Care Medicine. 2003;29:691-8.
17. Krupicka MI, Bratton SL, Sonnenthal K. Impact of a pediatric pharmacists in the pediatric intensive care unit. Critical Care Medicine. 2002;30:919-21.
18. Dooley MJ, Allen KM, Doecke CJ, Galbraith KJ, Taylor GR, Bright J, et al. A prospective multicentre study of pharmacist initiated changes to drug therapy and patient management in acute care government funded hospital. British Journal of Clinical Pharmacology. 2003;57:513-21.
19. Rooney JJ, Heuvel LV. Root cause analysis for beginners. Quality Progress. 2004;37:45-53.
20. Wu AW, Lipshutz AKM, Pronovost PJ. Effectiveness and efficiency of root cause analysis in medicine. Journal of American Medical Association. 2008;299:685-7.

21. Wallace LM. From root cause analysis to safer systems : international comparison of nationally sponsored healthcare staff training programmes. Quality and Safety in Health Care. 2006;15:400-2.
22. Tang CW, Feng WM, Bao Y, Zhu Y. Medication safety for children in China. The Lancet. 2014;383:1462-8.
23. Roughhead L, Semple S, Rosenfeld E. Literature review: medication safety in Australia. Sydney: Australian Commission on Safety and Quality in Health Care, 2013.
24. Kimland E, Nydert P, Odlind V, Battiger Y, Lindermalm S. Paediatric drug use with focus on off-label prescriptions at Swedish hospital - a nationwide study. Acta Paediatrica. 2012;10:772-8.
25. Hoppo K, Anabwani G, Garcia-Bournissen F, Gazarian M, Kearns GL, Nakamura H. The status of paediatric medicine initiatives around the world - what has happened? what has not? European Journal of Clinical Pharmacology. 2012;68:1-10.
26. Aronson J. Medication errors: definitions and classification. British Journal of Clinical Pharmacology. 2009;67:599-604.
27. American Society of Health-System Pharmacists. Suggested definitions and relationships among medication misadventures, medication errors, adverse drug events, and adverse drug reactions. American Journal of Health-System Pharmacy. 1998;55:165-6.
28. Otero MJ, Schmitt E. Clarifying terminology for adverse drug events. Annals of Internal Medicine. 2005;142:77-8.
29. Manasse HR. Medication use in an imperfect world drug misadventuring as an issue of public policy. part 1. American Journal of Health-System Pharmacy. 1989;46:929-44.
30. Malone PM, editor. *Drug information : a guide for pharmacists*. 3rd ed. New York: McGraw-Hill; 2006.
31. Kilbridge P, Noirot L, Reichley R, Berchelmann K, Schneider C, Heard K, et al. Computerized surveillance of adverse drug events in a pediatric hospital. Journal of the American Medical Informatics Association. 2009;16:607-12.
32. Bates DW, Cullen DJ, Laird N, Petersen LA, Small SD, Servi D, et al. Incidence of Adverse Drug Events and Potential Adverse Drug Events. Journal of American Medical Association. 1995;274:29-34.
33. Tam KWT, Kwok HK, Fan YMC, Tsui KB, Ng KK, Ho KYA, et al. Detection and prevention of medication misadventures in general practice. International Journal for Quality in Health Care. 2008;20:192-9.
34. Bates D, Boyle D, Vliet M, Schneider J, Leape L. Relationship between medication errors and adverse drug events. Journal of General Internal Medicine. 1995;10:199-205.
35. National Coordinating Council for Medication Error Reporting and Prevention. About medication error 1998. Available from: http://www.nccmerp.org/aboutMedErrors.html.
36. Cohen MR. Risk management of medication errors must include a careful look at the specific systems involved. Hospital pharmacy. 1996;31:454-62.
37. Kopp BJ, Erstad BL, Allen ME. Medication errors and adverse drug events in an intensive care unit : direct observation approach for detection. Critical Care Medicine. 2006;34:415-25.
38. World Health Organization. International drug monitoring: the role of national centres. Geneva: 1972.
39. Trinkle R, Wu J. Errors involving pediatric patients receiving chemotherapy : a literature review. Medical and Pediatric Oncology. 1996;26:344-51.
40. Roughead EE, Semple SJ. Medication safety in acute care in Australia : where are we now? Part 1 : a review of the extent and causes of medication problems 2002-2008. Australia and New Zealand Health Policy. 2009;6:18.
41. Kalisch LM, Caughey GE, Roughead EE, Gilbert AL. The prescribing cascade. Australian Prescriber. 2011;34:162-6.

42. Nebekker JR, Barach P, Samore MH. Clarifying adverse drug events : a clinician's guide to terminology, documentation and reporting. Annals of Internal Medicine. 2004;140:795-801.
43. Tam KWT, Kwok KH, Fan YMC, Tsui KB, Ng KK, Ho KYA. Detection and prevention of medication misadventures in general practice. International Journal for Quality in Health Care. 2008;20:192-9.
44. Classen DC, Pesstotnik SL, Evans ES, Lloyd JF, Burke JP. Adverse drug events in hospitalized patients : excess length of stay, extra costs and attributable mortality. Journal of American Medical Association. 1997;277:301-6.
45. Lewis PJ, Dornan T, Taylor D. Prevalence, incidence and nature of prescribing errors in hospital inpatients : a systematic review. Drug Safety. 2009;32:379-89.
46. Runciman WB, Roughead EE, Semple SJ, Adams RJ. Adverse drug events and medication errors in Australia. International Journal for Quality in Health Care. 2003;15:i49-i59.
47. Runciman WB. Lessons from the Australian patient safety foundation: setting up a national patient safety surveillance system—is this the right model? Quality and Safety in Health Care. 2002;11:246-51.
48. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients : a meta-analysis of prospective studies. Journal of American Medical Association. 1998;279:1200-5.
49. Ghaleb MA, Barber N, Franklin BD, Wong ICK. The incidence and nature of prescribing and medication administration errors in paediatric inpatients. Archives of Disease in Childhood. 2010;95:113-8.
50. Kaushal R, Bates DW, Landrigan C, McKenna KJ, Clapp MD, Federico F, et al. Medication errors and adverse drug events in pediatric inpatients. Journal of American Medical Association. 2001;285:2114-20.
51. France DJ, Cartwright J, Jones V, Thompson V, Whitlock JA. Improving pediatric chemotherapy safety through voluntary incident reporting: lessons from the field. Journal of Pediatric Oncology Nursing. 2004;21:200-6.
52. Miller MR, Robinson KA, Lubomski LH, Rinke ML, Pronovost PJ. Medication errors in paediatric care: a systematic review of epidemiology and an evaluation of evidence supporting reduction strategy recommendations. Quality and Safety in Health Care. 2007;16:116-26.
53. Kaushal R, Jaggi T, Walsh K, Fortescue EB, Bates DW. Pediatric medication errors: what do we know? what gaps remain? Ambulatory Pediatrics. 2004;4:73-81.
54. Schumock GT. Methods to assess the economic outcomes of clinical pharmacy services. Pharmacotherapy. 2000;20:S243-S52.
55. Physician Insurers Association of America. Medication errors symposium white papers. Washington, DC: Physician Insurers Association of America, 2000.
56. Johnson JA, Bootman JL. Drug-related morbidity and mortality and the economic impact of pharmaceutical care. American Journal of Health-System Pharmacy. 1997;54:554-8.
57. Bates DW, Spell N, Cullen DJ. The costs of adverse drug events in hospitalized patients. Journal of American Medical Association. 1997;277:307-11.
58. Department of Health. An organisation with a memory. London: Stationery Office, 2000.
59. Australian Institute of Health and Welfare. Australian Hospital Statistics 1999-00. Canberra: 2002.
60. World Health Organization. World alliance for patient safety : forward programme. France: World Health Organization, 2004.
61. American Society of Hospital Pharmacists. ASHP guidelines on preventing medication errors in hospitals. American Journal of Hospital Pharmacy. 1993;50:305-14.

62. Leape LL, Bates DW, Cullen DJ. System analysis of adverse drug events. Journal of American Medical Association. 1995;274:35-43.
63. Joint Commission on Accreditation of Healthcare Organizations. Sentinel event statistics 2002. Available from: http://www.jcaho.org/accredited+organizations/ambulatory+care/sentinel+events.htm.
64. Taxis K, Dean B, Barber M. Causes of intravenous medication errors: an ethnographic study. Quality and Safety in Health Care. 2003;12:343-8.
65. Lesar T, Briceland L, Stein D. Factors related to errors in medication prescribing. Journal of American Medical Association. 1997;277:312-7.
66. Likic R, Maxwell SRJ. Prevention of medication errors: teaching and training. British Journal of Clinical Pharmacology. 2009;67:656-61.
67. The United States Pharmacopeial Convention. Summary of information submitted to MedMARx in the year 2002: charting a course for change. 2002.
68. Stebbing C, Wong ICK, Kaushal R, Jaffe A. The role of communication in paediatric drug safety. Archives of Disease in Childhood. 2007;92:440-5.
69. Williams MV, Parker RM, Baker DW. The role of health literacy in patient-physician communication. Family Medicine. 2002;34:383-9.
70. Dean B, Schachter M, Vincent C, Barber N. Prescribing errors in hospital inpatients: their incidence and clinical significance. Quality and Safety in Health Care. 2002;11:340-4.
71. Wright K. Student nurses need more math to improve their drug calculating skills. Nurse Education Today. 2007;27:278-85.
72. Preston R. Drug errors and patient safety: the need for a change in practice. British Journal of Nursing. 2004;18:201-5.
73. Stebbing C, Wong ICK, Kaushal R, Jaffe A. The role of communication in paediatric drug safety. Archives of Disease in Childhood. 2007;92:440-5.
74. Angley M, Ponniah A, Bong J, Padhye V, Shakib S, Spurling L. Implementing and evaluating a parallel post-discharge home medicines review (HMR) model: The Pharmacy Guild of Australia; 2010. Available from: http://www.guild.org.au/iwov-resources/documents/The_Guild/PDFs/CPA%20and%20Programs/4CPA%20General/IIG-011/IIG011%20Final%20Report.pdf.
75. Wong ICK, Basra N, Yeung V, et al. Supply problems of unlicensed and off-label medicines after discharge. Archives of Disease in Childhood. 2006;91:686-8.
76. Nutbeam D. Health literacy as a public health goal: a challenge for contemporary health education and communication strategies into the 21st century. Health Promotional International. 2000;15:259.
77. Dolder CR, Lacro JP, Leckband S, et al. Interventions to improve antipsychotic medication adherence : review of recent literature. Journal of Clinical Psychopharmacology. 2003;23:389-99.
78. Tates K, Meeuwesen L. Doctor-parent-child communication: a review of the literature. Social Science and Medicine. 2001;52:839-59.
79. Kripalani S, LeFevre FP, Williams MV, Basaviah P, Baker DW. Deficits in communication and information transfer between hospital-based and primary care physicians: implications for patient safety and continuity of care. Journal of American Medical Association. 2007;297:831-41.
80. Joint Commission on Accreditation of Healthcare Organizations. National patient safety goals 2003. Available from: http://www.jcaho.org/accredited+organizations/patient+safety/npsg/npsg_03.htm.
81. Krass I, Smith C. Impact of medication regimen reviews performed by community pharmacists for ambulatory patients through liaison with general medication practitioners. International Journal of Pharmacy Practice. 2000;8:111-20.
82. Safety and Quality Council. Second national report on patient safety, improving medication safety. Canberra: Australian Council for Safety and Quality in Health Care, 2002.

83. Davis NM. Performance lapses as a cause of medication errors. Hospital Pharmacy. 1996;31:1524-5.
84. Fu-In T, Shuh C, Jen S, Shu Y, Ien-Lan W, Ching-Huey C. Nurses relate the contributing factors involved in medication errors. Journal of Clinical Nursing. 2007;16:676.
85. Steering Committee on Quality Improvement Management and Committee on Hospital Care. Principles of pediatric patient safety: reducing harm due to medical care. Pediatrics. 2011;127:1199-210.
86. American Society of Hospital Pharmacists. ASHP guidelines on preventing medication errors in hospitals. Am J Hosp Pharm. 1993;50:305-14.
87. The Joint Commission. Sentinel event alert : preventing pediatric medication errors Washington D C: The Joint Commission; 2008. Available from: http://www.jointcommission.org/assets/1/18/SEA_39.pdf.
88. Dundee FK, Dundee DM, Noday DM. Pediatric counseling and medication management services : Opportunities for community pharmacists. Journal of American Medical Association. 2002;42:556-67.
89. Wassmer E, Minnaar G, Abdel AN. How do paeditricians communicate with children and parents? European Journal of Pediatrics. 2004;93:1501-6.
90. Rowe C, Koren T, Koren G. Errors by paediatric residents in calculating drug doses. Archives of Disease in Childhood. 1998;79:56-8.
91. Yappe SJ, Aranda JV. Neonatal and Pediatric Pharmacology. Therapeutic Principles in Practice. 3rd ed. Philadelphia: Lippincott Williams and Wilkins; 2005.
92. Blumer JL, Reed MD. Neonatal pharmacology. In: Aranda JS, editor. *Neonatal and pediatric pharmacology : therapeutic principle in practice*. 3rd ed. Philadelphia: Lippincott, Williams and Wilkins; 2005.
93. Kearns GL. Developmental pharmacology : drug disposition, action and therapy in infants and children. New England Journal of Medicine. 2003;349:1157.
94. Chan DS, Kotzin DA. Adult vs paediatric clinical intervention trends : a four year retrospective report. Journal of Pediatric Pharmacy Practice. 1998;3:144-9.
95. Kozer E, Scolnik D, MacPherson A. Using a preprinted order sheet to reduce prescription errors in pediatric emergency department : a randomized, controlled trial. Pediatrics. 2005;116:1299-302.
96. Sheridan-Leos N, Schulmeister L, Hartranft S. Failure mode and effect analysis™: a technique to prevent chemotherapy errors. Clinical Journal of Oncology Nursing. 2005;10:393-8.
97. Weiss J, Krebs S, Hoffmann C, Werner U, Neubert A, Brune K, et al. Survey of adverse drug reactions on a pediatric ward : a strategy for early and detailed detection. Pediatrics. 2002;110:254-7.
98. Rozich JD. Standardization as a mechanism to improve safety in health care. The Joint Commission Journal on Quality and Patient Safety. 2004;30:5-14.
99. Wong ICK, Ghaleb M, Dean-Franklin B, Barber N. Incidence and nature of dosing errors in paediatric medications : a systematic review. Drug Safety. 2004;27:661-70.
100. Chappell K, Newman C. Potential tenfold drug overdoses on a neonatal unit. Archives of Disease in Childhood Fetal Neonatal Edition. 2004;89:F483-F4.
101. Tan E, Cranswick NE, Rayner CR, et al. Dosing information for paediatric patients : are they really "therapeutic orphans"? Medical Journal of Australia. 2003;179:195-8.
102. Budetti PP. Ensuring safe and effective medications for children. Journal of American Medical Association. 2003;290:970-1.
103. Roberts R, Rodriguez W, Murphy D. Pediatric drug labeling : improving the safety and efficacy of pediatric therapies. Journal of American Medical Association. 2003;290:905-11.
104. Ghaleb M, Wong I. Medication errors in paediatric patients. Archives of Disease in Childhood Education and Practice Edition. 2006;91:ep20-ep4.

105. Budetti P. Ensuring safe and effective medications for children. Journal of American Medical Association. 2003;290:970-1.
106. Largent E, Miller F, Pearson S. Going off-label without venturing off-course. Archives of Internal Medicine. 2009;169:1745-7.
107. Conroy S, Choonara I, Impicciatore P, Mohn A, Arnell H, Rane A. Survey of unlicensed and off label drug use in paediatric wards in European countries. European network for drug investigation in children. British Medical Journal. 2000;320:79-82.
108. Radley D, Finkelstein S, Stafford R. Off-label prescribing among office-based physicians. Archives of Internal Medicine. 2006;166:1021-6.
109. Sullivan J, Buchino J. Medication errors in pediatrics--the octopus evading defeat. Journal of surgical oncology. 2004;88(3):182-8.
110. Walsh k, Kaushal R, Chessare J. How to avoid paediatric medication error : a user's guide to the literature. Archives of Disease in Childhood. 2005;90:698-702.
111. Sandlin D. Pediatric medication error prevention. Journal of Perianesthesia Nursing. 2008;23:279-81.
112. Scavuzzo J, Gamba N. Bridging the gap : the virtual chemotherapy unit. Journal of Pediatric Oncology Nursing. 2004;21:27-32.
113. Womer RB, Tracy E, Soo-Hoo W, Bickert B, DiTaranto S, Barnsteiner JH. Multidisciplinary systems approach to chemotherapy safety : rebuilding processes and holding the gains. Journal of Clinical Oncology. 2002;20:4705-12.
114. Phillips J, Beam S, Brinker A, Holquist C, Honig P, Lee L, et al. Retrospective analysis of mortalities associated with medication errors. American Journal of Health-System Pharmacy. 2001;58:1835-41.
115. Muller T. Typical medication errors in oncology : analysis and prevention strategies. Onkologie. 2003;26:539-44.
116. Sheridan-Leos N. A model of chemotherapy education for novice oncology nurses that supports a culture of safety. Clinical Journal of Oncology Nursing. 2007;11:545-51.
117. Schulmeister L. Look-alike, sound-alike oncology medications. Clinical Journal of Oncology Nursing. 2006;10:35.
118. Berman A. Reducing medication errors through naming, labeling and packaging. Journal of Medical Systems. 2004;28:9-29.
119. Gandhi T, Bartel S, Shulman L, Verrier D, Burdick E, Cleary A, et al. Medication safety in the ambulatory chemotherapy setting. Cancer. 2005;104:2477-83.
120. Ogletree RL. Preventing medication errors in oncology. Hospital Pharmacy. 2002;15:47-52.
121. SHPA Committee of Specialty Practice in Clinical Pharmacy. SHPA standards of practice for clinical pharmacy. Journal of Pharmacy Practice and Research. 2005;35:122-46.
122. Peterson G, Tenni P, Jackson S, Bereznicki L, Hughes J, Kong D, et al. Documenting clinical intervention in community pharmacy : PROMISe III2010. Available from: www.guild.org.au/iwov-resources/...Guild/.../RFT0809_FinalReport.pdf.
123. Cohen CR, Anderson RW, Attilio RM, et al. Preventing medication errors in cancer chemotherapy. American Journal of Health-System Pharmacy. 1996;53:737-46.
124. Kloth DD. Assuring safe care for patients through an organized multidisciplinary team effort. Hospital Pharmacy. 1997;32:s21-s5.
125. Donyai P, O'Grady K, Jacklin A. The effects of electronic prescribing on the quality of prescribing. British Journal of Clinical Pharmacology. 2007;64:1-8.
126. Reynolds ER, Boyce RW, Haxby DG, Goldberg BA, Stennett DJ. Intervention assessment in an Indian health service pharmacy. Journal of American Pharmeutical Association. 2000;40:41-5.
127. Barber ND, Batty R, Ridout DA. Predicting the rate of physician-accepted interventions by hospital pharmacists in the United Kingdom. American Journal of Health-System Pharmacy. 1997;54:397-405.

128. Johnston J, Vienet MD, editors. SHPA standards of practice for clinical pharmacy. Melbourne: The Society of Hospital Pharmacists of Australia; 1996.
129. Alderman CP, Farmer C. A brief analysis of clinical pharmacy interventions undertaken in an Australian teaching hospital. Journal of Quality in Clinical Practice. 2001;21:99-103.
130. Lau PM, Stewart K, Dooley M. The ten most common adverse drug reactions (ADRs) in oncology patients : do they matter to you? Support Care Cancer. 2004;12:626-33.
131. Bond CA, Raehl CL. Clinical pharmacy services, hospital pharmacy staffing and medication errors. Pharmacotherapy. 2002;22:134-47.
132. Fischer DS, Alfano S, Knobf MT, et al. Improving the cancer chemotherapy use process. Journal of Clinical Oncology. 1996;14:3148-55.
133. American Society of Health-System Pharmacists. ASHP guidelines on preventing medication errors with antineoplastic agents. American Journal of Health-System Pharmacy. 2002;59:1648-68.
134. Attilio RM. Caring enough to understand: the road to oncology medication error prevention. Hospital Pharmacy. 1996;31:17-26.
135. Kohler ADR, Montello MJ, Green L. Standardizing the expression and nomenclature of cancer treatment regimens. American Journal of Health-System Pharmacy. 1998;55:137-44.
136. Hepler CD, Strand LM. Opportunities and responsibilities in pharmaceutical care. American Journal of Hospital Pharmacy. 1990;47:533-43.
137. Chung MK, Bartfield JM. Knowledge of prescription medications among elderly emergency department patients. Annals of Emergency Medicine. 2002;39:605-8.
138. Bedell SE, Jabbour S, Goldberg R. Discrepancies in the use of medications : their extent and predictors in an outpatient practice. Archives of Internal Medicine. 2000;160:2129-34.
139. Gardner B, Graner K. National patient safety goals: pharmacists' medication reconciliation-related clinical interventions in a children's hospital. The Joint Commission Journal on Quality and Patient Safety. 2009;35:278-82.
140. Easton K, Morgan T, Williamson M. Medication safety in the community : a review of literature. Sydney: National Prescribing Service, 2009.
141. The Joint Commission. Sentinel event alert 2006. Available from: www.jointcommission.org/SentinelEvents/SentinelEventAlert/sea-35.htm.
142. Joint Commission on Accreditation of Healthcare Organizations. Preventing medication errors : strategies for pharmacists. Illinois: Joint Commission Resources, Inc; 2001.
143. Rozich JD, Howard RJ, Justeson JM, et al. Patient safety standardisation as a mechanism to improve safety in health care. Joint Commission Journal on Quality and Patient Safety. 2004;30:5-14.
144. Carter M. Pharmacist-acquired medication histories in a university hospital emergency department. American Journal of Health-System Pharmacy. 2006;63:2500-3.
145. deClifford JM, Caplygin FM, Lam SS, Leung BK. Impact of an emergency department pharmacist on prescribing errors in an Australian hospital. Journal of Pharmacy Practice and Research. 2007;37:284-6.
146. Kim JM, Park SJ, Sohn YM, Lee YM, Gwak HS, Lee BK, et al. Development of clinical pharmacy services for intensive care units in Korea. Springer Plus. 2014;3:34.
147. Dodd C. Assessing pharmacy interventions at Salisbury health care NHS trust. Hospital Pharmacy. 2003;10:451-6.
148. Folli HL, Poole RL, Benitz WE, Russo JC. Medication error prevention by clinical pharmacists in two children's hospitals. Pediatrics. 1987;79:718-22.

149. Hatoum HT, Catizone C, Hutchinson RA. An eleven-year review of the pharmacy literature : documentation of the value and acceptance of clinical pharmacy. Drug Intelligence and Clinical Pharmacy. 1986;20:33-48.
150. Fernandez-Llamazares CM, Manrique-Rodriguez S, Peres-Sanz C, Duran-Garcia ME, Sanjurjo-Saez M, Calleja-Hernandez MA. Validation of a method for recording pharmaceutical interventions. Journal of Clinical Pharmacy and Therapeutics. 2012;37:459-63.
151. van-Mill JWF, Westerlund T, Hersberger T, Schaefer MA. Drug-related problem classification systems. Annals of Pharmacotherapy. 2004;38:859-67.
152. Basger BJ, Moles RJ, Chen TF. Application of drug-related problem (DRP) classification systems: a review of the literature. European Journal of Clinical Pharmacology. 2014;70:799-815.
153. Zaidi STR, Hassan Y, Postma MJ, Ng SH. Impact of pharmacist recommendations on the cost of drug therapy in ICU patients at a Malaysian hospital. Pharmacy World and Science. 2003;25:299-302.
154. Lee AJ, Boro MS, Knapp KK, Meier JL, Korman NE. Clinical and economic outcomes of pharmacist recommendations in a veterans affairs medical center. American Journal of Health-System Pharmacy. 2002;59:2070-7.
155. Bond CA, Raehl CL, Franke T. Interrelationships among mortality rates, drug costs, total cost of care and length of stay in United States hospitals: summary and recommendations for clinical pharmacy services and staffing. Pharmacotherapy. 2001;21:129-41.
156. Lada P, Delgado G, Jr. Documentation of pharmacists' interventions in an emergency department and associated cost avoidance. American Journal of Health-System Pharmacy. 2007;64:63-8.
157. Olson LM, Desai S, Soto ML, Namazifard S, Quelland AK, Erstad BL. Evaluation of pharmacists' interventions at a university teaching hospital. Canadian Journal of Hospital Pharmacy. 2001;58:20-5.
158. vandenBemt PMLA, Postma MJ, vanRoom EN, Chow MC, Fijn R, Brouwers JRBJ. Cost-benefit analysis of the detection of prescribing error by hospital pharmacy staff. Drug Safety. 2002;25:135-43.
159. Ridjt TD, Willems L, Simoens S. Economic effects of clinical pharmacy interventions: a literature review. American Journal of Health-System Pharmacy. 2008;65:1161-72.
160. Sutcliffe KM. Defining and classifying medical error : lessons for learning. Quality and Safety in Health Care. 2004;13:8-9.
161. Boyer MM. Root cause analysis in perinatal care : health care professionals creating safer health care systems. Journal of Perinatal and Neonatal Nursing. 2001;15:40-54.
162. The Canadian Patient Safety Institute. Canadian root cause analysis framework : a tool for identifying and addressing the root causes of critical incidents in healthcare. 2005.
163. Leape L. Error in medicine. Journal of American Medical Association. 1994;272:1851-7.
164. Voekler R. Treat systems, not errors, experts say. Journal of American Medical Association. 1996;276:1537-8.
165. Bagian JP. Patient safety : what is really at issue? Frontiers of Health Services Management. 2005;22:3-16.
166. Reason J. *Human error*. New York: Cambridge University Press; 2003.
167. Reason J. Human error : models and management. British Medical Journal. 2000;320:768-70.
168. Department of Veterans Affairs, Veterans Health Administration, National Center for Patient Safety. Root cause analysis. 2009.

169. Wald H, Shojania KG. Root cause analysis. In: Shojania KG, McDonald KM, Watcher RM, editors. *Making health care safer : a critical analysis of patient safety practices*: Agency for Healthcare Research and Quality; 2001.
170. Shinn JA. Root cause analysis : a method of addressing errors and patient risk. Progress in Cardiovascular Nursing. 2000;15:24-5.
171. Bagian JP, Lee C, Gosbee J. Developing and deploying a patient safety program in a large health care delivery system : you can't fix what you don't know. The Joint Commission Journal on Quality Improvement. 2001;27:522-32.
172. Stecker MS. Root cause analysis. Journal of Vascular and Interventional Radiology. 2007;18:5-8.
173. Iedema RA, Jorm C, Long D, Braithwaite J, Travaglia J, Westbrook M. Turning the medical gaze in upon itself : root cause analysis and the investigation of clinical error. Social Science and Medicine. 2006;62:1605-15.
174. Handle C. Quality improvement through root cause analysis. Hospital Material Management Quarterly. 2000;21:74-8.
175. Bagian JP, Gosbee J, Lee CZ. The Veteran Affairs root cause analysis system in action Joint Commission Journal on Quality Improvement. 2002;28:531-45.
176. Woloshynowych M, Rogers S, Taylor-Adams S, Vincent C. The investigation and analysis of critical incidents and adverse events in healthcare. Health Technology Assessment. 2005;9:31-6.
177. Sutton I. Incident investigation and root cause analysis. Process risk and reliability management

Elsevier Inc; 2010.
178. Flynn EA, Barker KN, Pepper GA, Bates DW, Mikeal RL. Comparison of methods for detecting medication errors in 36 hospitals and skilled-nursing facilities. American Journal of Health-System Pharmacy. 2002;59:436-46.
179. Kiekkas P, Karga M, Lemonidou C, Aretha D, Karanikolas M. Medication errors in critically ill adults: a review of direct observation evidence. American Journal of Critical Care. 2011;20:36-44.
180. Fahimi F, Ariapanah P, Faizi M, Shafaghi B, Namdar R, Ardakani MT. Errors in preparation and administration of intravenous medications in the intensive care unit of a teaching hospital: an observational study. Australian Critical Care. 2008;21:110-6.
181. Calabrese A, Erstad B, Brandl K, Barletta J, Kane S, Sherman D. Medication administration errors in adult patients in the ICU. Intensive Care Medicine. 2001;27:1592-8.
182. Tissot E, Cornette C, Demoly P, Jacquet M, Barale F, Capellier G. Medication errors at the administration stage in an intensive care unit. Intensive Care Medicine. 1999;25:353-9.
183. Boardman H, Fitzpatrick R. Self reported clinical pharmacist interventions underestimate their input to patient care. Pharmacy World and Science. 2001;23:55-9.
184. Condren ME, Haase MR, Luedtke SA, Gaylor AS. Clinical activities of an academic pediatric pharmacy team. Annals of Pharmacotherapy. 2004;38:574-8.
185. Davydov L, Caliendo GC, Smith LG, Mehl B. Analysis of clinical intervention documentation by dispensing pharmacists in a teaching hospital. Hospital Pharmacy. 2003;38:346-50.
186. The International Statistical Classification of Diseases and Related Health Problems 10th Revision. Geneva: The World Health Organization, 2010.
187. Steliarova-Foucher E, Stiller C, Lacour B, Kaatsch P. International classification of childhood cancer, third edition. Cancer. 2005;103:1457-67.
188. Pharmaceutical Society of Australia, The Royal Australian College of General Practitioners, Australasian Society of Clinical and Experimental Pharmacologists and

Toxicologists. *Australian Medicines Handbook 2014*. Adelaide: Australian Medicines Handbook; 2014.
189. *British National Formulary*. 56th ed. London: BMJ Group & RPS Publishing; 2008.
190. Condren ME, Haase MR, Luedtke SA, Taylor AS. Clinical activities of an academic pediatric pharmacy team. The Annals of Pharmacotherapy. 2004;38:574-8.
191. Hosmer DW, Lemeshow S. *Applied Logistic Regression*. 2nd ed. New York: Wiley; 2000.
192. Fleiss JL. Measuring nominal scale agreement among many raters. Psychological Bulletin. 1971;76:378-82.
193. Patient Safety Directorate. Clinical incident management toolkit. Perth: Western Australia Department of Health; 2011.
194. Industrial Relation Commisssion of New South Wales. Health employee's pharmacists (state) award 2012. Available from: www.health.nsw.gov.au/careers/conditions/Awards/hsu_he_pdf.
195. Miles J, Shevlin M. *Applying regression and correlations : a guide for students and researchers*. London: Sage; 2001.
196. Bright JM, Tenni PC. The clinical services documentation (CSD) system for documenting clinical pharmacists' services. Australian Journal of Hospital Pharmacy. 2000;30:10-5.
197. Fernández-Llamazares CM, Calleja-Hernandez MA, Manrique-Rodriguez S, Pérez-Sanz C, Duran-García E, Sanjurjo-Saez M. Impact of clinical pharmacist interventions in reducing paediatric prescribing errors. Archives of Disease in Childhood. 2012;97:564-8.
198. Coutsouvelis J, Corallo CE, Dooley MJ, Foo J, Whitfield A. Implementation of a pharmacist-initiated pharmaceutical handover for oncology and hematology patients being transferred to critical care units. Support Care Cancer. 2010;18:811-6.
199. Maat B, Au YS, Bollen CW, vanVught A, Egberts TCG, Rademaker CMA. Clinical pharmacy interventions in paediatric electronic prescriptions. Archives of Disease in Childhood. 2013;98:222-7.
200. Guy J, Persaud J, Davies E, Harvey D. Drug errors: what role do nurses and pharmacists have in minimizing the risk? Journal of Child Health Care. 2003;7:277-90.
201. Kaushal R, Bates DW, Abramson EL, Soukup JR, Goldmann DA. Unit-based clinical pharmacists' prevention of serious medication errors in pediatric inpatients. American Journal of Health-System Pharmacy. 2008;65:1254-60.
202. Bedouch P, Charpiat B, Conort O, Rose FX, Escosier L, Juste M, et al. Assessment of clinical pharmacists' interventions in French hospitals: results of a multicenter study. Annals of Pharmacotherapy. 2008;42:1095-103.
203. Stemer G, Laml-Wallner G, Kuegler I, Poelzleitner P, Messner S, Steininger S, et al. Comprehensive evaluation of clinical pharmacists' interventions in a large Austrian tertiary care hospital. Europen Journal of Hospital Pharmacy. 2012:10.1136/ejhpharm-2012-000131.
204. Virani A, Crown N. The impact of a clinical pharmacist on patient and economic outcomes in a child and adolescent mental health unit. Canadian Journal of Hospital Pharmacy. 2003;56:158-62.
205. Zhang C, Zhang L, Huang L, Luo R, Wen J. Clinical pharmacists on medical care of pediatric inpatients: a single-center randomized controlled trial. PLoS ONE. 2012;7:e30856.
206. Waddell JA, Solimando DA, Strickland WR, Smith BD, Wray MK. Pharmacy staff interventions in a medical center hematology-oncology service. Journal of American Pharmaceutical Association. 1998;38:451-6.
207. Sanghera N, Chan P, Khaki ZF, Planner C, Lee KKC, Cranswick NE, et al. Interventions of hospital pharmacists in improving drug therapy in children. Drug Safety. 2006;29:1031-47.

208. Ruder AD, Smith DL, Madsen MT, Kass FH. Is there a benefit to having a clinical oncology pharmacist on staff at a community oncology clinic? Journal of Oncology Pharmacy Practice. 2011;17:425-32.
209. Wong S, Gray ES. Clinical pharmacy services in oncology clinics. Journal of Oncology Pharmacy Practice. 1999;5:49-54.
210. Abdel-Qader DH, Harper L, Cantrill JA, Tully MP. Pharmacists' interventions in prescribing errors at hospital discharge. Drug Safety. 2010;33:1027-44.
211. Shah S, Dowell J, Greene S. Evaluation of clinical pharmacy services in a hematology/oncology outpatient setting. Annals of Pharmacotherapy. 2006;40:1527-32.
212. Serrano-Fabiá A, Albert-Marí A, Almenar-Cubell D, Jiménez-Torres NV. Multidisciplinary system for detecting medication errors in antineoplastic chemotherapy. Journal of Oncology Pharmacy Practice. 2010;16:105-12.
213. Wilson S, Wahler R, Brown J, Doloresco F, Monte SV. Impact of pharmacist intervention on clinical outcomes in the palliative care setting. American Journal of Hospital Palliative Care. 2011;28:316-20.
214. Lee J, McPherson M. Outcomes of recommendations by hospice pharmacists. American Journal of Health-System Pharmacy. 2006;63:2235-9.
215. Wang HY, Chan ALF, Chen MT, Liao CH, Tian YF. Effects of pharmaceutical care intervention by clinical pharmacists in renal transplant clinics. Transplant Proceeding. 2008;40:2319-23.
216. Mogensen CB, Olsen I, Thisted AR. Pharmacist advice is accepted more for medical than surgical patients in an emergency department. Danish Medical Journal. 2013;60:A4682.
217. Klopfer JD, Einarson TR. Acceptance of pharmacists' suggestions by prescribers: a literature review. Hospital Pharmacy. 1990;25:830-6.
218. Friesner DL, Scoot DM, Dewey MW, Johnson TA, Kessler ML. What types of nursing facilities are more likely to adopt a pharmacist's medication review recommendations? Consultant Pharmacist. 2013;28:490-501.
219. Abu-Ramaileh AM, Shane R, Churchill W. Evaluating and classifying pharmacists' quality interventions in the emergency department. American Journal of Health-System Pharmacy. 2011;68:2271-5.
220. Wilson S, Wahler R, Brown J, Doloresco F, Monte SV. Impact of Pharmacist Intervention on Clinical Outcomes in the Palliative Care Setting. American Journal of Hospice and Palliative Medicine. 2010.
221. Taegtmeyer AB, Curkovic I, Corti N, Rosen C, Egbring M, Russmann S, et al. Drug-related problems and factors influencing acceptance of clinical pharmacologists' alerts in a large cohort of neurology inpatients. Swiss Medical Weekly. 2012;142:w13615.
222. Pereira PN, Guy MC, Sweaney AM, Boesen KP. Evaluation of prescriber responses to pharmacist recommendations communicated by fax in a medication therapy management program (MTMP). Journal of Managed Care Pharmacy. 2011;17:345-54.
223. Almeida-Neto AC, Chen TF. When pharmacotherapeutic recommendations may lead to the reverse effect on physician decision-making. Pharmacy World and Science. 2008;30:3-8.
224. Ranelli PL, Biss J. Physicians' perceptions of communication with and responsibilities of pharmacist. Journal of American Pharmaceutical Association. 2000;40:625-30.
225. The National Coordinating Council for Medication Error Reporting and Prevention. NCC MERP index for categorizing medication error 2001. Available from: http://www.nccmerp.org/pdf/indexColor2001-06-12.pdf.
226. Bosma L, Jansman FGA, Franken AM, Harting JW. Evaluation of pharmacist clinical interventions in a Dutch hospital setting. Pharmacy World and Science. 2007;30:31-8.

227. Overhage J, Lukes A. Practical, reliable, comprehensive method for characterizing pharmacists' clinical activities. American Journal of Health-System Pharmacy. 1999;56:2444-50.
228. Collier J. Paediatric prescribing: using unlicensed drugs and medicines outside their licensed indications. British Journal of Clinical Pharmacology. 1999;48:5-8.
229. Sircar-Ramsewak F, Baliramsingh S, Seepersad V, Sasanerine-Persad S. Global impact of pharmacist intervention on patient care and cost: a descriptive study at a Trinidad hospital. Pro Newsletter. 2007;38:24-6.
230. Al-Rahbi HAM, Al-Sabri RM, Chitme HR. Interventions by pharmacists in outpatient pharmaceutical care. Saudi Pharmaceutical Journal. 2014;22:101-6.
231. Pham DQ. Evaluating the impact of clinical interventions by PharmD students on internal medicine clerkships: the results of a 3 year study. Annals of Pharmacotherapy. 2006;40:1541-5.
232. McLennan DN, Dooley MJ, Brien JE. Beneficial clinical outcomes resulting from pharmacist interventions. Journal of Oncology Pharmacy Practice. 1999;5:184-9.
233. Kunac DL. Inter- and intra-rater reliability for classification of medication related events in paediatric inpatients. Quality and Safety in Health Care. 2006;15:196-201.
234. Marimoto T, Gandhi TK, Seger AC. Adverse drug events and medication errors: detection and classification methods. Quality and Safety in Health Care. 2004;13:306-14.
235. Forrey RA, Pedersen CA, Schneider PJ. Interrater agreement with a standard scheme for classifying medication errors. American Journal of Health-System Pharmacy. 2007;64:175-81.
236. King WJ, Paice N, Rangrej J, Forestell GJ, Swartz R. The effect of computerized physician order entry on medication errors and adverse drug events in pediatric inpatients. Pediatrics. 2003;112:506-9.
237. Potts AL, Gregory DF. Computerized physician order entry and medication errors in a paediatric critical care unit. Pediatrics. 2004;113:59-63.
238. Kozer E, Scolnik D, Macpherson A. Variables associated with medication errors in pediatric emergency medicine. Pediatrics. 2002;110:737-42.
239. Snyder RA, Abarca J, Meza JL, Rothschild JM, Rizos A, Bates DW. Reliability evaluation of the adapted national coordinating council medication error reporting and prevention (NCC MERP) index. Pharmacoepidemiology and Drug Safety. 2007;16:1006-13.
240. Selbt S, Fein JA, Osterhoudt K, Wayne HO. Medication errors in a paediatric emergency department. Pediatric Emergency Care. 1999;15:1-4.
241. Crowley E, Williams R, Cousins D. Medication errors in children: a descriptive summary of medication error reports submitted to the United States Pharmacopeia. Current Therapy Research. 2001;26:627-40.
242. Wong ICK, Wong LYL, Cranswick NE. Minimising medication errors in children. Archives of Disease in Childhood. 2009;94:161-4.
243. Cunningham KJ. Analysis of clinical interventions and the impact of pediatric pharmacists on medication error prevention in a teaching hospital. Journal of Pediatric Pharmacology and Therapeutics. 2012;17:365-73.
244. Ghaleb MA, Barber N, Franklin BD, Yeung VWS, Khaki ZF, Wong ICK. Systematic review of medication errors in pediatric patients. Annals of Pharmacotherapy. 2006;40:1766-76.
245. Kaushal R. Using chart review to screen for medication errors and adverse drug events. American Journal of Health-System Pharmacy. 2002;59:2323-5.
246. Kim Y, Schepers G. Pharmacist intervention documentation in US health care system. Hospital Pharmacy. 2003;12:1141-7.
247. McLennan DN, Dooley MJ. National survey of clinical activity documentation practices. Australian Journal of Hospital Pharmacy. 2000;30:6-9.

248. Tenni PC, Hughes JD. National survey of clinical pharmacy services. Australian Journal of Hospital Pharmacy. 1996;26:416-27.
249. Pederson CA, Schneider PJ, Santell JP, Kelly EJ. ASHP national survey of pharmacy practice in acute care settings: monitoring, patient education, and wellness. American Journal of Health-System Pharmacy. 2000;57:2171-87.
250. Millar T, Sandilya R, Tordoff J, Ferguson R. Documenting pharmacist's clinical interventions in New Zealand hospitals. Pharmacy World and Science. 2008;30:99-106.
251. Dooley MJ, McLennan DN, Galbraith KJ, Burgess NG. Multicentre pilot study of a standard approach to document clinical pharmacy activity. Australian Journal of Hospital Pharmacy. 2000;30:150-5.
252. Reilly JC, Wallace M, Campbell MM. Tracking pharmacist interventions with a hand-held computer. American Journal of Health-System Pharmacy. 2001;58:158-61.
253. Simonian AI. Documenting pharmacist interventions on an intranet. American Journal of Health-System Pharmacy. 2003;60:151-5.
254. William M, Peterson GM, Tenni P, Bindoff IK, Curtain C, Hughes J, et al. Drug related problems detected in Australian Community Pharmacies: the Promise Trial. Annals of Pharmacotherapy. 2011;45:1067-76.
255. Lau A, Balen RM, lam R, Malyuk DL. Using a personal digital assistant to document clinical pharmacy services in an intensive care unit. American Journal of Health-System Pharmacy. 2001;58:1229-32.
256. Pugh CB. Documenting the clinical interventions of pharmacists. Topics in Hospital Pharmacy Management 1992;11:30-43.
257. American Society of Health-System Pharmacists. ASHP guidelines on documenting pharmaceutical care in patient medical records. American Journal of Health-System Pharmacy. 2003;60:705-7.
258. Royal Pharmaceutical Society of Great Britain. Guidance on recording interventions. The Pharmaceutical Journal. 2006;276:517-8.
259. Schaff RL, Schumock GT, Nadzam DM. Development of the Joint Commission's indicators for monitoring the medication use system. Hospital Pharmacy. 1991;26:326-9.
260. De Rijdt T, Willems L, Simoens S. Economic effects of clinical pharmacy interventions: a literature review. American Journal of Health-System Pharmacy. 2008;65:1161-72.
261. Catania HF, Yee WP, Catania PN. The next step in clinical intervention programs. Topics in Hospital Pharmacy Management. 1992;11:80-5.
262. McKee M, Frei BL, Garcia A, Fike D, Soefje SA. Impact of clinical pharmacy services on patients in an outpatient chemotherapy academic clinic. Journal of Oncology Pharmacy Practice. 2011;17:387-94.
263. Bond CA, Raehl CL. Clinical pharmacy services, pharmacy staffing and hopital mortality rates. Pharmacotherapy. 2007;27:481-93.
264. Scarsi KK, Fotis MA, Noskin GA. Pharmacist participation in medical rounds reduce medication errors. American Journal of Health-System Pharmacy. 2002;59:2089-92.
265. Ling JM, Mike LA, Rubin J, Abraham P, Howe A, Patka J, et al. Documentation of pharmacist interventions in the emergency department. American Journal of Health-System Pharmacy. 2005;62:1783-93.
266. Zimmerman C, Smolarek R, Stevenson J. Peer review and continuous quality improvement of pharmacists' clinical interventions. American Journal of Health-System Pharmacy. 1997;54:1722-7.
267. Nurgat Z, Al-Jazairi A, Abu-Shraie N, Al-Jedai A. Documenting clinical pharmacist intervention before and after the introduction of a web-based tool. International Journal of Clinical Pharmacy. 2011;33:200-7.
268. Berg BL. Focus group interviewing. In: Berg BL, editor. *Qualitative research methods for the social sciences*. Boston: Allyn and Bacon; 2004.

269. Creswell JW. *Educational research: planning, conducting, and evaluating quantitative and qualitative research*. Upper Saddle River: Pearson Education; 2005.
270. Sharts-Hopko NC. Focus group methodology: when and why? Journal of the Association of Nurse in AIDS Care. 2001;12:89.
271. Starre CVD, Dijk MV, Bos AVD, Tibboel D. Paediatric critical incident analysis: lessons learnt on analysis, recommendations and implementation. European Journal of Pediatrics. 2014;173:1449-57.
272. Kruk R. Patient safety and clinical quality program: third report on incident management in the new South Wales public health system 2005-2006. Sydney: New South Wales Department of Health, 2006.
273. Haig KM, Sutton S, Whittington J. SBAR: a shared mental model for improving communication between clinicians. Journal of Quality and Patient Safety. 2006;32:167-75.
274. Mills PD, Neily J, Kinney LM, Bagian J, Weeks WB. Effective interventions and implementation strategies to reduce adverse drug events in the Veterans Affairs (VA) system. Quality and Safety in Health Care. 2008;17:37-46.
275. The United States of Pharmacopeia. USP release fourth annual report on medication errors in US hospitals2003. Available from: http:www.usp.or/newscenter.
276. Buckley MS, Erstad BL, Kopp BJ, Theodorou AA, Priestley G. Direct observation approach for detecting medication errors and adverse drug events in a pediatric intensive care unit. Pediatric Critical Care Medicine. 2007;8:145-52.
277. Winterstein AG, Johns TE, Rosenberg EI, Hatton RC, Gonzalez-Rothi R, Kanjanarat P. Nature and causes of clinically significant medication errors in a tertiary care hospital. American Journal of Health-System Pharmacy. 2004;61:1908-16.
278. Westbrook JI, Li L, Lehnbom EC, Baysari MT, Braithwaite J, Burke R, et al. What are incident reports telling us? A comparative study at two Australian hospitals of medication errors identified at audit, detected by staff and reported to an incident system. International Journal for Quality in health Care. 2015:1-9.
279. Wittich CM, Burkle CM, Lanier WL. Medication errors: an overview for clinicians. Mayo Clinic Proceedings. 2014;89:1116-25.
280. American Academy of Pediatrics Committee on Drugs, American Academy of Pediatrics Committee on Hospital Care. Prevention of medication errors in the pediatric inpatient setting. Pediatrics. 2003;112:431-6.
281. Levine SR, Cohen MR, Blanchard NR. Guidelines for preventing medication errors in pediatrics. Journal of Pharmacy Practice and Therapeutics. 2001;6:426-42.
282. Kim GR, Chen AR, Arceci RJ. Error reduction in pediatric chemotherapy: computerized order entry and failure modes and effect analysis. Archives of Pediatric and Adolescent Medicine. 2006;160:495-8.
283. Ghaleb MA, Wong ICK. Medication errors in paediatric patients. Archives of disease in childhood - Education & practice edition. 2006;91(1):ep20.
284. Bates DW, Teich JM, Lee J, Seger D, Kuperman GJ, Ma'Luf N, et al. The impact of computerized physician order entry on medication error prevention. Journal of American Medical Informatics Association. 1999;6:313-21.
285. White CS. Advanced practice prescribing: Issues and strategies in preventing medication error. journal of Nursing Law. 2011;14:120-7.
286. Koppel R, Metlay JP, Cohen A. Role of computerized physician order entry systems in facilitating medication errors. Journal of American Medical Association. 2005;293:1197-203.
287. Bates DW, Kuperman GJ, Wang S, Gandhi T, Kittler A, Volk L, et al. Ten Commandments for Effective Clinical Decision Support: Making the Practice of Evidence-based Medicine a Reality. Journal of the American Medical Informatics Association. 2003;10:523-30.

288. Kaushal R, Jha AK, Franz C, Glaser J, Shetty KD, Jaggi T, et al. Return on investment for a computerized physician order entry system. Journal of the American Medical Informatics Association. 2006;13:261-6.
289. Simms ER, Slakey DP, Garstka ME, Tersigni SA, Korndorffer JR. Can simulation improve the traditional method of root cause analysis? a preliminary investigation. Surgery. 2012;152:489-97.
290. Wakefield JG, McLaws ML, Whitby M, Patton L. Patient safety culture: factors that influence clinical invilvement in patient safety behaviours. Quality and Safety in Health Care. 2010;19:585-91.
291. Leonard MS, Cimino M, Shaha S, McDougal S, Pilliod J, Brodsky L. Risk reduction for adverse drug events through sequential implementation of patient safety initiatives in a children's hospital. Pediatrics. 2006;118:e1124-e9.
292. Sandra VD. Pediatrician–parent–child communication: problem-related or not? Patient Education and Counseling. 2004;52:61-8.
293. Taitz J, Genny K, Brooks V, Ross D, Ryan K, Schumack B, et al. System-wide learning from root cause analysis: a report from the New South Wales Root Cause Analysis Review Committee. Quality and Safety in Health Care. 2010;19:e63.
294. Ranelli PL, Bartsch K, London K. Pharmacists' perceptions of children and families as medicine consumers. Psychology and Health. 2000;15:829 -40.
295. Cronrath P, Lynch TW, Gilson LJ, Nishida C, Sembar MC, Spencer PJ, et al. PCA oversedation: application of Healthcare Failure Mode Effect (HFMEA) analysis. Nursing Economics. 2011;29:79-87.
296. Pham JC, Natterman JP. ReCASTing the RCA: an improved model for performing root cause analyses. American Journal of Medical Quality. 2010;25:186-91.

Appendix 1: Data Collection Form (Direct Observation Study)

Attach Patient Sticker	Date of admission: Date of discharge: Ward:

Presenting complaints	
History of presenting complaints	
Medical history	
Medication history	
ADR/allergy history	
On admission medication(s)	Current medication(s)
Description of intervention & medication(s) implicated	
Cause of intervention	
Trigger of intervention	
Intervened health care personnel	
Degree of acceptance	

Appendix 2: Approval from Princess Margaret Hospital for Children Institutional Review Board

Government of **Western Australia**
Department of **Health**
Child and Adolescent Health Service

Dr Shalini Kassam
Pharmacy
Princess Margaret Hospital
Roberts Road
SUBIACO WA 6008

Dear Dr Kassam

Audit 337QP – Pharmacist interventions in minimising medication misadventure in children – 2923-05/11

This letter confirms that the above audit has been reviewed and approved by the relevant Hospital Quality Improvement Committee and approved by Executive Director of Medical Services in accordance with the National Statement 2007 (clauses 5.1.18 to 5.1.23).

The Executive Director has recommended this audit be noted by the Ethics Committee and requested a number for the purpose of publication.

Yours sincerely,

pp **Marlene Clayton**
Ethics Committee Secretary

1 July 2011

Princess Margaret Hospital for Children
Roberts Road Subiaco WA 6008
GPO Box D184 Perth WA 6840
Tel: (08) 9340 8222 Fax: (08) 9340 8111
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Appendix 3: Approval from Curtin University Human Ethics Committee

Curtin University

Memorandum

To	Hesty Ramadaniati, School of Pharmacy
From	A/Prof Stephan Millett, Chair, Human Research Ethics Committee
Subject	Protocol Approval **PH-14-11**
Date	14 September 2011
Copy	Jeff Hughes, School of Pharmacy

Office of Research and Development

Human Research Ethics Committee

Telephone 9266 2784
Facsimile 9266 3793
Email hrec@curtin.edu.au

Thank you for your "Form C Application for Approval of Research with Low Risk (Ethical Requirements)" for the project titled *"Pharmacist Interventions in Minimising Medication Misadventures in Children with Cancer"*. On behalf of the Human Research Ethics Committee I am authorised to inform you that the project is approved.

Approval of this project is for a period of twelve months **14-09-11** to **14-09-12**.

The approval number for your project is **PH-14-11**. *Please quote this number in any future correspondence*. If at any time during the twelve months changes/amendments occur, or if a serious or unexpected adverse event occurs, please advise me immediately.

Yours sincerely,

Associate Professor Stephan Millett
Chair Human Research Ethics Committee

Please Note: The following standard statement must be included in the information sheet to participants:
This study has been approved by the Curtin University Human Research Ethics Committee (Approval Number PH-14-11). If needed, verification of approval can be obtained either by writing to the Curtin University Human Research Ethics Committee, c/- Office of Research and Development, Curtin University, GPO Box U1987, Perth, 6845 or by telephoning 9266 2784 or hrec@curtin.edu.au

Appendix 4: Participant Information Sheet (Direct Observation Study)

Participant Information Sheet

Pharmacists' Interventions in Minimising Medication Misadventure in Children with Cancer: Direct Observation

My name is Hesty Ramadaniati. I am a PhD student enrolled in School of Pharmacy at Curtin University.

Purpose of Research

The aims of the project are evaluating the role of pharmacists' interventions in minimising the occurrence of medication misadventure in children and investigating the causes and contributing factors to medication misadventure in this population.

Your Role

I am inviting the ward pharmacists to participate in this study. You will be observed by researcher during your day to day professional practice. The researcher will minimise any distraction during observation so you can perform your routine tasks in a natural manner. If I notice any adverse interventions that are likely to cause imminent harm to the patients, I will notify senior pharmacists and/or pharmacy director immediately.

Consent to Participate

Your participation in this research is voluntary. You have the right to withdraw at any stage and there is no penalty for withdrawing from participation. When you have signed the consent form I will assume that you have agreed to participate and allow me to use your data in this research.

Confidentiality

The information collected will be kept confidential and data collection sheets along with the electronic data files will be kept in a secure archive in the School of Pharmacy for five years before they will be destroyed.

Further Information

This research has been reviewed and given approval by Curtin University Human Research Ethics Committee (Approval number xxxx) and Permission from Princess Margaret Hospital Authority (Registration Number : 2923). If you have any questions about this research, please contact me on 0468930200 or by email : h.ramadaniati@postgrad.curtin.edu.au .

Alternatively, you can contact my supervisor Prof. Jeff Hughes on (+618) 9266 7367 or J.D.Hughes@curtin.edu.au. If needed, verification of approval can be obtained either by writing to the Curtin University Human Research Ethics Committee, c/- Office of Research and Development, Curtin University of Technology, GPO Box U1987, Perth 6845 or by telephoning 9266 2784 or emailing hrec@curtin.edu.au.

Thank you very much for your time. Please keep this letter for your information.

Appendix 5: Participant Consent Form (Direct Observation Study)

CONSENT FORM

Pharmacists' Interventions in Minimising Medication Misadventure in Children with Cancer: Direct Observation

I _____ have read the information on the attached letter. I have been given and have understood an explanation of this research project. I have had an opportunity to ask questions and have them answered to my satisfaction. I understand that I may withdraw myself (or any information I have provided) from this project without penalty of any sort.

I understand that any information will be kept confidential to the researcher. I agree that research gathered for this study may be published provided name or any other information that may identify me is not used.

Name_____ Signature_____

Date_____

Investigator_____Signature_____

Appendix 6: Case Vignettes for Expert Panel Assessment

The expert panel assessed 42 cases. Each case was followed by the same questions. For brevity, the questions were presented after Case 1 and not repeated in the other cases.

GENERAL MEDICAL WARD FOR INFANTS

Case 1

A 27-day-old female (weight: 3.97 kg) was admitted to the emergency department because of fever over the last few days. The mother said that the baby was a little more sleepy than usual and did not drink milk well. The mother and her older sister had sore throats, and cousins had croup and in contact with her. She was born full-term without any complications. Medical history: insignificant. Regular medications: nil. Allergy/ADR history: nil. She was initially diagnosed with sepsis. During hospitalisation, she was prescribed the following medications:

Domperidone 10 mg TDS oral
Normal saline 3 mL IV PRN
Paracetamol 60 mg QID oral
Gentamicin 28 mg OD IV
Aciclovir 80 mg TDS IV
Cefotaxime 200 mg QID IV
Amoxycillin 20 mg QID oral

The following day, the pharmacist reviewed the medication chart and noticed that the patient was prescribed domperidone 10 mg TDS and the dose was high for the patient (max dose 9 mg/day). The pharmacist contacted the doctor and was informed that the medication was for the mother's nausea and not for the baby. However, there was no sticker/alert that said the medication was for the mother and not the baby. The pharmacist attached the alert sticker that the medication was not for the patient.

Examination of the cerebrospinal fluid, nasopharyngeal aspirate, blood and urine culture was negative for the presence of bacteria and virus. The final diagnosis was viral illness with fever of unexplained origin. The baby improved and was discharged home 4 days after admission without any medications.

QUESTIONS

1. From the case above, how do you rate the clinical significance of pharmacist's intervention? (**Please tick the most appropriate rating**)

- ☐ Unsure
- ☐ No clinical significance
- ☐ Minor: small adjustments and optimisation of therapy, not expected to significantly alter hospital stay or clinical outcome
- ☐ Moderate: adjustments expected to enhance effectiveness of drug therapy, producing minor reductions in patient morbidity
- ☐ Major: intervention is expected to prevent or address very serious drug related problem
- ☐ Life saving

2. In your opinion, does the case described above involve a medication misadventure?

(Medication misadventure is any iatrogenic hazard or incident associated with drug therapy.)

- ☐ Unsure
- ☐ Yes
- ☐ No

3. If you answer yes to **question 2**, what type of medication misadventure best describes the case? **(Please tick any that apply)**

- ☐ Adverse drug event: any injury resulting from a medication or lack of an intended medication
- ☐ Adverse drug reaction: any unexpected, unintended, undesired or excessive response to a drug, with or without an injury
- ☐ Medication error: any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of health professionals, patient, or consumer

4. If the case involves medication error, what is the most appropriate category for the error? **(Please tick one category only)**

- Unsure
- Drug omission (the failure to prescribe the required medication)
- Dose omission (the failure to administer an ordered dose)
- Improper dose (over dosage, under dosage, extra dose)
- Wrong strength/concentration
- Wrong drug
- Wrong dosage form
- Wrong techniques of administration
- Wrong route of administration
- Wrong rate (too fast or too slow)
- Wrong duration
- Wrong time
- Wrong patient
- Monitoring errors (includes contraindicated drugs, drug-drug interaction, drug-food interaction, drug-disease interaction, and documented allergy)
- Deteriorated drug error (dispensing drug error which has expired)
- Other (any medication error that does not fall into one of the above)

5. How do you rate the potential severity of the error involved in the case? **(Please tick the most appropriate category)**

- Unsure
- Category A: circumstances or events that have the capacity to cause error
- Category B: an error occurred, but the medication did not reach the patient
- Category C: an error occurred that reached the patient but did not cause patient harm
- Category D: an error occurred that resulted in the need for increased patient monitoring but no patient harm
- Category E: an error occurred that resulted in the need for treatment or intervention or caused temporary patient harm
- Category F: an error occurred that resulted in initial or prolonged hospitalisation and caused temporary patient harm
- Category G: an error occurred that resulted in permanent patient harm

- Category H: an error occurred that resulted in a near-death event (e.g. anaphylaxis, cardiac arrest)
- Category I: an error occurred that resulted in patient death

---

Case 2

A 9-month-old male was admitted to hospital because of vomiting, reduced feeding, fever and irritability. The family had returned from a holiday in Indonesia 2 weeks ago. Medical history: insignificant. Regular medications: nil. His mother had thalassemia minor and was diagnosed with hepatitis A one week ago. During hospitalisation, the baby was diagnosed with typhoid fever and received the following medications:

Ceftriaxone 680 mg OD IV
Azithromycin 180 mg OD oral
Paracetamol 140 mg QID oral PRN
Ibuprofen 90 mg TDS oral PRN
Normal saline 5 mL 6-hourly IV PRN

On Day 2 he was receiving azithromycin 180 mg once daily. According to hospital policy for *Salmonella* infection, the azithromycin dose is Day 1: 20 mg/kg and Days 2 to 6: 10 mg/kg. As he weighed 9 kg and it was Day 2, the pharmacist recommended the doctor reduce the dose to 90 mg once daily until Day 6. The recommendation was accepted.

Case 3

A 1-year-old female (weight: 8.95 kg) was admitted due to cystic fibrosis-associated pulmonary exacerbation. She had symptoms of upper respiratory tract infection for 2 to 3 weeks. Medical history: cystic fibrosis with pancreatic insufficiency (diagnosed during newborn screening program). Allergy/ADR history: nil.

Medications on admission
Vit ABDECK® (multivitamin) ½ OD oral
Sodium chloride 3.5 mL BD oral
Creon® (pancreatic enzyme) I oral PRN
Augmentin Duo® (amoxycillin + clavulanic acid) BD oral

Current medications	Day 1	2	3	4	5	6	7	8	9	10	11	12	13
Vit ABDECK® (multivitamin) ½ OD oral	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Sodium chloride 3.5 mL BD oral	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Creon® (pancreatic enzyme) I oral PRN	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Timentin® (ticarcillin + clavulanic acid) 900 mg TDS IV	x	x	x	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Tobramycin 90 mg OD IV	✓	✓	✓	✓	x	x	x	x	x	x	x	x	x
Tobramycin 120 mg OD IV	x	x	x	x	✓	✓	✓	✓	✓	✓	✓	✓	✓
Augmentin Duo 180 mg BD oral	✓	✓	✓	x	x	x	x	x	x	x	x	x	x
Azithromycin 90 mg 3x/ week on Mon,Wed,Fri	✓	x	✓	x	✓	x	x	✓	x	✓	x	✓	x
Pulmozyme 2.5 mg neb BD pre-physiotherapy	x	x	x	x	✓	✓	✓	✓	✓	✓	✓	✓	✓
Normal saline flush 3-5 mL IV PRN	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

During hospitalisation, she was prescribed tobramycin 90 mg once daily IV (10 mg/kg/day). After the third dose, the AUC level was 68 mg/L/h (target range: 70-100) and below therapeutic level. Based on tobramycin pharmacokinetic calculations, the pharmacist recommended the doctor increase the dose to 120 mg once daily IV; maximum dose for patient: 750 mg once daily IV (15 mg/kg/day). The recommendation was accepted.

She was discharged 14 days after admission with discharge medications: sodium chloride 3.5 mL BD oral, Vit ABDECK® ½ daily oral and Augmentin Duo® 200 mg BD oral. She was to be reviewed at the cystic fibrosis clinic 2 weeks post-discharge.

GENERAL MEDICAL WARD FOR YOUNG CHILDREN

Case 4

An 11-year-old male was admitted because of pneumonia. His medical history was complicated: born premature 23/40 weeks, cerebral palsy, chronic lung disease, global developmental delay, epilepsy, on bilevel positive airway pressure, on Percutaneous Endoscopic Gastrostomy (PEG) and infusaport, severe subglottic stenosis, recurrent persistent *Candida* infection, pseudomonas colonisation, ligation of partial ducts, submandibular gland removal. Multiple antibiotic allergies (Bactrim® [trimethoprim + sulfamethoxazole], amoxycillin, cephalexin, Timentin® [ticarcillin + clavulanic acid], meropenem, fluconazole, penicillin, vancomycin, amikacin, amphotericin, ciprofloxacillin).

Medications on admission	Current medications
Benztropine 0.5 mg *nocte* PEG	Benztropine 0.5 mg *nocte* PEG
Melatonin 10 mg *nocte* PEG	Melatonin 10 mg *nocte* PEG
Movicol® (macrogol laxative) ½ sachet OD PEG	Movicol® (macrogol laxative) ½ sachet OD PEG
Magnesium chloride 3.7 mL BD PEG	Magnesium chloride 3.7 mL BD PEG
Nitrazepam 5 mg *nocte* PEG	Nitrazepam 5 mg *nocte* PEG
Baclofen 2.5 mg TDS PEG	Baclofen 2.5 mg TDS PEG
Clobazam 5 mg TDS PEG	Clobazam 5 mg TDS PEG
Phenobarbitone 60 mg *nocte* PEG	Phenobarbitone 60 mg *nocte* PEG
Levetiracetam 500 mg *mane* PEG	Levetiracetam 500 mg *mane* PEG
Levetiracetam 1000 mg *nocte* PEG	Levetiracetam 1000 mg *nocte* PEG
Epilim® (valproate) (200 mg/mL) 12.5 mL BD PEG	Epilim® (valproate) (200 mg/mL) 12.5 mL BD PEG
Dantrolene 4 mL BD PEG	Dantrolene 4 mL BD PEG
Aztreonam 900 mg 8-hourly IV	Aztreonam 900 mg 8-hourly IV
Teicoplanin 300 mg OD IV	Teicoplanin 300 mg OD IV
Diazepam 2 mg TDS PEG	Diazepam 2 mg TDS PEG
Centrum® (multivitamin) I OD PEG	Centrum® (multivitamin) I once daily PEG
Heparin saline 5 mL TDS PRN IV	Heparin saline 5 mL TDS PRN IV
Panadol® (paracetamol) 450 mg QID PRN PEG	Panadol® (paracetamol) 450 mg QID PRN PEG
Loratadine 6 mg OD PEG	Loratadine 6 mg OD PEG
Posaconazole 5 mL BD PEG	Posaconazole 5 mL BD PEG
Inner Health Plus® (probiotic) ½ tablespoon BD PEG	Inner Health Plus® (probiotic) ½ tablespoon BD PEG
Normal saline neb 10 mL PRN	Normal saline neb 10 mL PRN

During hospitalisation, he was prescribed aztreonam 900 mg 8-hourly IV, which was charted twice. The pharmacist double checked with the nurse and was informed that one of the aztreonam orders was for the hospital-in-the-home (HITH) service. There were no notes on the medication chart that it was for HITH. The pharmacist attached the alert sticker on the other medication chart that it was for HITH.

Case 5

A 1-year-11-month-old (weight: 10.8 kg) was admitted due to HIV encephalopathy, cardiomyopathy and disseminated tuberculosis. He had experienced 10 days of fever, cough, vomiting, lethargy, chronic thrush and long-standing developmental regression. He had had several infections since he was 14 months old, e.g. thrush, ear infection, measles and pneumonia. He had recently been diagnosed with HIV in Indonesia and his parents decided to take him to Perth. His condition was unstable. He had renal and liver impairment, severe immunosuppression, failure to thrive,

blood transfusion and nasogastric feeds. He also presented with spasticity in all limbs. Allergy/ADR history: nil.

Current medications	**Discharge medications**
Fluconazole 125 mg OD IV	Montelukast 4 mg *nocte* oral
Tazocin® (piperacillin + tazobactam) 1 g TDS IV	Prednisolone 5 mg/mL 1.5 mL OD oral
Aciclovir 259 mg 8-hourly IV	Isoniazid 100 mg II *mane* oral
Nilstat® (nystatin) 1 mL QID oral	Lamivudine 10 mg/mL 5 mL BD oral
Montelukast 4 mg *nocte* oral	Nevirapine 50 mg/5 mL 7 mL BD oral
Ibuprofen 100 mg TDS oral PRN	Clonidine 10 mcg/mL 1 mL QID oral
Oxycodone 1 mg OD oral	Rifampicin 100 mg/5 mL 7.5 mL *nocte* oral
Paracetamol 150 mg 6-hourly oral PRN	Moxifloxacin 400 mg ¼ tablet *nocte* oral
Augmentin Duo® (amoxycillin + clavulanic acid) 225 mg BD oral	Ethambutol 100 mg II *nocte* oral
Valganciclovir 200 mg OD IV	Abacavir 100 mg/5 mL 4.25 mL BD oral
Prednisolone 5 mg/mL 1.5 mL OD oral	Captopril 5 mg/5 mL 1.5 mL TDS oral
Isoniazid 100 mg II *mane* oral	Frusemide 50 mg/5 mL 1 mL *mane* oral
Lamivudine 10 mg/mL 5 mL BD oral	Diazepam 10 mg/10 mL 1 mL TDS oral
Nevirapine 50 mg/5 mL 7 mL BD oral	Posaconazole 200 mg/5 mL 2.75 mL BD oral
Clonidine 10 mcg/mL 1 mL QID oral	Amphotericin lozenges QID
Rifampicin 100 mg/5 mL 7.5 mL *nocte* oral	
Moxifloxacin 400 mg ¼ tablet *nocte* oral	
Ethambutol 100 mg II *nocte* oral	
Abacavir 100 mg/5 mL 4.25 mL BD oral	
Captopril 5 mg/5 mL 1.5 mL TDS oral	
Frusemide 50 mg/5 mL 1 mL *mane* oral	
Diazepam 10 mg/10 mL 1 mL TDS oral	
Posaconazole 200 mg/5 mL 2.75 mL BD oral	
Amphotericin lozenges QID	

During hospitalisation, he was prescribed fluconazole, which was charted twice for different routes of administration: intravenous and oral. The pharmacist spoke to the nurse and was informed that initially it was planned for intravenous use. As the line could not be found, the order was changed to oral. However, the intravenous order was not deleted. The pharmacist recommended the doctor cross out the intravenous fluconazole order. The recommendation was accepted.

He was discharged 102 days after admission with monthly routine monitoring at the immunology clinic.

Case 6

A 6-year-11-month-old female (weight: 28 kg) with a history of cystic fibrosis presented to hospital for elective admission for peripherally inserted central catheter insertion. Medical history: insignificant. Allergy/ADR history: nil.

Medication on admission	Current medications
Augmentin Duo® (amoxycillin + clavulanic acid) 6 mL BD oral	Timentin® (ticarcillin + clavulanic acid) 2.8 g TDS IV
Ventolin® (salbutamol) 1-2 puffs 2-4 hourly PRN	Tobramycin 280 mg OD IV (10 mg/kg)
Vit ABDECK® (multivitamin) I OD oral	Vit ABDECK® (multivitamin) I OD oral
Salt solution 15 mL OD oral	Salt solution 15 mL OD oral
	Augmentin Duo® (amoxycillin + clavulanic acid) 6 mL BD oral
	Paracetamol 400 mg QID oral PRN
	Ondansetron 3 mg QID oral PRN
	Normal saline 5 mL IV PRN
	Heparin saline 5 mL IV PRN

Tobramycin AUC level was taken after the fourth dose and the level was lower (AUC: 35 mg/L/h) than the target level (target AUC: 70-100 mg/L/h). The pharmacist recommended the doctor increase the tobramycin dose from 280 mg to 420 mg once daily IV and that 420 mg once daily IV (15 mg/kg/day) was the maximum dose for the patient. The recommendation was accepted.

Case 7

A 7-year-9-month-old male (weight: 30 kg) was transferred from another hospital with a 3-day history of right eye pain and swelling. He had been unwell for one week with fever and vomiting. He was diagnosed with right eye periorbital cellulitis and sinusitis. Medical history: severe atopic eczema. Regular medications: nil. Allergy/ADR history: peanut and bee string (may cause anaphylaxis), honey (airway swelling), egg (may cause rash and gastrointestinal reactions). Family medical history: allergic asthma and lactose intolerance (mother), hay fever (older brother), lactose intolerance and recurrent otitis (older sisters).

Current medications	Day 1	2	3
Ceftriaxone 750 mg BD IV	✓	✓	✓
Flucloxacillin 1.5 g QID IV	✓	✓	✓
Vancomycin 450 mg OD IV	✓	✓	x
Paracetamol 500 mg QID oral	✓	✓	✓
Nasonex® (mometasone furoate) spray topical II *nocte*	✓	✓	✓
Nurofen® (ibuprofen) 200 mg TDS oral PRN	✓	✓	x
Heparinised saline 5 mL IV PRN	✓	✓	✓
Sinus rinse topical BD right eye	✓	✓	✓
Chloramphenicol eye drops topical I QID right eye	✓	✓	✓
Timolol drops 0.25% topical I OD right eye	✓	✓	✓

Discharge medications
Amoxycillin/clavulanate 400 mg/57 mg per 5 mL suspension 5 mL BD oral for 10 days
Clindamycin 150 mg TDS oral for 10 days
Mometasone furoate 50 mcg/dose nasal spray II spray each nostril *nocte* for 10 days
Xylometazoline 0.05% nasal drops 2 drops each nostril QID for 5 days

During hospitalisation, he was prescribed ceftriaxone 750 mg IV twice daily. According to the *Paediatric Pharmacopoeia*, the dose is 50 mg/kg 12-hourly = 1.5 g twice daily. The pharmacist recommended the ophthalmologist increase the dose. The recommendation was rejected because the patient was being discharged and the antibiotic would be ceased.

Case 8

A 5-year-2-month-old (weight: 16.7 kg) was admitted to a regional hospital on 25 March 2012 because of fever and abdominal pain from suspected appendicitis. He had a one-week history of cough, fever (up to 39 degrees) and grunting. Chest X-ray showed pleural effusion. He was transferred from the regional hospital to Princesss Margaret Hospital on 26 March 2012.

Medical history: eczema (2 months ago), facial and tooth injury after falling on paving (2008). Family medical history: brother had croup one week before. Allergies/ADR history: nil. Regular medications: nil. Other comorbidities: nil.

He was on 2 L oxygen via nasal prongs with soft grunting. He had bilateral crackles and a trial of salbutamol was not effective. He was diagnosed with right para-pneumonic effusion and empyema (confirmed by chest X-ray). Microbiological culture and sensitivity test of pleural fluid (29 and 30 March) showed *Staphylococcus aureus* sensitive to flucloxacillin. Viral serology was negative.

On 29 March, a right pigtail drain was inserted for drainage of empyema. Another chest X-ray (2 April) showed the empyema had reduced in size, although a considerable amount of right-sided pleural fluid remained. The mediastinum was displaced towards the left and there was underlying infiltrate in the right mid and lower zone. The left lung field and pleural space remained clear.

Medications on admission
Benzylpenicilin 600 mg QID IV (had received 5 doses)
Azithromycin 170 mg OD oral (had received 1 dose)

Current medications	**Day 1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**
Azithromycin 170 mg OD oral	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Ceftriaxone 850 mg BD IV	✓	✓	✓	✓	✓	✓	✓	✓	x	x	x	x	x	x	x
Lincomycin 250 mg TDS IV	x	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	x
Teicoplanin 170 mg BD 3 doses and then 170 mg OD IV	x	x	x	x	x	x	x	x	✓	✓	✓	✓	✓	✓	✓
Alteplase 1.6 mg once daily through chest drain for 2 days	x	x	x	x	x	✓	✓	x	x	x	x	x	x	x	x
Paracetamol 240 mg QID oral PRN	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Ondansetron 2 mg 6-hourly oral PRN	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Loratadine 5 mg OD oral PRN	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Oxycodone IR 1.5-3 mg 4-hourly oral PRN	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Ibuprofen 180 mg TDS oral PRN	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

During hospitalisation, the patient slowly improved and the doctor decided to prescribe teicoplanin 170 mg IV twice daily. According to hospital policy,

teicoplanin is to be used 10 mg/kg/dose 12-hourly for 3 doses and then 6-10 mg/kg once daily (max dose 800 mg/day). As the patient had had received 3 doses, the pharmacist recommended the doctor reduce the frequency to once daily. The recommendation was accepted.

The patient had slow resolution of symptoms and was discharged on 17 April with clindamycin 125 mg QID oral for 4 weeks and an outpatient appointment 1 week after discharge.

GENERAL MEDICAL WARD FOR ADOLESCENTS

Case 9

A 16-year-old was admitted due to cerebral palsy-associated severe dystonia. Recent admission was 3 months previously for adjustment of medications and nasogastric (NG) rehydration. Allergy/ADR history: nil. Medication history: baclofen 10 mg TDS NG, tetrabenzine 12 mg BD NG, clonidine 50 mg TDS NG.

Medications on admission	**Current medications**
Diazepam 5 mg QID NG	Diazepam 5 mg 3-hourly NG PRN
Diazepam 3 mg NG PRN	Benzhexol 2 mg BD NG
	Melatonin 4 mg OD NG
	Clonazepam 0.1 mg *nocte* NG
	Ibuprofen 340 mg TDS NG PRN
	Diazepam 5 mg QID NG
	Paracetamol 500 mg TDS NG

During hospitalisation, she was prescribed clonazepam 0.1 mg *nocte* via PEG. However, the medication had been left off when recharted. The pharmacist recommended the doctor represcribe it. The recommendation was accepted.

Case 10

An 18-year-old was admitted because of chronic lung disease. Medical history: scleroderma, chronic lung disease, inflammatory arthritis, blind, vasculitis, vocal cord palsy, recurrent cellulitis, recurrent pancreatitis, pneumonia and osteomyelitis. Allergy/ADR history: nil.

Medications on admission	Current medications
Omeprazole 20 mg BD oral	Omeprazole 20 mg BD oral
Vit E 1000 unit *mane* oral	Vit E 1000 unit *mane* oral
Aspirin 100 mg *nocte* oral	Aspirin 100 mg *nocte* oral
Amitriptyline 25 mg *nocte* oral	Amitriptyline 25 mg *nocte* oral
Caltrate® (calcium) I OD oral	Caltrate® (calcium) I OD oral
Centrum® (multivitamin) I *mane* oral	Centrum® (multivitamin) I *mane* oral
Flunarizine 10 mg *nocte* oral	Flunarizine 10 mg *nocte* oral
Folic acid 1 mg *mane* oral	Folic acid 1 mg *mane* oral
Methotrexate 5 mg weekly	Paracetamol 1 g QID oral PRN
Melatonin 20 mg *nocte* oral	Oxycodone IR 5 mg 6-hourly oral PRN
Metoclopramide 10 mg TDS oral	Flucloxacilin 2 g QID IV
Hydroxychloroquine 200 mg OD oral	Normal saline 5 mL QID IV PRN
Resprim® (trimethoprim + sulfamethoxazole) 160 mg 3x/week oral	Heparin saline 5 mL QID IV PRN
Meloxicam 7.5 mg BD oral	Ondansetron 4-8 mg 8-hourly IV PRN
	Ibuprofen 400 mg 8-hourly oral PRN
	Melatonin 20 mg *nocte* oral
	Metoclopramide 10 mg TDS oral
	Hydroxychloroquine 200 mg OD oral
	Resprim® (trimethoprim + sulfamethoxazole) 160 mg 3x/week oral

She had been taking meloxicam 7.5 mg twice daily regularly, which was not charted during hospitalisation. The pharmacist recommended the doctor prescribe meloxicam. The recommendation was accepted.

Case 11

An 18-year-old presented for elective admission for revision of rhinoplasty with castocartilageal graft. Medical history: Binder syndrome (rhinoplasty 2010). Regular medication: nil. Allergy/ADR history: morphine (itch and rash).

Current medications	Discharge medications
Diclofenac 50 mg TDS oral	Diclofenac 50 mg TDS oral for 5 days
Augmentin Duo Forte® (amoxycillin + clavulanic acid) BD oral	Augmentin Duo Forte ® (amoxycillin + clavulanic acid) BD oral for 5 days
Gabapentin 200 mg TDS oral	Gabapentin 200 mg TDS oral for 2 weeks
Paracetamol 1 g QID oral	Paracetamol 1 g QID oral for 5 days
Tramadol IR 100 mg 4-hourly oral PRN	Tramadol IR 100 mg 4-hourly oral PRN
Ibuprofen 400 mg TDS oral	
Timentin® (ticarcillin + clavulanic acid) 3 g QID IV	
Tramadol SR 100 mg BD oral	
Oxycodone IR 6-12 mg 2-hourly oral PRN	
Ondansetron 4 mg 6-hourly IV PRN	
Metoclopramide 10 mg 6-hourly IV PRN	
Normal saline 5 mL IV PRN	
Oxycodone SR 10 mg BD oral	
Movicol® (macrogol laxative) 1-2 sachet OD oral PRN	
Loratadine 10 mg OD oral PRN	

During hospitalisation, she was prescribed ibuprofen and diclofenac. Due to duplication of non-steroidal anti-inflammatory drugs, the pharmacist recommended the doctor cease one of the orders. The recommendation was accepted and ibuprofen was ceased.

Case 12

A 15-year-old patient was admitted due to cystic fibrosis-associated pulmonary exacerbation. Medical history: asthma. Allergy/ADR history: erythromycin, cephalexin, penicillin (rash and itch).

Medications on admission	Current medications
Creon® (pancreatic enzyme) 10,000 variable dose oral PRN	Creon® (pancreatic enzyme) 10,000 variable dose oral PRN
Salbutamol inh 1-2 puffs 4-6-hourly PRN	Salbutamol inh 1-2 puffs 4-6-hourly PRN
Hypertonic saline neb PRN	Hypertonic saline neb PRN
Rifabutin 150 mg OD oral	Rifabutin 150 mg OD oral
Clarithromycin 500 mg OD oral	Clarithromycin 500 mg OD oral
Omeprazole 20 mg OD oral	Omeprazole 20 mg OD oral
Benefiber® (fibre) 1 tablespoon OD oral	Benefiber® (fibre) 1 tablespoon OD oral
Melatonin 40 mg *nocte* oral	Melatonin 40 mg *nocte* oral
Vit ABDECK® (multivitamin) II OD oral	Vit ABDECK® (multivitamin) II OD oral
Caltrate® (calcium) I OD oral	Caltrate® (calcium) I OD oral
Ondansetron 4 mg QID oral PRN	Ondansetron 4 mg QID oral PRN
Lactulose 20 mL BD oral	Lactulose 20 mL BD oral
	Normal saline 5 mL IV PRN
	Heparin saline 5 mL IV PRN
	Xylocaine Viscous 10 mL oral PRN
	Ceftazidime 2 g TDS IV
	Moxifloxacin 400 mg OD IV
	Paracetamol 750 mg QID oral
	Amikacin 800 mg OD IV

During hospitalisation, she was prescribed Xylocaine Viscous 10 mL PRN without frequency. The pharmacist recommended the doctor specify the frequency: every two hours. The recommendation was accepted.

Case 13

A 16-year-old female was admitted due to perianal celulitis. A perianal abscess had been present for one week. Patient complained of pain but no fever. She also had a skin rash that had started 3 weeks ago. Medical history: Crohn's disease, Sweet's syndrome, and abscess left inguinal region. Allergy/ADR history: nil.

Medications on admission	Current medications
Mesalazine 1 g BD oral	Mesalazine 1 g BD oral
Azathioprine 100 mg *mane* oral	Azathioprine 100 mg *mane* oral
Adalimumab 40 mg SC fortnightly	Adalimumab 40 mg orally fortnightly
Multivitamin I OD oral	Metronidazole 120 mg 8-hourly IV
	Ciprofloxacin 500 mg BD oral
	Paracetamol 1 g QID oral PRN
	Ibuprofen 400 mg TDS oral PRN
	Normal saline flush 5-10 mL QID IV PRN

During hospitalisation, she was charted for adalimumab 40 mg per oral. In Australia, adalimumab is only available as a subcutaneous injection. The pharmacist recommended the doctor change the route of administration from oral to subcutaneous. The recommendation was accepted.

Case 14

A 13-year-old male was admitted due to exacerbation of asthma. He had a one-day history of breathing difficulty and it was not improved after taking 3-hourly Ventolin® (salbutamol). His comorbidity included obesity. Allergy/ADR history: nil.

Medications on admission	Current medications
Seretide® (salmeterol) inh 125/25 2 puffs BD	Seretide® (salmeterol) inh 125/25 2 puffs BD
Ventolin® (salbutamol) inh 1-2 puffs 3-hourly PRN	Ventolin® (salbutamol) inh 1-2 puffs 3-hourly PRN
	Tamiflu 75 mg OD oral for 5 days
	Prednisolone 60 mg OD oral for 5 days
	Paracetamol 1 g QID oral PRN
	Normal saline 5-10 mL IV PRN

During hospitalisation, he was prescribed Tamiflu 75 mg once daily oral for influenza prophylaxis. The lab result showed that the patient was positive for influenza virus. According to hospital policy and the *Australian Medicines Handbook*, the treatment regimen is Tamiflu 75 mg BD oral for 5 days. The pharmacist recommended the doctor change the regimen from prophylaxis (once daily) to treatment (twice daily). The recommendation was accepted.

GENERAL SURGICAL WARD

Case 15

A 7-year-10-month-old was admitted due to sigmoid sinus thrombosis and mastoidectomy. Medical history: myringoplasty. Regular medications: nil. Allergy/ADR history: nil.

Current medications
Paracetamol 500 mg QID oral
Clexane® (enoxaparin) 40 mg BD SC
Ceftriaxone 1.95 g OD IV
Vancomycin 900 mg QID IV
Oxycodone IR 2-4 mg 4-hourly oral PRN
Heparinised saline 5 mL IV PRN
Ondansetron 5.94 mg QID oral PRN
Ibuprofen 390 mg TDS oral PRN

During hospitalisation, she was prescribed ondansetron 5.94 mg four times daily. As the dose is not easy to measure, the pharmacist recommended the doctor change the dose to one that is measurable (6 mg QID). The recommendation was accepted.

Case 16

A 11-year-old was admitted for bilateral reimplantation of ureter (bilateral grade IV vesicoureteral reflux). Allergy/ADR history: nil.

Medications on admission	Current medications
Bactrim® (trimethoprim + sulfamethoxazole) 8 mL nocte oral	Oxybutynin patch 10 mg for 3.5 days
Oxybutynin 5 mg BD oral	Ibuprofen 300 mg TDS oral PRN
	Oxycodone IR 3-7 mg 3-hourly oral PRN
	Promethazine 7 mg TDS IV PRN
	Loratadine 10 mg OD oral PRN
	Pethidine 35 mg 4-hourly IV PRN
	Cephazolin 540 mg TDS IV
	Cotrimoxazole® (trimethoprim + sulfamethoxazole) 70 mg *nocte* oral
	Paracetamol 500 mg QID oral

During hospitalisation, she was prescribed oxybutynin patch 10 mg for 3.5 days. According to the *Paediatric Pharmacopoeia* and the *Australian Medicines Handbook*, the dose is 3.9 g/day or 13 mg for 3.5 days. The pharmacist recommended the doctor increase the dose. The recommendation was accepted.

Case 17

An 8-year-10-month-old (weight: 25 kg) was admitted for removal of a left ovary teratoma. She had a 6-day history of altered bowel habits with vomiting and urinary obstruction. The mother noticed a suprapubic mass which improved on opening

bowel/passing urine. After investigation, she was planned for teratoma hysterectomy. The left ovary teratoma was removed 3 days after admission. Medical history: unremarkable. Regular medications: nil. Allergy/ADR history: nil.

Current medications	**Discharged medications**
Oxybutynin ½ patch every third day	Oxycodone IR 2.5 mg 2-hourly oral PRN
Paracetamol 400 mg QID oral	Clindamycin 150 mg TDS oral for 4 days
Cephazolin 300 mg TDS IV	
Lincomycin 390 mg TDS IV	
Lactulose 20 ml BD oral PRN	
Oxycodone IR 2.5 mg 2-hourly oral PRN	
Buscopan 10 mg TDS oral PRN	
Loratadine 10 mg OD oral	

During hospitalisation, she was prescribed oxycodone immediate release 2.5 mg 2-hourly PRN. According to the *Paediatric Pharmacopoeia*, the oxycodone immediate-release dose for children is 0.1-0.2 kg/dose 4- to 6-hourly. The pharmacist recommended the doctor reduce the frequency to 4- to 6-hourly. The recommendation was accepted.

Case 18

A 10-year-old (weight: 76.14 kg, height: 160 cm) was transferred from a regional health clinic with abdominal pain, vomiting and fever for 2 days. On admission to Princess Margaret Hospital, he was diagnosed with appendicitis. Medical history: asthma, obesity (more than 9th centile), and eczema. He was on Seretide® (salmeterol) inhaler 125/25 BD and Ventolin® (salbutamol) inhaler PRN.

Allergy/ADR history: peanut (may cause anaphylaxis), penicillin and grasses (may cause rash).

On Day 1, he underwent a laproscopic appendicectomy and the result confirmed a perforated appendix with gangreneous inflammation. The other relevant results included:

Peritoneal fluid microsopy – *Streptococcus milleri* (sensitive to penicillin)

Stool specimen microsocpy: mucus (not seen), leukocytes (not seen), erythrocytes (not seen), yeast cell (moderate number)

Stool specimen-culture: *Clostridium difficile* toxin (not detected), *Clostridium difficile* (not isolated), *Salmonella* (not isolated), *Shigella* (not isolated), *Campylobacter* (not isolated).

He was treated with intravenous triple antibiotics post operatively. He developed nausea and vomiting and explosive diarrhoea, as well as contact dermatitis on his left hip/buttock.

Medications on admission
Seretide® (salmeterol) inhaler 125/25 BD
Ventolin® (salbutamol) inhaler 2 puffs 4-hourly PRN

Current medications	**Day 1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Seretide® (salmeterol) inh 125/25 BD	✓	✓	✓	✓	✓	✓	✓	✓
Ventolin® (salbutamol) inh 1-2 puffs 4-6-hourly PRN	✓	✓	✓	✓	✓	✓	✓	✓
Ceftriaxone 1 g BD IV	✓	✓	✓	✓	✓	✓	✓	x
Metronidaxole 500 mg TDS IV	✓	✓	✓	✓	x	x	x	x
Gentamicin 160 mg OD IV	✓	✓	✓	✓	✓	✓	x	x
Paracetamol 1 g QID oral	✓	✓	✓	✓	✓	✓	✓	✓
Oxycodone IR 5 mg 4-hourly oral PRN	x	x	✓	✓	✓	✓	✓	✓
Ibuprofen 400 mg TDS oral PRN	✓	✓	✓	✓	✓	✓	✓	✓
Tramadol 50 mg 4-hourly oral PRN	✓	x	✓	✓	✓	✓	✓	✓
Morphine PCA 1 mg/ml lock out 5 minutes	x	✓	x	x	x	x	x	x
Ondansetron 4 mg BD oral PRN	✓	✓	✓	✓	✓	✓	✓	✓
Metoclopramide 5 mg BD oral PRN	✓	✓	✓	✓	✓	✓	✓	✓
Nilstat® (nystatin) drops 1 ml QID oral	x	x	✓	✓	✓	✓	✓	✓

According to the hospital antibiotic protocol for prophylaxis and treatment of appendiceal surgery with ruptured and gangrenous appendix for patients with non-anaphylactic penicillin allergy, is two intravenous antibiotics: ceftriaxone 50 mg/kg (max 1 g) 6-hourly plus metronidazole 12.5 mg/kg IV (max 500 mg) 8-hourly for up to 5 days. It is common practice to add a third antibiotic: gentamicin 7 mg/kg once daily IV (max 500 mg/day).

During hospitalisation, he was prescribed gentamicin 160 mg IV once daily. The patient was obese (BMI: 29.7 kg/m^2) and his ideal body weight was 35 kg. The gentamicin dose is calculated using ideal body weight = 7 mg/kg/day (max 500

mg/day) = 245 mg IV once daily. One wrong dose had been given before the pharmacist recommended the doctor increase the dose to 245 mg once daily. The recommendation was accepted.

The patient was also prescribed paracetamol 1 g QID oral. The paracetamol dose should be calculated using ideal body weight = 15 mg/kg /dose 4-6 hourly = 525 mg 4-6 hourly ≈ 500 mg 4-6 hourly oral. Three wrong doses had been given before the pharmacist recommended the doctor reduce the dose to 500 mg QID oral. The recommendation was accepted.

Case 19

A 17-year-old presented for elective admission due to spina bifida for Mitrofanoff procedure and bladder augmentation. Medical history: spinal dysraphism. Allergy/ADR history: latex and IV contrast.

Medications on admission	Current medications
Vesicare® (solifenacin) 10 mg OD oral	Vesicare® (solifenacin) 5 mg OD oral
	Bactrim® (trimethoprim + sulfamethoxazole) 160/800 mg I OD oral
	Paracetamol 1 g QID oral
	Metronidazole 400 mg TDS oral
	Loperamide I TDS oral
	Oxycodone IR 5 mg 4-hourly oral PRN
	Ondansetron 4 mg TDS SL PRN
	Mucomyst® (acetylcysteine) 1-5 mL PRN via catheter
	Normal saline 5-10 mL PRN via catheter

During hospitalisation, she was prescribed prophylaxis Bactrim® 160/800 mg once daily. According to the *Therapeutic Guidelines*, the prophylaxis trimethoprim+sulfamethoxazole dose is 80/400 mg-160/800 mg once daily, and for treatment 80/400 mg-160/800 mg 12-hourly. The pharmacist recommended the doctor change the dose to 80/400 mg once daily as it was for prophylaxis and not for treatment. The recommendation was accepted.

The patient was discharged on loperamide, paracetamol and metronidazole.

Case 20

An 8-year-8-month-old (weight: 33 kg) was admitted for pain management secondary to urine extravasation into abdominal wall tissue. He presented with abdominal pain and left flank and scrotal swelling four days after cystoscopy, nephrostomy and JJ stent insertion. He also had decreased urine output over time.

Medical history: Vater syndrome, urinary incontinence secondary to Vater syndrome, Tetralogy of Fallot, anorectal malformation (repaired and closed), enuresis, faecal encoperesis, and solitary kidney. Allergy/ADR history: brown tape.

Medications on admission	**Current medications**
Oxybutynin patch 1.95 mg every 3.5 days	Oxybutynin patch 1.95 mg every 3.5 days
	Paracetamol 500 mg QID oral PRN
	Ondansetron 4 mg QID IV PRN
	Oxycodone IR 5 mg 4-hourly oral PRN
	Bactrim® (trimethoprim + sulfamethoxazole) 120 mg BD oral
	Cephazolin 400 mg TDS IV
	Tazocin® (piperacillin + tazobactam) 2.9 g BD IV
	Amoxycillin 600 mg TDS oral
	Loperamide 2 mg *mane* oral

During hospitalisation, he was prescribed oral Bactrim 120 mg twice daily. As the available formulation of Bactrim tablets was 80/400 mg, the pharmacist recommended the doctor reduce the dose to Bactrim 80 mg/400 mg one tablet 12-hourly or change to liquid formulation with the dose of 0.5 mL/kg/dose 12-hourly = 15 mL 12-hourly. The recommendation was rejected.

Discharge medications
Loperamide 2 mg *mane* oral
Oxybutynin patch (3.9 mg/24 h) ½ patch/3.5 days
Bactrim® (trimethoprim + sulfamethoxazole) 200 mg/400 mg 120 mg BD oral

The patient was discharged with a clinic appointment within 3 weeks of discharge. He also needed repeat cystoscopy within 6 weeks post-discharge for stenosed urine output and redo reimplantation.

Case 21

A 14-year-old was admitted due to multiple traumas following a quad bike accident. Computed tomography scan of abdomen in another hospital revealed significant intraabdominal trauma. On admission, he underwent surgery for splenectomy, left nephrectomy and insertion of intercostal catheter for drainage of left pneumothorax. His recovery was complicated by persistent hypertension. Medical history: attention deficit hyperactivity disorder (previously on Ritalin). Regular medication: nil. Allergy/ADR history: nil.

Current medications	**Discharge medications with follow-up appointment for adjusting antihypertensives**
Omeprazole 20 mg OD oral	Lisinopril 20 mg *mane* oral
Metoclopramide 10 mg QID oral	Lisinopril 10 mg *nocte* oral
Domperidone 10 mg QID oral	Ondansetron wafer 4 mg PRN
Ondansetron 4 mg QID oral	Phenoxymethylpenicilin 250 mg tablet II *mane* for 10 days
Promethazine 12.5 mg TDS oral	
Hydralazine 15 mg 4-hourly IV	
Coloxyl with senna I BD oral	
Lactulose 30 mL BD oral	
Lisinopril 20 mg OD oral	
Oxycodone IR 5-10 mg 4-hourly oral PRN	
Paracetamol 1 g QID oral	
Timentin® (ticarcillin + clavulanic acid) 3 g QID IV	
Clonidine 150 mg TDS IV	
Heparinised saline 5 mL OD IV	
Ibuprofen 400 mg QID oral PRN	

During hospitalisation, she was prescribed four antiemetics: metoclopramide 10 mg QID oral, domperidone 10 mg QID oral, ondansetron 4 mg QID oral and promethazine 12.5 mg TDS oral. As the patient's nausea was not too bad, the pharmacist recommended the doctor change antiemetics from regular to if required. The recommendation was accepted and three antiemetics (metoclopramide, ondansetron and promethazine) were changed from regular to if required.

Case 22

A 14-year-old male (weight: 80 kg) was admitted due to epiblepharon correction (bilateral upper eye lid repositioning). Medical history: obstructive sleep apnoea, mild asthma, Prader Willi syndrome (morbid obesity and day time somnolence) and bilateral cryptorchidism. Allergy/ADR history: nil.

Medications on admission	Current medications
Concerta® (methylphenidate) 36 mg OD oral	Concerta® (methylphenidate) 36 mg OD oral
	Cephalexin 500 mg 8-hourly oral
	Ibuprofen 400 mg TDS oral

During hospitalisation, he was prescribed cephalexin 500 mg 8-hourly oral. According to the *Paediatric Pharmacopoeia*, the cephalexin dose for children is 6.25-12.5 mg/kg 6-hourly. The pharmacist recommended the doctor increase the frequency to 6-hourly in order to achieve therapeutic level. The recommendation was accepted.

Case 23

A 5-year-1-month-old male (weight: 22 kg) was admitted due to a penetrating right eye injury. He had a sore right eye and yellowish discharge. He was referred by his general practitioner. Medical history: finger laceration in 2011 with plastic surgery. Regular medication: nil. Allergy/ADR history: nil.

Current medications
Ciprofloxacin 200 mg BD IV
Metoclopramide 3.4 mg OD IV
Paracetamol 140 mg QID oral PRN
Ibuprofen 220 mg TDS oral PRN

During hospitalisation, he was prescribed ciprofloxacin 200 mg BD IV. As ciprofloxacin IV was restricted in the hospital, the pharmacist recommended the doctor change the dose form to oral. The recommendation was rejected.

HAEMATOLOGY-ONCOLOGY WARD

Case 24

A 14-year-old female with newly diagnosed osteogenic sarcoma (September 2011) was admitted to receive her first chemotherapy cycle. Medical history: insignificant. Regular medication: nil. Allergy/ADR history: nil

Current medications
Cisplatin 102 mg IV over 4 hours
Doxorubicin 64 mg IV over 15 minutes
Flucloxacillin 1.4 g QID IV for 4 doses
Dexamethasone 8 mg OD IV pre-chemotherapy for 2 days
Dexamethasone 4 mg BD IV
Paracetamol 1 g QID oral PRN
Oxycodone IR 5-10 mg 2-hourly oral PRN
Ondansetron 4 mg TDS IV PRN
Metoclopramide 10 mg TDS oral PRN

As the patient was still nauseated, the pharmacist recommended the doctor add lorazepam 1-2 mg 6-hourly oral PRN as antiemetic post-chemotherapy. The recommendation was accepted.

Case 25

A 17-year-old patient was hospitalised due to pain and electrolyte imbalance post bone marrow transplant. Medical history: sickle cell disease (bone marrow transplant 14 months ago). Allergy/ADR history: nil.

Current medications	**Current medications**
Gabapentin 300 mg TDS oral	Oxycodone IR 5-10 mg 3-6-hourly oral PRN
Sirolimus 2.1 mg OD oral	Levetiracetam 500 mg BD oral
Prednisolone 25 mg *mane* oral	Lorazepam 1 mg *nocte* oral
Prednisolone 12.5 mg *nocte* oral	Posaconazole 200 mg TDS IV
Omeprazole 40 mg OD oral	Resprim® (trimethoprim + sulfamethoxazole) II BD 3 days/week
Potassium chloride III BD oral	Penicillin V 250 mg BD oral
Ondansetron 8 mg TDS oral PRN	Magnesium aspartate 500 mg BD oral
Nifedipine 10 mg OD oral PRN	Cholecalciferol 5000 unit OD oral
Loratadine 10 mg OD oral PRN	Sodium bicarbonate II TDS oral
Loperamide I-II oral PRN	Amphotericin lozenge I QID oral
Budesonide 9 mg OD oral	Budesonide 9 mg OD oral
Enalapril 10 mg OD oral	Vancomycin 760 mg TDS IV
Valganciclovir 900 mg OD oral	

During hospitalisation, she was prescribed posaconazole three times daily IV. When the pharmacist looked at administration record on the medication chart, it seemed that the medicine was given twice daily. The pharmacist reminded the nurse to give it three times daily instead of twice daily.

Case 26

A 9-year-old male (weight 26.7 kg) was admitted due to febrile neutropenia. Medical history: acute lymphoblastic leukaemia/ALL (consolidation phase diagnosed 3 months ago) and seizure. Allergy/ADR history: vancomycin (Redman's syndrome), ceclor (rash and diarrhoea).

Medications on admission	**Current medications**
Mercaptopurine 75 mg oral on Sunday	Mercaptopurine 75 mg oral on Sunday
Mercaptopurine 50 mg OD oral except Sunday	Mercaptopurine 50 mg OD oral except Sunday
Fluconazole 200 mg *nocte* oral	Fluconazole 200 mg *nocte* oral
Levetiracetam 3 mL BD oral	Levetiracetam 3 mL BD oral
Resprim I BD 3 days/week oral	Resprim® (trimethoprim + sulfamethoxazole) I BD 3 days/week oral
Dexamethasone 3.4 mg *mane* oral	Dexamethasone 3.4 mg *mane* oral
Dexamethasone 3.3 mg *nocte* oral	Dexamethasone 3.3 mg *nocte* oral
	Vancomycin 2.1 g IV infusion over 24 hours

He was prescribed vancomycin 2.1 g IV infusion but the dose was high. According to the hospital policy for febrile neutropenia, the vancomycin dose is 60-80 mg/kg/day via continuous infusion. The pharmacist recommended the doctor reduce the dose to 1.6 g IV infusion over 24 hours. The recommendation was accepted.

Case 27

A 17-year-old female post bone marrow transplant was admitted due to pain and electrolyte imbalance. Medical history: sickle cell disease (bone marrow transplant 14 months ago). Allergy/ADR history: nil

Current medications	Current medications
Gabapentin 300 mg TDS oral	Oxycodone IR 5-10 mg 3-6 hourly oral PRN
Sirolimus 2.1 mg OD oral	Levetiracetam 500 mg BD oral
Prednisolone 25 mg *mane* oral	Lorazepam 1 mg *nocte* oral
Prednisolone 12.5 mg *nocte* oral	Posaconazole 200 mg TDS oral
Omeprazole 40 mg OD oral	Resprim® (trimethoprim + sulfamethoxazole) II BD 3 days/week
Potassium chloride III BD oral	Penicillin V 250 mg BD oral
Ondansetron 8 mg TDS oral PRN	Magnesium aspartate 500 mg BD oral
Nifedipine 10 mg OD oral PRN	Cholecalciferol 5000 unit OD oral
Loratadine 10 mg OD oral PRN	Sodium bicarbonate II TDS oral
Loperamide I-II oral PRN	Amphotericin lozenge I QID oral
Budesonide 9 mg OD oral	Budesonide 9 mg OD oral
Enalapril 10 mg OD oral	Vancomycin 960 mg TDS IV
Valganciclovir 900 mg OD oral	

During hospitalisation, budesonide was charted twice. The pharmacist recommended the doctor cease one of the orders. The recommendation was accepted.

Patient passed away the following month due to intracerebral haemorrhage and multi organ failure.

Case 28

A 14-year-old female with newly diagnosed osteogenic sarcoma (September 2011) was admitted to receive her chemotherapy cycle. Medical history: insignificant. Regular medication: nil. Allergy/ADR history: nil

Medications on admission	Current medications
Bactrim 800 mg BD oral	Ranitidine 150 mg BD oral
Fluconazole 200 mg *nocte* oral	Bactrim 800 mg BD oral
	Fluconazole 200 mg *nocte* oral
	Metoclopramide 10 mg TDS oral PRN
	Lorazepam 1-2 mg BD oral PRN
	Coloxyl II BD oral PRN
	Parachoc 20 mL OD oral PRN
	Ondansetron 8 mg TDS oral PRN
	Methotrexate 20 g IV over 4 hours

During hospitalisation, the patient received ondansetron as an antiemetic but continued to be nauseous. The pharmacist recommended the doctor change ondansetron to tropisetron 5 mg daily IV because tropisetron may be more effective in adolescents. The recommendation was accepted.

Case 29

A 10 year-old male with osteosarcoma was admitted to receive his chemotherapy. He was diagnosed with osteosarcoma last month. Medical history: insignificant. Allergy/ADR history: nil.

Medications on admission	Current medications
Fluconazole 100 mg OD oral	Fluconazole 100 mg OD oral
Resprim® (trimethoprim + sulfamethoxazole) I BD 3 days/week oral	Resprim® (trimethoprim + sulfamethoxazole) I BD 3 days/week oral
	Ondansetron 6 mg TDS oral PRN
	Diphenhydramine 3 mg QID IV PRN
	Dexamethasone 2 mg BD oral
	High-dose methotrexate 1 g IV over 4 hours
	Calcium folinate 18 mg QID IV (24 hours after high-dose methotrexate)
	Doxorubicin 46 mg IV over 15 minutes
	Cisplatin 73 mg IV over 4 hours

The pharmacist recommended the doctor prescribe ondansetron and dexamethasone at discharge to overcome nausea and vomiting post chemotherapy. The recommendation was accepted.

Case 30

A 10-year-4-month-old male with osteosarcoma was admitted to receive his chemotherapy. He was diagnosed with osteosarcoma last month. Medical history: insignificant. Allergy/ADR history: nil.

Medications on admission	Current medications
Fluconazole 100 mg OD oral	Fluconazole 100 mg OD oral
Resprim® (trimethoprim + sulfamethoxazole) I BD 3 days/week oral	Resprim® (trimethoprim + sulfamethoxazole) I BD 3 days/week oral
	Ondansetron 5 mg TDS IV
	Diphenhydramine 3 mg QID IV PRN
	Dexamethasone 2 mg BD oral
	High-dose methotrexate 1 g IV over 4 hours
	Calcium folinate 18 mg QID IV (24 hours after high-dose methotrexate)
	Doxorubicin 46 mg IV over 15 minutes
	Cisplatin 73 mg IV over 4 hours

At discharge, Resprim® was not highlighted as one of the discharge medications. The pharmacist recommended the doctor prescribe Resprim® at discharge in addition to fluconazole as the patient's regular medications for antibacterial and antifungal prophylaxis, respectively. The recommendation was accepted.

Case 31

A 9-year-3-month-old male with newly diagnosed metastatic neuroblastoma (diagnosed one month ago) was admitted due to febrile neutropenia. Medical history: eczema. Allergy/ADR history: vancomycin (Redman's syndrome).

Medications on admission	**Current medications**
Resprim® (trimethoprim + sulfamethoxazole) I BD oral 3x/week	Resprim® (trimethoprim + sulfamethoxazole) I BD oral 3x/week
Fluconazole 100 mg *nocte* oral	Fluconazole 100 mg *nocte* oral
	Movicol® (macrogol laxative) Junior I BD oral
	Lactulose 10 mL TDS oral
	Ondansetron 4 mg TDS oral
	Lugol's iodine 0.2 mL TDS oral
	Oxycodone SR 15 mg BD oral
	Vancomycin 620 mg TDS IV
	Tobramycin 340 mg OD IV
	Tazocin® (piperacillin + tazobactam) 3 g QID IV
	Metoclopramide 4-5 mg TDS oral PRN
	Loratadine 10 mg OD oral PRN
	Paracetamol 500 mg QID oral PRN
	Promethazine 5 mg QID oral PRN
	Oxycodone IR 5 mg 6-hourly oral PRN

The consultant decided to prescribe oxycodone SR 15 mg once daily after the ward meeting. During hospitalisation, the resident prescribed this medicine twice daily instead of once daily. The pharmacist recommended the resident reduce the frequency of oxycodone SR. The recommendation was accepted.

Case 32

A 3-year-2-month-old female with ALL was admitted due to back pain for investigation and neutropenia. Medical history: insignificant. Allergy/ADR history: nil.

Current medications
Ranitidine 37.5 mg BD oral
Parachoc® (liquid paraffin) 10 mL OD oral
Ondansetron 2 mg TDS oral PRN
Oxycodone IR 2 mg QID oral PRN
Paracetamol 180 mg QID oral PRN

Patient had been neutropenic for a month and the high-dose methotrexate schedule had been withheld twice. However, during the neutropenic period, the patient was not on Bactrim as antibacterial prophylaxis. The pharmacist recommended the doctor prescribe Bactrim 3.5 mL bd oral three times weekly. The recommendation was accepted.

Case 33

A 4-year-old female with ALL (maintenance phase) was admitted due to fever. Medical history: duplex left kidney. Allergy/ADR history: vancomycin (Redman's syndrome), tegaderm (rash).

Medications on admission	Current medications
Mercaptopurine 50 mg OD oral 6 days/week	Mercaptopurine 50 mg OD 6 days/week
Mercaptopurine 75 mg OD oral 1 day/week	Mercaptopurine 75 mg OD oral 1 day/week
Methotrexate 15 mg weekly oral	Methotrexate 15 mg weekly oral
Resprim® (trimethoprim + sulfamethoxazole) 5 mL BD oral 3 days/week	Resprim® (trimethoprim + sulfamethoxazole) 5 mL BD oral 3 days/week
	Tazocin® (piperacillin + tazobactam) 1.9 g QID IV
	Movicol® (macrogol) ½ sachet OD oral PRN
	Parachoc® (liquid paraffin) 10 mL BD oral PRN

During hospitalisation, methotrexate oral was prescribed without a specific day for administration. According to the parent and oral chemotherapy diary, the patient took her oral chemotherapy every Friday. The pharmacist recommended the doctor specify the day on the medication chart because Resprim® and methotrexate should not be given on the same due to additive antifolate activity. The recommendation was accepted.

Case 34

A 4-year-old female with ALL (maintenance phase) admitted due to fever. Medical history: duplex left kidney. Allergy/ADR history: vancomycin (Redman's syndrome), tegaderm (rash)

Medications on admission	Current medications
Mercaptopurine 50 mg OD oral 6 days/week	Mercaptopurine 50 mg OD oral 6 days/week
Mercaptopurine 75 mg OD oral 1 day/week	Mercaptopurine 75 mg OD oral 1 day/week
Methotrexate 15 mg weekly oral	Methotrexate 15 mg weekly oral
Resprim® (trimethoprim + sulfamethoxazole) 5 mL BD oral 3 days/week	Resprim® (trimethoprim + sulfamethoxazole) 5 mL BD oral 3 days/week
	Tazocin® (piperacillin + tazobactam) 1.9 g QID IV
	Movicol® (macrogol) ½ sachet OD oral PRN
	Parachoc® (liquid paraffin) 10 mL BD oral PRN

During hospitalisation, no antiemetic was charted. The pharmacist recommended lorazepam 0.5 mg OD oral and ondansetron 3 mg TDS oral as antiemetics. The recommendation was accepted.

Case 35

A 1-year-10-month-old male with posterior fossa tumor was admitted for investigation. Medical history: hyperextension of lumbar spine, left sided corticolis, mesenteric adenitis and developmental delay. Allergy/ADR history: nil.

Medications on admission	Current medications
Glycopyrrolate 250 mcg BD NG	Glycopyrrolate 250 mcg BD NG
Domperidone 5.5 mg TDS NG	Domperidone 5.5 mg TDS NG
Hydrocortisone 15 mg QID NG	Hydrocortisone 15 mg QID NG
Lactulose 10 mL *mane* NG	Lactulose 10 mL *mane* NG
Levetiracetam 130 mg BD NG	Levetiracetam 130 mg BD NG
Sodium chloride 1 mL BD NG	Sodium chloride 1 mL BD NG
	Filgrastim 75 mg OD SC
	Omeprazole 15 mg BD NG
	Paracetamol 210 mg QID IV
	Vincristine 0.9 mg IV over 10 minutes
	Carboplatin 230 mg IV over 1 hour
	Cyclophosphamide 600 mg IV over 1 hour
	Mesna 120 mg IV over 15 minutes

During hospitalisation, he was prescribed omeprazole. The pharmacist recommended the doctor cease omeprazole as it can affect the metabolism of most antineoplastic drugs. The recommendation was accepted.

Case 36

A 6-year-4-month-old male patient with T-cell ALL post consolidation phase (diagnosed last year) was admitted to receive his chemotherapy. Medical history: deep vein thrombosis (last year), urticarial rash, asthma. Allergy/ADR history: vancomycin (Redman's syndrome), platelet (swelling, itch), ambisome (swelling, itch).

Medications on admission	Current medications
Fluconazole 100 mg *nocte* oral	Fluconazole 100 mg *nocte* oral
Bactrim 6 mL BD oral 3x/week	Bactrim 6 mL BD oral
Ventolin neb 2.5 mg BD	Ventolin neb 2.5 mg BD
Thioguanine 40 mg 5 days/week	Thioguanine 40 mg 5 days/week
Thioguanine 60 mg 2 days/week	Thioguanine 60 mg 2 days/week
	Ondansetron 3 mg TDS oral PRN
	Methotrexate 120 mg IV over 25 minutes
	Vincristine 1.1 mg IV over 2 hours

During hospitalisation, he was prescribed daily Bactrim as bacterial infection prophylaxis. The pharmacist recommended the doctor change the regimen to three times/week since it was the standard dosing for this patients based on his treatment protocol.

Case 37

A 16-year-old female with newly diagnosed osteogenic sarcoma (diagnosed 9 months ago) was admitted to receive her chemotherapy. Medical history: insignificant. Regular medication: nil. Allergy/ADR history: nil

Medications on admission	Current medications
Bactrim® (trimethoprim + sulfamethoxazole) 800 mg BD oral	Ranitidine 150 mg BD oral
Fluconazole 200 mg *nocte* oral	Bactrim® (trimethoprim + sulfamethoxazole) 800 mg BD oral
	Fluconazole 200 mg *nocte* oral
	Metoclopramide 10 mg TDS oral PRN
	Lorazepam 1-2 mg BD oral PRN
	Coloxyl® (poloxamer) II BD oral PRN
	Parachoc® (liquid paraffin) 20 mL OD oral PRN
	Cisplatin 102 mg IV over 4 hours
	Doxorubicin 64 mg IV over 15 minutes
	Ondansetron 8 mg TDS oral PRN

During the ward round, the doctor mentioned that the patient's vitamin D level was low. The pharmacist recommended the doctor prescribe cholecalciferol. The recommendation was accepted.

Case 38

A 7-month-old male with newly diagnosed acute myelogenous leukaemia was admitted to receive his chemotherapy. Medical history: nil. Allergy/ADR history: nil.

Medications on admission	Current medications
Bactrim® (trimethoprim + sulfamethoxazole) 2.5 mL BD oral 3x/week	Bactrim® (trimethoprim + sulfamethoxazole) 2.5 mL BD oral 3x/week
Fluconazole 50 mg *nocte* oral	Fluconazole 50 mg *nocte* oral
	Ranitidine 20 mg BD oral
	Heparin saline 5 mL IV PRN
	Codeine 8 mg 4-6 hourly oral PRN
	Paracetamol 80 mg QID oral PRN
	Ondansetron 1.5 mg 8-hourly oral PRN
	Cytarabine 280 mg IV over 1 hour
	Bortezomib 0.5 mg IV push
	Mitozantrone 3.4 mg IV over 30 minutes

Five days post chemotherapy ondansetron was still charted even though the patient was not nauseated anymore. The pharmacist recommended the doctor change ondansetron to if required. The recommendation was accepted.

Case 39

A 3-year-3-month-old male with newly diagnosed neuroblastoma was admitted due to fever, diarrhoea and vomiting. Medical history: tonsillectomy and adenoids. Allergy/ADR history: vancomycin (Redman's syndrome), etoposide (anaphylaxis), lincomycin (rash).

Medications on admission	**Current medications**
Fluconazole 90 mg *nocte* oral	Fluconazole 90 mg *nocte* oral
Bactrim® (trimethoprim + sulfamethoxazole) 5 mL BD oral 3x/week	Rectinol® (anorectal) ointment topical TDS
	Flucloxacillin 340 mg QID IV for 4 doses
	Ondansetron 2 mg TDS oral PRN
	Codeine 7-14 mg 4-hourly oral PRN

During hospitalisation, he was not prescribed Bactrim® as antibacterial prophylaxis. The pharmacist recommended the doctor to chart Bactrim® as it is supportive medication for haematology-oncology patients. The recommendation was accepted.

HAEMATOLOGY-ONCOLOGY PHARMACY (DURING DISPENSING)

Case 40

A 6-year-6-month-old male with ALL-maintenance phase was admitted to the oncology clinic to receive chemotherapy. Medical history: insignificant. Allergy/ADR history: nil.

Medications on admission	**Medications during clinic admission**	**Discharge medications**
Resprim ½ tablet BD oral 3 days/week	Vincristine 1.3 mg in 60 mL N/S IV infusion over 5-15 minutes	Resprim ½ tablet BD oral 3 days/week
Mercaptopurine 50 mg OD oral 3 days/week		Mercaptopurine 50 mg OD oral 3 days/week
Mercaptopurine 75 mg OD oral 4 days/week		Mercaptopurine 75 mg OD oral 4 days/week
Methotrexate 25 mg weekly oral		Methotrexate 35 mg weekly oral

He was prescribed oral methotrexate 35 mg weekly (100% dose) at discharge. According to protocol, the patient should receive 75% dose (25 mg weekly). The pharmacist recommended the doctor reduce the dose. The recommendation was accepted.

Case 41

A 4-year-10-month-old female with newly diagnosed stage 4 neuroblastoma was admitted to the oncology clinic to receive chemotherapy (cyclophosphamide). Medical history: insignificant. Allergy/ADR history: nil.

Medications on admission	**Medications during clinic admission**	**Discharge medications**
Fluconazole 90 mg *nocte* oral	Cyclophosphamide 260 mg in 84 mL N/S IV infusion over 30 minutes	Fluconazole 90 mg *nocte* oral
Bactrim® (trimethoprim + sulfamethoxazole) 5 mL BD oral 3 days/week	Topotecan 0.8 mg in 57 mL N/S IV infusion over 30 minutes	Bactrim® (trimethoprim + sulfamethoxazole) 5 mL BD oral 3 days/week
	Dexamethasone 2 mg TDS IV	Ondansetron 2 mg TDS oral PRN
	Ondansetron 2 mg *stat* IV pre-chemotherapy	

When the pharmacist was about to make cyclophosphamide, she noticed that the total volume printed on the label (by another pharmacist) was 80 mL instead of 84 mL according to the parenteral cytotoxic medication order (yellow sheet). The manufacturing pharmacist recommended the other pharmacist change the label.

Case 42

A 6-year-4-month-old male patient with ALL (maintenance phase) was admitted to the oncology clinic to receive chemotherapy. Medical history: insignificant. Allergy/ADR history: nil.

Medications on admission	**Medications during clinic admission**	**Discharge medications**
Fluconazole 100 mg *nocte* oral	Methotrexate 12 mg intrathecal push	Fluconazole 100 mg *nocte* oral
Bactrim® (trimethoprim + sulfamethoxazole) 6 ml BD oral 3 days/week	Methotrexate 80 mg in 60 mL N/S IV infusion over 10-15 minutes	Bactrim® (trimethoprim + sulfamethoxazole) 6 mL BD oral 3 days/week
Valaciclovir 50 mg OD oral	Vincristine 1.1 mg in 60 mL N/S IV infusion over 5-15 minutes	Valaciclovir 50 mg OD oral
Thioguanine I oral 5 days/week		Thioguanine I oral 5 days/week
		Ondansetron 3 mg TDS oral

At discharge he was prescribed mercaptopurine oral with 50% dose at discharge. According to protocol, the patient was assigned to receive full dose. The pharmacist recommended the doctor increase the dose. The recommendation was accepted.

Appendix 7: Data Collection Form (Snapshot Periods)

CLINICAL SERVICES DOCUMENTATION

Snapshot Date: **Pharmacist:**

Clinical Service	Ward :					
	Mon	Tues	Wed	Thu	Fri	Total
Number of medication charts reviewed						
Number of patients seen						
Number of interventions						
Number of enquiries received by page or phone and not documented as a						

Other clinical activities: Presentation Teaching Quality Improvement Publications Protocols reviewed	

INTERVENTION DETAILS

Date/UMRN	Drug	Description

Appendix 8: Participant Information Sheet (Focus Group Discussion)

Curtin University

PARTICIPANT INFORMATION SHEET

Focus Group Discussion: Snapshot versus Continuous Documentation of Pharmacists' Interventions - Is Snapshot Worthwhile?

My name is Hesty Ramadaniati. I am a PhD student enrolled in School of Pharmacy at Curtin University.

Purpose of Research

The aims of this project are to gather pharmacists' perceptions and comments regarding the results of interventions documented through a prospective observational method compared to those documented through the established snapshot documentation method. Furthermore, this project aims to identify barriers to pharmacists documenting their interventions during snapshot period, and to seek suggestions on how to improve the documentation of pharmacists' clinical interventions on wards.

Your Role

I am inviting pharmacists in this hospital to participate in this focus group discussion. I would like to discuss several issues surrounding pharmacists' intervention documentation during snapshot period. In addition, I am interested in finding out your opinion on the ways to improve the documentation pharmacists' clinical interventions.

During focus group discussion, the facilitator will ask you several questions and you are free to answer the questions and discuss them with other fellow pharmacists. This process will take approximately 45-50 minutes and the discussion will be audio recorded and transcribed verbatim. I will also take written notes for cross checking.

Consent to Participate

Your participation in this research is voluntary. You have the right to withdraw at any stage and there is no penalty for not participating or for withdrawing from the study. When you have signed the consent form I will assume that you have agreed to participate and allow me to use your data in this research.

Confidentiality

The information you provide will be kept separate from your personal details and only the principal investigator will have access to this. The discussion transcripts will not have your name or any other identifying information on it and in adherence to university policy, the recording tapes and transcription will be kept in a secure archive in the School of Pharmacy for five years after which they will be destroyed.

Further Information

This research has been reviewed and given approval by Curtin University Human Research Ethics Committee (Approval number PH-11-13) and Permission from Princess Margaret Hospital Authority (Registration Number: 2923). If you have any questions or would like to receive further information about this research, please contact me, Hesty Utami Ramadaniati, on 0426135272 or by email: h.ramadaniati@postgrad.curtin.edu.au.

Alternatively, you can contact my supervisor Prof. Jeff Hughes on (+618) 9266 7367 or J.D.Hughes@curtin.edu.au. If needed, verification of approval can be obtained either by writing to the Curtin University Human Research Ethics Committee, c/- Office of Research and Development, Curtin University of Technology, GPO Box U1987, Perth 6845 or by telephoning 9266 2784 or emailing hrec@curtin.edu.au.

Thank you very much for your time. Please keep this letter for your information.

Appendix 9: Participant Consent Form (Focus Group Discussion)

CONSENT FORM

Focus Group Discussion: Snapshot versus Continuous Documentation of Pharmacists' Interventions:

Is Snapshot Worthwhile?

I _____ have read the information on the attached Participant Information Sheet. I have been given thorough explanation on this project. I have had an opportunity to ask questions and have them answered to my satisfaction. I understand that I may withdraw from this project without penalty of any sort and any information I have provided will be deleted.

I understand and agree that the focus group discussion will be audio recorded.

I understand that any information collected during the study will be kept confidential to the researcher and the published results will not use my name, and that no opinions will be attributed to me in any way that will identify me.

Name_____ Signature_____

Date_____

Investigator_____Signature_____

Page **1** of **1**

Appendix 10: Approval Letter from Curtin University Human Ethics Committee (Focus Group Discussion)

Curtin University

Memorandum

To	Hesty Ramadaniati
From	Alison Smith, R&D Coordinator, School of Pharmacy
Subject	Protocol Approval **PH-11-13**
Date	8 May 2013
Copy	Jeff Hughes

Faculty of Health Sciences

School of Pharmacy

TELEPHONE 9266 7418
FACSIMILE 9266 3793
EMAIL A.J.Smith@curtin.edu.au

Thank you for your "Form C Application for Approval of Research with Low Risk (Ethical Requirements)" for the project titled *"Snapshot versus Continuous Documentation of Pharmacists' Interventions: Is Snapshot Worthwhile?"*. On behalf of the Human Research Ethics Committee I am authorised to inform you that the project is approved.

Approval of this project is for a period of twelve months **08/05/2013** to **08/05/2014**.

The approval number for your project is **PH-11-13**. *Please quote this number in any future correspondence*. If at any time during the twelve months changes/amendments occur, or if a serious or unexpected adverse event occurs, please advise me immediately.

Sincerely,

Alison Smith
Research & Development Support Coordinator
School of Pharmacy

This study has been approved by the Curtin University Human Research Ethics Committee PH-11-13 If needed, verification of approval can be obtained either by writing to the Curtin University Human Research Ethics Committee, c/- Office of Research and Development, Curtin University, GPO Box U1987, Perth, 6845 or by telephoning 9266 2784 or hrec@curtin.edu.au

CRICOS Provider Code 00301J

Appendix 11: Questionnaire for Root Cause Analysis

Code:

MEDICATION ERRORS IN CHILDREN:
ROOT-CAUSE ANALYSIS USING SIMULATED SCENARIOS

Root cause analysis (RCA) is a systematic and comprehensive approach used to uncover the root of problems. It can be used to identify the gaps in hospital systems and processes of care that may not be immediately apparent and which may have contributed to the incident or near-miss (medication error). Some paediatric studies have reported that medication errors occur in nearly 6% of all medication orders. Despite the available literature on medication errors, less is known about such errors in children than adults.

INSTRUCTIONS

Please indicate your answer to each of the following questions by ticking the appropriate box(es) or entering your response in the space provided. The questionnaire should take about 30 minutes to complete. Please return the completed questionnaire **by 17 October 2014** in the sealed envelope provided and mail it to the return address. Please retain the information sheet for future reference.

SECTION 1: GENERAL INFORMATION, QUALIFICATIONS AND PROFESSIONAL EXPERIENCES

1. Please indicate your age by ticking the relevant box:

- ☐ 21 – 30 years
- ☐ 31 – 40 years
- ☐ 41 – 50 years
- ☐ >50 years

2. What is your gender?

- ☐ Female
- ☐ Male
- ☐

3. What is your role?

- Doctor → **Go to question 3a**
- Nurse → **Go to question 3b**
- Pharmacist → **Go to question 3c**

3a. As a doctor, what position do you currently hold in the hospital?

- Intern
- Resident
- Registrar
- Consultant/specialist

3b. As a nurse, what position do you currently hold in the hospital?

- Registered nurse/midwife
- Clinical nurse/clinical midwives/clinical development nurse
- Clinical nurse consultant/clinical midwifery consultant
- Clinical nurse specialist/clinical midwifery specialist
- Nurse practitioner
- Clinical nurse manager/clinical midwifery manager
- Director of nursing/director of midwifery

3c. As a pharmacist, what position do you currently hold in the hospital?

- Intern pharmacist
- Registered pharmacist (medication safety, clinical trial, manufacturing, inpatient/outpatient dispensary)
- Clinical pharmacist
- Senior clinical pharmacist
- Pharmacy Director/Deputy Director

4. How long have you been working as a health professional?

- < 5 years
- 5-10 years
- 11-20 years
- >20 years

5. How long have you been working in the area of paediatrics?

- □ < 5 years
- □ 5-10 years
- □ 11-20 years
- □ >20 years

SECTION 2: SCENARIOS AND ROOT CAUSE ANALYSIS

The goal of RCA is to find out: What happened? Why did it happen? What can be done to prevent it from happening again?. In this section, five simulated case studies are presented in paediatric patients. Each case study is followed by questions on the clinical significance of medication errors and the potential contributing factors of the error. You will be given an opportunity to give your opinion on how such errors may be prevented in the future.

Please indicate your answer to each of the following questions by ticking inside the appropriate box(es) or entering your response in the space provided.

SECTION 2: CASE STUDY 1 (INAPPROPRIATE DOSE)

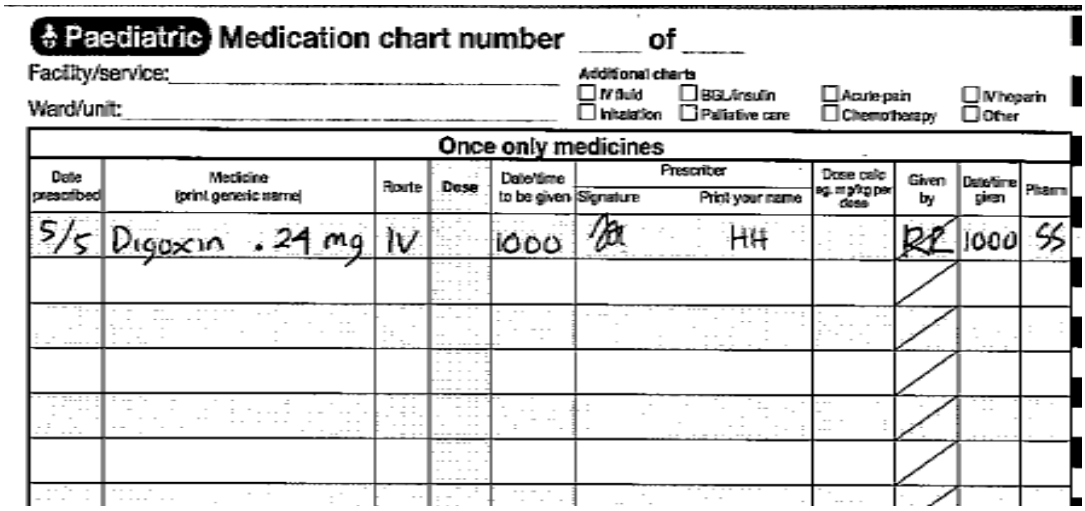
A 6-month-old baby (weight: 8 kg) was admitted with a diagnosis of congestive heart failure and pneumonia. The main complaints on admission were 10-day history of increased respiration, wheezing, general agitation, and persistent vomiting. She was born full-term and had a history of cardiac abnormalities. Past surgeries included open heart surgery for repair of the congenital heart defect and gastrotomy tube replacement. There was no history of allergies or ADR.

A resident who started his rotation in Paediatrics a week earlier prescribed the following medications without consulting the registrar, as he did not want to bother the registrar during the hectic morning.

Benzylpenicillin 120 mg (15 mg/kg) q8h IV
Normal saline 3 mL IV PRN
Paracetamol 120 mg (15 mg/kg) q6h IV

Frusemide 8 mg (1-2 mg/kg) q12h IV

The resident also wrote up digoxin as per the National Inpatient Medication Chart (below).



Paediatric Medication chart number ____ of ____

Facility/service:_____

Ward/unit:_____

Additional charts: ☐ IV fluid ☐ BSL/insulin ☐ Acute pain ☐ IV heparin ☐ Inhalation ☐ Palliative care ☐ Chemotherapy ☐ Other

Once only medicines

Date prescribed	Medicine (print generic name)	Route	Dose	Date/time to be given	Prescriber: Signature	Prescriber: Print your name	Dose calc eg. mg/kg per dose	Given by	Date/time given	Pharm
5/5	Digoxin .24 mg	IV		1000		HH		RR	1000	SS

The orders were sent back to the ward along with the medications. The nurse believed all the orders to be correct, as the doctor and the pharmacist had checked them. He then administered the digoxin to the patient, who within 2 hours began vomiting and went into respiratory distress, with arrhythmias ranging from bradycardia to ventricular fibrillation, and subsequently went into cardiac arrest. The registrar requested the patient be transferred to the Intensive Care Unit. However, 12 hours after her cardiac arrest, she again exhibited evidence of chronic heart failure with respiratory distress. She had low systolic blood pressure (75 mmHg), decreased breath sounds, and oxygen saturation readings of 74-78%. She went into cardiac arrest, and was pronounced dead an hour later due to the inappropriate dose of digoxin.

1. From the case above, how do you rate the clinical significance of the medication error involved? (**Please tick the most appropriate rating**)

(Medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of health professionals or patient or carer.)

- ☐ Unsure
- ☐ No clinical significance

- ☐ Minor: trivial error not expected to significantly alter hospital stay or clinical outcome
- ☐ Moderate: the error reduces the effectiveness of drug therapy, producing minor reductions in patient morbidity
- ☐ Major: the error results in a very serious drug related problem
- ☐ Life threatening

2. Which health professional(s) do you think were responsible for the error?

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3. Having reviewed the case what do you believe may be contributing factors? Please complete the table below.

3a.	Were specific patient issues a factor in this event?	☐ Yes ☐ No ☐ Unsure	If yes, describe the patient factors that may have contributed. **Description:**
3b.	Was dismissal of policies/procedure or guidelines a factor in this event?	☐ Yes ☐ No ☐ Unsure	If yes, tick the appropriate box(es) **AND** describe how it appeared to contribute. ☐ Patient misidentification ☐ Error/omission in medication reconciliation ☐ Clinical guidelines ☐ Coordination of care ☐ Medical record documentation ☐ Level and frequency of monitoring of patient **Description:**

3c.	Were there issues related to human resources in this event?	☐ Yes ☐ No ☐ Unsure	If yes, tick the appropriate box(es) **AND** describe how it appeared to contribute. ☐ Staff workload and inadequate staffing ☐ Recruitment ☐ Staff training and competencies ☐ Staff supervision **Description:**
3d.	Was miscommunication a factor in this event?	☐ Yes ☐ No ☐ Unsure	If yes, tick the appropriate box(es) **AND** describe the perceived deficiency. ☐ Miscommunication between staff ☐ Miscommunication between staff and patient and/or family **Description:**
3e.	Was the physical environment of the health service a factor in this event?	☐ Yes ☐ No ☐ Unsure	If yes, describe how it appeared to contribute. ☐ Noise ☐ Lighting ☐ Space **Description:**

3f.	Was control/provision of medication an issue in this event?	□ Yes □ No □ Unsure	If yes, describe how it appeared to contribute. □ Medication storage □ Labelling □ Documentation of administration □ Internal transfer of medications **Description:**
3g.	Is there any other factor(s) that could have contributed to this error?	□ Yes □ No □ Unsure	If yes, describe the other factors that may have contributed. **Description:**

4. What are your suggestions to prevent the recurrence of the error?

SECTION 2: CASE STUDY 2 (DISPENSING ERROR)

A 7-year-old girl, who had been hospitalised for 4 days following seizures, was scheduled to be discharged in the afternoon. The ward pharmacist checked her discharge medication orders (one of the medications was primidone 250 mg twice daily) and found everything was correct. The pharmacist then sent the medication orders to the Pharmacy Department during lunch time. A locum pharmacist received the orders and dispensed the medications. The medications in the dispensary are arranged alphabetically by generic name and not by therapeutic class so primidone was located next to prednisolone 25 mg. The lighting in the dispensary was poor, and the pharmacist's vision was reduced due to a cracked lens that he had not been able to replace. He picked prednisolone and dispensed a 1-month supply with her other antiepileptic medications. The other pharmacists were having lunch, so the medication orders were sent back to the ward without following the dispensary checking procedure. The nurse on the ward received the medications and gave them to patient's mother. The nurse knew that the ward pharmacists had checked the discharge medication orders in the morning, and thought it unnecessary to check them again. The discharge procedure requires that nurses double-check the medications against the prescriptions.

Two weeks later the patient was admitted to the ED due to lethargy, blurred vision, increased urination, thirst and dry mouth. Physical examiniation and laboratory results revealed that this patient was hyperglycaemic. After assessment of her medical condition and medication history, it was revealed that her condition was caused by a dispensing error by taking prednisolone instead of primidone to treat her seizures.

1. From the case above, how do you rate the clinical significance of the medication error involved? (**Please tick the most appropriate rating**)

(Medication error any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of health professionals or patient or carer.)

- Unsure
- No clinical significance
- Minor: trivial error not expected to significantly alter hospital stay or clinical outcome
- Moderate: the error reduces the effectiveness of drug therapy, producing minor reductions in patient morbidity
- Major: the error results in a very serious drug related problem
- Life threatening

2. Which health professional(s) do you think were responsible for the error?

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3. Having reviewed the case what do you believe may be contributing factors? Please complete the table below.

3a.	Were specific patient issues a factor in this event?	Yes No Unsure	If yes, describe the patient factors that may have contributed. **Description:**

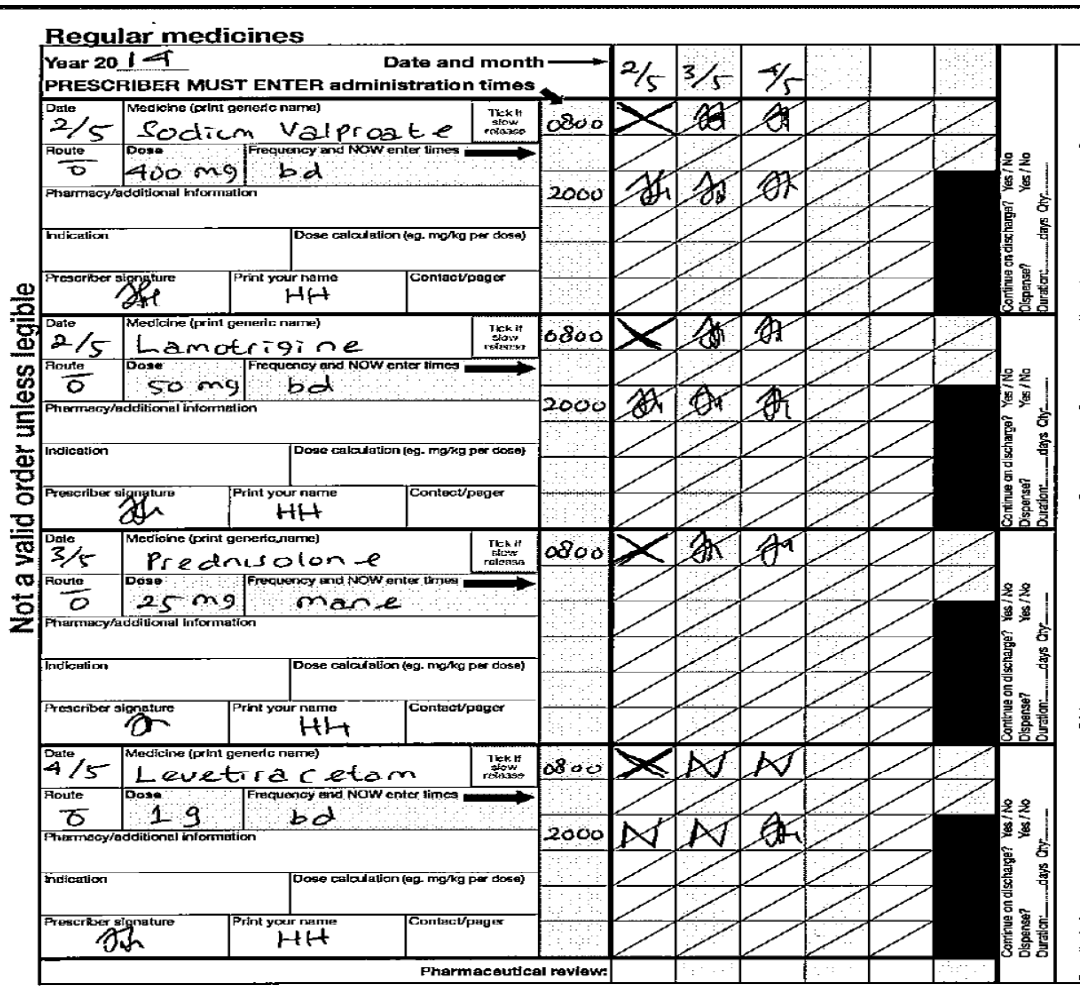
3b.	Was dismissal of policies/procedure or guidelines a factor in this event	☐ Yes ☐ No ☐ Unsure	If yes, tick the appropriate box(es) **AND** describe how it appeared to contribute. ☐ Patient misidentification ☐ Error/omission in medication reconciliation ☐ Clinical guidelines ☐ Coordination of care ☐ Medical record documentation ☐ Level and frequency of monitoring of patient **Description:**
3c.	Were there issues related to human resources in this event?	☐ Yes ☐ No ☐ Unsure	If yes, tick the appropriate box(es) **AND** describe how it appeared to contribute. ☐ Staff workload and inadequate staffing ☐ Recruitment ☐ Staff training and competencies ☐ Staff supervision **Description:**
3d.	Was miscommunication a factor in this event?	☐ Yes ☐ No ☐ Unsure	If yes, tick the appropriate box(es) **AND** describe the perceived deficiency. ☐ Miscommunication between staff ☐ Miscommunication between staff and patient and/or family **Description:**

3e.	Was the physical environment of the health service a factor in this event?	☐ Yes ☐ No ☐ Unsure	If yes, describe how it appeared to contribute. ☐ Noise ☐ Lighting ☐ Space **Description:**
3f.	Was control/provision of medication an issue in this event?	☐ Yes ☐ No ☐ Unsure	If yes, describe how it appeared to contribute. ☐ Medication storage ☐ Labeling ☐ Documentation of administration ☐ Internal transfer of medications **Description:**
3g.	Is there any other factor(s) that could have contributed to this error?	☐ Yes ☐ No ☐ Unsure	If yes, describe the other factors that may have contributed. **Description:**

4. What are your suggestions to prevent the recurrence of the error?

SECTION 2: CASE STUDY 3 (DRUG OMISSION)

A 15-year-old male was taken to the ED of a suburban hospital on Friday afternoon. He complained of difficulty breathing and wheezing history of asthma, long-standing history of a seizure disorder. His medications on presentation included sodium valproate, lamotrigine, levetiracetam, Ventolin (salbutamol) inhaler and Seretide (fluticasone/salmeterol) inhaler. The ED physician conducted a physical examination that revealed signs of an acute exacerbaton of his asthma. Chest X-ray did not show any sign of pneumonia. The patient was transferred to the ward and prescribed oral prednisolone 25 mg once daily, which resulted in a gradual improvement in his respiratory symptoms. He was also prescribed Ventolin (salbutamol) inhaler 2 puffs PRN, and Seretide (fluticasone/salmeterol) inhaler 125/25 2 puffs BD.



At 11 pm on Saturday, one of the nurses found him convulsing on the floor of his room and called the overnight medical team. The team responded quickly and gave

him intravenous medications (diazepam 15 mg IV every 15-30 minutes and phenytoin 250 mg IV for 3 doses within 6 hours) to stop his seizure. After his mental status improved, the patient complained of pain in his left shoulder and elbow. An X-ray of these joints showed evidence of traumatic fracture from his fall. On Sunday morning, the medical team reviewed the medication chart and the medication administration record and found that one of his seizure medications, levetiracetam, had not been given during his admission. There was a note in the medication administration chart from the daytime nurse indicating that levetiracetam was out of stock but the nurse did not notify the doctors, the pharmacy or the night shift nurse during handover. On Friday afternoon before the patient was admitted, the ward pharmacist noticed that the levetiracetam in the imprest room was low in stock, but the pharmacist was busy and forgot to notify the pharmacy assistant to restock the levetiracetam. The patient experienced the episode of seizure because of drug omission of one of his anticonvulsant medications, levetiracetam.

1. From the case above, how do you rate the clinical significance of the medication error involved? (**Please tick the most appropriate rating**)

(Medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of health professionals or patient or carer.)

- ☐ Unsure
- ☐ No clinical significance
- ☐ Minor: trivial error not expected to significantly alter hospital stay or clinical outcome
- ☐ Moderate: the error reduces the effectiveness of drug therapy, producing minor reductions in patient morbidity
- ☐ Major: the error results in a very serious drug related problem
- ☐ Life threatening

2. Which health professional(s) do you think were responsible for the error?

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3. Having reviewed the case what do you believe may be contributing factors? Please complete the table below.

3a.	Were specific patient issues a factor in this event?	☐ Yes ☐ No ☐ Unsure	If yes, describe the patient factors that may have contributed. **Description :**
3b.	Was dismissal of policies/procedure or guidelines a factor in this event?	☐ Yes ☐ No ☐ Unsure	If yes, tick the appropriate box(es) **AND** describe how it appeared to contribute. ☐ Patient misidentification ☐ Error/omission in medication reconciliation ☐ Clinical guidelines ☐ Coordination of care ☐ Medical record documentation ☐ Level and frequency of monitoring of patient **Description:**
3c.	Were there issues related to human resources in this event?	☐ Yes ☐ No ☐ Unsure	If yes, tick the appropriate box(es) **AND** describe how it appeared to contribute. ☐ Staff workload and inadequate staffing ☐ Recruitment ☐ Staff training and competencies ☐ Staff supervision **Description:**

3d.	Was miscommunication a factor in this event?	☐ Yes ☐ No ☐ Unsure	If yes, tick the appropriate box(es) **AND** describe the perceived deficiency. ☐ Miscommunication between staff ☐ Miscommunication between staff and patient and/or family **Description:**
3e.	Was the physical environment of the health service a factor in this event?	☐ Yes ☐ No ☐ Unsure	If yes, describe how it appeared to contribute. ☐ Noise ☐ Lighting ☐ Space **Description:**
3f.	Was control/provision of medication an issue in this event?	☐ Yes ☐ No ☐ Unsure	If yes, describe how it appeared to contribute. ☐ Medication storage ☐ Labeling ☐ Documentation of administration ☐ Internal transfer of medications **Description:**
3g.	Is there any other factor(s) that could have contributed to this error?	☐ Yes ☐ No ☐ Unsure	If yes, describe the other factors that may have contributed. **Description:**

4. What are your suggestions to prevent the recurrence of the error?

SECTION 2: CASE STUDY 4 (MONITORING ERROR-DOCUMENTED ALLERGY)

A 4-year-old female (weight: 15 kg) was referred by her GP with abdominal pain, vomiting and fever for 2 days. She was accompanied by her mother whose English was very poor. The patient's family had migrated to Australia 6 months ago. Medical history: insignificant. Regular medications: nil. She was diagnosed with appendicitis, and scheduled for surgery the following morning. She was precribed paracetamol 225 mg QID oral PRN, ibuprofen 150 mg TDS oral PRN, oxycodone immediate-release 2.5 mg QID oral PRN and ondansetron 2 mg TDS oral PRN. In the morning, the pharmacist went to the ward to take the patient's medication history and noticed a referral letter from the GP stating that the patient was allergic to penicillin, but there was no description of the reaction. The pharmacist tried to speak to the patient's mother, but this was impeded by the language barrier. The pharmacist then telephoned the GP for more details about the patient's allergy, but had to leave a message with the receptionist for the GP to return the call. In the meantime, the pharmacist annotated the chart with 'penicillin allergy' and attached an ADR sticker.

In the afternoon, the doctor prescribed prophylaxis antibiotic before surgery. According to the hospital's antibiotic protocol, prophylaxis for appendectomy in a patient with non-anaphylactic penicillin allergy is two intravenous antibiotics: cephazolin 25 mg/kg and metronidazole 12.5 mg/kg. The doctor was aware that the

patient was allergic to penicillin, but did not check further as he thought the reaction was not serious. He presumed it was safe to prescribe cephazolin because the pharmacist had reviewed the patient. The next morning, one hour before surgery, the nurse administered cephazolin and metronidazole. Around five minutes after the antibiotics were administered, the patient became agitated and developed a diffuse erythematous rash across her chest and back. She also developed difficulty breathing and an audible wheeze. The patient was transferred to the Intensive Care Unit and treated with intravenous corticosteroid, antihistamine and nebulised salbutamol. The patient's condition improved and she returned to the ward 2 days later and the surgery was rescheduled. The monitoring error had occurred as the patient had received penicillin although there was documentation of penicillin allergy.

1. From the case above, how do you rate the clinical significance of the medication error involved? (**Please tick the most appropriate rating**)

(Medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of health professionals or patient or carer.)

- ☐ Unsure
- ☐ No clinical significance
- ☐ Minor: trivial error not expected to significantly alter hospital stay or clinical outcome
- ☐ Moderate: the error reduces the effectiveness of drug therapy, producing minor reductions in patient morbidity
- ☐ Major: the error results in a very serious drug related problem
- ☐ Life threatening

2. Which health professional(s) do you think were responsible for the error?

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3. Having reviewed the case what do you believe may be contributing factors? Please complete the table below.

3a.	Were specific patient issues a factor in this event?	☐ Yes ☐ No ☐ Unsure	If yes, describe the patient factors that may have contributed. **Description :**
3b.	Was dismissal of policies/procedure or guidelines a factor in this event?	☐ Yes ☐ No ☐ Unsure	If yes, tick the appropriate box(es) **AND** describe how it appeared to contribute. ☐ Patient misidentification ☐ Error/omission in medication reconciliation ☐ Clinical guidelines ☐ Coordination of care ☐ Medical record documentation ☐ Level and frequency of monitoring of patient **Description:**
3c.	Were there issues related to human resources in this event?	☐ Yes ☐ No ☐ Unsure	If yes, tick the appropriate box(es) **AND** describe how it appeared to contribute. ☐ Staff workload and inadequate staffing ☐ Recruitment ☐ Staff training and competencies ☐ Staff supervision **Description:**

3d.	Was miscommunication a factor in this event?	□ Yes □ No □ Unsure	If yes, tick the appropriate box(es) **AND** describe the perceived deficiency. □ Miscommunication between staff □ Miscommunication between staff and patient and/or family **Description:**
3e.	Was the physical environment of the health service a factor in this event?	□ Yes □ No □ Unsure	If yes, describe how it appeared to contribute. □ Noise □ Lighting □ Space **Description:**
3f.	Was control/provision of medication an issue in this event?	□ Yes □ No □ Unsure	If yes, describe how it appeared to contribute. □ Medication storage □ Labeling □ Documentation of administration □ Internal transfer of medications **Description:**
3g.	Is there any other factor(s) that could have contributed to this error?	□ Yes □ No □ Unsure	If yes, describe the other factors that may have contributed. **Description:**

4. What are your suggestions to prevent the recurrence of the error?

SECTION 2: CASE STUDY 5 (TRANSCRIBING ERROR)

A 7-month-old male (weight: 8 kg) with newly diagnosed acute myeloid leukaemia (AML) was admitted to the oncology ward to receive his first chemotherapy. Medical history: premature birth and seizures. Allergy/ADR history: nil. Post chemotherapy, the patient remained in hospital due to his low neutrophil level and severe vomiting. His condition improved slowly. During hospitalisation, he was prescribed the following medications:

Trimethoprim-sulphametoxazole (40 mg-200 mg/5 mL) 2.5 mL BD 3 times/week
Fluconazole 50 mg *nocte* oral
Clonidine 20 mcg/mL 0.6 mL TDS oral
Clonazepam 2.5 mg BD oral
Levetiracetam 100 mg/mL 2.4 mL BD oral
Paracetamol 120 mg QID oral
Codeine 7.5 mg QID oral PRN
Oxycodone IR 1 mg 1-hourly oral PRN
Ranitidine 15 mg/mL 1 mL BD oral
Ondansetron 1 mg TDS oral
Hydrocortisone 2 mg TDS oral

One day before the start of the Christmas break, the doctor transcribed all the medication orders onto a new medication chart. The doctor was fatigued from writing discharge prescriptions, and did not notice that she had not written up the fluconazole (antifungal prophylaxis) on the new chart. The next day, the nurse administered the medications as charted. The nurse was not familiar with the oncology ward, as she was deployed from another ward due to staff shortages over the holiday period. She was not aware that one medication had been left off, and the ward pharmacist was only available on call. Consequently, the patient did not receive the antifungal. On the fourth day of not receiving fluconazole, the patient developed febrile neutropenia. The patient was prescribed intavenous antibiotics and an antifungal. His stay in the hospital was prolonged because of a transcribing error.

1. From the case above, how do you rate the clinical significance of the medication error involved? (**Please tick the most appropriate rating**)

(Medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of health professionals or patient or carer.)

- ☐ Unsure
- ☐ No clinical significance
- ☐ Minor: trivial error not expected to significantly alter hospital stay or clinical outcome
- ☐ Moderate: the error reduces the effectiveness of drug therapy, producing minor reductions in patient morbidity
- ☐ Major: the error results in a very serious drug related problem
- ☐ Life threatening

2. Which health professional(s) do you think were responsible for the error?

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3. Having reviewed the case what do you believe may be contributing factors? Please complete the table below.

3a.	Were specific patient issues a factor in this event?	☐ Yes ☐ No ☐ Unsure	If yes, describe the patient factors that may have contributed. **Description :**
3b.	Was dismissal of policies/procedure or guidelines a factor in this event?	☐ Yes ☐ No ☐ Unsure	If yes, tick the appropriate box(es) **AND** describe how it appeared to contribute. ☐ Patient misidentification ☐ Error/omission in medication reconciliation ☐ Clinical guidelines ☐ Coordination of care ☐ Medical record documentation ☐ Level and frequency of monitoring of patient **Description:**
3c.	Were there issues related to human resources in this event?	☐ Yes ☐ No ☐ Unsure	If yes, tick the appropriate box(es) **AND** describe how it appeared to contribute. ☐ Staff workload and inadequate staffing ☐ Recruitment ☐ Staff training and competencies ☐ Staff supervision **Description:**

3d.	Was miscommunication a factor in this event?	□ Yes □ No □ Unsure	If yes, tick the appropriate box(es) **AND** describe the perceived deficiency. □ Miscommunication between staff □ Miscommunication between staff and patient and/or family **Description:**
3e.	Was the physical environment of the health service a factor in this event?	□ Yes □ No □ Unsure	If yes, describe how it appeared to contribute. □ Noise □ Lighting □ Space **Description:**
3f.	Was control/provision of medication an issue in this event?	□ Yes □ No □ Unsure	If yes, describe how it appeared to contribute. □ Medication storage □ Labeling □ Documentation of administration □ Internal transfer of medications **Description:**

3g.	Is there any other factor(s) that could have contributed to this error?	□ Yes □ No □ Unsure	If yes, describe the other factors that may have contributed. **Description:**

4. What are your suggestions to prevent the recurrence of the error?

THANK YOU FOR YOUR PARTICIPATION

Appendix 12: Participant Information Sheet (Root Cause Analysis)

PARTICIPANT INFORMATION SHEET

Medication Error in Children: Root-Cause Analysis (RCA)

Using Simulated Scenarios

My name is Hesty Ramadaniati. I am a PhD student enrolled in the School of Pharmacy at Curtin University.

Purpose of Research

Root-cause analysis (RCA) is a systematic and comprehensive methodology to identify the gaps in hospitals' systems and processes of care that may not be immediately apparent and which may have contributed to an incident or near-miss. The goal of RCA is to find out 'What happened? Why did it happen? and What can be done to prevent it from happening again?'

This study is a part of larger study looking at the role of pharmacists' interventions in minimising the occurrence of medication misadventure in children. This study aims to investigate the contributing factors to medication errors in a set of simulated scenarios involving paediatric patients.

Your Role

I am inviting different groups of health care professionals including doctors, nurses, and pharmacists to participate in this study in order to obtain their perspectives on the contributing factors to medication error in a series of simulated cases involving paediatric patients.

You will be given a questionnaire that you can fill out in your own time. The questionnaire should take around 30 minutes to complete. Once you have completed the questionnaire, please return using the Reply-Paid envelope provided.

Consent to Participate

Your participation in this research is voluntary. You have the right to withdraw at any stage, and there is no penalty for not participating or for withdrawing. When you have signed the consent form, I will assume that you have agreed to participate and allow me to use your data in this research.

Confidentiality

The information you provide will be kept separate from your personal details and only the principal investigator will have access to this. The transcripts of the information on the questionnaire will not include your name or any other identifying information and in adherence to university policy, the questionnaire will be kept in a secure archive in the School of Pharmacy Curtin University for five years before it will be destroyed.

Further Information

This study has been approved under Curtin University's process for lower-risk studies (Approval number: PH-14-11) and Permission from Princess Margaret Hospital Authority (Registration Number: 2923). This process complies with the National Statement on Ethical Conduct in Human Research (Chapter 5.1.7 and Chapter 5.1.18-5.1.21). If you have any questions or would like to receive further information about this research, please contact me on 0469602565 or by email: h.ramadaniati@postgrad.curtin.edu.au .

Alternatively, you can contact my supervisor Professor Jeff Hughes on (+618) 9266 7367 or J.D.Hughes@curtin.edu.au. If needed, verification of approval can be obtained either by writing to the Curtin University Human Research Ethics Committee, c/- Office of Research and Development, Curtin University of Technology, GPO Box U1987, Perth 6845 or by telephoning 9266 2784 or by emailing hrec@curtin.edu.au.

Thank you very much for your time.

Appendix 13: Participant Consent Form (Root Cause Analysis)

CONSENT FORM

Medication Error in Children: Root-Cause Analysis (RCA)
Using Simulated Scenarios

I _____, have read the information on the attached letter and understand the requirement of this study. I have had an opportunity to ask questions and had them answered to my satisfaction. I understand that I may withdraw myself (or any information I have provided) from this study without penalty of any sort at any time.

I understand that all information will be kept confidential and only the principal investigator will have access to this information. I agree that information collected for this study may be published, provided my name or any other identifying information is not used.

Name_____ Signature_____

Date_____

Investigator_____Signature_____