

The Effect of the Unit Dose Dispensing System on Medication Preparation and Administration Errors in Intravenous (IV) Drugs in a Chinese Hospital: Inpatient

by

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Abstract

Intravenous (IV) errors are considered dangerous since IV drugs usually go directly into the patient's vein. Chinese patients receive more than twice the IVs of all other patients, yet the nature of "medication errors" is understudied.

The purpose was to study and test a method for reducing medication errors involving IVs in a Chinese hospital.

The objectives were to (1) explore and measure the frequency of medication errors and identify clues to the causes of medication errors in Chinese hospital inpatient units, (2) identify the clinical relevance of the errors, and (3) investigate the effect of a Unit Dose Dispensing System on medication errors involving IV drugs.

A General Surgery Patient Ward in a tertiary hospital with more than 1,300 beds in Beijing was selected as a convenience sample. An exploratory study was conducted for 4 weeks. Then a Cluster Randomized Trial design was used for an explanatory study of the effect of installing a Unit Dose Dispensing System. The patients' doses for the two units on the study ward were randomly assigned to the Control group or the Experimental group by flipping a coin.

The direct observation method was used on the day shift from 8 AM to 3 PM to detect medication errors. The preparation and administration processes for Total Parenteral Nutrition (TPN) doses were directly observed by the Principal Investigator for 10 consecutive days for each group, both before and after the Unit Dose Dispensing

System was installed in the Experimental group. An Analysis of Covariance (ANCOVA) showed a statistically significant effect on reducing overall medication error rates ($F_{1,17} = 19.77$, $P = 0.0004$), wrong dose error rates ($F_{1,17} = 12.37$, $P = 0.0026$), and omission error rates ($F_{1,17} = 5.52$, $P = 0.03$).

The Unit Dose Dispensing System produced a significantly higher accuracy in the preparation and administration of TPN doses.

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List of Abbreviations

ADEs	Adverse Drug Events
ADM	Automated Dispensing Machine
ANCOVA	Analysis of Covariance
ANOVA	Analysis of Variance
ASHP	American Society of Health-System Pharmacists
BCMA	Bar-Code Medication Administration
BID	Twice Daily
BMI	Basic Medical Insurance List
CDSS	Clinical Decision Support System
CPOE	Computerized Prescription Order Entry
EAMC	East Alabama Medical Center
EHR	Electronic Health Record
E-MAR	Electronic Medication Administration Record
FDA	Food and Drug Administration
GIS	Government Insurance Scheme
HIS	Hospital Information System
ICU	Intensive Care Unit
IRB	Institutional Review Board

ISMP	Institute for Safe Medication Practices
IU	International Unit
IV	Intravenous
JCAHO	Joint Commission on Accreditation of Healthcare Organizations
LIS	Labor Insurance Scheme
MAR	Medication Administration Record
MERP	Medication Errors Reporting Program
MOH	Ministry of Health
MRI	Magnetic Resonance Imaging
NCMS	New Cooperative Medical System
NICU	Neonatal Intensive Care Unit
PIVAS	Pharmacy Intravenous Admixture Center Service
SOE	State-Owned Enterprise
TID	Three Times Daily
T.O.E.	Total Opportunity for Error
TPN	Total Parenteral Nutrition
USP	The United States Pharmacopeia
WHO	World Health Organization

Chapter 1: Introduction

General Problem

High volume usage of intravenous (IV) continuous infusion therapy can be considered as a unique aspect of the culture of Chinese healthcare. In the 18th Meeting of the 11th National People's Congress, Zhixin Zhu, the Deputy Director of the National Development and Reform Commission, revealed that China used 10.4 billion infusion bottles annually in 2009 (China Daily, 2011). This number of infusions was the equivalent to approximately 8 infusion bottles per capita for 1.3 billion Chinese people, much higher than 2.5 - 3.3 bottles of the international level (China Daily, 2011).

Given the high frequency of the use of intravenous medications in daily practice, it is surprising the degree to which information regarding the safety of these intravenous drug administrations for Chinese patients is limited. The Chinese people now don't have a very clear picture of the concept of IV medication errors: how frequently do IV medication errors happen and what variables affect IV medication errors?

Flynn and colleagues (Flynn, Pearson, & Barker, 1997) reported that the mean error rate in IV admixture compounding detected by observation at five U.S. hospital pharmacies was 9%. The study showed that for total parenteral nutrition solutions (TPN) that were prepared manually had 37% error rate and 22% error rate prepared partly using automation. If the error rate of 9% was applied to the Chinese hospitals where intravenous infusions were administered, about 900

million errors involving intravenous infusions would have occurred annually in Chinese hospitals in 2009.

The preparation and administration of intravenous drugs is a complex process with multiple steps which include the selection of correct drugs, the selection of correct diluents (if needed), the dissolving of powder, and the transfer of injectable fluid from the original vial or ampoule into a base solution infusion bag.

Since IV drugs usually go directly into the patient's vein via injection or infusion, IV drugs are considered as high-risk-harm drugs. Data between 2002 and 2006 from the United States Pharmacopeia's (USP's) MEDMARX program, a central internet-based voluntary reporting system that was designed to report, track and help users detect trends in medication errors by using a standardized-entry form and allowing anonymous error data comparisons between the facilities enrolled, showed that parenteral medication errors were nearly three times as likely to cause harm or death (3%) compared with other drug form errors (1.2%) (MEDMARX Database 2002-2006, 2008). The majority (79%) of harmful or fatal parenteral errors involved IV route of administration. Fifty eight percent of the parenteral errors originated during the administration step of the medication-use process (MEDMARX Database 2002-2006, 2008).

The wide range of error rates from 6 to 83% (Hartley & Dhillon, 1998; O'Hara, Bradley, Gallagher, & Shields, 1995; Taxis & Barber, 2003b; Thur, Miller, & Latiolais, 1972; Van den Bemt, Fijn, van der Voort, Gossen, Egberts, & Brouwers, 2002) in preparing and administering intravenous drugs suggest the need for more exploratory studies. Those studies yielded a wide error rate range because they combined the IV medication errors in both the preparation and administration processes. However IV medication administration errors should be studied as a

terminal outcome of medication safety because the errors that happen in the preparation processes might be corrected before the medications reach the patient.

A Council of Europe report attributed these IV errors to the lack of unit-dose injectable medications and insufficient pharmacy staffing resources (Armitage & Knapman, 2003). In 2002, the Chinese Ministry of Health mandated that unit dose based dispensing should be used for oral drugs in all hospital inpatient pharmacies. Zhang and colleagues first introduced the unit dose dispensing concept to a Chinese hospital pharmacy in 2005. Several Chinese hospital inpatient pharmacies such as the Shanghai Institute of Hepatobiliary Surgery and Fuzhou Hospital have used the Unit Dose Dispensing System in oral medicines for the inpatients since 2005 and 2006, respectively. According to one Chinese pharmacy director, about 60-70% of inpatients and 80% of outpatients use intravenous drugs in Chinese hospitals (Jing Zhang, 2008). However, the unit dose dispensing concept has not been widely accepted for IV drugs in Chinese hospital pharmacies. Nurses continue to prepare or mix the IV drugs in the treatment room in the patient wards as they have done traditionally. One study (Li, Huang, Li, Sun, & Ying, 2009) surveyed hospitals by questionnaire and reported that only 19.1% (9 out of 47) of hospitals in Beijing had a unit dose based Pharmacy Intravenous Admixture Center Service (PIVAS).

The Unit Dose Dispensing System concept and applications were developed by Barker and Heller in 1963-1964 (Barker & Heller, 1963a). Their study showed that a Unit Dose Dispensing System can effectively reduce medication errors in a hospital. A “unit dose” is defined as “the physical quantity of a drug specified by a prescriber to be administered to a specified patient at one time, in a labeled ready-to-administer form with no further physical or chemical alterations required” (Barker & Heller, 1963a). Further, the Unit Dose Dispensing System proposed by Barker and Heller (Barker & Heller, 1963a) must have all unit-doses stored

in a central pharmacy and all drugs in a unit dose form at the time they are dispensed . The use of the word “dispensed” assumed the involvement of a pharmacist. From 1964 to 1976, four published studies reported the reduction of medication errors based on the Unit Dose Dispensing System compared to the conventional dispensing system (Barker, 1969; Hynniman, Conrad, Urch, Rudnick, & Parker, 1970; Means, Derewicz, & Lamy, 1975; Schnell, 1976). Today the Unit Dose Dispensing System is widely adopted in many hospitals in the US. A 2008 national survey of drug dispensing and administration practice (Pedersen, Schneider, & Scheckelhoff, 2009) indicated that about 86.7% hospitals dispensed a majority of oral medications in a unit dose form for noncritical care patients and about 69.6% hospitals dispensed a majority of injectable medications in a unit dose form for critical care and noncritical care patients, in which a unit dose was defined as a dose dispensed by the pharmacy that is ready to administer to a patient (e.g., no further dosage calculation or manipulation is required).

The above results were based on reports from hospitals in western countries, however it was uncertain if a unit dose system that works for United States hospitals for example would work for Chinese hospitals. Because of very limited information available regarding the effects of unit dose systems on medication errors in Chinese hospitals, such research is needed.

The first goal of this study was to explore the frequency of intravenous medication errors and identify clues to their cause. The second goal was to identify the potential clinical relevance of the detected errors. The third goal was to investigate the effect of a Unit Dose Dispensing System on medication administration errors for IV drugs.

Significance

IV medications are considered to be particularly dangerous because of the immediate onset of systemic effects, low therapeutic index of many IV medications, and difficulty reversing pharmacologic effects after IV administration (MEDMARX Database 2002-2006, 2008). Despite these dangers, China has an overwhelming usage of IVs compared to other countries and the nature of “medication errors” is poorly examined and understood.

The following two examples illustrate this. First, death of a two and half year old boy in Hainan Province involving a IV medication labeled with the wrong patient’s name on the bottle was reported (Gao, 2011). The hospital didn’t consider it as a medication error, and claimed that the bottle which was labeled with the wrong patient’s name was a sealed bottle of 5% Glucose Solution without adding any additive. The explanation given by the hospital to the death was “unpreventable infusion allergy event”. Second, a one-year-old boy in Anhui Province died during the infusion of Cefathiamidine without any previous skin allergy test (Dragon TV, 2010). However, the physician said that the allergy test was not necessary this time because this boy has previously used Cefathiamidine. Thus, due to the lack of the knowledge of the existence and nature of medication errors, the reasons for the deaths were unclear to the hospitals, the patients’ family, as well as the public. The normal processes for such cases are to analyze the chemicals in the infused bottle and examine the dead body for pathology evidence, which can be very costly.

Medication errors have been understudied in China. Although the Regulation of Hospital Pharmacy Administration has required hospital pharmacies to dispense medications in a unit dose since 2002, the Unit Dose Dispensing System has been slowly adopted. The first unit dose system was installed for use with oral medications in a Chinese hospital in 2005. No study was conducted to study the effect of the new system on medication errors.

Unlike medication error reporting systems used in the United States (e.g., USP's MEDMARX, the ISMP Medication Error Reporting Program, or FDA's MedWatch in the US) there is no national medication error reporting system in China. Thus the absence of research to describe the nature and frequency of medication errors in the Chinese healthcare system is not surprising. Without the knowledge of the nature and frequency of IV medication errors, the patients to whom they administered are at high risk. Better understanding of the nature, frequency and causes of IV medication errors may help guide hospital administrators to improve their system to enhance the quality of care provided to the Chinese.

This research used the undisguised observation method to detect and measure the rate of medication errors, which is capable of producing the most valid results compared to other methods. Measuring the effect of a new IV drug distribution system can provide valuable information for healthcare evaluate and redesign an optimum IV drug distribution systems for Chinese hospitals. The results may also serve to analyze and highlight the potential clinical importance which will hopefully increase the attention of the public to medication administration errors and thereby improve the safety of inpatients in Chinese hospitals.

Scope

This study involved the following two phases:

Phase I: Exploratory Study

1. An exploratory review of the literature was performed to identify the variables and interventions that may contribute to reducing medication errors. The operational definitions of the independent variable and dependent variables were developed during this phase. The hospital to be studied was identified by offering the opportunity to

participate in the study to the director of the pharmacy who attended the ASHP midyear meeting at Anaheim, California in 2007. The sample size was estimated using the effect size calculations and power analysis.

2. The direct observation was used during the first visit in December 2009 in order to obtain the detailed information on describing the TPN medication distribution system used by this hospital. The operational definitions were tested, refined and retested. The flow chart of TPN drug distribution processes was produced using Microsoft Visio.
3. The selection of a patient ward for study was discussed with the Director of the Pharmacy. A General (Gastrointestinal) Surgery Patient Ward was offered by the hospital.
4. Direct observation was used again in July 2010 to improve the familiarity of the observer with the observation environment before the explanatory study.
5. The plan for installing a Unit Dose Dispensing System was discussed with the Director of the Pharmacy and the Chief Head Nurse on the study ward. Only TPN doses were approved by the hospital for the unit dose trial.

Phase II: Explanatory study

The effect of a Unit Dose Dispensing System on TPN medication errors was studied based on a cluster randomized control-experimental design in a General Surgery Patient Ward in a tertiary hospital in Beijing.

Chapter 2: Statement of the Problem

Study Objectives

The first objective of this study was to explore the frequency of intravenous medication errors and identify the clues that may cause medication errors in Chinese hospital inpatient units.

The second objective was to identify the potential clinical relevance of the detected errors.

The third objective was to investigate the effect of a Unit Dose Dispensing System on medication administration errors for IV drugs.

Research Questions

1. What is the nature and frequency of IV preparation and administration errors among Chinese hospital inpatients?
2. What are the clues that may contribute to IV medication preparation and administration errors among Chinese hospital inpatients?
3. What is the effect of a Unit Dose Dispensing System upon IV preparation and administration errors in a Chinese hospital: inpatient?
4. What is the potential clinical significance of the detected medication preparation and administration errors?

Research Hypotheses

H_{A0}: A Unit Dose Dispensing System will not significantly affect overall IV preparation and administration errors for inpatients in a Chinese hospital.

H_{A1}: A Unit Dose Dispensing System will significantly reduce IV preparation and administration errors overall for inpatients in a Chinese hospital.

H_{B0}: A Unit Dose Dispensing System will not significantly affect IV preparation and administration errors, by error types, for inpatients in a Chinese hospital.

H_{B1}: A Unit Dose Dispensing System will significantly reduce IV preparation and administration errors, by error types, for inpatients in a Chinese hospital.

Concepts

1. Unit dose (Barker & Heller, 1963a): Any physical quantity of a drug specified by a physician to be administered to a patient at one time, and not requiring any significant physical or chemical alterations before being administered.
2. Unit dose dispensing: The IV drugs to be administered to one patient at one time are prepared (premixed) in the pharmacy, packaged in an individual package, labeled, and delivered in ready-to-use form to the patient unit within 1-2 hours before the administration time is due.
3. Medication Administration Error (Barker & McConnell, 1962): A deviation from the physician's interpretable orders as written on the patient's chart.

4. An Opportunity for Error (O.E.) (Barker, Kimbrough, & Heller, 1966): The basic unit of data, defined as any dose observed to be given by an observed nurse, or any dose ordered but omitted. One opportunity for error can be only correct, or incorrect in one or more ways.
5. Total Opportunities for Error (T.O.E.s) (Barker, Kimbrough, & Heller, 1966): The total doses ordered (including omissions) plus the number of unordered doses given.
6. Medication administration error rate (Barker, Kimbrough, & Heller, 1966): The number of detected medication errors is divided by the Total Opportunities for Error with the result multiplied by 100.

Flynn and Barker noted that the error categories may not be mutually exclusive; therefore, the rates for different error types cannot always be simply added to obtain an overall error rate (Allan & Barker, 1990).

7. Medication Error Categories (Allan & Barker, 1990; Flynn & Barker, 2000; Flynn, Pearson, & Barker, 1997):

The allowable deviation from the physician's order for measured doses and the range of acceptable times for medication administration must be clearly stated (Allan & Barker, 1990).

- *An unordered or unauthorized drug error*: The administration of a dose of medication that was never ordered for that patient.
- *An extra dose error*: A dose is given in excess of the total number of times ordered by the physician, such as a dose given on the basis of an expired order, after a drug has been discontinued, or after a drug has been put on hold. For example, if a physician

- orders a drug to be given only in the morning and the patient receives a dose in the evening as well, an extra dose error has occurred.
- *Omission error*: A patient fails to receive a dose of medication that was ordered before the next dose is due. If the patient refuses the medication, it is not generally counted as an omission error or an opportunity for error (O.E.). Doses withheld according to conditional order or policy (e.g., “nothing by mouth before surgery”) are not counted as errors or O.E.s.
 - *A wrong dose or wrong strength error*: A dose is given that contains the wrong number of preformed dosage units (such as tablets) or is, in the judgment of the observer, more than 17% greater or less than the correct dosage. The origin of the use of plus or minus 17% was derived from the error commonly encountered by the researchers in the measuring devices commonly supplied to the nurses by the hospital for measuring out oral doses. For injectable doses, a narrower definition was used - any dose that is more than 10% different from the correct dosage would be in error. Wrong dose errors are counted for the intravenous medications and base-solutions (the volume and concentration of the medication) only when the dose was quantitatively specified by the physician and quantitatively measurable by the observer, e.g., Sodium Chloride Injection Concentrate (10%) 20 ml or Sodium Chloride Injection (0.9%) 10 ml was give when Sodium Chloride Injection Concentrate (10%) 10 ml was ordered.
 - *Wrong route error*: A medication is administered by a route that is different from the one ordered, such as giving the patient Sodium Chloride Injection Concentrate (10%) 10 ml by mouth which was ordered intravenously.

Wrong time error: The administration of a dose more than 30 minutes before or after the scheduled time of administration in the absence of an acceptable reason, e.g., when the patient is not in his or her room because of undergoing a procedure elsewhere in the hospital. Although each hospital may determine its own acceptable time range for administration of a dose, 30 minutes is commonly used because it has been shown that nurses can usually administer all their medications within 1 hour. The schedule programmed into the pharmacy's computer system may be used to define correct administration times. If the physician didn't record the time at which an order was written, wrong time errors shouldn't be recorded for doses given on that day until a second dose is given. The first dose given according to the standard administration schedule is considered to establish the schedule in effect, and subsequent doses on the same day may then be examined for wrong time errors.

- *Wrong form error:* The container used to deliver the dose to the patient is incorrect. For example, a syringe was used for the dose instead of a 50 ml IV mini bag.
- *Wrong administration rate error:* The rate of administration of Infusions of intravenous fluids differs from the rate specified by the physician. An infusion given as a bolus can be defined in this category. An intravenous infusion rate exceeding 20 meq/hr of a solution containing potassium chloride can lead to hyperkalemia and, ultimately, cardiac arrhythmias.
- *A deteriorated drug error:* The physical or chemical integrity of a medication dosage form has been compromised, as with expired drugs or intravenous medications requiring refrigeration that are left at room temperature.

- *Wrong administration technique error*: an inappropriate procedure during administration of a drug. For example, not wiping an injection site with alcohol is included in this category.
- *Wrong preparation technique error*: Aseptic technique is violated (e.g., needle contamination, improper decontamination of vials and materials, improper syringe selection, not using a filter needle to inject the reconstituted product when this is normal procedure, improper needle use, lack of hand washing, improper air injection, improper vial venting, improper shaking), or there are deviations from hospital policies and procedures that affected the accuracy or sterility of the final product.
- *Wrong reconstitution procedure*: The volume or solution used to reconstitute the product is contraindicated in medication's package insert or reconstitution is incomplete.

Operational Definitions

- 1) IV Preparation and Administration Error: The TPN preparation and administration processes by the trained IV preparation nurses were observed, noted and compared with the interpretable physician's orders of TPN drugs written on the patient chart in the General Surgery Patient Ward by an observer trained to detect an error.
- 2) Total Opportunities for Error (T.O.E.s): TPN doses ordered by the physician, interpretable to the observer, plus unordered TPN doses observed to be given to the patients in the General Surgery Patient Ward.
- 3) Medication error rate: The detected medication errors are divided by the Total Opportunities for Error with the result multiplied by 100.

4) Categories of IV Medication Administration Errors are listed as below:

- *An unordered drug error:* A dose was added in the Kabiven PI bag (1440 ml) and administered to the patient that was not ordered for that patient.
- *An omission error:* An additive, which was ordered to be added in the Kabiven PI bag (1440 ml) as a group, was failed to be mixed in the Kabiven PI bag (1440 ml) and administered to the patient.
- *A wrong dose error:* An additive, which was ordered in a group of TPN, was given more than 10% volume and concentration greater or less than the correct dosage, in the judgment of the observer.
- *An extra-dose error:* A dose given in excess of the total number of times ordered by the physician, such as a dose given on the basis of an expired order, after a drug has been discontinued, or after a drug has been put on hold.
- *A wrong time error:* The mixed Kabiven PI bag (1440 ml) was administered more than 60 minutes before or after the scheduled administration time.
- *A wrong route error:* The mixed Kabiven PI bag (1440 ml) was administered via a different location or site on the patient's body than was ordered.
- *A wrong administration rate error:* The mixed Kabiven PI bag (1440 ml) was administered at a $\pm 17\%$ deviation as the ordered rate.

5) Procedures of a Unit Dose System

A. Order Processing

1. A pharmacist reviews paper drug orders for prescribing accuracy, consulting with physician if necessary.
2. Orders are re-entered into the master order file (Excel Office 2007) by a pharmacist

- for each patient including patient's full name, age, bed number, dosage form, dosage (insulin dosage is calculated into volume), and administration time.
3. Medication orders are filed, updated and sent to the nurse division.
 4. Orders are printed out by a pharmacist in cumulative list of all active drug orders for each patient (drug list or pick list) at both the pharmacy (drug profile) and the nursing division Medication Administration Record (MAR).

B. IV Dispensing

1. The auxiliary worker uses the pick list to pick all doses scheduled for administration to each patient at one administration time, places them in a separate basket for each patient, signs or initials on the labels, and has them verified by a pharmacist.
 - 1.1. A pharmacist checks doses for deterioration visually, and expiry date, before admixture.
2. Label is generated, reviewed by pharmacist for changes needed, comparing label to order.
 - 2.1. Name and bed number are prominent on top of label.
 - 2.2. Name of base fluid is on label.
 - 2.3. Name of each active ingredient and the amount of dose with unit of concentration are on label.
 - 2.4. Brand name is close to generic name.
 - 2.5. Administration time is on label.
 - 2.6. Initials of pickers, preparing admixture technicians and review pharmacist are on label.
 - 2.7. Signature space for administration nurse name is on label.

- 2.8. Date Dispensed is on label
3. Labeled Refrigerate is stored in refrigerator

C. IV Preparation

1. The drugs dispensed are checked with the drug list before the preparation.
2. Doses are admixed and labeled by the IV preparation nurse.
 - 2.1. Sealed disposable syringe contains only one drug
 - 2.2. Sterile drugs will be prepared in laminar air flow hood (when available) using aseptic technique
3. Final product is verified by a pharmacist, corrected if needed, and signed initial on the label.

D. IV Delivery

1. IVs prepared are delivered in separate compartments (ex. drawer) labeled with patient name, I.D. number if possible, bed number and nursing unit name.
2. Doses are delivered 1-2 hours before administration time.
3. New/updated Medication Administration Record (MAR) is delivered to the nursing station.
4. Dispensing, inventory & financial records are updated in pharmacy.

E. IV Administration

1. Checks the label of each prepared IV received with the MAR Drug List for each patient.
2. Places all drugs in an individual compartment labeled with patient name and bed

number.

3. Proceeds down the hall and to administer the doses.
 - 3.1. Checks patient name, I.D. number if possible, and bed number on the patient such as on a wrist band.
 - 3.2. IV Push: the label is checked for the correct rate of administration.
 - 3.3. Administers doses.
 - 3.4. Signs initials and administration time on the MAR at patient bedside

F. Other Changes

1. All changes are limited to TPN IVs only, unless and until notified otherwise
2. Doses ordered PRN, chemotherapy and the patient's own drugs may require special handling.
3. For solutions pre-mixed by the manufacturer, records the lot numbers.
4. All communications are typed through the computer without handwritten (Excel Office 2007).
5. The nurse records all doses at the time of administration.
6. Dispensing includes picking by the IV nurses (or technicians) if checked by pharmacist.
7. The label on dose dispensed will match that in edited and pharmacist-reviewed order.
8. Bar coding is recommended for dose and patient identification if available.

Chapter 3: Literature Review

Both English and Chinese articles were reviewed to illustrate the significance of this study and the rationale for conducting it. The purposes were to obtain a broad background relevant to the research topics, to critique the articles that addressed the questions relevant to the research questions, and to identify the gaps of the previous studies on IV preparation and administration errors.

Online databases, Google Scholar and manual searches were performed. The following databases and sources were used to conduct the literature search:

- International Pharmaceutical Abstracts (1970 to March 2011)
- Ovid MEDLINE(R) (1948 to March Week 4 2011)
- Auburn Journals Ovid
- Journals Ovid Full Text (Updated to April 1 2011)
- Cochrane Database of Systematic Reviews
- CINAHL (1982 to present)
- PsycINFO (1806 to present)
- Dissertations & Theses Abstracts
- CNKI -China Academic Literature Full-text Database (1960 to March 2011)
- CNKI- China Doctoral Dissertations Full-text Database (1999 to Present)
- CNKI- China Masters' Theses Full-text Database (1999 to Present)

The following keywords were cross linked to conduct the literature search:

- “Medication Error(s)”
- “Inpatient(s)”
- “Medication Use System” or “Medication Delivery System”
- “Safety” or “Patient Safety”
- “Intravenous” or “Infusion” or “IV”
- “Unit Dose” or “Unit Dose Dispensing”
- “Observation”

The Medication Use System in Inpatient Units in Hospitals

System, Medication Use System, and System Safety

A system is defined as “A combination of people, procedures, facility, and/or equipment all functioning within a given or specified working environment to accomplish a specific task or set of tasks” (Stephenson, 1991).

System safety is defined as “ A sub-discipline of systems engineering, that applies scientific engineering, and management principles to ensure adequate safety, the timely identification of hazard risk, and initiation of actions to prevent or control those hazards throughout the life cycle and within the constraints of operational effectiveness, time, and cost” (Stephenson, 1991).

The comprehensive drug system was summarized as a chain of multiple steps, beginning at the manufacturer and ending at the patient’s bedside, as shown below (Aspden, 2007; Barker & Pearson, 1986).

At the manufacturer:

1. Drug research and development

2. Drug approval by the FDA agent
3. Order processing
4. Production and filling
5. Marketing and distribution

At the physician office:

6. Patient assessment
7. Order formulated

At the pharmacy:

8. Ordering/receiving
9. Storing
10. Preparation for dispensing (including compounding, measuring, packaging, and labeling)
11. Dispensing
12. Transportation to nursing unit

At the nursing unit:

13. Ordering/receiving
14. Storing
15. Preparation for administration (including compounding, measuring, packaging, and labeling)
16. Administration to patient
17. Monitoring the patients

The medication use system when medications are ordered for inpatients contains steps 6-17 in the hospital. The perspective of the medication use system for the health care providers was to collaboratively promote efforts to achieve the optimal therapeutic goals and encourage the

enhancement of high-reliable and high-quality care, which was the six key dimensions identified by the Committee on Quality of Health Care in America in the 2001 IOM report, as listed below (Committee on Quality of Health Care in America Institute of Medicine, 2001; Corrigan, Donaldson, Kohn, Maguire, & Pike, 2001).

- Safe: avoiding injuries to patients from the care that is intended to help them.
- Effective: providing services based on scientific knowledge to all who could benefit, and refraining from providing services to those not likely to benefit.
- Patient-centered: providing care that is respectful of and responsive to individual patient preferences, needs, and values, and ensuring that patient values guide all clinical decisions.
- Timely: reducing waits and sometimes harmful delays for both those who receive and those who give care.
- Efficient: avoiding waste, including waste of equipment, supplies, ideas, and energy.
- Equitable: providing care that does not vary in quality because of personal characteristics such as gender, ethnicity, geographic location, and socioeconomic status.

Drug Distribution System in Hospitals

In general, there are three types of drug distributions systems for the inpatients in hospitals: (1) the floor stock system, (2) the patient prescription system, and (3) the Unit Dose Dispensing System. The role of the hospital pharmacists is changing from the dispensing-oriented to the professional knowledge- based and patient-centered.

Floor Stock System

Historically multiple doses were dispensed as a bulk supply of drug products from the pharmacy to the patient care units at one time, known as the floor stock system. In this system, the nurses prepared all doses of medications (including compounding of IV admixtures) near the patient's bedside when the administration was due. Although the lines of communication for drug orders and dose preparations are short and decentralized (the pharmacist is excluded) and distribution from the pharmacy to the patient care units can be done on a batch rather than a continuous basis, this system didn't work well because the drug knowledge required in the dose preparation processes was beyond that of the typical nurse and the drug inventory management requirements exceeded the capabilities of the nursing personnel managing the typical unit (Barker & Pearson, 1986).

As the automated dispensing devices such as Pyxis are used on the nursing units in many hospitals today, current floor stock is also be called "Automated Floor Stock System".

Patient Prescription System

The patient prescription system is distinguished from the floor stock system by the facts that the pharmacists reviewed the original order without relevant patient information and multiple doses were labeled for a specific patient in each container. In this system, the doses were usually sent in 2 to 5-day supply, and the nurse maintained the bottles in stock and used a reminder system to determine when the medication was to be administered (Black & Nelson, 1992). This system fell closer to the Unit Dose Dispensing System when the doses were in single unit form and multiple doses of different drugs (e.g., a 24- hour supply) were sent all at one time

(Barker & Pearson, 1986). This is consistent with the ASHP statement on unit dose drug distribution (American Society of Hospital Pharmacists, 1989): “for most medications not more than a 24 hour supply of doses is delivered to or available at the patient care area at any time.”

In both the floor stock system and the patient prescription system, the nurse rather than the pharmacist played the major role in drug order evaluation and drug preparation (Black & Nelson, 1992).

Unit Dose Dispensing System

The Unit Dose Dispensing System as a revolution activating and expanding the role of pharmacist in the hospital drug distribution system, was created and investigated at the University of Arkansas Medical Center in 1960s, and soon afterwards at the University of Iowa (Barker & Heller, 1963a, 1963b, 1964; Barker, Heller, & Brennan, 1964; Barker, Heller, Brennan, & Sheldon, 1964; Barker, Heller, & Sheldon, 1964; Black & Tester, 1964).

The fundamental elements of the Unit Dose Dispensing System were summarized by Barker and Pearson as follows: (1) theoretically, the unit dose form could be created anywhere along the chain of steps beginning with the delivery by the pharmaceutical manufacturer and ending with the nurse who administered the unit dose; (2) All drugs were retained in the pharmacy until just 1-2 hours prior to use. In the model system at the University of Arkansas Medical Center, this was calculated to require as many as 14 deliveries a day according to the model distribution curve of the demand for doses by time of day; (3) All medication orders were edited in the pharmacy before dispensing; and (4) all Drug Distribution Control Information would come from this source only (Barker & Pearson, 1986).

The Unit Dose Concept in Medication Use Systems

Two major pioneering research teams devoted themselves to developing applications of the unit-dose dispensing system concept from 1961 to 1964. A centralized Unit Dose Dispensing System project was developed at the University of Florida in 1961 (McConnell, Barker, & Garrity, 1961) and continued at the University of Arkansas Medical Center featured the preparation of all medications in the pharmacy (Barker, 1969; Barker & Heller, 1963a, 1963b, 1964; Barker, Heller, & Brennan, 1964; Barker, Heller, Brennan, & Sheldon, 1964; Barker, Heller, & Sheldon, 1964). A decentralized model of a Unit Dose Dispensing System was developed and tested at the University of Iowa in which the medication was prepared by a pharmacist on each nursing floor (Tester, 1964).

Centralized Unit Dose Dispensing System (CUDD)

Exploratory Study

The purpose of developing a centralized unit dose dispensing (CUDD) system was to improve medication administration accuracy (Barker & McConnell, 1962), establish an effective information program to support the nurses in medication administration (McConnell, Barker, & Garrity, 1961), and reduce the waste of medications on the floor (Barker & Heller, 1963b).

The procedures of the Unit Dose Dispensing System were established for an exploratory study on the pediatric floor (35 beds) of the University of Florida Teaching Hospital (250 beds), as shown below (McConnell, Barker, & Garrity, 1961):

1. A carbon copy of the order was simultaneously produced when a physician wrote a medication order, and was sent by the floor clerk to the pharmacy by pneumatic tube.

2. A central secretary in the pharmacy received the copy of the order, transcribed the drug order, order change, or discontinued order onto a patient medication record. Both the copy of the order and the transcribed patient medication record were checked for accuracy and initialed by the pharmacist. After checking, the central secretary placed a signal tab on the top margin of the patient medication record to indicate the time of day the next dose was due.
3. One hour before medication were scheduled to be given, the central secretary pulled all patient medication records and wrote medicine cards for each dose due for every patient the next hour. Medication cards were used and filled by the pharmacy technician.
4. The pharmacy technician prepared the individual packaged medications and placed each dose in a properly identified plastic drawer of a special metal cabinet mounted on a wheeled cart. Each drawer was identified with the patient's name, hospital number, and location. An appropriate pharmacy note for the nurse was placed in each drawer with each dose.
5. The checking pharmacist checked each dose and medicine card in the filled cabinet against the patient medication record and validated the medicine card by stamping the date, time of day, and her initial.
6. The pharmacy messenger delivered the cabinets, which also contained an assortment of disposable needles, syringes, cotton swabs, alcohol, pencils, and note paper to the appropriate patient care unit.
7. The nurse wheeled the cabinet to the door of the patient's room and gave the medications to the patient. With each dose of medication the nurse was supplied a single dose of correct medication except in the use of multiple dose vials, a medicine card in the

traditional format with dilutions pre-calculated and any special remarks included, and pharmacy notes for the nurse - a card-size resume of drug information pertinent to administration and observation of effects of the drug.

8. After administration, the nurse kept the pharmacy notes for reference (in case of unusual symptoms or reactions in the patient) and the medicine cards for charting her medicines. She removed the PRN medications from the cabinet by placing them in the patient's cubicle at the nursing station, and placed the drug cabinet in position for returning to the pharmacy. The medicine cards were to be destroyed after use. If the medication cards were to be re-used, instead of a white card, a yellow medicine card was prepared by the central secretary.
9. The pharmacy technicians cleared the returned cabinets, placing returned and unused medications and extra pharmacy notes for the nurse in a special section where they remained for the subsequent dose of the same medication to be given. Special notes placed in the drawers by the nurses were given to the pharmacist, such as those requesting duplicate doses to be sent for a patient who frequently loses the first one.
10. At the end of each day the central secretary pulled the copies of each patient medication record, priced the doses listed and sent the charge to the business office.
11. Special provisions for special situations: (1) Stat orders and orders requiring compounding: these were separated from the rest of the Unit Dose Dispensing System. (2) PRN orders: the nurse was instructed to transfer the medication and drug information card from the cabinet to the patient's cubicle at the nursing station. (3) Narcotics, Barbiturates, Sedatives, and PRN analgesics: these were kept as floor stock. Emergency drugs were also kept as floor stock for emergency night orders or by the on-call

pharmacist. (4) Night orders: those written after 5 PM were filled by the night or on-call pharmacist with enough medication to last till morning.

No measure of the Medication Errors comparing the two systems (centralized Unit Dose Dispensing System and floor stock system) was obtained as this was considered outside the scope of this exploratory study to test the workability of the system (McConnell, Barker, & Garrity, 1961).

The time study data were not sufficient to support the hypothesis that the Unit Dose Dispensing System can reduce the nursing time required, due to the small sample size of medications administered on a pediatric floor (McConnell, Barker, & Garrity, 1961).

Explanatory Study

In the fall of 1961, an explanatory investigation of the effect of a fully developed centralized Unit Dose Dispensing System was funded by the U.S. Public Health Service, and conducted in the University of Arkansas Medical center (Heller, 1964). For this study, the pharmacy was remodeled as a small pharmaceutical manufacturing firm to prepare the packaging of all doses as unit doses: an automated conveyor elevator system delivered the doses to all floors, and the pharmacy staff was expanded and retrained to include new personnel such as pickers.

The qualitative results confirmed that the centralized unit dose dispensing process under the pharmacy permitted three important improvements (Barker & Heller, 1963b): (1) use of efficient and accurate mechanical and electronic equipment, (2) an improved working environment for personnel performing this task, and (3) supervision of the process by a pharmacist.

The quantitative results (Barker, 1969; Barker, Heller, Brennan, & Sheldon, 1964) showed that the centralized Unit Dose Dispensing System significantly reduced medication errors. The pilot study (Barker, Heller, Brennan, & Sheldon, 1964) results showed that the average error rates with wrong time errors were 16.1% in the control period and 7.2% in the experimental period (14.4% in the control period and 1.8% in the experimental group if wrong time errors were excluded). The error rates by types showed that the Unit Dose Dispensing System effectively reduced errors of omission, wrong dose, extra dose, unordered drug, and wrong route. Wrong time errors were not reduced significantly.

The utilization of nurse and pharmacist time was improved (Barker, Heller, & Sheldon, 1964). Nursing time spent in drug preparation was reduced 13.7% by the experimental systems, and 57% of the saved time (7.7% of total time) was transferred into such desirable categories as bedside nursing, administration of drugs, and division management. The pharmacists' time saved was 39.4%, of which 63% (24.9% of total time) was transferred to the desirable tasks of editing medication files and providing drug information to assist the physicians in the selection of drugs and direct the nurses for the proper administration.

The control period (floor stock system) was studied for 6 months on 6 nursing divisions in 1964. The experimental period (unit dose system) was studied for 2 months on 2 nursing divisions in 1965 due to the limitation of funds (Barker, 1969). The results showed that medication error rate with wrong time errors but excluding “wrong brand” as errors was 25.9% in the control group and 12% in the experimental group (13% in the control group and 1.9% in the experimental group without wrong time errors and “wrong brand errors”). The authors of the study also recognized that extraneous factors such as historical events occurring between the two periods could have influenced the data due to the time lapse between the two evaluation periods.

Decentralized Unit Dose Dispensing

The goals of a research group at the University of Iowa were to study a version of the Unit Dose dispensing concept operationalized around a pharmacy substations on each nursing floor, as shown below (Tester, 1964):

1. Reduction of medication errors,
2. Reduction of nursing time devoted to medication activities,
3. Increased utilization of pharmacists in line with their training,
4. Reduction of drug inventory,
5. Greater control over drugs,
6. Provision of a check by a pharmacist on prescriptions written by medical staff, and
7. Evaluation of the system by medical, nursing, and pharmacy staffs.

Operational Definitions: Differences

The operational definitions of terms related to medication errors and unit dose dispensing were defined somewhat differently in studies subsequent to the original definitions proposed by Barker and colleagues (Barker, Kimbrough, & Heller, 1966).

Unit dose packaging was defined as the process of enclosing a single dose of medication within a single compartment including proper identification of this compartment (Black & Tester, 1964).

Unit dose dispensing was defined as the practice of providing to the nursing station a quantity of medication sufficient for one dose in a single compartment, just prior to the scheduled administration time (Black & Tester, 1964).

Decentralized pharmacy was defined as a pharmacy substation which replaced the drug storage areas in four nursing stations and provided pharmacy service on a 24-hour basis directly to these four wards (Black & Tester, 1964, 1967).

Medication error was defined as any deviation during the demonstration period of interpretation and transcription, preparation and administration (Black & Tester, 1967). This definition of medication error defined by Black and Tester was found to be difficult to replicate because it is confusing regarding how many errors should be counted in when an error happened in the period of transcription and was not prevented in the period of preparation and administration, and what the denominator of the error rate was if one dose experienced three different errors during that period.

The results of this study were reported as follows (Black & Tester, 1967):

1. Medication errors dropped from 2.2% in the conventional system to 0.5% in the decentralized unit dose system, and discrepancies were reduced from 1.1 to 0.3%.
2. The amount of nursing time required for medication activities was reduced by an average of 14.49 hours per day for the four medical wards.
3. The availability and utilization of the pharmacist as a drug consultant to the physician and nurse was perceived to be improved. But no evidence was offered.
4. The revenue loss to the hospital as a result of patient charges lost showed 0.028 of each dollar lost as compared to 0.377 in the conventional system.
5. The drug inventory throughout the hospital was claimed to be minimized as drug deterioration, obsolescence, pilferage, and capital investment were reduced.

6. The amount of floor space required for medication storage on each nursing station was reduced. The pharmacy substation occupied 183.5 square feet plus 85.0 additional square feet for storage, as compared to 325.2 square feet within the wards areas.

Although this research group reported using observation as a method to detect medication errors, no details were provided on the methods or the results obtained. No statistical analysis was applied to compare the two systems.

Subsequent Studies of the Unit Dose Dispensing System

Subsequent studies testing the effect of the Unit Dose Dispensing System were reported, and positive results were obtained (Hynniman, Conrad, Urch, Rudnick, & Parker, 1970; Means, Derewicz, & Lamy, 1975; Schnell, 1976). The following describes these studies.

Hynniman and colleagues compared the error rate at the University of Kentucky Hospital which used a Unit Dose Dispensing System with the error rates in four hospitals of similar bed size (Hynniman, Conrad, Urch, Rudnick, & Parker, 1970). The hospital with a Unit Dose Dispensing System had an error rate of 3.5% compared with error rates ranging from 8.3 to 20.6% (specifically 8.3%, 9.9%, and 20.6%) in the three hospitals with the prescription order system and 11.5% in the hospital with the floor stock system. A significant limitation was that the observers didn't accompany the nurse to the patient's bedside. Hence, several types of errors including wrong route, wrong administration rate, and wrong administration technique errors couldn't be captured by the observer. Also, the denominator for calculating the medication error rate was defined as the number of medication doses administered but not including those ordered but omitted. This study would have yielded a larger percentage of error rate than what was reported if Barker's definition of total opportunities for errors (T.O.E.s) was used.

Means et al (1975) compared the medication error rates of a multi-dose dispensing system with a computer-based Unit Dose Dispensing System in the Johns Hopkins Hospital. Two similar adult, medical, 30-bed patient care units, each serviced by a different drug distribution system (multi-dose and computer-based unit dose distribution system), were studied for 60 days. The error rates were 7.35% in the patient care unit with multi-dose dispensing system and 1.61% in the patient care unit with the computer-based Unit Dose Dispensing System. The limitation included the exclusion of omission errors. The author explained that omission errors were not included because the observer couldn't observe all the doses administered and the doses might be administered by a physician or another nurse without the knowledge of the observer. The author commented that if omission errors had been included, the medication administration error rate for the study hospital would be higher.

Schnell and colleagues measured the error rates for two months in two phases before and after the installation of the Unit Dose Dispensing System in four Canadian hospitals (Schnell, 1976). The overall error rates in Hospital B, C, and D decreased from 42.9 to 23.3%, 20.1 to 7.8%, and 38.5 to 23.1% (14.5 to 12.9%, 7.7 to 2.0%, and 9.6 to 3.7%, excluding wrong-time errors). However, the error rate was unexpectedly increased from 37.2 to 38.5% in hospital A (8.9 to 14.6%, excluding wrong-time errors). The author explained that the increase in hospital A was due to an increase in the number of extra dose errors which were caused by less strict adherence to procedures of enforcement of the hospital's automatic stop order policy by the pharmacist in the unit dose system. If the wrong-time errors and extra dose errors were excluded in hospital A, the error rates would be 8.5% before and 5.8% after the installation of the Unit Dose Dispensing System. For all hospitals the mean error rates would be 10.3% before and 5.9% after the installation of the Unit Dose Dispensing System excluding wrong-time errors. Schnell

graded errors for potential clinical significance by assigning a number on a scale of 0 to 100 according to the error categories. The overall index of significance was calculated by adding the numbers the number of errors in each category multiplied by its index value and the sum of the total was divided by the total number of errors. Schell calculated the index of clinical significance at the range from 28 to 47.1 in the Unit Dose Dispensing System and from 32.8 to 38.6 in the traditional multi-dose drug distribution system. If wrong time errors with an index value of 20 which influenced the index of significance to less severe were excluded, the index of clinical significance would jump to the range from 63 to 69.9 in the Unit Dose Dispensing System and from 68.4 to 73.5 in the traditional multi-dose drug distribution system.

Barker and colleagues evaluated a Unit Dose Dispensing System at a large teaching hospital, proposed recommendations to improve the existing system and re-evaluated the new system after the recommendations were implemented to varying extents (Barker, Harris, Webster, Stringer, Pearson, Mikeal, Glotzhober, & Miller, 1984a, 1984b, 1984c). Four nursing units were studied over 17-day period observations in the initial study (Barker et al., 1984a). The total medication error rate for initial study was 9% excluding wrong-time errors. The error rate excluding wrong-time errors was 3-5 times greater than the rates in other five hospitals in 1960-1970s after they installed unit dose system (Barker, Heller, Brennan, & Sheldon, 1964; Barker, Kimbrough, & Heller, 1966; Hynniman, Conrad, Urch, Rudnick, & Parker, 1970; Means, Derewicz, & Lamy, 1975; Schnell, 1976). The consultant group proposed 14 recommendations for improving the existing Unit Dose Dispensing System (Barker et al., 1984c). The hospital fully implemented three recommendations: cancellation of the use of pharmacy substations, assigning pharmacy to prepare and maintain the primary medication order records, and creation of strategic workload attack teams to go to nursing units during the peak workload periods. The

last two recommendations were expected to reduce error rates and response time. Six recommendations were partially implemented. Four of them were expected to reduce error rate: using dispensing envelopes, increase unit dose packaging, increasing the frequency of deliveries, and dispensing PRN medications on request. Five recommendations were not implemented: using computer to control medication and communicate, increasing the use of pneumatic tube, redesigning pharmacy facilities, reduction of lead time for IV orders, and developing and posting operational definitions for the terms “stat”, “now”, and “emergency” throughout the hospital. One and half years after the fourteen recommendations were implemented to different extents, another study was conducted to measure the medication error rates and the response times (Barker et al., 1984b). Response times for routine medication orders decreased by 55%. No significant differences in medication error rates for any of the error types were found. The errors were evaluated again to find the clues that explained the failure to achieve a significant reduction in medication errors. The errors were primarily attributed to the failure of implementation of these recommendations: computer printing and sorting of orders, use of dispensing envelopes for medications delivered in true unit dose form, and packaging of all medications in unit dose form. This in-depth evaluation indicated the importance of fully implementation of the Unit Dose Dispensing System and the need for close monitoring the performance standards to achieve the expected lowest error rate.

Dean et al compared the medication error rates (mostly oral drugs) in a U.S. hospital with those in a U.K. hospital (Dean, Allan, Barber, & Barker, 1995). The U.K. hospital had a ward-based system without transcription of orders in which a pharmacist visited each ward several times daily, reviewed each patient’s medication chart, and wrote additional instructions to the nurse regarding administration. The U.S. hospital used a partially automated Unit Dose

Dispensing System with a MedStation device for controlled drugs, some first doses, and PRN doses. The medication error rate in the U.S. hospital was 6.9%, significantly higher than the 3.0% rate in the U.K. hospital. The authors attributed the difference of error rates in two health care systems to (1) The U.K. hospital eliminated transcription process which reduce the risk of errors induced by transcription, and (2) The U.K. hospital had the greater availability of pharmacists on the ward.

In 2005, Zhang et al reported that they had first introduced an application of the unit dose dispensing concept to oral medications in a Chinese hospital pharmacy (Zhang, Zhao, Li, Wang, & Gong, 2005). The authors introduced the background and implementation of the Unit Dose Dispensing System in US hospital pharmacies and described the trends and likelihood of the Unit Dose Dispensing System in Chinese hospital pharmacies. However, the effect of their Unit Dose Dispensing System on medication errors was not reported in the article.

Advantages and Disadvantages of the Unit Dose Dispensing System

The advantages of the unit dose system over alternative distribution procedures were cited as follows in the official statement of the American Society of Hospital Pharmacists (ASHP) (American Society of Hospital Pharmacists, 1975):

1. A reduction in the incidence of medication errors,
2. A decrease in the total cost of medication-related activities,
3. A more efficient usage of pharmacy and nursing personnel, allowing for more direct patient-care involvement by pharmacists and nurses,
4. The improvement of overall drug control and drug use monitoring,
5. More accurate patient billings for drugs,

6. The elimination or minimization of drug credits,
7. Greater control by the pharmacist over pharmacy workload patterns and staff scheduling,
8. A reduction in the size of drug inventories located in patient-care areas, and
9. Greater adaptability to computerized and automated procedures.

The ASHP 1975 Statement identified and summarized four distinctive elements common to all the Unit Dose Dispensing Systems (American Society of Hospital Pharmacists, 1975).

1. Medications are contained in, and administered from, single unit or unit dose packages;
2. Medications are dispensed in ready-to-administer form to the extent possible;
3. Not more than a 24-hour supply of doses is provided to or available at the patient-care area at any time for most medications; and
4. A patient medication profile is concurrently maintained in the pharmacy for each patient.

The growth of the Unit Dose Dispensing System was tracked by the ASHP in a national survey repeated every few years. The ASHP's statement and periodic survey demonstrated confusion among hospital pharmacists about the concept of the Unit Dose Dispensing System and the variety of the system's implementations (Barker & Pearson, 1986).

The limitations of the the Unit Dose Dispensing System then being implemented were summarized, as shown below (Barker & Pearson, 1986):

1. The frequency of scheduled deliveries was lower than the expectation to be more or equal to 9-10 times per day based on the average number of patient doses administered in the hospital. The frequency of dose delivery times in the model system in the study at UAMC was 14 times/day. The evidence showed that infrequent deliveries produced the need for a greater number of adjustment doses to be sent to the floor for placement in the cart by

the nurses, which had the effect of increasing the rate of medication errors (Barker & Pearson, 1986).

2. The first dose of PRN orders was not being sent to the patient care areas in advance of need, which increased the opportunity for omission errors.
3. Another limitation of systems claimed to be unit dose was the extent to which not all doses were dispensed in true unit dose packages. The dosage forms such as injectables, ointments, eye drops, and oral liquids were more difficult for the pharmacist to measure and package (Barker & McConnell, 1962).

The ASHP national survey in 2008 reported that 86.7% of hospitals dispensed a majority of oral medications in unit dose form and 70% of hospitals dispensed a majority of injectable medications in unit dose form (Pedersen, Schneider, & Scheckelhoff, 2009). However, the results were confounded with the percentage of hospitals who also claimed to have Automated Dispensing Cabinets (ADCs) using the original Pyxis matrix drawer configuration that allows access to all medications stocked in that drawer, which falls closer to the definition of floor stock. The survey in 2008 reported that a majority of hospitals (83%) used automated dispensing cabinets (ADCs) in their medication distribution systems (Pedersen, Schneider, & Scheckelhoff, 2009). However, only 51.5% of hospitals used individually secured pockets in a matrix drawer while 48.5% of hospitals used the original Pyxis matrix drawer configuration that allows access to all medications stocked in that drawer (Pedersen, Schneider, & Scheckelhoff, 2009).

The Intravenous (IV) Medication Use Systems

Intravenous (IV) medication administration refers to the process of giving medication directly into a patient's vein (Martelli, 2002). Methods of administering IV medication may

include giving the medication by rapid injection (push) into the vein using a syringe, giving the medication intermittently over a specific amount of time using an IV secondary line, or giving the medication continuously mixed in the main IV solution. IV medications are most often given through a peripheral line or saline IV lock, but may also be administered direct IV, through an implanted vascular access port or through a central line (Martelli, 2002).

The administration techniques on IV medication delivery usually included IV push, retrograde system, volumetric-chamber set, piggyback systems, and syringe pump (Reilly, 1987).

IV drug delivery systems currently include manufacturer-prepared products, pharmacy-based IV admixture system, point-of-care activated systems, IV push systems, augmented IV push systems (such as syringe pumps), and volume-control chambers (Sanborn, Gabay, & Moody, 2009). The systems were ranked using a decision analysis methodology by an independent, interdisciplinary experts panel based on 4 domains: safety, cost, simplicity of use, and education and training needed for operation (Sanborn, Gabay, & Moody, 2009). Manufacture prepared products were considered to be the safest drug delivery systems overall. However, the recent event of TPN contamination in six hospitals in Alabama resulting in over 10 deaths showed that IV products prepared by outsourcing this service to centralized providers may not be safe as expected (Institute for Safe Medication Practices, 2011).

Evaluation of Medication Use System Performance

The theoretical principles recommended for the design and evaluation of a medication use system were summarized by Barker and Pearson as below (Barker & Pearson, 1986):

1. The law of requisite variety,
2. Simplification,

3. Standardization,
4. Mechanization and automation,
5. Specialization,
6. Improved utilization of personnel, and
7. Centralization

The criteria for the measurement of the performance of a medication use system were cited by Barker and Pearson as below (Barker & Pearson, 1986).

1. Quality (accuracy),
2. Efficiency,
3. Control of inventory,
4. Utilization of personnel,
5. Lost inventory, and
6. Lost charges

Medication error or medication accuracy was considered as the No. 1 objective to measure for the performance of the medication use system (Barker & Pearson, 1986). Traditional efforts at error reduction have focused on individuals and episodes, using training, exhortation, rules and sanctions to improve performance (Leape, 1994). Human factors specialists and error experts reject this traditional approach, noting that it is more effective to change the system as a whole to reduce the likelihood of accidents (Moray, 1994). Focusing on the nurse's individual performance merely to give the right medication to the right patient in the right dose by the right route at the right time (5 rights) was far from enough to ensure the safety of medication use system. Poor system design makes errors difficult to detect in order for them to be intercepted before injury occurs (Leape, Bates, Cullen, Cooper, Demonaco, Gallivan, Hallisey, Ives, Laird,

& Laffel, 1995). Although an individual's performance may be identified as the proximate cause of the event, an assessment of the entire system is necessary to identify risk points, or weak links, that may have facilitated the individual's less-than-optimal performance (Cousins, 1998).

Problem of Medication Administration Errors and Detection Technologies

Although errors can happen at any stage of the medication use system, the ultimate outcome measure of the medication use system from the patient's perspective is the rate of errors which reach the patient at the point of administration. This was first offered as the measure of the quality of a hospital medication system at the time when a Unit Dose Dispensing System was being developed. Thus, prescribing errors, transcribing errors, dispensing errors and self-administration errors were excluded from the focus of this dissertation. The study of prescribing errors for example typically involves expert judgment on whether each medication was prescribed appropriately and effectively for treating the disease state of particular patients.

In 1962, the frequency of medication errors was first studied by Barker and McConnell by disguised direct observation method at a rate of 16.2% (1 error every 6 doses administered) and 14.7% without wrong time errors (Barker & McConnell, 1962). Between 1960 and 1990, medication error studies were mostly focused on the diffusion of the Unit Dose Dispensing System in hospitals. After 1990, medication error studies were focusing on the effect of environmental factors, automations, and technologies.

The operational definitions and categories of medication administration errors are important to critique the validity of the research on medication errors, which were described under the Concepts and Operational Definition.

Clinical Significance

The issue of measuring and comparing the relative severity of errors has been addressed in numerous studies. The operational definitions used have differed widely. Barker and colleagues' study indicated that 66.1 to 74.2% of all medication errors could be considered serious depending upon whether wrong time errors were included or not (Barker, Kimbrough, & Heller, 1966). Hynniman et al. reported that 59.1% of medication administration errors detected were considered as serious (Hynniman, Conrad, Urch, Rudnick, & Parker, 1970). Schnell reported that the index of clinical significance of medication administration errors they created ranged from 28.0 to 47.1 (including wrong-time errors) and from 63.0 to 73.5 (excluding wrong-time errors) (Schnell, 1976). Dean and Barber developed a method of scoring the severity of medication errors on the basis of potential clinical outcomes without the knowledge of patient outcomes (Dean & Barber, 1999). Thirty professional from four U.K. hospitals scored potential patient outcomes of 50 selected medication errors on the scale of 0 to 10, where 0 represented a case with no potential clinical effect on the patient and 10 represented a case with potential clinical effects of death. The results showed that 57.5% agreement on the severity of a medication error between any two assessments, regardless of the judge and the occasion on which the case was assessed. In order to achieve a Generalizability Coefficient of 0.8, at least four judges would have to score each case, each on one occasion, with the mean score used as a severity indicator. The reliability and validity were not affected by the professions of the judges or the number of the occasions on which the errors were assessed.

Medication Errors Detection Methods

The methods that have been used or proposed were summarized by Flynn and Barker as below (Flynn & Barker, 2007):

1. Direct observation,
2. Chart review,
3. Incident reports,
4. The critical incident technique,
5. Anonymous self-reports,
6. Attending medical rounds to listen for clues that an error has occurred,
7. Detecting omission errors on the basis of doses returned on the medication cart,
8. Urine testing - omitted or unauthorized drugs,
9. Examination of death certificates,
10. Stimulated self-report using interview,
11. MAR comparison to physician orders,
12. Computer-assisted monitoring,
13. Attending nurses change-of-shift report,
14. Comparison of drugs removed from automated dispensing device for a patient with physician orders , including override, and
15. Data mining

Observation

A direct observation technique which was capable of capturing more valid medication errors in the medication use system than other error detection methods was widely accepted and used in medication error studies since 1960s.

The disguised direct observation technique in the medication error study was developed by Barker and McConnell (Barker & McConnell, 1962). In this study, an observer randomly selected a nurse giving medication and witnessed the preparation and administration of each dose. The nurses selected for observing were only told that the purpose of the study was to optimize the medication distribution system and were not aware of the real purpose of the error study. If the nurse was aware of the goal of error study, an undisguised direct observation method was used. The observer wrote notes on what the subject did in the preparation and administration processes. The notes were later compared with the physician's order. An error was counted if the nurse didn't carry out the order accurately. The results estimated that 51,200 errors probably occurred when extrapolating the 2-week data collected by direct observation on morning, evening, and night shifts, compared with 36 official incident reports in the hospital over a one year period.

A study of medication administration errors by direct observation was conducted in 36 health care facilities (Barker, Flynn, Pepper, Bates, & Mikeal, 2002). The medication administration error rate was reported as 19% (excluding wrong time errors, the rate was 10%). The most frequent errors were wrong time errors (43%), omission errors (30%), wrong dose errors (17%), and unordered drug errors (4%).

The direct observation method was recognized as superior due to the following advantages (Barker, Flynn, & Pepper, 2002):

- Knowledge of errors by subjects is not required,
- Willingness to report is not required,
- Remembering is not required,
- The ability to communicate is not required,

- Selective perception of subjects is unrelated,
- Observer inference is involved, and
- The effect of the observer on the observed is not significant when the observer is trained to be non-intrusive and the subject is busy at work.

The major disadvantages of direct observation method are fatigue and Hawthorne Effect (Note: the alteration of behavior by the subjects of a study because they are being observed) of the observer on the subjects (Dean & Barber, 2001; Flynn & Barker, 2000). Dean and Barber conducted a study on the validity and reliability of observational methods for studying medication errors at a U.K. hospital (Dean & Barber, 2001). The results showed that observation of nurses during drug administration and discreet intervention by the observer didn't significantly affect the medication administration error rate. It has been demonstrated that individuals and groups adapt quickly to an observer's presence and act as they would usually act and if the observer takes care to be unobtrusive and not to give the subjects observed the feeling that judgments are being made, the observer as an influential stimulus is nullified (Kerlinger & Lee, 1999).

Chart Review

Chart review was often used in the studies of Adverse Drug Events (ADEs) (Leape et al., 1995) and the clinical significance of medication errors (Flynn & Barker, 2000). The limitation of chart review is that sometime the drug use related symptoms were not always listed on the patient chart.

Incident Report

In the United States today, medication error reports collected and analyzed on national level are (1) JCAHO Sentinel Event Reporting System, (2) MedWatch, which is operated by the Food and Drug Administration (FDA), (3) U.S. Pharmacopeia Institute for Safe Medication Practice Medication Errors Reporting Program (USP-ISMP MERP), and (4) MEDMARX, a national database of medication errors for use by hospitals (Cousins & Calnan, 2000; Smetzer & Cohen, 2007). The goal of the USP-ISMP MERP and MedWatch is to identify the circumstances in which errors occur and to educate the health professional so that the chances of recurring errors are lessened (Cousins & Calnan, 2000).

Error reports should be categorized to the severity of patient outcome according to the index from the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP), as shown below (Cousins & Calnan, 2000):

No Error

- Category A: Circumstance or events that have the capacity to cause error

Error, No Harm

- Category B: An error occurred but the error didn't reach the patient
- Category C: An error occurred that reached the patient but didn't cause patient harm
- Category D: An error occurred that resulted in the need for increased patient monitoring but no patient harm.

Error, Harm

- Category E: An error occurred that resulted in the need for treatment or intervention and caused temporary patient harm.

- Category F: An error occurred that resulted in initial or prolonged hospitalization 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.

Error, Death

- Category I: An error occurred that resulted in patient death.

The limitation of the self-report is that the person is aware that an error occurred and is willing to report. Barker and McConnell found that even though the nurse is aware of the error, she is still hesitant to report it if a physician advises against reporting the error, the nurse believes that the error will not harm the patient, or the error is omission or wrong time error.

The direct observation method was confirmed to be able to detect more medication errors than the other two methods: chart review and incident report (Flynn, Barker, Pepper, Bates, & Mikeal, 2002). In this study, observers detected 300 of 457 pharmacist-confirmed errors made on 2556 doses (11.7% error rate) compared with 17 errors detected by chart reviewers (0.7% error rate) and 1 error detected by incident report review (0.04% error rate).

Errors in IV Medication Use

There are 41 steps in the path from the prescription of an infusion to its administration (Fraind, Slagle, Tubbesing, Hughes, & Weinger, 2002). Medication errors may be introduced during any of these steps of this complex process.

Recently, serious and life-threatening IV medication errors have been heavily reported. For example, in 2006, 1,000 times stronger than recommended dosages of IV heparin caused the deaths of three infants in Methodist Hospital in Indianapolis (Davies, 2006). Similarly in 2007, a

massive overdose of heparin was given to three infants at Cedars-Sinai Medical Center in Hollywood (Phend, 2007). In 2008, more than 100 times the recommended dosage of IV heparin was given to 17 children in Neonatal Intensive Care Unit (NICU) at a hospital in Corpus Christi, Texas (Gray, 2008).

The USP's MEDMARX database between 2002 and 2006 revealed that parenteral medication errors were nearly three times as likely to cause harm or death (3.0%) compared with other drug form errors reported (1.2%). The majority (79%) of harmful or fatal parenteral errors involved the IV route of administration, and 58% of parenteral errors originated during their administration (MEDMARX Database 2002-2006, 2008).

Based on self reports submitted to the USP-ISMP MERP, the ISMP created and periodically updated a list of potential high-alert medications (Institute for Safe Medication Practices, 2008). During February-April 2007, 770 practitioners responded to an ISMP survey designed to identify which medications were most frequently considered high-alert drugs by individuals and organization.

Most of the high-alert medications were IV drugs, which are highlighted in Figure 1.

Classes/Categories of Medications

Adrenergic agonists, IV (e.g., epinephrine, phenylephrine, norepinephrine)
Adrenergic antagonists, IV (e.g., propranolol, metoprolol, labetalol)
Anesthetic agents, general, inhaled and IV (e.g., propofol, ketamine)
Antiarrhythmics, IV (e.g., lidocaine, amiodarone)
Antithrombotic agents (anticoagulants), including warfarin, low-molecular-weight heparin, IV unfractionated heparin, Factor Xa inhibitors (fondaparinux), direct thrombin inhibitors (e.g., argatroban, lepirudin, bivalirudin), thrombolytics (e.g., alteplase, reteplase, tenecteplase), and glycoprotein IIb/IIIa inhibitors (e.g., eptifibatide)
Cardioplegic solutions
Chemotherapeutic agents, parenteral and oral
Dextrose, hypertonic, 20% or greater
Dialysis solutions, peritoneal and hemodialysis
Epidural or intrathecal medications
Hypoglycemics, oral
Inotropic medications, IV (e.g., digoxin, milrinone)
Liposomal forms of drugs (e.g., liposomal amphotericin B)
Moderate sedation agents, IV (e.g., midazolam)
Moderate sedation agents, oral, for children (e.g., chloral hydrate)
Narcotics/opiates, IV, transdermal, and oral (including liquid concentrates, immediate and sustained release formulations)
Neuromuscular blocking agents (e.g., succinylcholine, rocuronium, vecuronium)
Radiocontrast agents, IV
Total parenteral nutrition solutions

Specific Medications

Colchicine injection***
Epoprostenol (Flolan), IV
Insulin, subcutaneous and IV
Magnesium sulfate injection
Methotrexate, oral, non-oncologic use
Opium tincture
Oxytocin, IV
Nitroprusside sodium for injection
Potassium chloride for injection concentrate
Potassium phosphates injection
Promethazine, IV
Sodium chloride for injection, hypertonic (greater than 0.9% concentration)
Sterile water for injection, inhalation, and irrigation (excluding pour bottles) in containers of 100 mL or more

Note: ***Although colchicine injection should no longer be used, it will remain on the list until shipments of unapproved colchicine injection cease in August 2008. For details, please visit: www.fda.gov/bbs/topics/NEWS/2008/NEW01791.html. (Institute for Safe Medication Practices, 2008)

Figure 1: ISMP List of High-Alert Medications

The concerns about the safety of intravenous drug therapy due to their severity were reported in the late 1960s. A survey conducted by Patterson et al in Louisville Veterans Administration Hospital showed that 86% of intravenous fluids infused to the inpatients contained more than one drug (some contained as many as 5 drugs) and the author expressed the concerns about drug incompatibilities and the length of time between preparation and administration (Patterson & Nordstrom, 1968).

Thur and colleagues in 1972 observed 331 parenteral admixtures prepared by nurses for a 10-day period on two medical-surgical nursing units in a 350-bed nongovernmental, general, short-term teaching hospital (Thur, Miller, & Latiolais, 1972). Error categories included the preparation of wrong drug or IV solution, wrong dosage, unordered drugs or preparation of admixtures containing incompatible drugs. Omission errors and wrong time errors were not included in the study. The inclusion criteria for wrong dosage errors and the calculation of error rates were not provided in the study. The results reported that the error rate of preparation of parenteral admixture by nurses was 21%. The major factors leading to parenteral admixture medication errors were non-adherence to written nursing procedures, transcription errors involving medication cards, number of interruptions during each admixture and non-use of available information sources.

A study by Perlstein et al evaluated Medical personnel (nurses, physicians, and pharmacists) on their ability to correctly calculate drug doses for sick newborns in a pediatric center (Perlstein, Callison, White, Barnes, & Edwards, 1979). Five registered pharmacists who were tested demonstrated far better computational skills than either the nursing or physician group. The five pharmacists had a higher mean score of drug calculation (96%) than the eleven pediatricians (89%) and the twenty seven nurses (75.6%). A repeat evaluation of 95 nurses

showed an 86.2% accuracy rate, with experienced nurses performing no better than inexperienced nurses.

O'Hara reported that 168 doses had at least one error in 179 observed IV doses (94%), Of the 132 doses given by senior house officers, 129 (98%) had at least one error, compared with 39 of the 47 doses (83%) given by nurses (O'Hara, Bradley, Gallagher, & Shields, 1995). This study indicate the accuracy problem in IV preparation and administration processes, but the data could not be compared with other studies because no details of medication errors were provided and the the error categories (Incorrect time, Incorrect rate, Incorrect volume, Incorrect diluents, Incorrect method, Dose duplication, and Dose omission) were different from other studies.

An observation study (Flynn, Pearson, & Barker, 1997) of errors in IV admixture compounding at five large hospital pharmacies detected a 9% error rate (147 errors per 1679 doses). The rate of errors that were potentially clinically significant was 1.5%. The most common type of error was wrong-dose, defined as a deviation of 5% or more from the dose listed on the pharmacy label. The product type with the highest error rate was Total Parenteral Nutrition (TPN) solutions (37% with manual preparation and 22% when some automation was used).

Schneider et al conducted an undisguised observation study of IV medication errors in the PICU at the university hospital in Lausanne, Switzerland (Schneider, Cotting, & Pannatier, 1998). The error categories were based on Guidelines on Preventing Medication Errors in Hospitals in 1993 (American Society of Hospital Pharmacists, 1993) and the error categories described by Allan and Barker in 1990 (Allan & Barker, 1990). The deviation of wrong dose error was defined as a dosage varying by $\pm 20\%$ to the medical instruction which is larger compared with the operational definition by Allan and Barker. The definitions of wrong

administration technique error and wrong preparation error were not clearly defined. Including wrong time errors, 74 errors were identified in the total opportunities for error of 275 (an error rate of 26.9%). When the wrong time errors were excluded, 50 errors were identified (an error rate of 18.2%). The most frequent errors were wrong time errors (32.4%), wrong administration technique errors (32.4%), and preparation errors (23%).

Hartley and Dhillon conducted a disguised observation study of IV medication administration errors at two general surgical wards (each with 26 beds) and one general medical ward in a 800-bed general hospital in the United Kingdom (Hartley & Dhillon, 1998). Excluding timing errors, 86 errors were observed in the total of 323 IV infusions observations, giving an intravenous medication error rate of 26.9%. The most frequent errors were omission errors (46.5%), wrong preparation technique (26.7%), wrong dose error (10.5%), and wrong administration technique (10.5%). The limitations of the article included that omission errors with acceptable reasons such as patients away from the ward were counted in but the denominator of the error rate didn't include omission errors. In addition, the deviation of wrong dose preparation error was not defined clearly such as not all powder dissolved.

Tissot et al conducted a 30 days undisguised observation study of medication errors described by the American Society of Health System Pharmacists in Guidelines on Preventing Medication Errors in Hospitals in 1993 (American Society of Hospital Pharmacists, 1993) in three 15-bed ICU units at a university hospital in France (Tissot, Cornette, Demoly, Jacwuet, Barale, & Capellier, 1999). The results showed that 132 errors were detected in 2009 observed nurses acts (6.6% error rate). The denominator was observed nurses' acts which differed from "Total opportunities for error" defined by Barker and McConnell (Barker & McConnell, 1962).

Bruce and Wong conducted a disguised observation method on the period of preparation and administration of parenteral medications by nursing staff during the day shift (Monday to Friday 8:00 AM - 4:30 PM) for four weeks on an acute admission ward in a U.K. hospital (Bruce & Wong, 2001). The operational definitions of medication errors and the total opportunities for error were adapted from the study of Barker and McConnell in 1961. The T.O.E.s were 107. An error rate of 25.2% including wrong time errors and 10.3% excluding wrong time errors were reported. Limitations in this study included the small sample size, unclear percentage of deviation of wrong rate of administration, and some of the error classifications involving personal judgments such as incomplete labeling unsatisfactory to the observer, deterioration in the judgment of the observer, and wrong preparation techniques such as failure to wash hands or use gloves.

Van den Bemt et al conducted a disguised observation study on medication errors in the ICUs of two Dutch hospitals (Van den Bemt et al., 2002). Including wrong time errors, 104 administrations with at least one error were detected in 233 total opportunities for error (44.6% of error rate). When wrong time errors were excluded, 77 administrations with at least one error were identified (33% of error rate). The acceptable deviations of wrong dose error, wrong dose preparation error, and wrong administration technique error were not clearly defined in the article.

Taxis and Barber used disguised observation to study the errors made by nurses who prepared and administered intravenous doses at a university teaching hospital and a non-teaching hospital in the United Kingdom (Taxis & Barber, 2003b). An intravenous drug error was defined as any deviation in the preparation or administration of a drug from a doctor's prescription, the hospital's intravenous policy, or the manufacturer's instructions in this study. The results showed

that one or more preparation or administration errors were detected in 212 of 430 prescribed IV doses observed, for an error rate of 49%. Three doses (1%) had potentially severe errors and 126 doses (29%) had potentially moderate errors. The error rates were overestimated due to the reasons that the denominator didn't include the unauthorized IV doses which were given to the patients, the percentage deviation of the dosage to be considered as a wrong dose error was not given, and percentage deviation of administration rate to be considered as a fast administration of bolus dose error was not given. The author concluded that at a 400-bed hospital with 300 intravenous doses administered per day, at least one patient is likely to experience a potentially serious IV error every day. The analysis showed that the two weak stages in the IV delivery system were (1) drugs that required multiple step preparation, and (2) administration of doses as a bolus.

A similar study was conducted on a surgical ward and a surgical intensive care unit in a German hospital by Taxis and Barber in 2004 (Taxis & Barber, 2004). The results showed that one or more preparation or administration errors were detected in 58 of 122 prescribed IV doses observed, for an error rate of 48%. About one-third of all IV doses were associated with a potentially harmful error. One of the strategies to reduce potentially harmful errors was the reduction in the number of ward-based IV drug preparations.

In another article, Taxis and Barber analyzed the causes of the detected intravenous medication errors using human error theory as a framework (Taxis & Barber, 2003a). A total of 265 errors were identified in 483 IV drug preparations and 447 drug administrations. Active failures were categorized as human errors of slips/lapses and mistakes, and violations. A main active failure was identified in 256 (97%) of the errors. There were 25 (10%) slips and lapses, 60 (23%) mistakes, and 171 (67%) violations. Most violations (n = 168, 98%) were fast

administration of bolus doses; in 116 cases (69%) the bolus dose was given in less than half the recommended time. Causes included a lack of knowledge of preparation or administration procedures, complex design of technology, the lack of communication between nurses and inadequate use of technology. The author discussed that IV drug errors were not only caused by the immediate act, but a range of organizational and managerial issues, including training, cultural context, choice of product, and design of technology. The author suggested that the IV drug errors can be reduced by the involvement of the clinical pharmacists as the key health professionals in ward practice, removing the nurses from the task of making up the IV drugs, restricting the supply and stock of concentrated potassium chloride on wards, and including the central preparation of IV medications.

Wirtz et al investigated the incidence and the severity of IV drug preparation and administration errors on two wards in one teaching hospital in the United Kingdom (with traditional British ward pharmacy service) and two teaching hospitals in Germany (one with a traditional ward stock service and one with a satellite pharmacy service with a unit dose system) (Wirtz, Taxis, & Barber, 2003). Of the 337 prepared doses, 88 (26%) preparation errors including omissions were identified and of the 287 administered doses, 93 (34%) administration errors were observed. The most common errors types were omission, wrong dose and wrong administration rates. More than 70% of IV medication errors had the potential for moderate or severe patient harm. The acceptable percentage deviation of wrong dose was not clearly defined in the study.

Parshuram et al performed a lab study using a direct observational study asking 118 health care professionals (20 anesthesia, 4 pharmacists, 17 pharmacy technicians, and 81 registered nurses) who would be involved in the preparation of intravenous medication infusion

in their regular clinical activities to perform 5 infusion preparation tasks (drug-volume calculation, rounding calculation, volume measurement, dose-volume calculation, and mixing) and 4 morphine infusion to specific concentrations in a structured nonclinical environment (Parshuram, To, & Seto, 2008). The results showed that the error rates were detected in 4.9% of drug-volume calculations, 2.5% of rounding calculation, 1.6% of volume measurements, 4% of dose-volume calculation, and 1.6% mixing. Concentration errors were found in 34.7% of infusion preparation tasks. The use of a calculator was found to reduce errors in dose volume calculations. The concentration errors were positively associated with fewer infusions prepared in the previous week, increased with number of years of professional experience, use of a concentrated stock solution, and the preparation of small dose volumes. Participants with more than 10 years experience were more likely than those with less experience to make at least one error in rounding calculations. In terms of the magnitude of errors, larger errors in infusion preparation were associated with sleeping fewer hours in the 24 hours before the study, use of the more concentrated stock solution, and preparation of smaller dose volumes (e.g., for children and neonates).

Recommendations for IV medication safety practice were offered by Parshuram et al (2008) as follows.

1. The use of electronic calculators by front line staff is likely to reduce calculation errors;
2. Centralized preparation of medications could be practical and have cost advantages (Armour, Cairns, Costello, Riley, & Davies, 1996);
3. Methods that reduce or better manage fatigue could improve technical performance;
4. The use of standardized infusion concentrations could reduce errors if the concentrations selected are matched to appropriately dilute stock concentrations; and

5. The use of pre-filled syringes or ready-mixed infusions prepared to industry standards could improve the accuracy of medication dosing and would better serve the therapeutic needs of children.

A major limitation of this study was that the participants performed preparation in a structured nonclinical environment without disturbances or distractions in normal work.

Effect of Automation and Technology on IV Medication Use

Automation and technologies offer the ability to relieve humans from highly repetitive and tedious workloads and enhance the reliability of their work. They also have the potential to reduce medication errors and improve system efficiency and safety. The human can then focus on the work that requires the abstract, thinking, judgment, and higher level cognitive processes at which humans excel (Felkey & Barker, 1995). However, technology by itself will rarely prevent medication errors unless it is effectively integrated into the existing medication use system and appropriately managed for it to positively impact patient safety (Rough & Temple, 2006). Full implementation of these technologies will take years to accomplish based on their relative advantage, compatibility, complexity or simplicity, trialability, and observability (Rogers, 1995). If the automation or technologies were not implemented appropriately or implemented without dedicated oversight on management, training, quality assurance and ongoing support and maintenance, new sources of errors might prevail and the automated system may be less safe than the manual system it replaced (Felkey & Barker, 2005; Rough & Temple, 2006).

Automation and technologies have been widely used in medication use systems for the primary function of entering prescriptions electronically and with decision support, dispensing doses, counting doses, packaging medications into unit dose, labeling, admixing IVs by a robot,

scanning the bar code for the correct medication and the correct patient's IDs, and setting up the rate through IV pump. The automations and technologies related to IV medication use are summarized as: Computerized Prescription Order Entry (CPOE) or Clinical Decision Support System (CDSS), Electronic Medication Administration Record (E-MAR), Bar Code Medication Administration (BCMA), Smart infusion pump, Automated Dispensing Machine (ADM), and automated admixture robot.

Franklin et al conducted an observational study before and after a closed-loop distribution system including electronic prescribing, automated dispensing, barcode patient identification and electronic medication administration record in a 28-bed general surgery patient ward of a London teaching hospital (Franklin, O'Grady, Donyai, Jacklin, & Barber, 2007). The results showed that the medication administration error rate reduced from 7.0% of 1,473 non-intravenous doses pre-intervention to 4.3% of 1,139 afterwards ($P = 0.005$). The generalization of this study is limited, because the impact an individual technology system on medication administration errors was not provided in this article if the hospital only installed one technology system.

Computerized Prescription Order Entry (CPOE)

CPOE technology was first designed and tried at the Brigham and Women's Hospital, a 720-bed major urban teaching hospital in Boston, in order to reduce response time and transcription problems (Teich, Hurley, Beckley, & Aranow, 1992). The cost of implementing CPOE in a large 500-bed hospital with 25,000 admissions annually was estimated at \$7.9 million of initial cost plus \$1.35 million of annual operating cost (First Consulting Group, 2003).

Bates et al conducted a prospective time series analysis with 4 periods on medication error rate before and after the CPOE implementation on three medical units (two general care medical units and one medical intensive care unit) at Brigham and Women's Hospital in Boston (Bates, Teich, Lee, Seger, Kuperman, Ma'Luf, Boyle, & Leape, 1999). The data showed that an 81% decrease in non-missed-dose medication errors, from 142 per 1,000 patient-days in the baseline period to 26.6 per 1,000 patient-days in the final period ($P < 0.0001$). Medication errors were detected in three ways: (1) pharmacists reported any prescribing errors, potential ADEs, or ADEs during the dispensing process; (2) medication sheets retrieved by the pharmacy; and (3) all medication charts. The medication errors detected could be limited regarding prescribing errors due to the detection method.

Bar Code Medication Administration (BCMA)

BCMA technology was first introduced by a nurse in the Colmery-O'Neil Veterans Affairs Medical Center (VAMC) in Topeka, Kansas in 1994, and was used throughout the Veterans Affairs (VA) health care systems from 1999 to 2003 (Schneider, Bagby, & Carlson, 2008). In 2008, 25.1% hospitals claimed the adoption of BCMA (Pedersen, Schneider, & Scheckelhoff, 2009). The BCMA system includes installing a computerized system of scanners, PDAs, bar coding equipment, and patient wristbands (Tucker, 2003). Including the training and bar code operating costs, the estimated first-year costs for a 191-bed hospital were \$369,000 with annual operating costs estimated to be \$312,000 (Tucker, 2003).

Thielke reported the medication administration errors before and after implementation of BCMA in a 28-bed hematology unit in the University of Wisconsin Hospital and Clinics (Thielke, 2003). The author reported that the baseline error rate pre-implementation was 9.09%

based on observation; the post-implementation error rate was 1.21% based on seventeen days data collection. The author estimated that 11,518 errors per year were eliminated on this unit. The overall error rate was reduced by 87%. The wrong dose and wrong dosage form errors were decreased 100%, followed by decreases for omitted dose (92%), wrong time (77%), and wrong drug (51%). The limitation of this article was that no details of methods and the timeframe were specifically stated.

Paoletti et al conducted a prospective direct observational study on medication administration errors before and after the implementation of electronic medication records (EMARs) and BCMA in a general hospital (Paoletti, Suess, Lesko, Feroli, Kennel, Mahler, & Sauders, 2007). The control group was a 20-bed cardiac telemetry unit. Intervention group 1 was also a 20-bed cardiac telemetry unit. Intervention group 2 was a 36-bed medical surgical unit. A 35.9% reduction of medication administration errors was found after EMARs and BCMA were installed in the intervention group 2, with 15.6% error rate in the Pre-implementation phase and 10% error rate in the Post-implementation phase. The reduction of medication errors was 54% if the wrong time and wrong technique errors were excluded, with 6.3% error rate in the Pre-implementation phase and 2.9% error rate in the Post-implementation phase. The author explained that the intervention group 1 was not as valid as a comparator with the control group because it had a lower variation in medication orders because of the aggregated cardiac patients and use of standardized order sets and a double-check by two nurses to verify the transcription of all medication orders. However, this does not make sense based on the results that no significant reduction of medication errors was found in the intervention group 1, with 25.3% error rate in the Pre-implementation phase and 19.2% error rate in the Post-implementation phase (with 1.6% error rate in the Pre-implementation phase and 1.6% error rate in the Post-implementation phase,

if wrong time and wrong technique errors were excluded). This study didn't give more details of the effects of EMARs and BCMA on reducing the subtypes of errors. Another limitation is that BCMA was embedded in the EMARs system.

Helmons et al conducted a prospective observational study of medication administration errors before and after the implementation of bar code assisted medication administration (BCMA) on two medical-surgical units and two medical and surgical intensive care units (ICUs) in a 386-bed academic teaching hospital (Helmons, Wargel, & Daniels, 2009). The results showed that more than 90% of medication administrations occurred during the 9 AM medication round in the medical-surgical units and medical and surgical ICUs. No differences were found for the overall error rate (12.6% before BCMA and 13.5% after BCMA), the error rate excluding wrong time errors (11.0% before BCMA and 9.9% after BCMA), and the error types (omission errors, wrong dose errors, wrong technique, and unauthorized drugs) before and after BCMA implementation on the ICUs. Increased wrong time errors after BCMA were observed in both the medical-surgical units and ICUs. Decreased omission errors were observed after BCMA in the medical surgical units.

DeYoung et al conducted a prospective direct observational study of medication administration errors in a 38-bed adult medical ICU in a 744-bed community teaching hospital before and after the implementation of BCMA (DeYoung, VanderKooi, & Barletta, 2009). The results showed that BCMA was most effective at reducing wrong administration time errors (reduced by 56% after the implementation of BCMA). There were no significant differences in omission errors, wrong dose errors, wrong drug errors, wrong route errors, and unauthorized drug errors before and after the BCMA.

Poon et al conducted a quasi-experimental study before and after an electronic medication administration system (bar-code eMAR) in an academic medical center (Poon, Keohane, Yoon, Ditmore, Bane, Levtzion-Korach, Moniz, Rothschild, Kachalia, Hayes, Churchill, Lipsitz, Whittemore, Bates, & Gandhi, 2010). Direct observations were made simultaneously in each unit 2 to 4 weeks before the bar-code eMAR and then 4 to 8 weeks afterward. Each error was classified by a member of the study staff and further adjudicated independently by two members of a multidisciplinary panel consisting of physicians, nurses and pharmacists to confirm the presence of an error and the potential ADEs. The results showed that the total medication error rate excluding wrong time errors reduced significantly ($P < 0.001$) from 11.5% on units that did not use the bar code eMAR to 6.8% on units that did use it. The contributors of the errors were wrong administration route (oral vs. nasogastric-tube administration) and wrong documentation errors. The rate of potential adverse drug events excluding wrong time errors fell from 3.1% without the use of the bar-code eMAR to 1.6% with its use ($P < 0.001$). The rate of timing errors fell from 16.7% without the use of the bar-code eMAR to 12.2% with its use ($P < 0.001$). The potential ADEs associated with wrong time errors didn't change significantly. Transcription errors fell from 6.1% without the use of the bar-code eMAR to 0 with its use. The results also showed that the wrong dose errors (2.0% before the bar-code eMAR and 1.1% after the bar-code eMAR) and wrong medication errors (1.0% before the bar-code eMAR and 0.4% after the bar-code eMAR) were significantly reduced ($p < 0.001$). One limitation of this study is that the BCMA was embedded in the eMAR system.

Automated Dispensing Machines (ADMs)

Barker and colleagues compared medication errors between an automated bedside dispensing system McLaughlin Dispensing Device (MD) and a decentralized pharmacy satellite unit dose distribution system on a 32-bed general surgery unit of an 848-bed acute care, non-profit general hospital in 1984 (Barker, Pearson, Hepler, Smith, & Pappas, 1984). A crossover study design with randomized assignment of subjects and treatments was used. A single pharmacist observer observed 14 days on both systems as the nurses administered medications on the day (7:30 AM - 12:30 PM) and evening shifts (5:30 PM - 10:30 PM). The mean error rate including wrong time errors was significantly reduced from 15.9% with the decentralized unit dose system to 10.6% with the bedside dispensing device ($P < 0.05$). No significant difference in the error rate between shifts was found. If wrong time errors were excluded, no significant difference in the error rate was found (6.7% with the decentralized unit dose system to 5.2% with the bedside dispensing device). The results showed that the automated bedside dispensing machine did not successfully prevent all the errors such as wrong dose errors, wrong route errors, and extra dose errors.

Borel et al conducted a disguised observational study of medication administration errors before and after the implementation of MedStation Rx (Pyxis, San Diego, CA) at a 600-bed hospital. The medication errors were reduced significantly from 16.9% before the implementation of Pyxis to 10.4% after the implementation of Pyxis ($P < 0.001$). Most of the errors were wrong-time errors.

Chinese Health Care Systems

Chinese Health Care System Summary

China is the home to one quarter of the world's population, and more of its 1.3 billion people have flocked into megalopolises (such as Shanghai, with more than 16 million people, and Beijing, with more than 13 million) that dwarf anything in the western world (Blumenthal & Hsiao, 2005). Much of the rural population, which numbers 900 million, lives in poverty and desperation that are reminiscent of the world's forgotten regions (Blumenthal & Hsiao, 2005).

The Chinese health care system is principally a hospital centered, three-tiered system, with public health network support at the primary care level (Hong & Yatsushiro, 2003). At each level, hospitals are divided further into three grade levels according to the quality of their services (Hong & Yatsushiro, 2003). The grade level of each hospital is decided by the Ministry of Health (MOH) according to its roles and functions, size, level of technology, and quality of medical services. Data confirmed that the Chinese health care system achieved enormous improvements after the establishment of the People's Republic in 1949 (Chinese Ministry of Health, 2009). Health care institutions increased to 278,337 in 2008 as compared to 3,670 in 1949. The Under-five mortality rate decreased from 225 per 1,000 births in 1960 to 22 per 1,000 births in 2007. Life expectancy increased from an average of 35 years in 1949 to an average of 74 years in 2007.

The distribution of general government health spending (e.g., including social health insurance spending) is heavily skewed to urban area within a province, and unequally distributed across provinces (Wagstaff, Yip, Lindelow, & Hsiao, 2009). These inequalities in government health spending are at least in part responsible for the geographic inequalities in the accessibility and quality of health facilities (poor inland provinces versus prosperous southeastern provinces),

their use and health outcomes (Wagstaff, Yip, Lindelow, & Hsiao, 2009). For example, the rate of hospital deliveries varies from 29.8% in Guizhou, a poor inland province, to 99.5% in Zhejiang, a prosperous southeastern province (Wagstaff, Yip, Lindelow, & Hsiao, 2009). The statistical data from the Ministry of Health in 2009 showed that Beijing had 6,497 health care institutions: about equal to the quantity of health care institutions in some provinces (Chinese Ministry of Health, 2009).

Chinese political commitment to health system reform was declared at the highest level when the President Hu Jintao stated in October 2006 that all Chinese people should have access to affordable essential health services (World Health Organization, 2009). The main objective is to provide universal coverage of basic health care by the end of 2020 (World Health Organization, 2009).

Chinese health care systems experienced three periods of reform since 1949 when the Communists assumed power of the Country: 1949-1978, 1978-2002, and 2002-now.

Chinese Health Care System 1949-1978

During Mao Tse-Tung's era, health insurance and to some extent health care delivery were organized around the workplace (Wagstaff, Yip, Lindelow, & Hsiao, 2009), which was typical of 20th-century communist societies that are now largely extinct (Blumenthal & Hsiao, 2005). There were three schemes for different groups of people in the country: the Cooperative Medical Scheme (CMS), the Labor Insurance Scheme (LIS) and Government Insurance Scheme (GIS). CMS financed health care for members of the agricultural commune; LIS financed health care for State-Owned Enterprise (SOE) workers; and GIS financed health care for government officials (Wagstaff, Yip, Lindelow, & Hsiao, 2009).

“Barefoot doctors” were farmers who received minimal basic medical and paramedical training to provide the basic medical needs of villagers in rural areas, and were attached to the agricultural commune and workplace clinics when they provided first-level care. Second-level care was provided in Township Health Centers (THCs) in rural areas and in district hospitals and enterprise hospitals in urban areas (Wagstaff, Yip, Lindelow, & Hsiao, 2009). Tertiary care was provided in county and city hospitals, and pharmacies were typically integrated into these facilities (Wagstaff, Yip, Lindelow, & Hsiao, 2009).

Communes, local and central governments all collected taxes which were used to pay demand-side subsidies to the health insurance programs and supply-side subsidies to providers (Wagstaff, Yip, Lindelow, & Hsiao, 2009). It was a near-universal health insurance with minimal out-of-pocket payments.

Chinese Health Care System 1978-2002

At the beginning of the 1980s, China was undergoing the epidemiologic transition seen in Western countries: infectious diseases were giving way to chronic diseases (e.g., heart disease, cancer, and stroke) as leading causes of illness and death (Chinese Ministry of Health, 2004).

In 1978, the second leader of China, Deng Xiaoping, reformed the command-and-control economy to the market-oriented economy. Within a few years, Chinese health care system transformed into the profit-making health system too. The agricultural commune was quickly replaced by household production, profit-making village and township enterprises were set up, and SOE was granted substantial financial autonomy (Wagstaff, Yip, Lindelow, & Hsiao, 2009). The breakup of the commune led to the almost total collapse of the CMS (Hsiao, 1984; Liu,

2004b). Financial autonomy for SOE meant many fell into financial difficulty; a large number closed and SOE employment levels fell (Cai, Park, & Zhao, 2008).

In 1990s, the central government focused its efforts on urban health insurance. Yip reported that government spending in urban areas was five to six times higher than in rural areas (Yip, 2009). Insurance coverage plummeted in rural areas, and declined in urban areas (Gao, Tang, Tolhurst, & Rao, 2001). From 1978 to 1999, the central government's share of national health care spending fell from 32% to 15% (Liu, 2004a). Out-of-pocket expenses accounted for 58% of health care spending in 2002, as compared with 20% in 1978 (Liu, Rao, & Hsiao, 2003). In order to regulate the price of drugs, a new scheme to cover all urban formal-sector workers (not including their dependents) was launched known as Basic Medical Insurance (BMI) in 1995.

From 1978 to 2002, the annual per capita spending on personal health services in China increased by a factor of 40, from roughly \$1.35 to \$55 (Blumenthal & Hsiao, 2005). Half of Chinese health care spending was devoted to drugs (as compared with 10% in the United States) (Hesketh & Zhu, 1997).

These consequences accompanied the transition to the market-oriented health care system, as shown below (Wagstaff, Yip, Lindelow, & Hsiao, 2009):

1. Heavy investment in high-tech equipment and a consequent shift from labor-intensive to capital-intensive care
 - a. Liu and Hsiao identified the rapid adoption of new technology as a major driver of the cost growth in Chinese health care system (Liu & Hsiao, 1995).
 - b. In Shanghai, Caesarean sections increased faster than could be explained by increases in risk factors (Cai, Marks, Chen, Zhuang, Morris, & Harris, 1998).

- c. In the late 1990s, China had more Magnetic Resonance Imaging (MRI) scanners per million people than more affluent Thailand or Mexico and around two and a half times as many as would be expected on the basis of its per capita income at the time (Wagstaff, Lindelow, Wang, & Zhang, 2009).
2. A high share of spending on drugs
 - a. In 2003, nearly 45% of total health spending was on drugs , compared with the Organization for Economic and Co-operation and Development (OECD) average of around 15% (Wagstaff, Lindelow, Wang, & Zhang, 2009).
3. The delivery of medically unnecessary care
 - a. For profit reasons, flu patients were often given unnecessary IV injections in dilapidated clinics (Yip, 2009).
 - b. About 75% of patients suffering from a common cold and 79% of hospital patients were prescribed antibiotics, compared with an international average of 30% (Yip, 2009).
 - c. Providers over-prescribed drugs and tests, and hospitals raced to introduce high-tech services and expensive imported drugs that gave them higher profit margins (Liu & Mills, 1999).
 - d. In order to increase their profits, village doctors bought fake or expired drugs at a cheap price and sold them to patients at the higher official price (Blumenthal & Hsiao, 2005).
4. Rapid cost escalation
 - a. Between 2003 and 2004, the average cost per case increased by as much as 15–20% in central and general township health centers and county hospitals, even after

adjusting for case mix (relative numbers of inpatient, emergency and outpatient care) and other factors such as bed stock and local income per capita (Wagstaff, Lindelow, Wang, & Zhang, 2009).

5. A larger share of out-of-pocket health spending
 - a. Using data from the National Health Survey (NHS), Yip reported that the out-of-pocket expenses associated with a single inpatient admission increased from 70 to 80% of per capita income in 1993 to more than 200% in 2003 (Yip, 2009).
 - b. Out-of-pocket spending as a share of total health spending grew from 29% in 1978 to over 60% in 2000 (Wagstaff, Lindelow, Wang, & Zhang, 2009).

Chinese Health Care System 2002-Now

In 2003, the Chinese government initiated the New Cooperative Medical System (NCMS), a government-run voluntary insurance program, with government subsidies targeting the poorer Western and Central regions (Central Committee of Communist Party of China, 2002). The primary goals of the NCMS are to prevent rural Chinese from being impoverished by medical expenses and to reduce inequalities in care between Chinese rich and poor areas (Yip & Hsiao, 2009).

Chinese political commitment to health system reform was declared at the highest level when President Hu, Jintao stated in October 2006 that all Chinese people should have access to affordable essential health services (World Health Organization, 2009). After three years of deliberation, in 2009, the government announced their national health reform blueprint with the main objective to provide universal coverage of basic health care by the end of 2020 (World Health Organization, 2009). Reforms are proposed in five areas: the public health system, the

medical care delivery system, the health security system, the pharmaceutical system, and pilot hospital reform (World Health Organization, 2009).

In the latest Basic Medical Insurance List (BMI), more than half of the drugs are in injectable dosage forms, which are common or high frequency drugs (Chinese Ministry of Labor and Social Security, 2004).

Rationale of the Study

The need for a broad descriptive study of the nature and frequency of IV medication errors that will identify clues to cause and suggest the potential clinical relevance of such errors is evident. The majority of observational studies of IV medication errors conducted in Europe had a broad error rate range from 6.6% to 50%, gathering at the error rate of 20%-50% (Bruce & Wong, 2001; Hartley & Dhillon, 1998; Schneider, Cotting, & Pannatier, 1998; Taxis & Barber, 2003a, 2003b; Taxis & Barber, 2004; Tissot et al., 1999; Van den Bemt et al., 2002; Wirtz, Taxis, & Barber, 2003). Two studies with higher error rates of 21% (Thur, Miller, & Latiolais, 1972) and 83% (O'Hara, Bradley, Gallagher, & Shields, 1995) in the US didn't give details of error categories and error rate calculation. One study in Canada was conducted in a nonclinical environment (Parshuram, To, & Seto, 2008). One study in the US provided a description of IV admixture compounding errors and said the most common type of error was wrong-dose. TPNs had the highest error rate with 22% even when prepared by some automation in the centralized IV preparation room in the hospital pharmacies (Flynn, Pearson, & Barker, 1997).

Some studies didn't clearly define the extent of deviation in the operational definitions of wrong dose errors (Hartley & Dhillon, 1998; Van den Bemt et al., 2002; Wirtz, Taxis, & Barber, 2003), wrong dose preparation errors (Hartley & Dhillon, 1998; Schneider, Cotting, & Pannatier,

1998; Van den Bemt et al., 2002), and wrong rate of administration errors (Bruce & Wong, 2001). Also, some studies gave inappropriate or vague definitions or involved personal judgments in the operational definitions of omission errors (Hartley & Dhillon, 1998), wrong preparation technique errors (Bruce & Wong, 2001), wrong administration technique error (Hartley & Dhillon, 1998; Schneider, Cotting, & Pannatier, 1998; Van den Bemt et al., 2002), deteriorated drugs (Bruce & Wong, 2001; Hartley & Dhillon, 1998), incomplete labeling (Bruce & Wong, 2001), and the total opportunities for error (Hartley & Dhillon, 1998; Tissot et al., 1999).

Some studies observed and analyzed IV preparation and administration errors separately (Taxis & Barber, 2003a, 2003b; Taxis & Barber, 2004; Wirtz, Taxis, & Barber, 2003). These studies would limit the wrong dose errors detection in the measurement of medication administration errors if the wrong dose errors were introduced in IV admixture preparation processes.

This dissertation used standardized operational definitions of medication errors with clear deviation percentages, total opportunities for error as the denominator, and error rate calculation. Both preparation and administration processes were observed in order to detect the wrong dose errors that may have occurred at the beginning of the preparation, but only medication administration errors were measured as the outcome at the end point of medication use system. The direct observation method was used in this dissertation to capture medication errors. This technique has been shown to be more valid than chart review and self report (Barker, Flynn, & Pepper, 2002; Dean & Barber, 2001).

Automation has been used and studied to prevent medication errors since the 1990s, but its effects on medication errors are still under study with results unproven.

CPOE automation was evaluated to achieve the potential effects on reducing prescribing errors, transcribing errors, and ADEs by the chart review method (Bates et al., 1999). However, the cost of implementing CPOE was not affordable by most non-profit hospitals as well as most Chinese hospitals with an estimation of \$7.9 million of initial cost plus \$1.35 million of annual operating cost of in a large 500-bed US hospital with 25,000 admissions annually (First Consulting Group, 2003).

One study in a general hospital showed that the integrated BCMA and EMAR system reduced medication errors significantly in one experimental group, but didn't reduce medication errors significantly in the other experimental group (Paoletti et al., 2007). Poon et al study in an academic medical center showed that BCMA reduced the total medication error rate significantly, but the contributors of the errors were wrong administration route (oral vs. nasogastric-tube administration) and wrong documentation errors (Poon et al., 2010). Two studies in ICUs showed that BCMA did not significantly reduce overall errors as well as subtypes of errors (omission errors, wrong dose errors, wrong technique errors, and unauthorized drug errors) (DeYoung, VanderKooi, & Barletta, 2009; Helmons, Wargel, & Daniels, 2009).

Two studies in hospitals showed that ADMs significantly reduced wrong time errors (Barker, Pearson, Hepler, Smith, & Pappas, 1984; Borel & Rascati, 1995).

The Unit Dose Dispensing System has already been installed as interventions for reducing oral medication dispensing errors in some Chinese hospitals since 2004, but its main effect on reducing medication errors has never been investigated and measured.

In summary, this study considered the current medication use system, labor and culture in the Chinese hospitals and then selected for testing the inexpensive intervention of the unit dose dispensing concept as tested and found effective in many US hospitals.

Chapter 4: Methodology

Study Setting

The study site is a General (Gastrointestinal) Surgery Patient Ward with 53 beds in two units, located at a tertiary A-level hospital with more than 1,300 beds in Beijing. The floor layout (not to scale) of the study Patient Ward is shown in Figure 2. The hospital offers integrated eastern-western medicinal therapy, which is a clinical medical research and teaching hospital.

The background of the hospital and the study site was obtained by the Principal Investigator from the exploratory study in December 2009. The hospital had five pharmacies: the Traditional Chinese Outpatient Pharmacy, the Traditional Chinese Inpatient Pharmacy, the Western Outpatient Pharmacy, the Western Inpatient Pharmacy, and the Special Pharmacy for the Children Emergency, the Infectious Disease, and the International Medical Departments. A total of 12 pharmacists in the Western Inpatient Pharmacy were responsible for dispensing all the injectable drugs to the inpatients in the hospital. Clinical pharmacists were only assigned to the Departments of Endocrinology, Hematology, Nephrology, and the Intensive Care Unit.

The research protocol was reviewed and approved by the Director of the Outpatient Pharmacy and the Clinical Research Ethical Review Board at the hospital, and the Auburn University Institutional Review Board (IRB) for the Use of Human Subjects in Research in May 2010 (Appendices B and C). The IRB was renewed in September 2011 (Appendices D).

The Director of the Outpatient Pharmacy agreed to provide collaborative support for the study. The General (Gastrointestinal) Surgery Patient Ward was offered by the hospital. This

patient ward housed 50% of cancer patients, served by 13 physicians and 18 employed nurses.

No clinical pharmacist was currently assigned to this ward. The majority (90%) of the prescribed orders for the patients on this ward were for IV drugs.

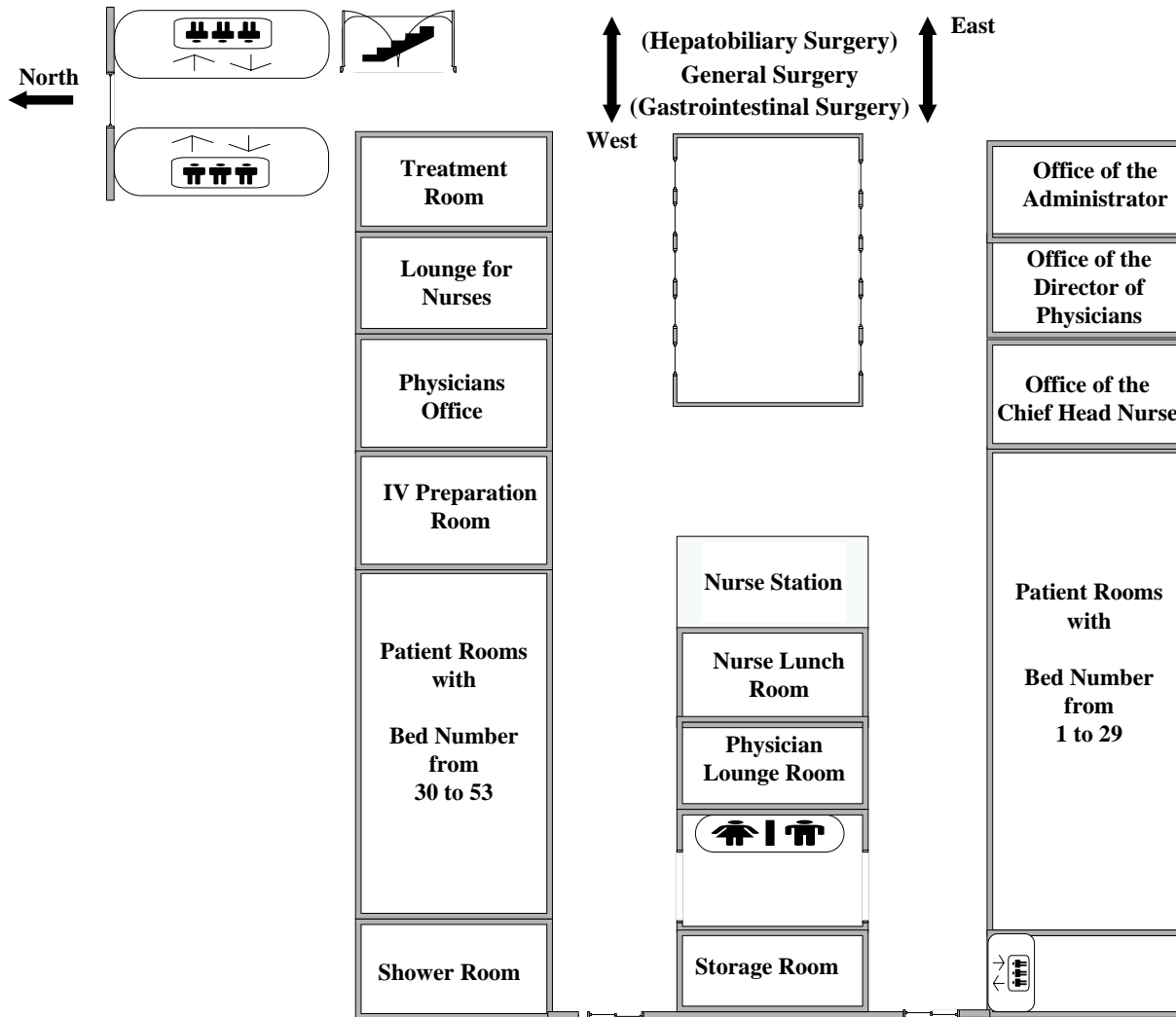


Figure 2: Floor Layout of the Study Patient Ward

Exploratory Level Study

Undisguised observation was performed in the western inpatient pharmacy and the study patient ward during the first visit from December 16 to December 30, 2009 and the second visit from July 12 to July 30, 2010. The objectives of the exploratory study were to obtain the information as follows:

1. Understand the current IV drug distribution process,
2. Understand the current IV drug preparation and administration processes,
3. Test the operational definition of medication administration errors,
4. Find the information needed to test the observation method,
5. Estimate the nature and rate of IV medication administration errors, and
6. Locate the source of the information of drug usage needed to identify the population of IV medications dispensed to each patient ward, and to estimate the sample size to be used in the explanatory study.

The characteristics of the independent variables and dependent variables of initial interest were defined at the level of an exploratory study.

Description of the Existing System

A new Hospital Information System (HIS), including nursing station and physician station, was installed on the General (Gastrointestinal) Surgery Patient Ward (the study site) in July 2010. However, handwriting on the patient charts was still the primary method of prescriptions.

Two printed forms were used by the ward: routine medication orders and non-routine medication orders.

The form for routine medication orders is shown in Figure 3. Routine medication orders were those given at regular and standardized intervals and were generally repeated more than twice, which were usually prescribed before 11 AM everyday. These orders were written on the form in black color. The patient identification number was on the top right corner of the page. The patient name, gender, age, the name of the department, the room number, and the bed number were required to appear on the top of the table. The medication orders included the starting date and time, drug names, dosage, route, administration frequency, discontinued date and time, and the signatures of the physician, the primary nurse, and the medical nurse. The physician, the primary nurse and the medicine nurse were required to sign after the starting time and the discontinuance time for routine orders.

The image shows a 'Long-term Medication Order' form (长期医嘱单) with handwritten entries. The form is titled '长期医嘱单' at the top center. It contains a table with columns for drug names, dosages, routes, and frequencies. The entries are written in black ink. There are several yellow star-shaped markers placed on the form, likely to highlight specific areas or errors. The form is placed on a surface, and a portion of a white bowl is visible on the left side.

Figure 3: Routine Medication Orders

The form for non-routine medication orders is shown in Figure 4. Non-routine medication orders were those repeated fewer than two times or were given at irregular intervals such as PRN orders and Pre-operation orders. Distinguished from the routine medication orders, they were written on the form in orange color. No expiration time was required. The physician only signed once after the starting time. The primary nurse and medical nurse signed once after the administration time.

医嘱时间	医嘱	医嘱剂量	执行时间
2010-7-10 8:30	NS 100ml		7:30
2010-7-10 8:45	NS 200ml		7:30
2010-7-10 9:00	NS 100ml		7:30
2010-7-10 9:15	NS 100ml		7:30
2010-7-10 9:30	NS 100ml		7:30
2010-7-10 9:45	NS 100ml		7:30
2010-7-10 10:00	NS 100ml		7:30
2010-7-10 10:15	NS 100ml		7:30
2010-7-10 10:30	NS 100ml		7:30
2010-7-10 10:45	NS 100ml		7:30
2010-7-10 11:00	NS 100ml		7:30
2010-7-10 11:15	NS 100ml		7:30
2010-7-10 11:30	NS 100ml		7:30
2010-7-10 11:45	NS 100ml		7:30
2010-7-10 12:00	NS 100ml		7:30
2010-7-10 12:15	NS 100ml		7:30
2010-7-10 12:30	NS 100ml		7:30
2010-7-10 12:45	NS 100ml		7:30
2010-7-10 13:00	NS 100ml		7:30
2010-7-10 13:15	NS 100ml		7:30
2010-7-10 13:30	NS 100ml		7:30
2010-7-10 13:45	NS 100ml		7:30
2010-7-10 14:00	NS 100ml		7:30
2010-7-10 14:15	NS 100ml		7:30
2010-7-10 14:30	NS 100ml		7:30
2010-7-10 14:45	NS 100ml		7:30
2010-7-10 15:00	NS 100ml		7:30
2010-7-10 15:15	NS 100ml		7:30
2010-7-10 15:30	NS 100ml		7:30
2010-7-10 15:45	NS 100ml		7:30
2010-7-10 16:00	NS 100ml		7:30
2010-7-10 16:15	NS 100ml		7:30
2010-7-10 16:30	NS 100ml		7:30
2010-7-10 16:45	NS 100ml		7:30
2010-7-10 17:00	NS 100ml		7:30
2010-7-10 17:15	NS 100ml		7:30
2010-7-10 17:30	NS 100ml		7:30
2010-7-10 17:45	NS 100ml		7:30
2010-7-10 18:00	NS 100ml		7:30
2010-7-10 18:15	NS 100ml		7:30
2010-7-10 18:30	NS 100ml		7:30
2010-7-10 18:45	NS 100ml		7:30
2010-7-10 19:00	NS 100ml		7:30
2010-7-10 19:15	NS 100ml		7:30
2010-7-10 19:30	NS 100ml		7:30
2010-7-10 19:45	NS 100ml		7:30
2010-7-10 20:00	NS 100ml		7:30
2010-7-10 20:15	NS 100ml		7:30
2010-7-10 20:30	NS 100ml		7:30
2010-7-10 20:45	NS 100ml		7:30
2010-7-10 21:00	NS 100ml		7:30
2010-7-10 21:15	NS 100ml		7:30
2010-7-10 21:30	NS 100ml		7:30
2010-7-10 21:45	NS 100ml		7:30
2010-7-10 22:00	NS 100ml		7:30
2010-7-10 22:15	NS 100ml		7:30
2010-7-10 22:30	NS 100ml		7:30
2010-7-10 22:45	NS 100ml		7:30
2010-7-10 23:00	NS 100ml		7:30
2010-7-10 23:15	NS 100ml		7:30
2010-7-10 23:30	NS 100ml		7:30
2010-7-10 23:45	NS 100ml		7:30
2010-7-10 24:00	NS 100ml		7:30

Figure 4: Non-Routine Medication Order

From 7:30 AM - 8:30 AM, the physicians checked the patients and adjusted IV orders orally to the medical nurses who would prepare the IV doses. Later, the physicians updated the orders on the patient charts.

The total IV doses were about 200-250 doses per day. Once daily was the most frequent administration (150-180 doses), followed by twice daily (BID) (30-40 doses) and three times daily (TID) (10-20 doses). The time for the once daily administration was 9 AM. The time for the BID administration was 9 AM and 3 PM. The time for the TID administration was 9 AM, 3 PM, and 9 PM.

TPN doses, which were all given peripherally by once daily, contained multiple additives such as Vitamin C injection, Sodium chloride injection concentrate (10%), Compound Amino Acid Injection (15-HBC) 250 ml, etc in the Kabiven TM PI fat emulsion bag. All the TPN doses were placed along the transcribed TPN doses the medication inspection sheet for each patient on the counter closely by an auxiliary worker. No label was provided on the Kabiven TM PI fat emulsion bag. The medical nurses prepared the TPN doses according to the transcribed TPN doses the medication inspection sheet. They transferred the ampoule additives into the glass solution bottles such as Compound Amino Acid Injection (15-HBC) 250 ml, and combined the glass solution bottles into the Kabiven TM PI fat emulsion bag using gravity flow. The patient name and the bed number were added on the Kabiven TM PI fat emulsion bag after the transferring process finished.

Non-TPN doses, which were given peripherally by once daily, BID or TID, contained one additive such as an antibiotic in a base solution of 250 ml of 5% Glucose Solution or 100 ml 0.9% Sodium Chloride Solution. The name of the additive, the dosage of the additive and the administration time were written on the back of the base solution bag. No patient information was marked on the base solution bag. The nurse added the additive into the base solution and mixed them as an assembly line. The patient name and

the bed number were added at the bedside before administering the mixed Non-TPN dose.

The orders for injectable medications were sent to the pharmacy before 11 AM through the HIS in an accumulated format on ward basis. In general, the delivery process would be finished within one hour, but during the rush hour it might take as long as two hours. The pharmacy delivered the accumulated injectable medications to each patient ward before 12 PM on a daily basis. For any emergency need, the HIS “prescription” would arrive at the pharmacy immediately. The average delivery times for non-routine injectable medication orders was 3-4 times/day.

The pharmacists were responsible for (1) receiving the medication orders from the nursing stations on the patient ward, (2) dispensing the IV drugs in bulk form upon their requisition, (3) dispensing the oral medicines in unit-dose forms upon their requisition, (4) maintaining the drug storage in the pharmacy, (5) providing clinical drug information to the nurses, and (6) collecting reports of adverse drug reactions from the patient wards.

Nurses were divided into four categories according to their duties: primary nurse, medicine nurse, medical nurse, and nursing care nurse.

The primary nurse was responsible for (1) attending the meeting with the physicians in the morning 7:30 - 8:30 AM, (2) transcribing the medical orders on the patient charts, (3) receiving new patients, transferring departments, changing beds and checking-out patients, (4) maintaining the medical item storage in the nursing station, and (5) assisting the communications among the physicians, the medicine nurses, and the medical nurses.

The medicine nurse was responsible for (1) receiving and confirming medication orders on the HIS, (2) comparing and checking the medication orders on the patient charts and on the HIS, (3) generating a whole list of medication orders for the entire day on the HIS, (4) sending the electronic whole list of medication orders to the pharmacy, (5) picking up the bulk package of medications from the pharmacy at 11:00 AM - 12:00 PM, and (6) checking the storage of medications in the unit.

The medical nurses were responsible for (1) transcribing IV medication orders to the medication inspection sheet with a carbon copy for each patient and putting the carbon copy on a patient's clip board, (2) transcribing IV medication orders for a whole day into a piece of paper as a "To Do List" for administration drugs, (3) preparing IV doses, (4) administering IV doses, checking the "To Do List" and signing the infusion speed and the signature on the patient clip board, and (5) circulating around the patient rooms to change the infusion bags as needed.

The Flowchart of the current medication distribution system is shown in Figure 5.

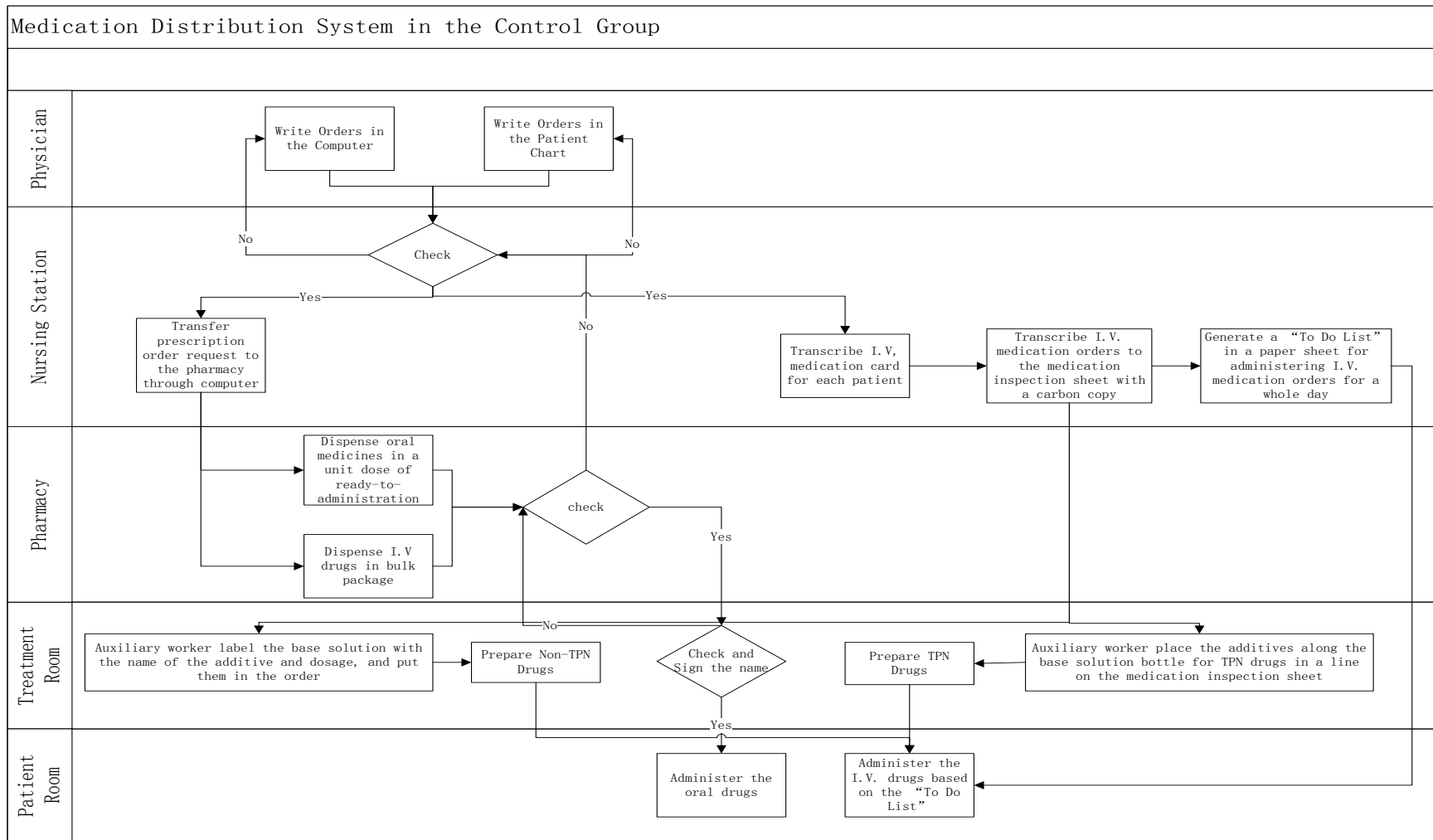


Figure 5: Flowchart of the Drug Distribution System in the Control Group

Explanatory Level Study

Population

The target population was defined as the TPN doses ordered, prepared and administered for the patients in the General Surgery Patient Ward during the observation period.

The 53 beds were 75%-90% occupied with 40 to 48 patients during the observation period. The TPN doses were about 50-100 doses for 10-15 patients per day and were all given once daily.

Sample

The sample was defined as the observed TPN doses, which were ordered, prepared and administered for the patients on the General Surgery Patient Ward.

The day shift from 8 AM to 3 PM was chosen for observation due to the high volume of IV administration doses given at this time period. A total of 517 ordered doses plus 4 unordered doses were observed in the Control group, 41.7% of the total prescribed TPN doses during the time periods of August 3 to August 13, 2011 and October 4 to October 13, 2011. A total of 675 ordered doses were observed in the Experimental group, 44.4% of the total prescribed TPN doses during the time periods of August 16 to August 25, 2011 and October 17 to October 26, 2011.

Sample Size Calculation

Cohen's d (Cohen, 1988) is defined as the difference between two means divided by a pooled standard deviation (S) for the data, shown in the following formula.

$$d = \frac{\bar{x}_1 - \bar{x}_2}{s}, \text{ where } s = \sqrt{\frac{(n_1 - 1)s_1^2 + (n_2 - 1)s_2^2}{n_1 + n_2}}, \text{ and}$$

$$s_N = \sqrt{\frac{1}{N} \sum_{i=1}^N (x_i - \bar{x})^2}.$$

Based on the pilot study that was used for the development of a Unit Dose Dispensing System with medication error rates for each individual observation period (shift) in the control and experimental groups at the University of Arkansas Medical Center by Barker and Colleagues (Barker, Heller, Brennan, & Sheldon, 1964), the effect size (Cohen's d) was calculated as 1.2 for two-tail test with α of 0.05. The sample size was estimated as 12 observation periods for each group with an average of 48 doses in each observation period with the power of 0.80.

Independent Variable (IV) and Dependent Variable (DV)

The Independent Variable was the intervention of the Unit Dose Dispensing System, which was installed in the Experimental group.

The Dependent Variable was medication errors of the TPN doses, which were observed and detected in the preparation and the administration processes.

The detailed characteristics of independent variable and dependent variable were described in the Concepts and Operational Definitions in Chapter 2.

Research Design

This study used Control and Experimental Design with the Cluster as the unit of

Randomization. A Cluster Randomized Trial or Group Randomized Trial (GRT) is a common design in clinical health care research in which clusters of individuals rather than individuals are randomly assigned into study groups (e.g., the group is randomly assigned, not the individual) (Murray, 1998).

The main reason to choose a Cluster Randomized Trial in this study was that the intervention of a Unit Dose Dispensing System could not be installed on individual basis. The clusters of doses for two units with 29 beds in one unit and 24 beds in the other unit on the General Surgery Ward were randomly assigned to the Control group or Experimental group by flipping a coin. It was also an administratively convenient design because the patients who had already been assigned into the beds according to their physicians were not affected by the group assignment.

The doses within each group were observed individually when they were prepared by the same group of medication nurses and administered to the patients at the routine time. Medication preparation and administration processes were directly observed by the Principal Investigator for each group both before and after the intervention of the Unit Dose Dispensing System was installed in the Experimental group. No changes were made in the Control group. The details of the observation method were described in the Data Collection Chapter.

The effect of the Unit Dose Dispensing System was measured by the Analysis of Covariance (ANCOVA) controlling the before-test as a covariate to find the difference of after-test between the Control and Experimental groups.

Structure

The structure of the study is shown in Figure 6 and Figure 7.

R O O

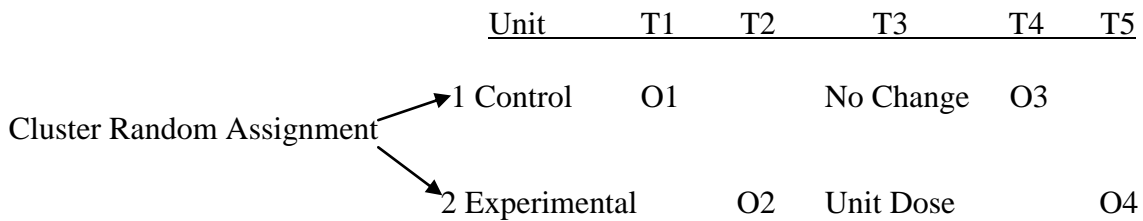
R O X O

R: Random Assignment

O: Measurement (Direct Observation)

X: Intervention in the Experimental group

Figure 6: Standard Control and Experimental Design with Random Assignment



T1, T2, T3, T4, T5: Time 1, Time 2, Time 3, Time 4, Time 5

O1 and O2: Observations before the intervention of Unit Dose

O3 and O4: Observations after the intervention of Unit Dose

Figure 7: Control and Experimental Design with Cluster Random Assignment

Controls

Selection Bias

The two units were selected from the same patient ward. The patients occupancy rates were similar in the two units.

The patients were assigned into the unit based on their physicians. Although the physicians in charge of each unit were different, the doses ordered in the two units had

similar nature and characteristics due to the similar disease states of the patients on the same ward.

The same group of nurses prepared the doses for both the Control group and Experimental group. These nurses worked for the two sections by rotation, which means the only difference for the two groups was the intervention.

The difference of additives per patient in the Control and Experimental groups were compared by one-way Analysis of Variance (ANOVA) in SPSS Software, Version 17.0. The results in Table 1 show that there was no significant difference ($F_{1,39} = 1.004$, $P = 0.323 > 0.05$) of the additives' complexity for the patient (prescribed additives for each patient) between the Control and Experimental groups. Further, their IV doses were prepared and administered by the same group of nurses centralized at the same time in the same room. Because of the above reasons, the two units used for the Control and Experimental groups were comparable at the same level.

Table 1: Difference of Additives per Patient between Control and Experimental Groups

Tests of Between-Subjects Effects

Dependent Variable: Doses_Per_Patient

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	3.361 ^a	1	3.361	1.004	.323
Intercept	2022.332	1	2022.332	603.993	.000
Group	3.361	1	3.361	1.004	.323
Error	130.582	39	3.348		
Total	2153.457	41			
Corrected Total	133.943	40			

a. R Squared = .025 (Adjusted R Squared = .000)

Random Errors

The doses in the two units were randomly assigned to the Control or Experimental group.

Internal Validities

During the observational periods, the observed nurses experienced no training or external education on medication safety and the observation instrument.

The purpose of the Control group was to minimize the external threats from maturation and instrumentation in the Experimental group. The doses were prepared and administered by the same group of medication nurses in both Control and Experimental groups, except for the difference of the Unit Dose Dispensing System. If the observed nurses in the Control group experienced influence from the maturation and observation instrument in the study, the effects should also be reflected in the Experimental group.

Data Collection Methods

The direct disguised observation method was first used as a method of detecting medication errors by Barker and McConnell (Barker & McConnell, 1962). In this study the direct undisguised observation method was used in both the preparation and administration processes to detect and measure the outcome of IV medication errors. The data collection forms are shown in Appendix E. After the purpose of the study was given to the observed nurses initially, the term “medication error” was purposely replaced by the term “medication accuracy” for acceptability to the observed nurses.

The observer was a current Ph.D. candidate in the Department of Pharmacy Care Systems at Auburn University, who obtained a B.S. of pharmacy from Shenyang Pharmaceutical University in China in 2000 and was trained and certified in the direct observation method (and skills) in July of 2008 at East Alabama Medical Center (EAMC) by Dr. Elizabeth Flynn.

The observation was performed in a non-judgmental and unobtrusive way. The observer accompanied the nurse who prepared the IV medications, witnessed the preparation processes, and recorded the information of the IV bag number, preparation time, patient's initial, room number and bed number, the base solution name, the volume of the base solution, the additive name, dosage form, strength, and the volume of the dose that the nurses added into the base solution bag. If the patient's information was not given on the base solution, the Principal Investigator put a number on the base solution bag as an identifier in order to match the the doses which were prepared and administered for the patient.

When the nurse administered the IV medications to the patients, the observer accompanied the nurse who delivered the IV bags and administered the IV bags at the bedside, wrote the patients' information and the administered IV information or the number marked on the IV bag by the Principal Investigator. The preparation notes and the administration notes were combined and matched for each patient and were later compared with the physician's orders to detect any IV medication errors.

The location of the observer and the layout (not to scale) of the IV preparation room are shown in Figure 8.

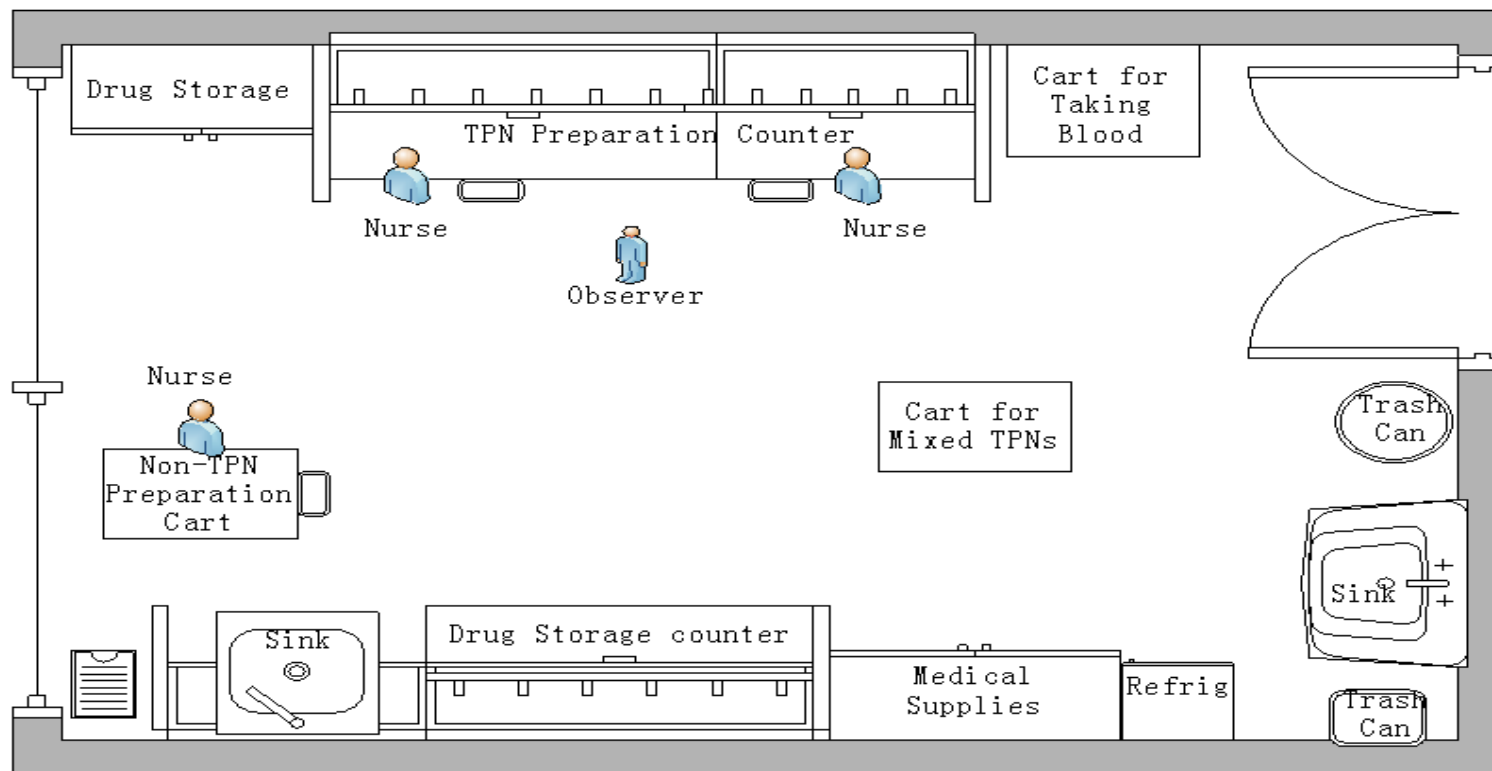


Figure 8: Layout of the IV Preparation Room and Location of the Observer

Chapter 5: Results

Data Collection

Study Subjects

After obtaining permission from the study hospital and approval from the Auburn University IRB (16-weeks of full board review process) on May 28, 2010, the summer months of 2010 were finally selected based on the convenience of the Principal Investigator.

After a lengthy discussion with the Director of pharmacy, a General Surgery Patient Ward with a high volume of IV medication orders was offered and approved for observation. The beds on this Patient Ward were divided into the two sides of the hallway (Racetrack design: rooms with #1-#29 beds on one side and rooms with #30-#53 beds on the other side). A Cluster Randomized Trial was selected for this study by flipping a coin to assign the beds on one side to the Control group and the beds on the other side to the Experimental group. The direct observation method was used to detect and measure medication errors.

Prior to data collection, the Principal Investigator had a meeting with the nurses who worked in the selected ward and who met the study inclusion criteria. The study inclusion criteria are described as follows:

1. Received a 3-year secondary nursing education and the Nursing Practice Certificate from the Ministry of Health,
2. Regularly employed more than one year at the study site,
3. Regularly prepared IV doses at the study site,

4. Regularly administered the IV doses at the study site, and
5. Age 19 or older.

Practical nursing students and new employees were excluded. Participating nurses were informed that their normal medication preparation and administration processes would be observed. The study was to evaluate the effect of the system changes, instead of the effect of the performance of individuals. Their personal information would not be released to anyone else including their supervisor. Confidentiality of data was established by coding the names of the nurses and the patients. The data were locked in a cabinet kept in the Principal Investigator's department with access by only the Principal Investigator herself. The observed nurses were those who agreed to participate in the investigation. Three out of the seventeen nurses were excluded due to pregnancy. The participants were told that they could withdraw from study at any time without jeopardizing the relationships between the participants and their employer. The observed nurses were asked not to change any of their normal routines and to continue their normal working performance during the observation.

Excluded Doses for Observation: Non-TPN, PRN and Chemotherapy

The Chief Head Nurse refused to install the Unit Dose Dispensing System on Non-TPN doses because of the concerns described as follows.

1. Extra workload might be involved if the Unit Dose Dispensing System is installed. If the Non-TPN doses were discontinued by the physician, the same doses can be kept for the use with another patient who was prescribed the same drugs without any extra work such as replacing the new label with a new patient's information.
2. The preparation time might be longer than the time in the existing system.

3. Nurses may be dissatisfied if they have to do extra work.
4. Currently, the Non-TPN doses were mixed as an assembly line; hence, the nurse used the same syringe to add the same additives to the same base solutions. If a unit dose system was installed, it may consume extra 50-60 syringes per day.
5. The current Non-TPN doses were labeled only with the additive to be added and the time of administration on the base solution bag. For example, the nurse only labeled “Ornidazole 2 ampoule, 9 AM” or “Ornidazole 2 ampoule, 3 PM” on the bag of 5% Glucose Solution. No patient’s information was labeled on the bag. Thus, if such an order for one patient is discontinued or changed, the mini bag can be kept for using without any label change for another patient who was ordered the same IV drugs. The Chief Head Nurse said that this would reduce the likelihood of complaint from rising incorrect patient information on the label.

PRN doses were excluded from the study because very few doses were ordered as PRN. Chemotherapy doses were also excluded from the study because of the safety issue. After regular IV doses were mixed, a medical nurse who prepared the chemotherapy drugs would ask other staff to leave the treatment room when she prepared the chemotherapy drugs. The protections included two layers of gloves (plastic and rubber gloves), cotton mask, and opening the windows. No laminar air flow hood was provided in the treatment room to prepare such chemotherapy drugs. This protocol would prohibit the observer from being present in the room while chemotherapy doses were prepared.

Included Doses for Observation: TPN doses

The Unit Dose Dispensing System was installed only on TPN doses. The data analysis was limited to TPN doses.

The day shift from 8 AM to 3 PM was chosen for observation due to the high volume of IV administration doses given at this time period. Since there was only one observer, each group was observed in sequence, both before and after the intervention was installed.

The observation of the Control group occurring before the intervention of the Unit-Dose Dispensing System was conducted from August 3 to August 13, 2010. The observation of the Control group occurring after the intervention of Unit-Dose Dispensing System was conducted from October 4 to October 13 2010. The Principal Investigator excluded 7 doses (pre-test) and 11 doses (post-test) from the T.O.E.s in the Control group because they did not meet apriori operational definitions. A final total of 517 ordered doses plus 4 unordered doses were analyzed for the statistical analysis in the Control group, 41.7% of the total prescribed TPN doses. The error frequencies detected for the Control group are shown in Table 2.

Table 2: TPN Error Frequencies and Rates in the Control Group

Error Category	Date (Year: 2010)											Overall
	Aug. 3	Aug. 4	Aug. 5	Aug. 6	Aug. 7	Aug. 8	Aug. 9	Aug. 10	Aug. 11	Aug. 12	Aug. 13	
Omission	4	0	0	0	0	1	0	0	0	0	0	5
Unordered dose	2	0	0	0	0	0	0	0	0	0	0	2
Wrong dose	2	2	1	1	1	0	0	1	1	0	0	9
Extra dose	0	0	0	0	0	0	0	0	0	0	0	0
Wrong time	0	0	0	0	0	0	0	0	0	0	0	0
Wrong route	0	0	0	0	0	0	0	0	0	0	0	0
Wrong administration rate	0	0	0	0	0	0	0	0	0	0	0	0
Total Errors	8	2	1	1	1	1	0	1	1	0	0	16
T.O.E.s	26	22	31	19	23	10	5	15	15	16	14	196
Patient Numbers	5	4	5	3	4	2	1	2	3	3	2	
Error Rate (%)	30.77	9.09	3.23	5.26	4.35	10.00	0	6.67	6.67	0	0	8.16
Error Category	Date (Year: 2010)											Overall
	Oct. 4	Oct. 5	Oct. 6	Oct. 7	Oct. 8	Oct. 9	Oct. 10	Oct. 11	Oct. 12	Oct. 13		
Omission	1	2	1	1	0	4	3	0	6	1	19	
Unordered dose	0	1	0	0	0	0	0	0	0	1	2	
Wrong dose	0	0	0	1	2	1	3	1	1	1	10	
Extra dose	0	0	0	0	0	0	0	0	0	0	0	
Wrong time	0	0	0	0	0	0	0	0	0	0	0	
Wrong route	0	0	0	0	0	0	0	0	0	0	0	
Wrong administration rate	0	0	0	0	0	0	0	0	0	0	0	
Total Errors	1	3	1	2	2	5	6	1	7	3	31	
T.O.E.s	27	21	39	25	25	44	40	33	36	35	325	
Patient Numbers	3	2	5	4	4	5	5	4	5	3		
Error Rate (%)	3.70	14.29	2.56	8.00	8.00	11.36	15.00	3.03	19.44	8.57	9.54	

The observation of the Experimental group occurring before the intervention of Unit-Dose Dispensing System was conducted from August 16 to August 25, 2010. The observation of the experiment group occurring after the intervention of Unit-Dose Dispensing System was conducted from October 17 to October 26 2010. The Principal Investigator excluded 14 doses (post-test) from the T.O.E.s because because they did not meet apriori operational definitions. A final total of 675 ordered doses were kept as the final observations for the statistical analysis in the Experimental group, 44.4% of the total prescribed TPN doses. The error frequencies detected for the Experimental group are shown in Table 3.

Table 3: TPN Error Frequencies and Rates in the Experimental Group

Error Category	Date (Year: 2010)										Overall
	Aug. 16	Aug. 17	Aug. 18	Aug. 19	Aug. 20	Aug. 21	Aug. 22	Aug. 23	Aug. 24	Aug. 25	
Omission	0	0	0	0	0	1	0	0	0	0	1
Unordered dose	0	0	0	0	0	0	0	0	0	0	0
Wrong dose	0	3	1	1	1	0	1	1	1	1	10
Extra dose	0	0	0	0	0	0	0	0	0	0	0
Wrong time	0	0	0	0	0	0	0	0	0	0	0
Wrong route	0	0	0	0	0	0	0	0	0	0	0
Wrong administration rate	0	0	0	0	0	0	0	0	0	0	0
Total Errors	0	3	1	1	1	1	1	1	1	1	11
T.O.E.s	23	25	25	29	35	31	31	22	27	27	275
Patient Number	4	5	5	6	6	6	6	4	4	4	
Error Rate (%)	0	12.00	4.00	3.45	2.86	3.23	3.23	4.55	3.70	3.70	4.00
Error Category	Date (Year: 2010)										Overall
	Oct. 17	Oct. 18	Oct. 19	Oct. 20	Oct. 21	Oct. 22	Oct. 23	Oct. 24	Oct. 25	Oct. 26	
Omission	0	1	0	0	1	0	0	2	1	0	5
Unordered dose	0	0	0	0	0	0	0	0	0	0	0
Wrong dose	0	0	0	0	0	0	0	0	0	0	0
Extra dose	0	0	0	0	0	0	0	0	0	0	0
Wrong time	0	0	0	0	0	0	0	0	0	0	0
Wrong route	0	0	0	0	0	0	0	0	0	0	0
Wrong administration rate	0	0	0	0	0	0	0	0	0	0	0
Total Errors	0	1	0	0	1	0	0	2	1	0	5
T.O.E.s	39	49	47	35	38	30	42	38	44	38	400
Patient Number	4	6	5	4	4	3	5	4	5	4	
Error Rate (%)	0	2.04	0	0	2.63	0	0	5.26	2.27	0	1.25

Deficiencies of the Current System

The Principal Investigator tabulated all the errors and listed the details (e.g., clues to cause) about the deviations from the physician orders. In the baseline of the Control and Experimental groups, deficiencies of the current system were summarized based on clues to the causes of the errors: (1) handwritten transcriptions, (2) lacking insulin volume label, (3) limited shelf space, and (4) lacking double check before the preparation.

Clues to the causes of the errors provided the information of deficiencies of the current system which were considered to design a Unit Dose Dispensing System for this Chinese hospital.

Handwritten Transcriptions

Among the 27 detected errors, 9 errors (33%) were due to miscommunication of badly handwritten transcriptions. Unit of volume was another big issue involved in badly handwritten transcriptions. Some nurses transcribed ampoule as the unit; some nurses transcribed International Unit (IU) as the unit; some nurses did not transcribe the unit; and some nurses transcribed Milliliter (ml) as the unit. Clues to the causes of errors indicated that the unit which was transcribed by the nurses caused confusion to the auxiliary worker who placed the doses on the counter before the preparation, resulting in errors.

Lacking Insulin Volume Label

Among the 27 detected errors, 9 wrong dose errors (33%) were due to wrong calculation of the insulin volume and 1 omission error (4%) was contributed by two nurses -- both of whom forgot to add insulin for the patient.

Physicians prescribed only the ratio of insulin to glucose -- the insulin volumes were not calculated when the nurses transcribed the orders. The preparation nurses calculated the insulin volume just at the time when they mixed the TPNs.

Limited Shelf Space

Among the 27 detected errors, 4 errors (15%) may have been due to limited shelf space. Some ampoules for one patient were accidentally mixed with the doses of the adjacent patient. The nurse usually opened all the ampoules to be added in the TPNs and placed them closely together. The opened ampoule sometimes fell over and the dose spilled on the counter.

Lacking Double Check before the Preparation

Among the 27 detected errors, 2 errors (7%) may have been prevented by a double check after the auxiliary worker failed to place the doses on the counter before the preparation. Although the preparation nurses were asked to double check the doses before the preparation, however, this activity was usually omitted during the rush hours in the morning or was interrupted by other on-call tasks, such as a telephone call, a question from a physician, or withdrawal of the patients' blood.

Error Descriptions Summary

The error descriptions for the Control group are shown in Table 4 and 5. The error descriptions for the Experimental group are shown in Table 6 and 7.

Table 4: TPN Error Descriptions in the Control Group, Before (August 3- August 14, 2010)

Day	Error Number	Patient	Order	Dose given	Error Category	Implications (Clues to cause)
1	1	2	15% KCl 10 ml, added in the TPN, once daily	15% KCl 8 ml was added in the TPN	Wrong dose	The nurse's elbow was hit by somebody accidentally when withdrawing the liquid
1	2	8	15% KCl 20 ml, added in the TPN, once daily	None	Omission	Reasons: 1. This patient's doses were mixed with the adjacent patient's doses; 2. The nurse was helping a new nurse to mix the TPN and missed checking the list
1	3	8	10% NaCl 20 ml, added in the TPN, once daily	None	Omission	Reasons: 1. This patient's doses were mixed with the adjacent patient's doses; 2. The nurse was helping a new nurse to mix the TPN and missed checking the list
1	4	8	Vitamin C 3 g (7.5 ml), added in the TPN, once daily	None	Omission	Reasons: 1. The auxiliary worker failed to place this dose on the counter; 2. The nurse was helping a new nurse to mix the TPN and missed checking the list
1	5	22	15% KCl 10 ml, added in the TPN, once daily	15% KCl 30 ml was added in the TPN	Wrong dose	Reasons: 1. Adjacent patient's doses were mixed with this patient's doses; 2. The nurse didn't check the list and added them all.
1	6	22	None	10% NaCl 20 ml was added in the TPN	Unordered dose	Reasons: 1. Adjacent patient's doses were mixed with this patient's doses; 2. The nurse didn't check the list and added them all.
1	7	23	Vitamin K1 20 mg, added in the TPN, once daily	None	Omission	Handwritten of "VK1 2 ampoules" looked like "V/C, 2 ampoules".

Table 4: (Continued)

Day	Error Number	Patient	Order	Dose given	Error Category	Implications (Clues to cause)
1	8	23	None	Vitamin C 2 Ampoules were added in the TPN	Unordered dose	Handwritten of “VK1 2 ampoules” looked like “V/C, 2 ampoules”.
2	1	8	15% KCl 30 ml, added in the TPN, once daily	15% KCl 20 ml was added in the TPN	Wrong dose	The nurse missed transcribing this because Physician added 15% KCl 10 ml to the existed 15% KCl 20 ml in the TPN on a different day.
2	2	23	Ratio of insulin to Glucose 1:2.5, added in the TPN, once daily	Insulin 24 IU (0.6 ml) was added in the TPN	Wrong dose	40 IU (1 ml) was the volume that should have been given. The nurse estimated wrong, without calculation. The ratio of insulin to glucose is 1:2.5. TPN included Kabiven TM PI (100 g glucose). 100 g glucose should add 40 IU insulin (Insulin=100/2.5=40 IU). The insulin strength is 400 iu: 10 ml.
3	1	29	Ratio of insulin to Glucose 1:4, added in the TPN, once daily	Insulin 24 IU (0.6 ml) was added in the TPN	Wrong dose	56 IU (1.4 ml) was the volume that should have been given. The nurse forgot to add 50% Glucose solution 250 ml when calculating total glucose. The ratio of insulin to glucose is 1:4. TPN included Kabiven TM PI (100 g glucose) and 50% Glucose solution 250 ml, therefore, TPN had 225 g glucose. 100 g glucose should add 56 IU insulin (Insulin=225/4=56 IU). The insulin strength is 400 iu: 10 ml.
4	1	29	Ratio of insulin to Glucose 1:4, added in the TPN, once daily	Insulin 24 IU (0.6 ml) was added in the TPN	Wrong dose	56 IU (1.4 ml) was the volume that should have been given. The nurse forgot to add 50% Glucose solution 250 ml when calculating total glucose.

Table 4: (Continued)

Day	Error Number	Patient	Order	Dose given	Error Category	Implications (Clues to cause)
5	1	29	Ratio of insulin to Glucose 1:4, added in the TPN, once daily	Insulin 24 IU (0.6 ml) was added in the TPN	Wrong dose	56 IU (1.4 ml) was the volume that should have been given. The nurse forgot to add 50% Glucose solution 250 ml when calculating total glucose.
6	1	3	Ratio of insulin to Glucose 1:5, added in the TPN, once daily	None	Omission	The first nurse added additives (Vitamin K1 2 mg, Vitamin C 2 g, and Potassium Aspartate and Magnesium Aspartate Injection 50 ml) into the bottle of N(2)-L-alanyl-L-glutamine for injection, except insulin. The second nurse forgot to add insulin when she filled the liquid in the bottle of N(2)-L-alanyl-L-glutamine for injection into the 1440 ml bag of Kabiven TM PI bag.
7	None	None	None	None	None	None
8	1	29	Ratio of insulin to Glucose 1:4, added in the TPN, once daily	Insulin 24 IU (0.6 ml) was added in the TPN	Wrong dose	56 IU (1.4 ml) was the volume that should have been given. The nurse forgot to add 50% Glucose solution 250 ml when calculating total glucose.
9	1	2	Ratio of insulin to Glucose 1:6, added in the TPN, once daily	Insulin 8 IU (0.2 ml) was added in the TPN	Wrong dose	16 IU (0.4 ml) was the volume that should have been given. Nurse estimated wrong, without calculation. The ratio of insulin to glucose is 1:6. TPN has Kabiven TM PI (100 g glucose). 100 g glucose should add 16 IU insulin (Insulin=100/6=16 IU). The insulin strength is 400 iu: 10 ml.
10	None	None	None	None	None	None
11	None	None	None	None	None	None

Table 5: TPN Error Descriptions in the Control Group, After (October 4- October 13, 2010)

Day	Error	Patient	Order	Dose given	Error Category	Implications (Clues to cause)
1	1	23	Ratio of insulin to Glucose 1:5, added in the TPN	None	Omission	One nurse left insulin to be added by the next nurse. It happened that both nurses didn't add insulin in the TPN.
2	1	7	Ratio of insulin to Glucose 1:5, added in the TPN	None	Omission	One nurse left insulin to be added by the next nurse. It happened that both nurses didn't add insulin in the TPN.
2	2	15	Water-Soluble Vitamin For Injection 0.5 g, added in the TPN, once daily	None	Omission	This dose was not placed on the counter by the auxiliary worker because there was no supply. The nurse intended to give the drug of Compound 12-Vitamins for Injection.
2	3	15	None	Compound 12-Vitamins for Injection 0.5 g was added in the TPN	Unordered dose	The nurse intended to give the drug of Compound 12-Vitamins for Injection for Injection because the Water-Soluble Vitamin for Injection was no delivered from the pharmacy.
3	1	17	Ratio of insulin to Glucose 1:4, added in the TPN, once daily	None	Omission	Insulin dose was transcribed on the top line of the TPNs, instead of the bottom line as normal, therefore, the nurse may not notice it when preparing.
4	1	7	Ratio of insulin to Glucose 1:5, added in the TPN, once daily	Insulin 28 IU (0.7 ml) was added in the TPN	Wrong dose	20 IU (0.5 ml) was the volume that should be given. The nurse estimated wrong, without calculation. The ratio of insulin to glucose is 1:5. TPN included Kabiven TM PI (100 g glucose). 100 g glucose should add 20 IU insulin (Insulin=100/5=20 IU). The insulin strength is 400 iu: 10 ml.

Table 5: (Continued)

Day	Error Number	Patient	Order	Dose given	Error Category	Implications (Clues to cause)
4	2	8	Vitamin C 3 g (7.5 ml), added in the TPN, once daily	None	Omission	The auxiliary worker failed to place this dose on the counter. The nurse checked but didn't find it when preparing.
5	1	7	Ratio of insulin to Glucose 1:5, added in the TPN, once daily	Insulin 24 IU (0.6 ml) was added in the TPN	Wrong dose	20 IU (0.5 ml) was the volume that should have been given. The volume was estimated by the nurse without calculation. The ratio of insulin to glucose is 1:5. TPN included Kabiven TM PI (100 g glucose). 100 g glucose should add 20 IU insulin (Insulin=100/5=20 IU). The insulin strength is 400 iu: 10 ml.
5	2	10	Vitamin C 3 g (7.5 ml), added in the TPN, once daily	Vitamin C 4 ml was added in the TPN	Wrong dose	The opened vitamin C ampoule fell over and some liquid spilled due to limited shelf space.
6	1	12	Ratio of insulin to Glucose 1:5, added in the TPN, once daily	None	Omission	The nurse was talking to another preparation nurse. The insulin 20 IU (0.5 ml) was not given in the TPN.
6		13	Vitamin C 3 g (7.5 ml), added in the TPN, once daily	One ampoule of already turned yellow.	Other	One ampoule of Vitamin C turned yellow. The nurse didn't change it.
6	2	13	Vitamin K1 20 mg (2 ml), add in the TPN, once daily	None	Omission	Usually Vitamin K1 will not be placed on the counter in order to avoid the sunshine. The preparation nurse only mixed the doses dispensed on the counter.

Table 5: (Continued)

Day	Error Number	Patient	Order	Dose given	Error Category	Implications (Clues to cause)
6	3	19	10% NaCl 50 ml, added in the TPN, once daily	None	Omission	The auxiliary worker didn't place this drug on the counter and the preparation nurse didn't notice it.
6	4	20	10% NaCl 50 ml, added in the TPN, once daily	None	Omission	The nurse transcribed 10% NaCl 50 on the top line of TPN. The auxiliary worker failed to place this drug and the preparation nurse didn't notice it.
6	5	24	15% KCl 30 ml, added in the TPN, once daily	15% KCl 20 ml was added in the TPN	Wrong dose	Physician changed the number 20 ml to 30 ml on the number itself. The nurse transcribed dosage as 20 ml on the drug list.
7	1	4	Ratio of insulin to the Glucose 1:4, added in the TPN, once daily	16 IU (0.4 ml) Insulin was added in the TPN	Wrong dose	24 IU (0.6 ml) was the volume that should be given. The ratio 1:4 was transcribed like 1:6
7	2	6	10% NaCl 20 ml, added in the TPN, once daily	10% NaCl 30 ml was added in the TPN	Wrong dose	One extra ampoule of 10% NaCl was placed on the counter and the nurse didn't notice it.
7	3	13	Vitamin C 3 g (7.5 ml), added into the TPN, once daily	None	Omission	The auxiliary worker didn't place Vitamin C on the counter. The preparation nurse didn't find it when preparing.
7	4	13	Vitamin K1 20 mg, added in the TPN, once daily	None	Omission	The preparation nurse didn't pick up the Vitamin K1 from the shelf when preparing.

Table 5: (Continued)

Day	Error Number	Patient	Order	Dose given	Error Category	Implications (Clues to cause)
7	5	15	10% Calcium Gluconate 10 ml, added in the TPN, once daily	10% Calcium Gluconate 2 ml was added in the TPN	Wrong dose	The nurse usually opened all the ampoules to be added in the TPN and placed them closely. The opened ampoule fell over and the drug spilled on the counter.
7	6	18	Trace Elements for Injection (Addammel) 10 ml, added in the TPN, once daily	None	Omission	The auxiliary worker failed to place this dose on the counter. The nurse didn't notice the omitted dose.
8	1	7	Ratio of insulin to Glucose 1:5, added in the TPN, once daily	Insulin 24 IU (0.6 ml) was added in the TPN	Wrong dose	30 IU (0.75 ml) was the volume that should be given. The nurse estimated wrong, without calculation. The ratio of insulin to glucose is 1:5. TPN included Kabiven TM PI and 10% Glucose solution 500 ml. Therefore, TPN had 150 g glucose. 100 g glucose should add 30 IU insulin (Insulin=150/5=30 IU). The insulin strength is 400 iu: 10 ml.
9	1	8	Sodium Glycerophosphate Injection 10 ml, added in the TPN, once daily	None	Omission	The auxiliary worker failed to place this dose on the counter. The nurse didn't find it.
9	2	18	15% KCl 20 ml, added in the TPN, once daily	None	Omission	The nurse didn't transcribe this dose on the drug list.

Table 5: (Continued)

Day	Error Number	Patient	Order	Dose given	Error Category	Implications (Clues to cause)
9	3	23	Sodium Glycerophosphate Injection 10 ml, added in the TPN, once daily	None	Omission	The auxiliary worker failed to place this dose on the counter. The nurse was talking to another nurse and didn't notice the omitted doses.
9	4	23	Trace Elements 10 ml, added in the TPN, once daily	None	Omission	The auxiliary worker failed to place this dose on the counter. The nurse was talking to another nurse and didn't notice the omitted doses.
9	5	23	Water-Soluble Vitamin For Injection, added in the TPN, once daily	None	Omission	The auxiliary worker failed to place this dose on the counter. The nurse was talking to another nurse and didn't notice the omitted doses.
9	6	23	Fat-Soluble vitamin injection 10 ml, added in the TPN, once daily	None	Omission	The auxiliary worker failed to place this dose on the counter. The nurse was talking to another nurse and didn't notice the omitted doses.
9	7	23	Ratio of insulin to Glucose 1:4, added into the TPN, once daily	Insulin 40 IU (1 ml) was added in the TPN	Wrong dose	50 IU (1.25 ml) was the volume that should be given. The nurse forgot to add 5% Glucose solution 1000 ml when calculating total glucose. The ratio of insulin to glucose is 1:4. TPN included Kabiven TM PI, 10% Glucose Solution 500 ml and 5% Glucose Chloride Sodium Solution 1000 ml. Therefore, TPN had 200 g glucose. 200 g glucose should add 50 IU insulin (Insulin=200/4=50 IU). The insulin strength is 400 iu: 10 ml.

Table 5: (Continued)

Day	Error Number	Patient	Order	Dose given	Error Category	Implications (Clues to cause)
10	1	3	Ratio of insulin to Glucose 1:3, added in the TPN, once daily	Insulin 32 IU (0.8 ml) was added in the TPN	Wrong dose	42 IU (1.05 ml) was the volume that should be given. The nurse forgot to add 5% Glucose solution 500 ml when calculating total glucose. The ratio of insulin to glucose is 1:3. TPN included Kabiven TM PI (100 g glucose) and 5% Glucose solution 500 ml. Therefore, TPN had 125 g glucose. 125 g glucose should add 42 IU insulin (Insulin=125/3=42 IU). The insulin strength is 400 iu: 10 ml.
10	2	23	Water-Soluble Vitamin Powder for Injection 0.5 g, added in the TPN, once daily	None	Omission	The auxiliary worker failed to place this dose on the counter because of no supply. The nurse omitted the dose of Water-Soluble Vitamin for injection because there was no supply. She gave the dose of 12 Vitamins for Injection instead.
10	3	23	None	Compound 12 Vitamins for Injection 0.5 g was dissolved and added in the TPN	Unordered dose	The auxiliary worker failed to place this dose on the counter because of no supply. The nurse omitted the dose of Water-Soluble Vitamin for injection because there was no supply. She gave the dose of 12 Vitamins for Injection instead.

Table 6: TPN Error Descriptions in the Experimental Group, Before (August 16- August 25, 2010)

Day	Error Number	Patient	Order	Dose given	Error Category	Implications (Clues to cause)
1	None	None	None	None	None	None
2	1	50	10% NaCl 100 ml, added in the TPN, once daily	10% NaCl 10 ml was added in the TPN	Wrong dose (10 fold)	Reasons: 1. The nurse transcribed as 10% NaCl 10, without a unit along with the number. 2. The auxiliary worker only dispensed 10 ml (1 ampoule) of 10% NaCl.
2	2	51	Vitamin C 3 g (7.5 ml), added in the TPN, once daily	Vitamin C 5 ml was added in the TPN	Wrong dose	7.5 ml was the volume should be added in the TPN. The handwritten 3 g looked like 2 g.
2	3	53	Vitamin C 3 g (7.5 ml), added in the TPN, once daily	Vitamin C 5 ml was added in the TPN	Wrong dose	7.5 ml was the volume should be added in the TPN. Reason: The handwritten 3 g looked like 2 g.
3	1	50	10% NaCl 100 ml, added in the TPN, once daily	10% NaCl 10 ml was added in the TPN	Wrong dose (10 fold)	Reasons: 1. The nurse transcribed as 10% NaCl 10, without a unit along with the number. 2. The auxiliary worker only dispensed 10 ml (1 ampoule) of 10% NaCl
4	1	50	10% NaCl 100 ml, added in the TPN, once daily	10% NaCl 10 ml was added in the TPN	Wrong dose (10 fold)	Reasons: 1. The nurse transcribed as 10% NaCl 10, without a unit along with the number. 2. The auxiliary worker only dispensed 10 ml (1 ampoule) of 10% NaCl
5	1	50	10% NaCl 100 ml, added in the TPN, once daily	10% NaCl 10 ml was added in the TPN	Wrong dose (10 fold)	Reasons: 1. The nurse transcribed as 10% NaCl 10, without a unit along with the number. 2. The auxiliary worker only dispensed 10 ml (1 ampoule) of 10% NaCl

Table 6: (Continued)

Day	Error Number	Patient	Order	Dose given	Error Category	Implications (Clues to cause)
6	1	44	15% KCl 10 ml, added in the TPN, once daily	None	Omission	The 15% KCl was not placed on the counter by the auxiliary worker.
7	1	40	N(2)-L-alanyl-L-glutamine for injection 100 ml, added in the TPN, once daily	N(2)-L-alanyl-L-glutamine for injection 150 ml was added in the TPN	Wrong dose	Previous nurse added additives of Vitamin C 3 g, and 10% NaCl 50 ml in the bottle of N(2)-L-alanyl-L-glutamine for injection 50 ml. The second nurse took an extra new N(2)-L-alanyl-L-glutamine for injection 50 ml, because she assumed that bottle only had additives.
8	1	44	Ratio of insulin to Glucose 1:6, added in the TPN, once daily	Insulin 20 IU (0.5 ml) was added in the TPN	Wrong dose	16 IU (0.4 ml) was the volume that should be given. The nurse estimated wrong, without calculation. The ratio of insulin to glucose is 1:6. TPN included Kabiven TM PI (100 g glucose). 100 g glucose should add 16 IU insulin (Insulin=100/6=16 IU). The insulin strength is 400 iu: 10 ml.
9	1	44	Ratio of insulin to Glucose 1:6, added in the TPN, once daily	Insulin 20 IU (0.5 ml) was added in the TPN	Wrong dose	16 IU (0.4 ml) was the volume that should be given. The volume was estimated by the nurse without calculation. The ratio of insulin to glucose is 1:6. TPN has Kabiven TM PI(100 g glucose). 100 g glucose should add 16 IU insulin (Insulin=100/6=16 IU). The insulin strength is 400 iu: 10 ml.
10	1	30	Ratio of insulin to Glucose 1:2.5, added in the TPN, once daily	Insulin 56 IU (1.4 ml) was added in the TPN	Wrong dose	50 IU (1.25 ml) was the volume that should be given. The nurse estimated wrong, without calculation. The ratio of insulin to glucose is 1:2.5. TPN included Kabiven TM PI and 5% Glucose and Sodium Chloride solution 500 ml. Therefore, TPN had 125 g glucose. 125 g glucose should add 50 IU insulin (Insulin=125/2.5=50 IU). The insulin strength is 400 iu: 10 ml.

Table 7: TPN Error Descriptions in the Experimental Group, After (October 17- October 26, 2010)

Day	Error Number	Patient	Order	Dose given	Error Category	Implications (Clues to cause)
1	None	None	None	None	None	None
2	1	36	Coenzyme Complex for Injection 200 IU, added in the TPN, once daily	None	Omission	Coenzyme Complex for Injections were not delivered from the Pharmacy - unavailable
3	None	None	None	None	None	None
4	None	None	None	None	None	None
5	1	47	Trace Elements 10 ml, added in the TPN, once daily	None	Omission	Trace elements were not delivered from the Pharmacy - unavailable
6	None	None	None	None	None	None
7	None	None	None	None	None	None
8	1	41	Coenzyme Complex for Injection 200 IU, added in the TPN, once daily	None	Omission	Coenzyme Complex for Injections were not delivered from the Pharmacy - unavailable
8	2	41	Water-Soluble Vitamin for Injection 0.5 g, added in the TPN, once daily	None	Omission	Water-Soluble Vitamin for Injections were not delivered from the Pharmacy - unavailable
9	1	41	Water-Soluble Vitamin for Injection 0.5 g, added in the TPN, once daily	None	Omission	Water-Soluble Vitamin for Injections were not delivered from the Pharmacy - unavailable
10	None	None	None	None	None	None

Negotiations of the Experimental System Changes for Unit Dose

After studying the HIS physician station information (Figure 9), the Principal Investigator found that it was possible to print electronic IV orders from the computer in the nurse's station.

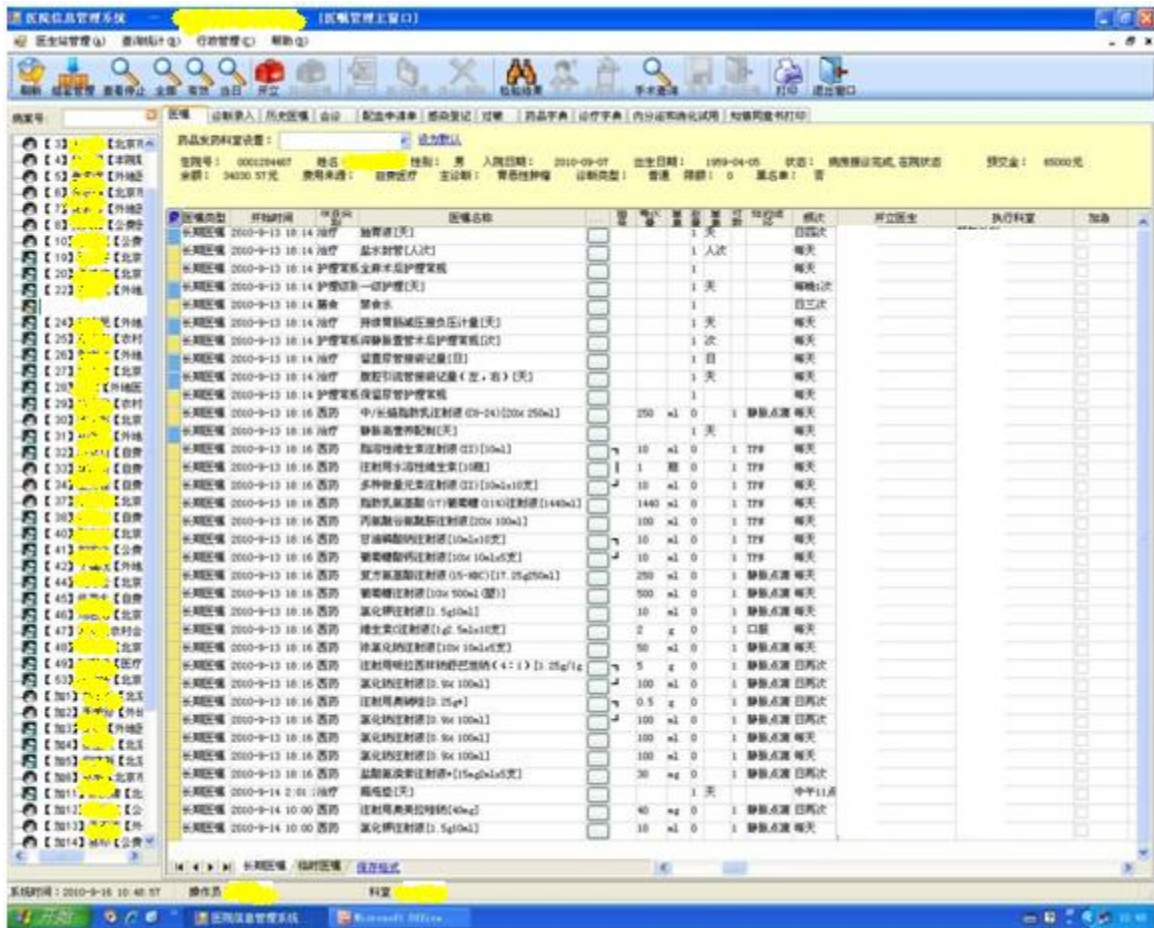


Figure 9: Physician Station of the HIS

However, in order to achieve the safety and efficiency of machine printed order in organized groups, the physicians would have to accept the suggested changes in prescribing as follows.

1. For TPN doses (Table 8):
 - a. Prescribe the base solution of Kabiven TM PI (1440 ml fat emulsion bag) as a main order,
 - b. Prescribe the additives which should be added into the base solution as the sub orders, and
 - c. Select the administration route as “TPN” in the HIS.

Table 8: The Suggestion for TPN Dose Prescription: an Example

	Drug Name	Volume	Route	Frequency
Main Order	Kabiven TM PI	1440 ml	TPN	Once Daily
Sub Order	20% Fat Emulsion Injection (C8-24)	250 ml		
Sub Order	10% Calcium Gluconate	10 ml		
Sub Order	15% KCl Injection (1.5 g: 10 ml)	20 ml		
Sub Order	Vitamin C Injection (1 g: 2.5 ml)	7.5 ml		
Sub Order	Insulin	0.8 ml		

2. For Non-TPN doses (Table 9):
 - a. Prescribe the base solution of Glucose Solution or Sodium Chloride Solution as a main order,
 - b. Prescribe the additive such as the antibiotic drug as a sub order, and
 - c. Select the administration route as “IV infusion” in the HIS.

Table 9: The Suggestion for Non-TPN Dose: an Example

	Drug Name	Volume	Route	Frequency
Main Order	5% Glucose Solution	250 ml	IV Infusion	BID
Sub Order	Orinidazole for Injection (0.25 g / ampoule)	0.5 g		

3. For the IV push doses (Table 10) : Select the administration route as the “IV push” in the HIS

Table 10: The Suggestion for IV Push Dose: an Example

	Drug Name	Volume	Route	Frequency
Order	Ambroxol Hydrochloride Injection (15 mg: 2 ml)	6 ml	IV Push	BID

On September 7 2010, the Principal Investigator met with the Director of the Pharmacy and a group of the clinical pharmacists, and introduced the Unit-Dose Dispensing System as would be defined to the Experimental group. The group was told of the potential problems which might be faced during the installation, and asked for their opinions and suggestions. Some

examples of errors detected were shown to the clinical pharmacists, after all were asked and agreed not to release any information about the errors to any nurse in the study patient ward.

After agreement on the changes to be made to the Unit Dose Dispensing System to be installed, a clinical pharmacist was assigned to assist as a part of the Unit Dose Dispensing System. Other agreements during this meeting which became part of the operational definition of the new system are as follows:

- If the doctor disagreed to the suggested changes in prescribing, the clinical pharmacist would try to help enter and generate a printable prescription (drug list and label).
- The Director of the Pharmacy would help the Principal Investigator discuss the preparation and administration changes with the Chief Head Nurse.
- The Director of the Pharmacy would help the Principal Investigator discuss physician cooperation with the Director of the Physicians on the study ward.

The Director of the Pharmacy arranged a meeting to negotiate the changes in the IV preparation and administration processes with the Chief Head Nurse. The Principal Investigator showed the Chief Head Nurse the evidence of some of the errors detected and the evidence of how such errors were typically prevented by Unit-Dose Dispensing Systems. The Chief Head Nurse only showed a great interest in the potential of machine-printed labels and the electronic IV orders to replace the handwritten transcriptions and improve the efficiency of their work, but she insisted on the status quo of the existing preparation and administration system procedures.

On September 14, 2010, the Director of Physicians agreed for the Principal Investigator to make a 10-minute PowerPoint presentation about the few changes the physicians would be asked to make in prescribing. Unfortunately, the presentation of the proposed changes was interrupted by the Director of the Physicians because he said there was no obvious improvement

in the efficiency for the physicians.

The Principal Investigator returned to the original idea of manually reentering each order in the Excel file (Office 2007). The Principal Investigator and the clinical pharmacist set up the medicine Excel file (Office 2007) for the patients on September 16-17, 2010. After the discussion with the Chief Head Nurse, the Unit-Dose Dispensing Concept was tested on the TPNs in the Experimental group from September 18-September 30, 2010 (Appendix I).

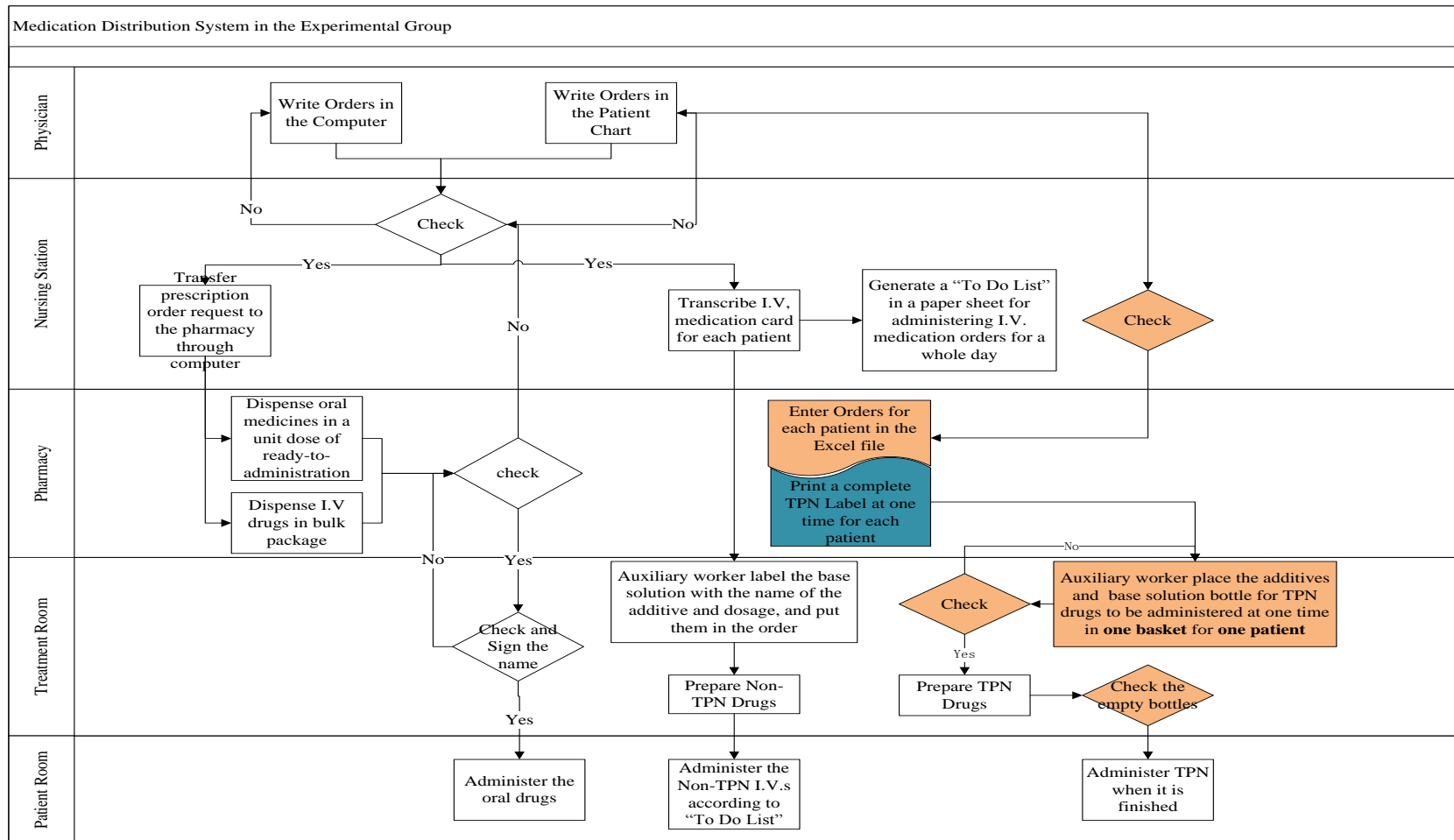
A checklist used to measure the progress of the installation of the Unit Dose Dispensing System is described in Table 11.

Table 11: Checklist for Measuring the Unit Dose Dispensing System Installation

A. IV ORDER	
1. Pharmacist reviews paper drug orders for prescribing accuracy, consulting with physician if necessary.	Checked
2. Orders are re-entered into the master order file (Excel Office 2007) for each patient including patient's full name, age, bed number, dosage form, dosage (insulin dosage is calculated into volume), and administration time.	Checked
3. Medication orders are filed, updated and sent to the nurse division.	Checked
4. Orders are printed out in cumulative list of all active drug orders for each patient (drug list or pick list) at both the pharmacy (drug profile) and the nursing division Medication Administration Record (MAR).	Checked
B. IV DISPENSING	
1. IV nurse (or auxiliary worker) uses Pick List to pick all doses scheduled for administration to each patient at one administration time, places them in a separate basket for each patient, signs or initials on the labels, and has them verified by a pharmacist.	Checked
1.1. Pharmacist checks doses for deterioration visually, and expiry date, before admixture.	Checked
2. Label is generated, reviewed by pharmacist for changes needed, comparing label to order.	Checked
2.1. Name and bed number are prominent on top of label.	Checked
2.2. Name of base fluid is on label	Checked
2.3. Name of each active ingredient and the amount of dose with unit of concentration are on label	Checked
2.4. Brand name is close to generic name.	Not Applicable

2.5. Administration time is on label.	Checked
2.6. Initials of pickers, preparing admixture technicians and review pharmacist are on label.	Checked
2.7. Signature space for administration nurse name is on label.	Checked
2.8. Date Dispensed is on label	Checked
3. Labeled Refrigerate is stored in refrigerator	Checked
C. IV PREPARATION	
1. The drugs dispensed are checked with the drug list.	Checked
2. Doses are admixed and labeled.	Checked
2.1. Sealed disposable syringe contains only one drug	Not Applicable
2.2. Sterile drugs will be prepared in laminar air flow hood (if possible) using aseptic technique	Not applicable
3. Final product is verified by a pharmacist, corrected if needed, and signed initial on the label.	Checked
D. IV DELIVERY	
1. IV bags prepared are delivered in separate compartments (e.g., basket) labeled with patient name, I.D. number if possible, bed number and nursing unit name.	Checked
2. Doses are delivered 1-2 hours before administration time.	Not Applicable
3. New/updated Medication Administration Record (MAR) is delivered to the nursing station.	Checked
4. Dispensing, inventory & financial records are updated in pharmacy.	Checked
E. IV Administration	
1. Checks the label of each prepared IV bag received with the MAR Drug List for each patient.	Checked
2. Places all drugs in an individual compartment labeled with patient name and bed number.	Checked
3. Proceeds down the hall to administer the doses.	Checked
3.1. Checks patient name, I.D. number if possible, and bed number on the patient such as on a wrist band.	Checked
3.2. IV Push: checks rate of administration.	Checked
3.3. Administers doses.	Checked
3.4. Signs initials and administration time on the MAR at patient bedside	Checked

The Flowchart of Experimental group procedures after the installation of the Unit Dose Dispensing System is shown in Figure 10.



Note: Gray scale areas are the unit dose intervention installed.

Figure 10: Flowchart of the Drug Distribution System in the Experimental Group

Description of Errors Detected

During the whole observation periods (including all Control and experimental phases), the following drugs were involved in omission errors (See Table 12).

1. Potassium Chloride Injection Concentrate (15%),
2. Sodium Chloride Injection Concentrate (10%),
3. Insulin,
4. Vitamin C,
5. Vitamin K1,
6. Sodium Glycerophosphate Injection,
7. Fat-Soluble Vitamin Injection,
8. Coenzyme Complex for Injection,
9. Trace Elements for Injection (Addammel), and
10. Water-Soluble Vitamin For Injection

Table 12: Drugs Involved in the Omission Errors

Drug ordered in the TPN (Once Daily) was omitted	Frequency
Potassium Chloride Injection Concentrate (15%) 20 ml	2
Potassium Chloride Injection Concentrate (15%) 10 ml	1
Sodium Chloride Injection Concentrate (10%) 50 ml	2
Sodium Chloride Injection Concentrate (10%) 20 ml	1
Vitamin C Injection 7.5 ml (3 g)	3
Vitamin K1 Injection 2 ml (20 mg)	3
Ratio of Insulin to Glucose 1:5	4
Ratio of Insulin to Glucose 1:4	1
Sodium Glycerophosphate Injection (Glycophos [®]) 10 ml	2
Fat-Soluble Vitamin Injection (II) (Vitalipid [®] N Adult) 10 ml	1
Coenzyme Complex for Injection 200 IU	2
Trace Elements for Injection (Addammel [®] N) 10 ml	3
Water-Soluble Vitamin for Injection (Soluvit [®] N) 0.5 g	5

The drugs involved in the wrong dose errors appear in Table 13.

1. Potassium Chloride Injection Concentrate (15%),
2. Sodium Chloride Injection Concentrate (10%),
3. Insulin,
4. Vitamin C,
5. Calcium Gluconate (10%), and
6. N(2)-L-Alanyl-L-Glutamine

Table 13: Drugs Involved in the Wrong Dose Errors

Drug Ordered in the TPN, Once Daily	Dose Given	Difference	% Error	Freq.
Potassium Chloride Injection Concentrate (15%) 10 ml	8 ml	2 ml	20	1
Potassium Chloride Injection Concentrate (15%) 10 ml	30 ml	20 ml	200	1
Potassium Chloride Injection Concentrate (15%) 30 ml	20 ml	10 ml	33	2
Sodium Chloride Injection Concentrate (10%), 20 ml	30 ml	10 ml	50	1
Sodium Chloride Injection Concentrate (10%), 100 ml	10 ml	90 ml	90	4
Ratio of Insulin to the Glucose (1:2.5) 40 units	24 units	16 units	40	1
Ratio of Insulin to the Glucose (1:4) 56 units	24 units	32 units	57	4
Ratio of Insulin to the Glucose (1:6) 16 units	8 units	8 units	50	1
Ratio of Insulin to the Glucose (1:5) 20 units	28 units	8 units	40	1
Ratio of Insulin to the Glucose (1:5) 20 units	24 units	4 units	20	1
Ratio of Insulin to the Glucose (1:4) 24 units	16 units	8 units	33	1
Ratio of Insulin to the Glucose (1:5) 30 units	24 units	6 units	20	1
Ratio of Insulin to the Glucose (1:4) 50 units	40 units	10 units	20	1
Ratio of Insulin to the Glucose (1:3) 42 units	32 units	10 units	23	1
Ratio of Insulin to the Glucose (1:6) 16 units	20 units	4 units	25	2
Ratio of Insulin to the Glucose (1:2.5) 50 units	56 units	6 units	12	1
Vitamin C Injection 3 g (7.5 ml)	4 ml	3.5 ml	47	1
Vitamin C Injection 3 g (7.5 ml)	5 ml	2.5 ml	33	2
10% Calcium Gluconate Injection (10 ml)	2 ml	8 ml	80	1
N(2)-L-Alanyl-L-Glutamine Injection (100 ml)	150 ml	50 ml	50	1

During the observation period, the drugs involved in unordered drug errors are shown in Table 14.

1. Sodium Chloride Injection Concentrate (10%),
2. Vitamin C, and
3. Compound 12-Vitamins Injection Powder

Table 14: Drugs Involved in Unordered Drug Errors

Unordered Drug was Given in the TPN	Frequency
Sodium Chloride Injection Concentrate (10%) 20 ml	1
Vitamin C Injection 2 ml	1
Compound 12-Vitamins Injection (powder) 0.5 g	2

Errors with Potential Clinical Importance

Because this study didn't include patient monitoring after administration, only the potential clinical severity of the errors to harm the patients could be assessed. The criteria for judging potential clinical importance was appearance in the ISMP's List of High-Alert Medications for 2008. The consequence of such error is a heightened risk of causing significant harm to the patient (Institute for Safe Medication Practices, 2008).

Potassium chloride for injection concentrate (15%), Sodium chloride for injection concentrate (10%), and Insulin errors were the most frequently occurring errors in the existing drug distribution systems involving both omission errors and wrong dose errors. Those three drugs were among the specific medications listed in the ISMP's High-Alert Medications in 2008 (Institute for Safe Medication Practices, 2008).

Both potassium chloride for injection concentrate and sodium chloride for injection concentrate are important for the maintenance of the body fluid and electrolyte

balance. The errors involving electrolyte drugs can cause electrolyte imbalance, extravasation or heart arrest.

The physician ordered insulin in a “Ratio of Insulin to the Glucose” format. The preparation nurses were required to calculate the actual volume of the insulin needed in the TPN at the time when they prepared the doses. Miscalculation appeared to be the cause of wrong dose errors of insulin. The dose discrepancy of insulin varied from 12% to 57%, and commonly occurred at 20% and above. The insulin was prescribed when the patient was considered in danger of experiencing hyperglycemia or extreme increases in blood sugar levels. The patient was at the risk for hypoglycemia when over-dosing insulin, hyperglycemia when under-dosing or omitted of insulin, or complications due to either hypoglycemia or hyperglycemia.

The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) considered insulin to be one of the top three “high-risk medications” in the inpatient setting (Institute for Safe Medication Practices, 2008). Analysis of data reported to USP’s MEDMARX reporting program over a two-year period (2000-2001) uncovered a total of 4,764 insulin errors with approximately 6.6% (N = 320) of these causing harm to the patient (Institute for Safe Medication Practices, 2003). Historically, the average harm threshold for error reports submitted to MEDMARX has been approximately 2.8%, indicating that when an insulin product is involved, it may be twice as likely to result in harm (Categories E-I) (Institute for Safe Medication Practices, 2003). Hellman found that 33% of the medical errors that caused death within 48 hours of the error involved insulin therapy and administration in the care of a hospitalized patient (Hellman, 2004).

Table 15 lists all the errors considered to have potential clinical significance.

Table 15: Errors with Potential Clinical Significance

Drug and Dose Ordered in the TPN, Once Daily	Prepared Dose
Insulin	
Ratio of Insulin to the Glucose (1:2.5) 40 units	24 units
Ratio of Insulin to the Glucose (1:4) 56 units	24 units
Ratio of Insulin to the Glucose (1:6) 16 units	8 units
Ratio of Insulin to the Glucose (1:5) 20 units	28 units
Ratio of Insulin to the Glucose (1:5) 20 units	24 units
Ratio of Insulin to the Glucose (1:4) 24 units	16 units
Ratio of Insulin to the Glucose (1:5) 30 units	24 units
Ratio of Insulin to the Glucose (1:4) 50 units	40 units
Ratio of Insulin to the Glucose (1:3) 42 units	32 units
Ratio of Insulin to the Glucose (1:6) 16 units	20 units
Ratio of Insulin to the Glucose (1:2.5) 50 units	56 units
Ratio of Insulin to the Glucose (1:5)	Omitted
Ratio of Insulin to the Glucose (1:4)	Omitted
Electrolytes: Potassium Chloride Injection Concentrate (15%)	
Potassium Chloride Injection Concentrate (15%) 10 ml	30 ml
Potassium Chloride Injection Concentrate (15%) 30 ml	20 ml
Potassium Chloride Injection Concentrate (15%) 20 ml	Omitted
Potassium Chloride Injection Concentrate (15%) 10 ml	Omitted
Electrolytes: Sodium Chloride Injection Concentrate (10%)	
Sodium Chloride Injection Concentrate (10%) 20 ml	30 ml
Sodium Chloride Injection Concentrate (10%) 100 ml	10 ml
Sodium Chloride Injection Concentrate (10%) 50 ml	Omitted
Sodium Chloride Injection Concentrate (10%) 20 ml	Omitted
	Unordered Sodium Chloride Injection Concentrate (10%) 20ml
Other	
N(2)-L-Alanyl-L-Glutamine Injection (100 ml)	150 ml
Vitamin K1 Injection 2 ml (20 mg)	Omitted
10% Calcium Gluconate Injection (10 ml)	2 ml
Vitamin C Injection 3 g (7.5 ml)	4 ml
Vitamin C Injection 3 g (7.5 ml)	5 ml
Vitamin C Injection 7.5 ml (3 g)	Omitted
Sodium Glycerophosphate Injection (Glycophos [®]) 10 ml	Omitted
Fat-Soluble Vitamin Injection (II) (Vitalipid [®] N Adult) 10 ml	Omitted
Coenzyme Complex for Injection 200 IU	Omitted
Trace Elements for Injection (Addammel [®] N) 10 ml	Omitted
Water-Soluble Vitamin for Injection (Soluvit [®] N) 0.5 g	Omitted

Statistical Analysis

Statistical analyses were performed with the use of SAS software, version 9.2 (SAS Institute). SAS codes are shown in Appendix F. The main effect of the Unit Dose Dispensing System, an independent variable randomly installed in the Experimental group, was evaluated by using the pre-test scores as a covariate in the Analysis of Covariance (ANCOVA). The alpha level was set at 0.05. The advantages of ANCOVA are the ability to reduce the error variance in the outcome measure and the ability to measure group differences after allowing for other differences between subjects (Munro, 2005). The result shows that the mean error rate differed between the Control group and the Experimental group before the installation of the Unit Dose Dispensing System. Therefore, the error variance is reduced by controlling for variation of pre-test in ANCOVA.

T-Test or ANOVA of the gain scores between the Control and Experimental groups or repeated measures ANOVA with one between-subjects factor (group) and one within-subjects factor (pre-post test) could not be used in this study because the error rate in the pre-test and post-test were based on the observational day instead of the same nurse or the same patient.

The assumptions for ANCOVA were summarized by Munro (2005):

1. The groups should be mutually exclusive.
2. The variances of the groups should be equivalent (homogeneity of variance).
3. The Dependent Variable should be normally distributed.
4. The covariate should be a continuous variable.
5. Required Assumption of the homogeneity of regression slopes across groups.

6. The covariate and the dependent variable must show a linear relationship. If the relationship between the covariate and the dependent variable is not linear, ANCOVA will have less benefit with little reduction in the error variance than ANOVA.

Descriptive of Means

Medication Errors Overall

The means of the overall medication error rates are shown in the Table 16.

The means of the overall medication error rates (%) in the Control group were 6.91 (SD = 8.66) before and 9.40 (SD = 5.62) after the Unit Dose Dispensing System was applied in the Experimental group.

The means of the overall medication error rates (%) in the Experimental group were 4.07 (SD = 3.04) before and 1.22 (SD = 1.80) after the Unit Dose Dispensing System was applied in the Experimental group.

Table 16: Means of the Overall Medication Error Rates

Group	N Obs	Variable	Mean	Std Dev	Minimum	Maximum
Control	11	Overall_Before	6.91	8.66	0	30.77
	10	Overall_After	9.40	5.62	2.56	19.44
Experimental	10	Overall_Before	4.07	3.04	0	12.00
	10	Overall_After	1.22	1.80	0	5.26

Wrong Dose Errors

The means of the wrong dose error rates are shown in the Table 17.

The means of the wrong dose error rates (%) in the Control group were 3.91 (SD = 3.46) before and 3.04 (SD = 2.86) after the Unit Dose Dispensing System was applied in the Experimental group.

The mean of the wrong dose error rates (%) in the Experimental group was 3.75 (SD = 3.30) before the Unit Dose Dispensing System was applied in the Experimental group. No wrong dose errors were found in the Experimental group after the Unit Dose Dispensing System was applied in the Experimental group.

Table 17: Means of the Wrong Dose Error Rates

Group	N Obs	Variable	Mean	Std Dev	Minimum	Maximum
Control	11	WrongDose_Before	3.91	3.46	0	9.09
	10	WrongDose_After	3.04	2.86	0	8.00
Experimental	10	WrongDose_Before	3.75	3.30	0	12.00
	10	WrongDose_After	0	0	0	0

Omission Errors

The means of the omission error rates are shown in the Table 18.

The means of the omission error rates (%) in the Control group were 2.31 (SD = 5.27) before and 5.59 (SD = 5.16) after the Unit Dose Dispensing System was applied in the Experimental group.

The means of the omission error rates (%) in the Experimental group were 0.32 (SD = 1.02) before and 1.22 (SD = 1.80) after the Unit Dose Dispensing System was applied in the Experimental group.

Table 18: Means of the Omission Error Rates

Group	N Obs	Variable	Mean	Std Dev	Minimum	Maximum
Control	11	Omission_Before	2.31	5.27	0	15.38
	10	Omission_After	5.59	5.16	0	16.67
Experimental	10	Omission_Before	0.32	1.02	0	3.23
	10	Omission_After	1.22	1.80	0	5.26

Statistical Significance between Groups

Medication Errors Overall

The results in Table 19 show that the covariate (pre-test) was not significantly related to the difference of post-test in the Control and Experimental groups ($P = 0.3719$), which indicated that the One-Way ANOVA on the mean difference (after) between the Control and Experimental groups would also get the similar significant results.

By controlling the pre-test as a covariate, the main effect of the intervention of Unit Dose Dispensing System had a statistically significant effect ($F_{1,17} = 19.77$, $P = 0.0004$) on the difference of the overall medication error rates (after) between the Control and Experimental groups.

Table 19: The Significance between Groups in ANCOVA: Overall Medication Error Rates

Source	DF	Type III SS	Mean Square	F Value	Pr > F
Group	1	347.3010	347.3010	19.77	0.0004***
Overall (Before)	1	14.7721	14.7721	0.84	0.3719
Error	17	298.6193	17.5658		
Corrected Total	19	647.5446			

Note: * $P < 0.05$, ** $P < 0.01$; *** $P < 0.001$

The results in Table 20 show that 54% (R-Square = 0.5388) of the variation in the post test of the overall medication error rates across the Control group and Experimental group was attributed to the installation of the Unit Dose Dispensing System in the Experimental group.

Table 20: R-Square in ANCOVA: Overall Error Rates

R-Square	Coeff Var	Root MSE	Overall After Mean
0.5388	78.9668	4.1912	5.31

Wrong Dose Errors

The results in Table 21 show that the covariate (pre-test) was not significantly related to the difference of post-test in the Control and Experimental groups ($P = 0.2173$), which indicated that the One-Way ANOVA on the mean difference (after) between the Control and Experimental groups would also get the similar significant results.

By controlling the pretest as a covariate, the main effect of the intervention of Unit Dose Dispensing System had a statistically significant effect ($F_{1,17} = 12.37$, $P = 0.0026$) on the difference of the wrong dose error rates (after) between the Control and Experimental groups.

Table 21: The Significance between Groups in ANCOVA: Wrong Dose Error Rates

Source	DF	Type III SS	Mean Square	F Value	Pr > F
Group	1	49.0068	49.0068	12.37	0.0026**
Wrong Dose (Before)	1	6.5032	6.5032	1.64	0.2173
Error	17	67.3292	3.9605		
Corrected Total	19	120.1621			

Note: * $P < 0.05$, ** $P < 0.01$; *** $P < 0.001$

The results in Table 22 show that 44% (R-Square = 0.4397) of the variation in the post test of the wrong dose error rates between the Control group and Experimental group was attributed to the installation of the Unit Dose Dispensing System in the Experimental group.

Table 22: R-Square in ANCOVA: Wrong Dose Error Rates

R-Square	Coeff Var	Root MSE	Wrong Dose After Mean
0.4397	130.7563	1.9901	1.52

Omission Errors

The results in Table 23 show that the covariate (pre-test) was not significantly related to the difference of post-test in the Control and Experimental groups ($P = 0.9765$), which indicated that the One-Way ANOVA on the mean difference (after) between the Control and Experimental groups would also get the similar significant results.

By controlling the pretest as a covariate, the main effect of the intervention of Unit Dose Dispensing System had a statistically significant effect ($F_{1,17} = 5.52, P = 0.03$) on the difference of the omission error rates (after) between the Control and Experimental groups.

Table 23: The Significance between Groups in ANCOVA: Omission Error Rates

Source	DF	Type III SS	Mean Square	F Value	Pr > F
Group	1	87.2024	87.20242	5.52	0.0311*
Omission (Before)	1	0.0141	0.0141	0.00	0.9765
Error	17	268.3405	15.7847		
Corrected Total	19	363.8391			

Note: * $P < 0.05$, ** $P < 0.01$; *** $P < 0.001$

The results in Table 24 show that 26% (R-Square = 0.2625) of the variation in the post test of the omission error rates between the Control group and Experimental group was attributed to the installation of the Unit Dose Dispensing System in the Experimental group.

Table 24: R-Square in ANCOVA: Omission Error Rates

R-Square	Coeff Var	Root MSE	Omission After Mean
0.2625	116.6814	3.9730	3.405

Mean Difference and 95% Confidence Interval

Medication Errors Overall

By controlling the pretest as a covariate, the adjusted post test mean difference of the overall medication error rates between the Control group and the Experimental group was 8.66% with a 95% Confidence Interval of 4.55 to 12.77% (Table 25).

Table 25: Adjusted Mean Difference of the Post Test: Overall Medication Error Rates

Least Squares Means for Effect Group				
i	j	Difference Between Means	95% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	8.66	4.55	12.77

Wrong Dose Errors

By controlling the pretest as a covariate, the adjusted post test mean difference of the wrong dose error rates between the Control group and the Experimental group was 3.14% with a 95% Confidence Interval of 1.26 to 5.03% (Table 26).

Table 26: Adjusted Mean Difference of the Post Test: Wrong Dose Error Rates

Least Squares Means for Effect Group				
i	j	Difference Between Means	95% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	3.14	1.26	5.03

Omission Errors

By controlling the pretest as a covariate, the adjusted post test mean difference of the omission error rates between the Control group and the Experimental group was 4.35% with a 95% Confidence Interval of 0.45 to 8.26% (Table 27).

Table 27: Adjusted Mean Difference of the Post Test: Omission Error Rates

Least Squares Means for Effect Group				
i	j	Difference Between Means	95% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	4.35	0.45	8.26

Required Assumptions Evaluation for ANCOVA

The assumptions for ANCOVA were tested for the normality, Levene's test for equal variances between the groups, and the homogeneity regression slopes across the groups as follows:

1. The normality of the residuals was evaluated by Shapiro-Wilk Test and Graphical method of Probability Plot in the Univariate Analysis.
2. The Levene's test of the adjusted post test means was evaluated by one-way ANOVA.
3. The Required Assumption of the homogeneity regression slopes across the groups: the slopes relating post-test scores to pre-test scores, which are assumed to be parallel for both the Control group and the Experimental group, were tested by the adding the interaction of Group*Pre-Test in the model of ANCOVA.

Some caution must be excised in interpreting the results if the assumptions of normality and the Levene's test for equal variance were violated. However, ANCOVA procedures are robust to mild to moderate violations of these assumptions.

The required assumption of the homogeneity regression slopes must be checked before using ANCOVA, because if that assumption is violated, ANCOVA can lead to improper interpretation of the results.

Medication Errors Overall

The Shapiro-Wilk test was not significant ($P = 0.1498 > 0.05$), which indicated that we failed to reject the null hypothesis that the data came from a normally distributed population (Table 28).

Probability plot in Figure 11 shows that the data were approximately distributed close to the straight normal line with a few residuals symmetrically departure on both sides of the normal line, which didn't cause a significant result in the Shapiro-Wilk Test.

Table 28: Normality Test: Overall Medication Error Rates

Tests for Normality				
Test	Statistic		p Value	
Shapiro-Wilk	W	0.9293	Pr < W	0.1498
Kolmogorov-Smirnov	D	0.2218	Pr > D	0.0106
Cramer-von Mises	W-Sq	0.1417	Pr > W-Sq	0.0281
Anderson-Darling	A-Sq	0.7280	Pr > A-Sq	0.0485

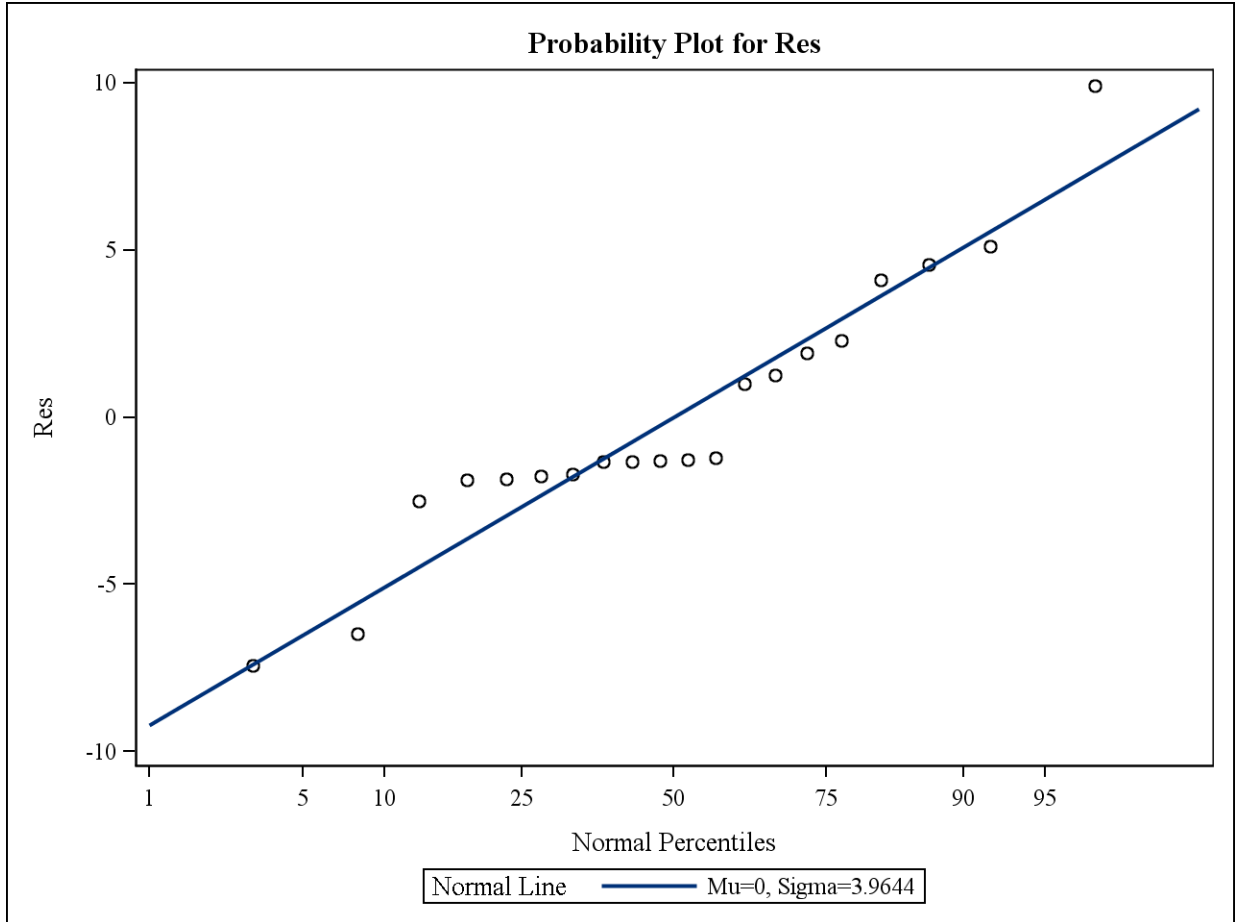


Figure 11: Probability Plot for Normality: Overall Medication Error Rates

Levene's Test was significant at the alpha level of 0.05 ($P = 0.0336 < 0.05$), which indicated that the null hypothesis of equal variances between the Control group and Experimental group was violated (Table 29).

If the alpha level was selected at 0.01, which didn't change the significance of results of post tests between groups in ANCOVA, Levene's Test was not significant ($P = 0.0336 > 0.01$), which indicated that the null hypothesis of equal variances between the Control group and Experimental group was not violated.

Table 29: Levene's Test: Overall Medication Error Rates

Levene's Test for Homogeneity of Overall Adjusted Variance					
ANOVA of Squared Deviations from Group Means					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Group	1	2630.6	2630.6	5.29	0.0336*
Error	18	8950.5	497.3		

Note: * $P < 0.05$, ** $P < 0.01$; *** $P < 0.001$

The interaction of pretest*Group was not significant ($P = 0.4868 > 0.05$), which indicated that the assumption of the common slopes of pre-test and post-test across the groups was met (Table 30).

Table 30: Common Slope Test: Overall Medication Error Rates

Source	DF	Type III SS	Mean Square	F Value	Pr > F
Group	1	216.7429	233.1380	11.98	0.0032
Overall (Before)	1	0.0001	0.0001	0.00	0.9983
Overall (Before)*Group	1	9.1661	9.1661	0.51	0.4868

Wrong Dose Errors

Shapiro-Wilk Test was significant at the alpha level of 0.05 ($P = 0.0434 < 0.05$), which indicated that the null hypothesis that the data came from a normally distributed population was rejected (Table 31).

The Probability Plot in Figure 12 shows that 70% of the residuals were closely distributed to the straight normal line, while at the upper right section 10% of the residuals departure to the right of the line and another 20% of the residuals departure to the left of the line, which caused the significant result in the Shapiro-Wilk Test.

Table 31: Normality Test: Wrong Dose Error Rates

Tests for Normality				
Test	Statistic		p Value	
Shapiro-Wilk	W	0.9012	Pr < W	0.0434*
Kolmogorov-Smirnov	D	0.2155	Pr > D	0.0160
Cramer-von Mises	W-Sq	0.1661	Pr > W-Sq	0.0139
Anderson-Darling	A-Sq	0.8844	Pr > A-Sq	0.0204

Note: * $P < 0.05$, ** $P < 0.01$; *** $P < 0.001$

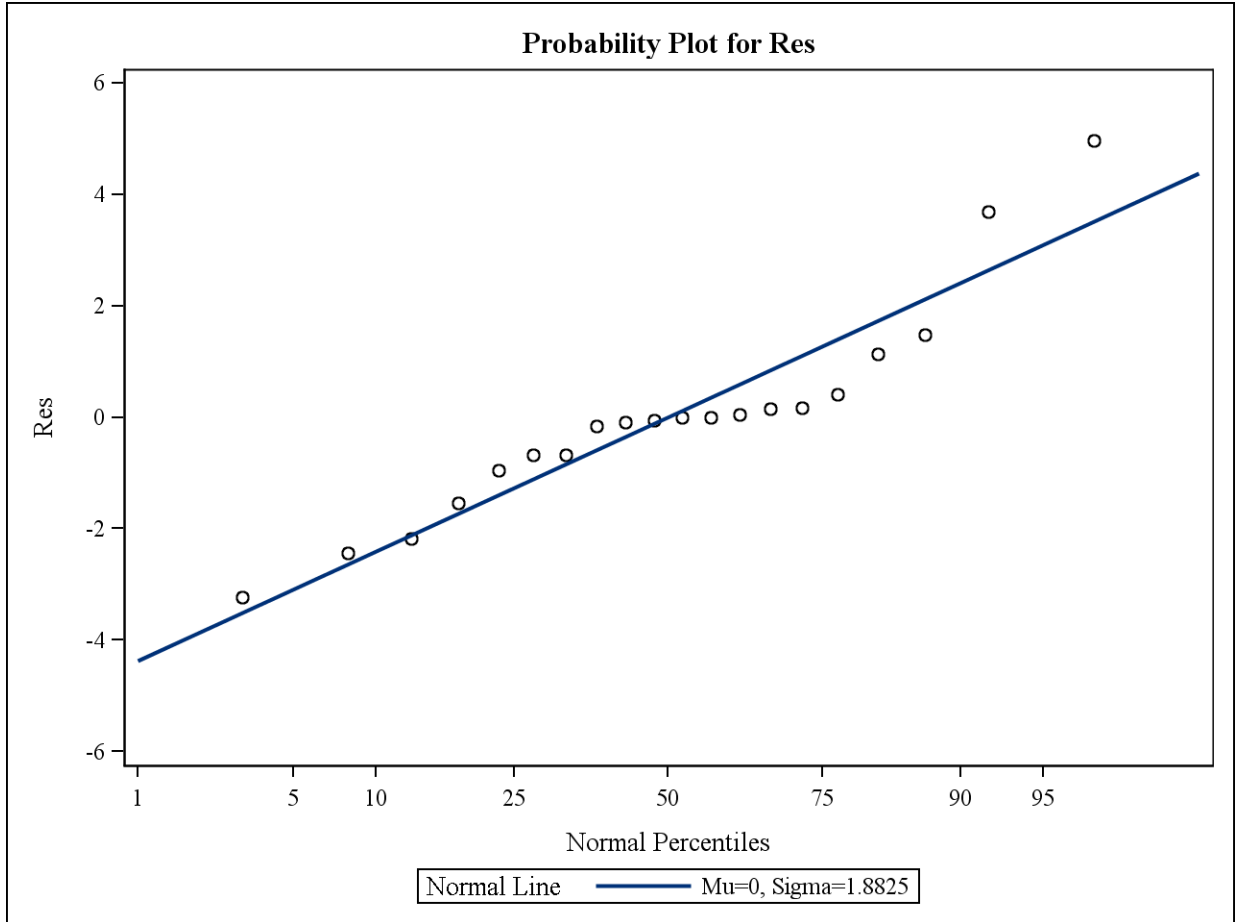


Figure 12: Probability Plot for Normality: Wrong Dose Error Rates

Levene's Test was significant at the alpha level of 0.05 ($P = 0.025 < 0.05$), which indicated that the null hypothesis of equal variances between the Control group and Experimental group was violated (Table 32).

If the alpha level was selected at 0.01, which didn't change the significant result of post tests between groups in ANCOVA, Levene's Test was not significant ($P = 0.025 > 0.01$), which indicated that the null hypothesis of equal variances between the Control group and Experimental group was not violated.

Table 32: Levene's Test: Wrong Dose Error Rates

Levene's Test for Homogeneity of WrongDose Adjusted Variance					
ANOVA of Squared Deviations from Group Means					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Group	1	186.0	186.0	5.98	0.025*
Error	18	560.3	31.1303		

Note: * $P < 0.05$, ** $P < 0.01$; *** $P < 0.001$

The interaction of pretest*Group was not significant ($P = 0.2218 > 0.05$), which indicated that the assumption of the common slopes of pre-test and post-test across the groups was met (Table 33).

Table 33: Common Slope Test: Wrong Dose Error Rates

Source	DF	Type III SS	Mean Square	F Value	Pr > F
Group	1	39.6449	39.6449	12.12	0.0053
Wrong Dose (Before)	1	6.1780	6.1780	1.62	0.2218
Wrong Dose (Before)*Group	1	6.1780	6.1780	1.62	0.2218

Omission Errors

Shapiro-Wilk Test was significant at the alpha level of 0.05 ($P = 0.031 < 0.05$), which indicated that the null hypothesis that the data came from a normally distributed population was rejected (Table 34).

The Probability Plot in Figure 13 shows that 50% of the residuals were closely distributed to the straight normal line with only 25% of the residuals asymmetrically departure to the left of the line which caused the significant result in the Shapiro-Wilk Test.

Although the Shapiro-Wilk Test suggested using a nonparametric test, however ANCOVA procedures are robust to the moderate violations ($W: 0.893$ vs. 0.905) of these assumptions, since the distribution of W is highly skewed, W of 0.905 was not significant with a sample of 20 at a critical level of 0.05.

Table 34: Normality Test: Omission Error Rates

Tests for Normality				
Test	Statistic		p Value	
Shapiro-Wilk	W	0.8933	Pr < W	0.031*
Kolmogorov-Smirnov	D	0.2270	Pr > D	<0.01
Cramer-von Mises	W-Sq	0.1293	Pr > W-Sq	0.0426
Anderson-Darling	A-Sq	0.7502	Pr > A-Sq	0.0437

Note: * $P < 0.05$, ** $P < 0.01$; *** $P < 0.001$

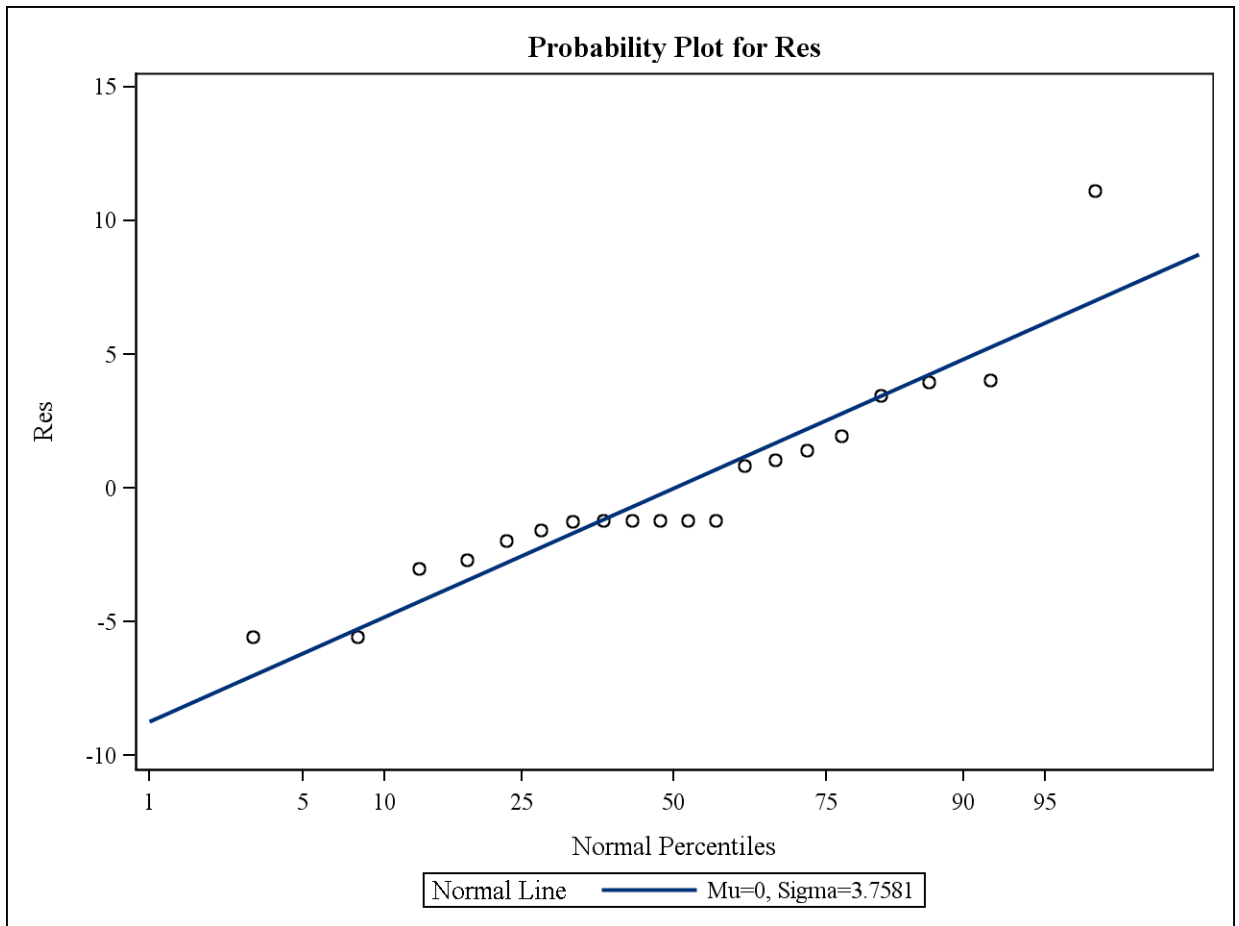


Figure 13: Probability Plot for Normality: Omission Error Rates

Levene's Test was not significant at the alpha level of 0.05 ($P = 0.0869 > 0.05$), which indicated that the null hypothesis of equal variances between the Control group and Experimental group was not violated (Table 35).

Table 35: Levene's Test: Omission Error Rates

Levene's Test for Homogeneity of Omission_Adjusted Variance					
ANOVA of Squared Deviations from Group Means					
Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Group	1	2209.2	2209.2	3.28	0.0869
Error	18	12129.8	673.9		

The interaction of pretest*Group was not significant ($P = 0.7488 > 0.05$), which indicated that the assumption of the common slopes of pre-test and post-test across the groups was met (Table 36).

Table 36: Common Slope Test: Omission Error Rates

Source	DF	Type III SS	Mean Square	F Value	Pr > F
Group	1	74.3885	74.3885	4.46	0.0507
Omission (Before)	1	1.4369	1.4369	0.09	0.7728
Omission (Before)*Group	1	1.7690	1.7690	0.11	0.7488

Boxplot of Error Rates

The BoxPlots were performed by One-Way Analysis of Variance (ANOVA) showing the mean changes before and after the installation of Unit Dose Dispensing System in the Experimental group between the Control group and Experimental group in Figures 14-19.

Medication Errors Overall

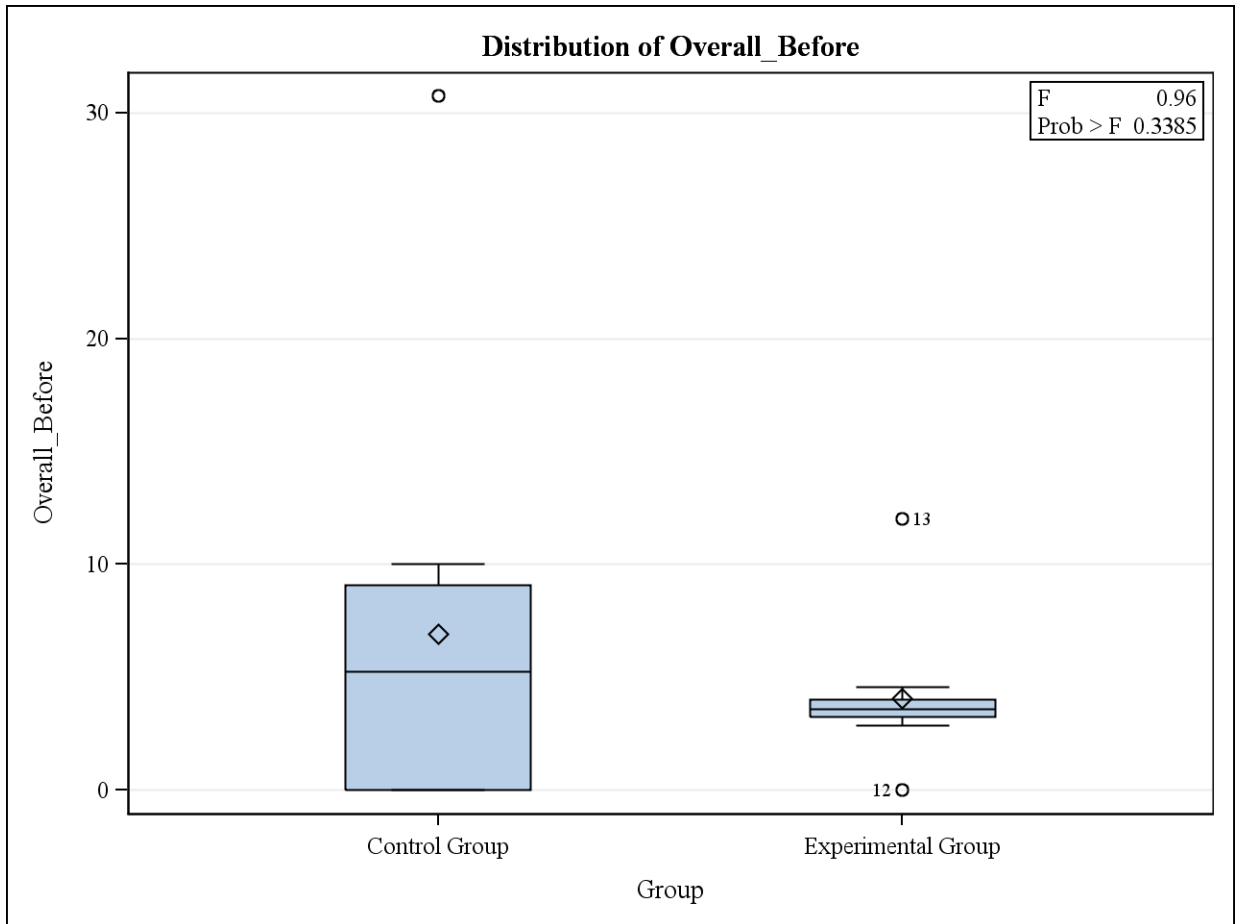


Figure 14: ANOVA of Mean Difference: Overall Medication Error Rates before the Unit Dose Dispensing

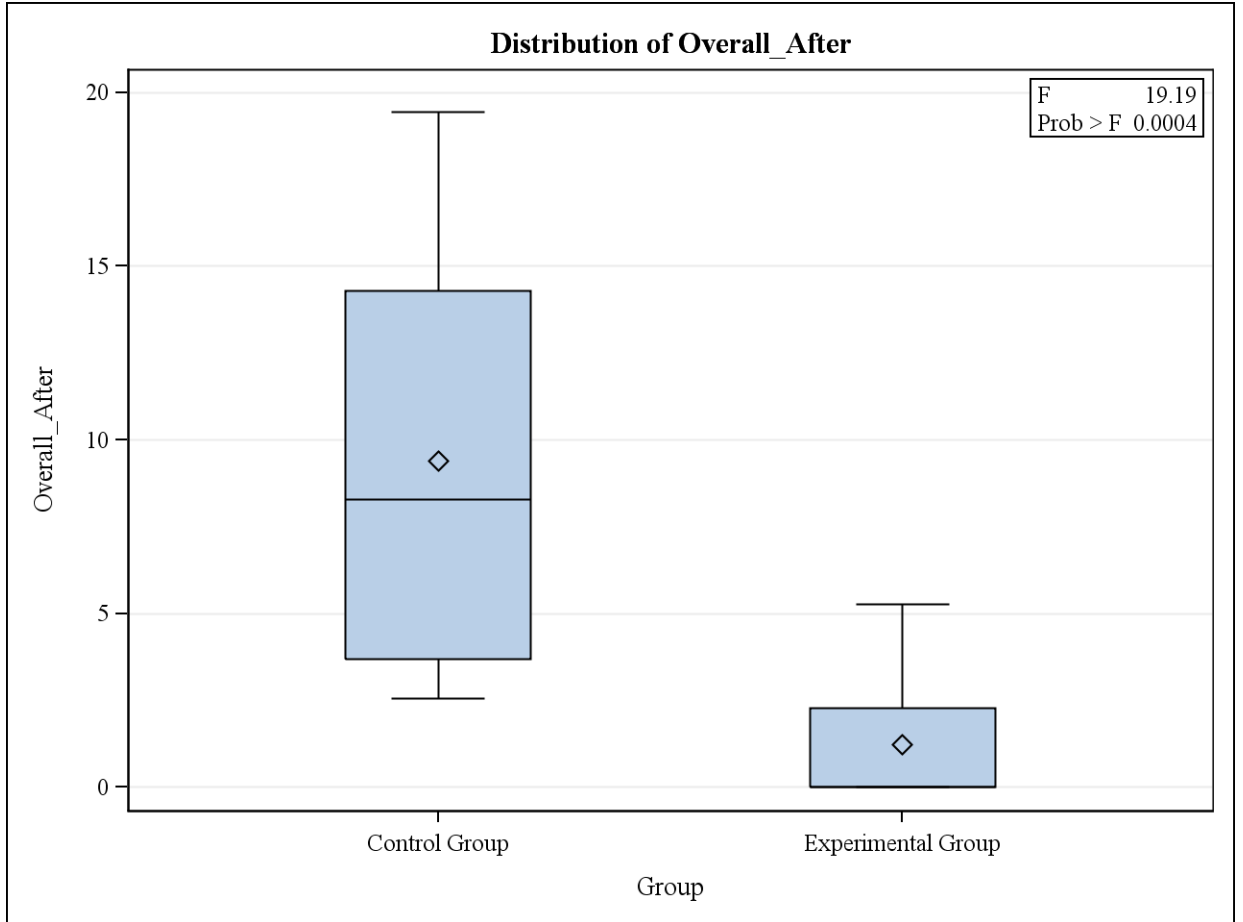


Figure 15: ANOVA of Mean Difference: Overall Medication Error Rates after the Unit
Dose Dispensing

Wrong Dose Errors

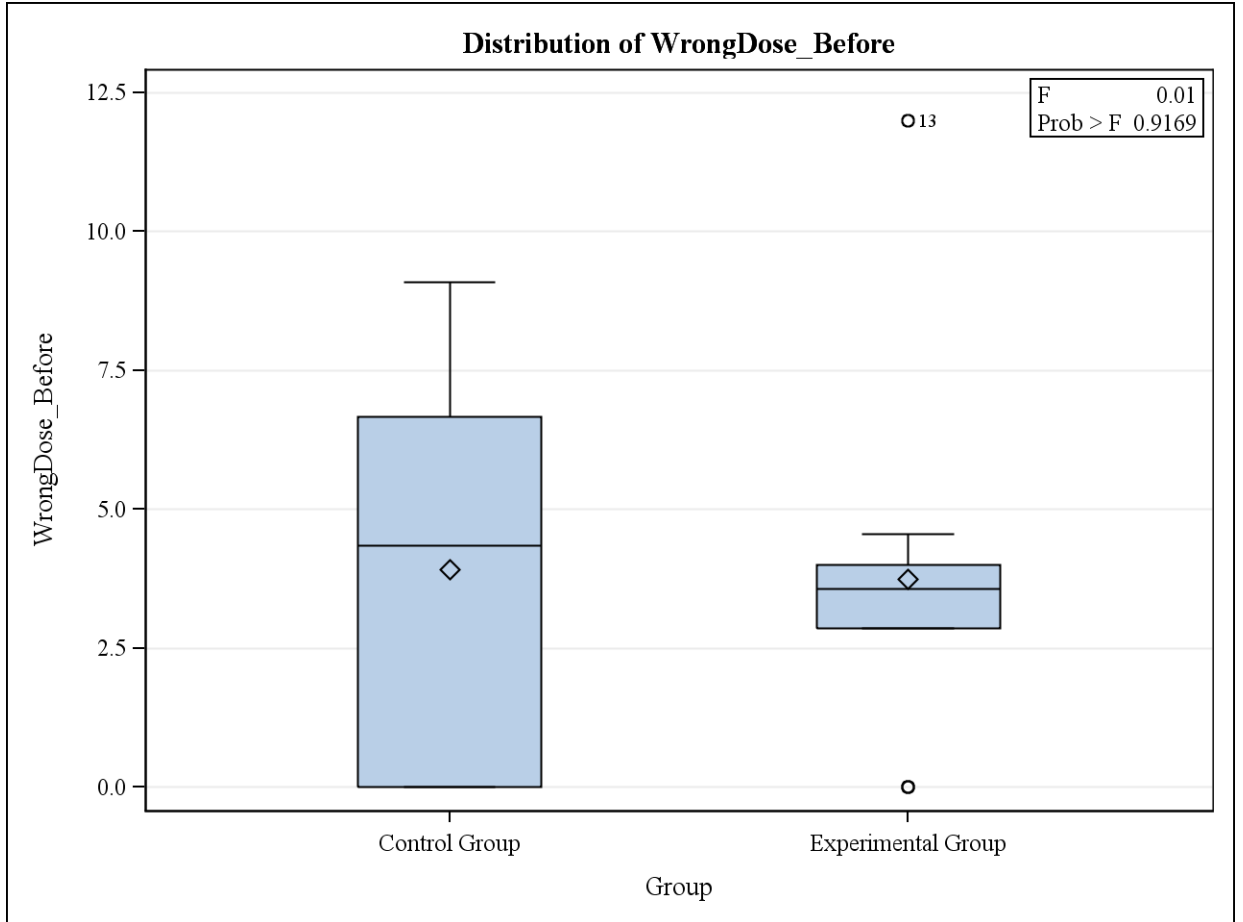


Figure 16: ANOVA of Mean Difference: Wrong Dose Error Rates before the Unit Dose Dispensing

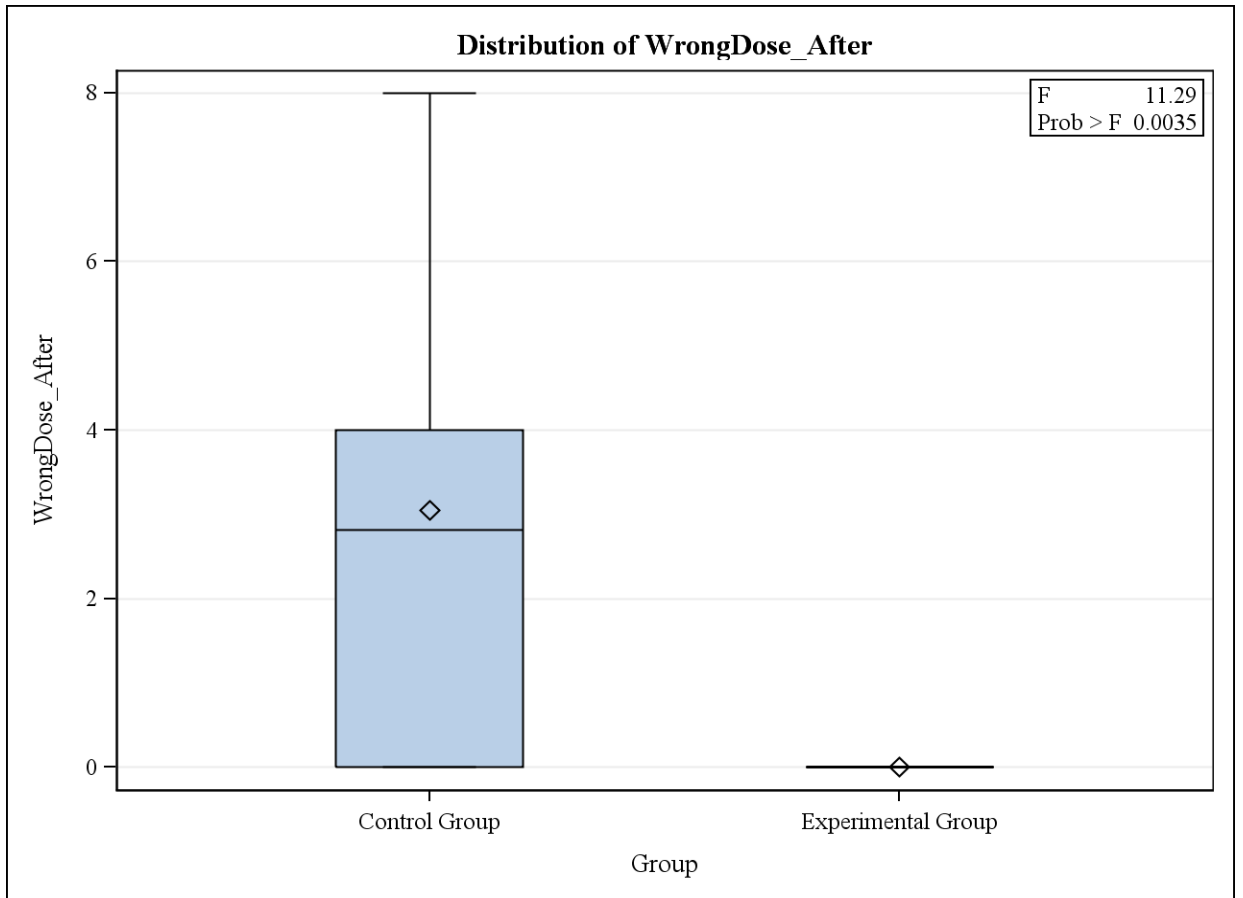


Figure 17: ANOVA of Mean Difference: Wrong Dose Error Rates after the Unit Dose Dispensing

Omission Errors

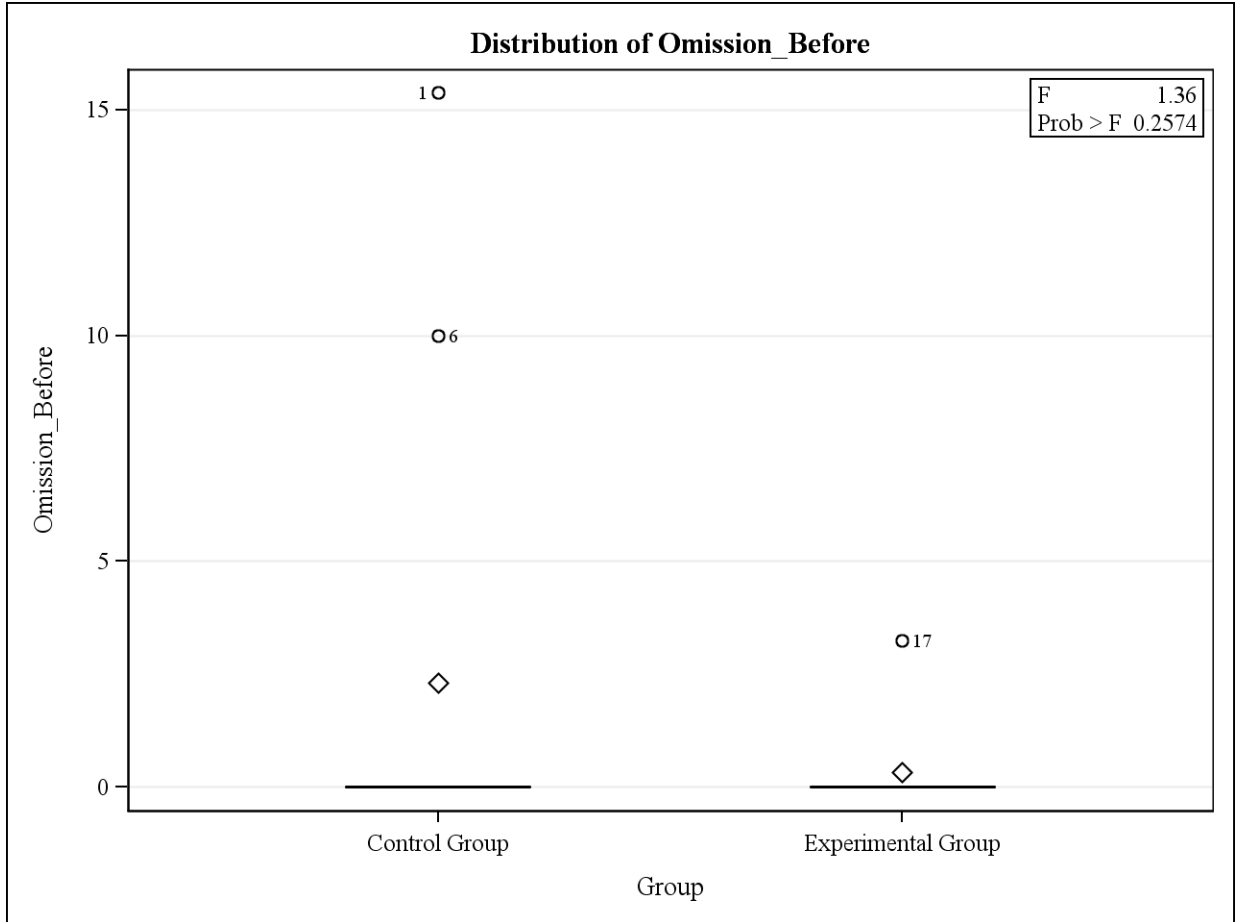


Figure 18: ANOVA of Mean Difference: Omission Error Rates before the Unit Dose Dispensing

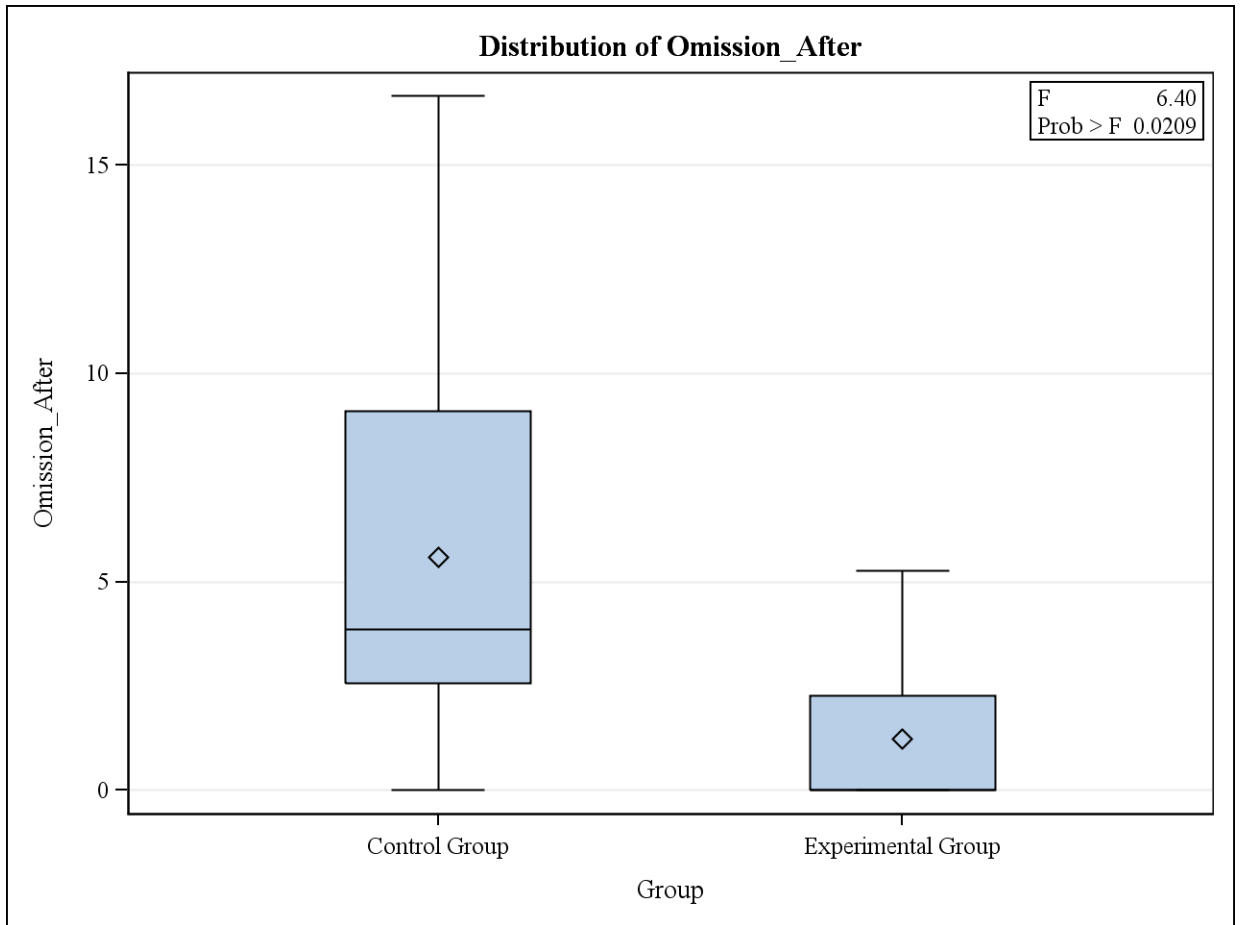


Figure 19: ANOVA of Mean Difference: Omission Error Rates after the Unit Dose
Dispensing

Outliers

The outliers detected in the Univariate analysis are shown in Table 37. The errors were evaluated by a panel of two persons, the Principal Investigator who conducted the observations and her advisor (Dr. Kenneth Barker), who is a recognized expert on this subject. The errors all appeared valid for reflecting the real medication processes and were included in the statistical analysis. The error for the first observation day in the Control group was more than 5 times the mean error rate. The statistical analysis was re-run after removing this extreme data, and the significant results didn't change.

The medication error rates by each observation day are presented in Appendix G.

Table 37: Extreme Observations

Overall Error Rate Extreme Observations				Wrong Dose Error Rate Extreme Observations				Omission Error Rate Extreme Observations			
Lowest		Highest		Lowest		Highest		Lowest		Highest	
Value	Obs	Value	Obs	Value	Obs	Value	Obs	Value	Obs	Value	Obs
0	41	12	13	0	41	7.5	28	0	41	9.09	27
0	38	14.29	23	0	40	7.69	1	0	38	9.52	23
0	37	15	28	0	39	8	26	0	37	10	6
0	35	19.44	30	0	38	9.09	2	0	35	15.38	1
0	34	30.77	1	0	37	12	13	0	34	16.67	30

Chapter 6: Conclusions and Discussion

Conclusions

An ANCOVA test was conducted for the difference between two means of the Control and Experimental groups, following the intervention of a Unit Dose Dispensing System. This was conducted for all error types combined at the 0.05 level of significance, where a the null hypothesis of no significant difference was rejected. Similar hypotheses were tested for individual error types and rejected except for unauthorized drug errors, wrong administration rate errors, and wrong time errors due to insufficient data.

Effect of the Unit Dose Dispensing System on IV Error Rates

The Unit Dose Dispensing System, compared with the existing system, ensured a higher accuracy during the IV preparation and administration processes as evidenced by reducing IV medication errors significantly in the Experimental group.

By controlling the pre test as a covariate, the adjusted post test mean difference of the overall medication error rates between the Control group and the Experimental group was 8.66% with a 95% Confidence Interval of 4.55 to 12.77%. The Unit Dose Dispensing System had a statistically significant effect ($F_{1,17} = 19.77$, $P = 0.0004$) on reducing the post test of the medication error rates in the Experimental group, by explaining 54% of the variation ($R\text{-Square} = 0.5388$) of the post test of the overall medication error rates between the Control group and Experimental group.

Effect of the Unit Dose Dispensing System on IV Error Rates, by Error Types

The results supported the hypotheses that the Unit Dose Dispensing System had a significant effect on IV preparation and administration errors, as well as on the sub types of the errors.

The adjusted post test mean difference of the wrong dose error rates between the Control group and the Experimental group was 3.14% with a 95% Confidence Interval of 1.26 to 5.03%. The Unit Dose Dispensing System had a statistically significant effect ($F_{1,17} = 12.37$, $P = 0.0026$) on reducing the post test of the wrong dose error rates in the Experimental group, by explaining 44% (R-Square = 0.4397) of the variation in the post test of the wrong dose error rates between the Control group and Experimental group.

The adjusted post test mean difference of the omission error rates between the Control group and the Experimental group was 4.35% with a 95% Confidence Interval of 0.45 to 8.26%. The Unit Dose Dispensing System had a statistically significant effect ($F_{1,17} = 5.52$, $P = 0.03$) on reducing of post test of the omission error rates in the Experimental group, by explaining 26% (R-Square = 0.2625) of the variation in the post test of the omission error rates between the Control group and Experimental group.

Due to insufficient data on other types of errors, the effect of the Unit Dose Dispensing System on unauthorized drug errors, wrong administration rate errors, and wrong time errors could not be evaluated in this study.

Discussion

Effect of the Unit Dose Dispensing System on Deficiencies of the Current System

This study indicated that the Unit Dose Dispensing System was effective in targeting the deficiencies of the current system.

Handwritten transcriptions

In the baseline of the Control and Experimental groups, 9 errors (33% of the total detected errors) appeared to be due to miscommunication via badly handwritten transcriptions. Handwritten transcriptions were eliminated in the Unit Dose Dispensing System. All the TPN orders were entered in the Excel file (Office 2007), and the labels of the TPN doses were generated from the Excel file (Office 2007). The unit of volume for liquids was standardized as a Milliliter (ml). The volume of the insulin was calculated and the unit for insulin volume was given by both Milliliter (ml) and International Unit (IU). The unit of volume for powder was standardized as mg or vial if the weight of the compounded powder was not given on the product.

Lacking Insulin Volume Label

In the baseline of the Control and Experimental groups, 9 wrong dose errors (33% of the total detected errors) were due to wrong calculation and 1 error (4% of the total detected errors) occurred when both nurses forgot to add insulin for the patient.

In the Unit Dose Dispensing System, the exact volume of the insulin was calculated in the Excel file (Office 2007) and the unit for insulin volume was given by both ml and iu. No extra calculations were needed by the preparation nurses before

mixing the TPN doses. This change may have prevented the omission errors and wrong dose errors for insulin doses under the current system.

Limited shelf space

In the baseline of the Control and Experimental groups, 4 errors (15% of the total detected errors) were likely due to limited shelf space. In the Unit Dose Dispensing System, all doses for one patient at one time were placed in a single container, and only one container was delivered to the preparation nurse at one time. This change avoided having all TPN doses placed closely together on the counter at one time and reduced the possibilities that one patient's doses were mixed with those for the adjacent patient.

Lacking Double Check before the Preparation

In the baseline of the Control and Experimental groups, 2 errors (7% of the total detected errors) lacked the required double check after the auxiliary worker failed to place the doses on the counter before the preparation. Even though the current system did ask for a double check, it was not performed by the preparation nurses assigned to do this double check before the task of mixing. In the Unit Dose Dispensing System, this task was assigned to a pharmacist (who did not prepare the TPN doses). Errors of extra or missing vials that appeared to be caused by the failure of the auxiliary worker were reduced in the Experimental group.

Errors that the Unit Dose Dispensing System Did not Prevent

The omission errors caused by the failure of the pharmacy to deliver the doses when due were not expected to be effected by the Unit Dose Dispensing System.

The wrong dose errors which occurred when the preparation nurse's elbow was hit by another nurse accidentally was not be prevented by the Unit Dose Dispensing System as installed, although such errors were not detected in the Experimental group after the intervention of the Unit Dose Dispensing System. However, it seems reasonable to speculate that such errors could be prevented by the ideal Unit Dose Dispensing System using a laminar flow hood.

The unauthorized dose error of compound 12-vitamins for injection which was given by a nurse as a substitute for water-soluble vitamin without the permission of the physician might have been caught and prevented by the involvement of the pharmacist in the Unit Dose Dispensing System.

Study Period

This study was planned such that both groups would be observed for 14 consecutive days before and after the intervention, and the time for the installation intervention of the Unit Dose Dispensing System would be 6 months. However, after the observer arrived on site and explained the plan again, serious disagreement occurred. After negotiation with the Director of the Physicians and the Chief Head Nurse, it was agreed that the intervention of the Unit Dose Dispensing System would be limited to TPN doses, and the study period compressed into a 3-month period with 10 consecutive days of the observation period for each group.

Advantages and Disadvantages of One Observer Versus Two Observers

One observer was used in this study. The use of two observers who were assigned to observe one nurse was used in the previous study to study intra-observer reliability (Barker, Kimbrough, & Heller, 1966). The reliability within one observer and reliability between two observers can both be measured by the Pearson Correlation Coefficient Analysis. The mean difference by T-Test or ANOVA can be measured between the two observations for the agreement of the operational definitions.

The advantages and disadvantages of one observer versus two observers are compared and listed in Table 38.

Table 38: Advantages and Disadvantages of One Observer Versus Two Observers

	Advantages	Disadvantages
One Observer	<ol style="list-style-type: none">1. No extra training and measurement for the agreement of the operational definitions.2. Physically possible in a small space.3. Economical.	<ol style="list-style-type: none">1. One observer could miss or incompletely record the information when workload is high.2. Need measure of inter-observer Reliability.
Two Observers	<ol style="list-style-type: none">1. Reduce missed or incompletely recorded information by one	<ol style="list-style-type: none">1. Need extra coordination of observer activities.2. Need for measures of reliabilities

	<p>observer.</p> <p>2. Double-check and reduce systematic errors by one observer.</p> <p>3. Opportunity for quality control by comparing results of observers.</p>	<p>within one observer and between two observers.</p> <p>3. Non-economical</p> <p>4. Need larger space for the two observers.</p> <p>5. Put more stress on the observed nurses and might get the project discontinued.</p>
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Comparison with Other Studies

This is the first study to evaluate the effects of the unit dose dispensing concept on IV medication administration errors in a Chinese hospital. First, this study extended the studies of the Unit Dose Dispensing System performed in the US and internationally (Barker, Heller, Brennan, & Sheldon, 1964; Dean, Allan, Barber, & Barker, 1995; Hynniman, Conrad, Urch, Rudnick, & Parker, 1970; Means, Derewicz, & Lamy, 1975; Schnell, 1976) by using control and experimental groups with cluster randomized design. Second, it filled the gap that no research by the observation method had been conducted on medication errors in a Chinese hospital, with the high volume usage of IV drugs in China. Third, the study showed that the inadequate labeling of the poor medication use system can hide IV medication errors. Fourth, this study showed that a change in the medication use system can significantly reduce IV medication errors, which should

attract the Chinese public and healthcare providers' attention to improve medication use safety.

This study improved the development and use of operational definition thus minimizing the use of subjective judgments (Bruce & Wong, 2001), and the unclear deviation percentage of wrong dose errors which were common in previous studies on IV medication errors (Bruce & Wong, 2001; Hartley & Dhillon, 1998; Van den Bemt et al., 2002; Wirtz, Taxis, & Barber, 2003). This study used standardized operational definitions of medication errors with clear deviation percentages, a defined total opportunities for error, and error rate calculations capable of providing comparable results for IV medication errors.

If the IV preparation processes and administration processes are studied separately, the results may compromise any clues to the causes of errors that reach the patients finally (Taxis & Barber, 2003a, 2003b; Taxis & Barber, 2004; Wirtz, Taxis, & Barber, 2003). In this study, although the preparation processes were observed, only the medication administration errors were measured and reported as the outcome at the endpoint of the medication use system.

Limitations

Convenience Sample

The study patient ward offered for the study was located in a teaching tertiary hospital was selected as a convenience in Beijing, the capital of China. Thus this was a convenience sample.

The distribution of general government health spending in China (e.g., including social health insurance spending) is heavily skewed to urban area within a province, and unequally distributed across provinces. (Wagstaff, Yip, Lindelow, & Hsiao, 2009). These inequalities in government health spending were at least in part responsible for the geographic inequalities in the accessibility and quality of health facilities (poor inland provinces versus prosperous southeastern provinces), their use and health outcomes (Wagstaff, Yip, Lindelow, & Hsiao, 2009). The statistical data from the Ministry of Health in 2009 showed that Beijing has 6,497 health care institutions: about equal to the quantity of health care institutions in some provinces (Chinese Ministry of Health, 2009).

Therefore, the generalization of the results from this hospital to other hospitals of different levels in other provinces may be limited.

Investigator Accuracy

The Principal Investigator accuracy was considered as a potential limitation because there was only one observer who observed and recorded the prescriptions, the preparation processes in the narrow IV preparation room, and the administration processes during a busy time. However, all the medication errors were considered valid after being double checked by the Principal Investigator and evaluated again by the major advisor, and the complete details of each error are included in this report for the scrutiny of the reader.

If the Principal Investigator failed to capturing all possible IV medication preparation and administration errors, then the under reporting could have contributed to

the systematic errors. However, the effect of this kind of systematic error should be minimized by the design with a Control group.

Insulin Doses (Small Volume)

When the preparation nurses added the insulin doses quickly, the small volume of insulin doses was difficult to observe. A total of 17 wrong dose errors were observed in the 39 ordered insulin doses in the Control group. Assuming that some of the rest corrected insulin doses (22 doses) were not accurately observed, a maximum estimation of such insulin doses was 4% of the ordered doses in the Control group. A total of 3 wrong dose errors were observed in the 16 ordered insulin doses in the Experimental group before the intervention of the Unit Dose Dispensing System. A maximum estimation of the incomplete insulin doses was 5% of the ordered doses. The insulin doses in the Experimental group after the intervention of the Unit Dose Dispensing System were not evaluated, because the doses of insulin were calculated and given in the volume before the preparation.

Observation of the Administration Processes

Not the entire process of the infusion was always observed. The observer didn't always know whether a TPN dose was stopped late in the day after the observation-period.

Exclusion of Doses

A total of 18 doses (3% of the ordered doses in the Control group) and 14 doses (2% of the ordered doses in the Experimental group) were excluded from the study (T.O.E.s) as falling outside of the operational definitions of the error categories. These thirty two errors involved the introduction of un-measurable volumes of liquids when sharing the tube and needle in transferring similar doses into the Kabiven TM PI bag (1440 ml) by gravity.

Sterility or Contamination

Sterility or Contamination problems were outside the scope of this study. The contamination errors were excluded by the observer in the study, because the operational definition required that any amount extra would be measurable, and measured. For example, the nurses used the discarded bottles of N (2)-L-alanyl-L-glutamine for injection or Compound Amino Acid Injection (15-HBC) which were used for the previous patient to transfer the ingredients into the Kabiven PI bag for the second or the third patient. However, these errors were not included in the statistical analysis because the observer could not detect what ingredients and the volumes were left in the reused bottle. The number of such doses was 18 doses (3% of the ordered doses) in the Control group and 14 doses (2% of the ordered doses) in the Experimental group.

TPN V.S. Non-TPN IV Doses Excluded

The nursing staff changed their mind and decided late in the study that they wanted Non-TPNs to be excluded. They decided that they would allow the Unit Dose

Dispensing System to be installed for TPN doses only (despite prolonged negotiations). Thus, Non-TPN doses including prefilled injectable syringes and the base solution containing one additive of antibiotics were excluded.

In the baseline observation, a total of 790 Non-TPN T.O.E.s were observed for an error rate of 10.5%.

Effect of the Nurses

No measure of the effect of individual nurses on the preparation and administration processes was recorded due to the possibilities that the doses for one patient could be prepared and administered by more than two nurses. Therefore, no intra-cluster correlation coefficients were analyzed. Even in the preparation process and especially in the Control group, the doses in a group of TPN orders for one patient could be prepared by two nurses. For example, one nurse transferred the additives from the ampoules into the 5% Glucose Solution and the second nurse continued by adding the insulin and transferring the liquid from the glucose solution bottle into the Kabiven TM PI bag (1440 ml) by gravity.

Effect of the Observation

The use of the observation method is always subject to the possibility of an effect of the observer upon the observed. Overall medication error rates were plotted by each observational day for both the Control group and the Experimental group in Appendix G. The error rate on Day 1 was the highest among the observational days. Except for this, a trend of increase or decrease of the error rates in two groups over the observational days

was not found on the graphs, which has been taken to indicate that such the “Hawthorne Effect” (the tendency that the subjects work nervously and poorly or perform better when they are under the observation in an experiment) was not found in the study.

Generalization

The study site was a patient ward in a teaching tertiary hospital in Beijing, the capital of China. The distribution of general government health spending (e.g., including social health insurance spending) is heavily skewed to urban area within a province, and unequally distributed across provinces. (Wagstaff, Yip, Lindelow, & Hsiao, 2009). These inequalities in government health spending were at least in part responsible for the geographic inequalities in the accessibility and quality of health facilities (poor inland provinces versus prosperous southeastern provinces), their use and health outcomes (Wagstaff, Yip, Lindelow, & Hsiao, 2009). The statistical data from the Ministry of Health in 2009 showed that Beijing has 6,497 health care institutions: about equal to the quantity of health care institutions in some provinces (Chinese Ministry of Health, 2009). Therefore, the generalization of the results from this hospital to other hospitals of different levels in other provinces may be limited.

Before the change to the Unit Dose Dispensing System, the HIS computerized system was already installed at both the physician’s station and the nurse’s station. Generalization to hospitals without this HIS system must be made with caution. It should be noted that the HIS system was used as a communication tool for requesting IV medications to be delivered in batch from the pharmacy, and for the charge process when the patient checked out from the patient ward. The existing IV preparation and

administration processes was generally representative of the current IV preparation and administration processes in the majority of large hospital without printable labels from the HIS system and a Centralized Pharmacy Intravenous Admixture Service (PIVAS) in pharmacy.

Therefore, the results are believed to be useful as the basis for considering the widespread introduction of the Unit Dose Dispensing System in the IV centralized preparation and administration processes.

Implications

Implications for Hospitals

The Chinese health care system is principally a hospital centered, three-tiered system, with public health network support at the primary care level (Hong & Yatsushiro, 2003). At each level, hospitals are divided further into three grade levels according to the quality of their services (Hong & Yatsushiro, 2003). The grade level of each hospital is decided by the Ministry of Health according to its roles and functions, size, level of technology, and quality of medical services.

The results of this study indicated that the current centralized IV preparation by the nurses in an IV preparation room in this tertiary A-level Chinese hospital had a high error rate. So, the quality of medication accuracy in the first and second tiered hospitals could be worse.

The total number of TPN medication errors observed in the Control and Experimental groups for the baseline study was 27 (T.O.E.s = 475), resulting in a total error rate of 6%.

The errors involving the clinically significant drugs in the ISMP high alert drugs list were: Potassium chloride injection concentrate (15%), Sodium chloride injection concentrate (10%), and Insulin. The clues to the causes of the errors suggested badly handwritten transcriptions (30%), lacking insulin volume label (33% wrong dose and 4% omission), limited shelf space (15%), and lacking double check before the preparation (7%).

The significance of this study is to strongly suggest that the Unit Dose Dispensing System designed for this Chinese hospital offers a reduction in the medication error rate of 70% at a relatively low cost. The cost should be relatively low because manual labor is used instead of automated systems which are very expensive.

The Unit Dose Dispensing System has been used in the Pharmacy Intravenous Admixture Center Service (PIVAS) at some Chinese military hospitals (Appendix J). Based on the results of this study, the Unit Dose Dispensing System is recommended for use at least for preparing TPN doses in other Chinese hospitals as well as the hospitals with similar IV preparation process in other developing countries.

Although the nursing staff changed their mind to exclude Non-TPNs from the Unit Dose Dispensing System late in the study, a total of 790 Non-TPN T.O.E.s were observed in the baseline study with a high error rate of 10.5%. A future study can address the clues to the causes of the errors in Non-TPN doses, and another study should focus on measuring the effect of the Unit Dose Dispensing System on reducing medication errors for Non-TPN doses.

Implications for Nurses

Nursing education varies greatly at multiple levels in China. There are about 862 secondary vocational nursing programs (2-3 years for high school graduates or 3-4 years for junior high school graduates), 307 diploma/associate programs (3 years for high school graduates), 192 baccalaureate programs (admits high school graduates through National University Admission Examinations), 65 masters programs and 10 doctoral programs in Chinese nursing education (Gao, Chan, & Cheng, 2011).

Several deficiencies in nursing IV preparation procedure which could potentially contribute to errors were found in this study: (1) no special precautions were observed when the nurses admixed high risk drugs; (2) the chemotherapy drugs were prepared in the same preparation room as TPN doses under no laminar air flow hood with limited protections (included two layers of gloves (plastic and rubber gloves), cotton mask, and opening the windows); (3) violations of the preparation procedures such that the tube and needle were shared for two patients in transferring similar additives into the Kabiven TM PI bags (1440 ml) were found; and (4) No labels containing the patient information and the additive drug information were placed on the base solution bag, such a system lacking labels seemed likely to raise the risk of errors and make them difficult to be detected in the system especially during the preparation process.

The findings of this study suggest that it is necessary to integrate the education of patient safety into the curriculum of the nursing education as well as continuing education or training during their practice.

Implications for Pharmacists

The findings of this study showed that although the preparation nurses were asked to double check the doses before the preparation, this activity was omitted due to the rushing hours in the morning or was interrupted by other on-call tasks, such as a telephone call, questions from a physician, need to withdraw the patients' blood, etc. The proposed Unit Dose Dispensing System for Chinese hospitals would integrate a pharmacist who does not prepare the TPN doses, but focuses on the role of editing order and checking labels in the medication use system.

If the hospital does not have enough pharmacists, a nurse can be considered for the role of editing orders and checking in the medication use system. However this nurse should not be the same nurse who perform the tasks of checking and preparing IV doses.

Implications for Pediatric Care

This study showed that more than 70% of the detected TPN errors (27 errors) observed in the Control and Experimental groups for the baseline study were wrong dose errors (19 errors). The Principal Investigator recognizes that the doses for children are more sensitive based on the age and weight of individuals.

Due to the high volume usage of prescribed infusion for Chinese people, especially for children it is highly recommended that the problem of IV medication errors for children, and potential effect of the Unit Dose Dispensing System on reducing medication errors for children be studied.

Recommendations for Future Studies

The recommendations for future studies are as follows:

1. It is recommended that the clues to the causes of the errors in Non-TPN doses and the effect of the Unit Dose Dispensing System on reducing medication errors for Non-TPN doses be studied.
2. It is highly recommended that the IV medication errors for children as well as the effect of the Unit Dose Dispensing System on reducing medication errors for children be studied.
3. It is recommended that the factors of inefficiencies, workload, and interruptions on the errors in the preparation of IVs receive further study.
4. The Principal Investigator recognized that E-Prescribing was available in the new installed HIS in this Chinese hospital although the physicians were not adapted to the full function. It is recommended that an explanatory study of the optimized utilization of technologies (e.g., E-Prescribing) should be incorporated into the Unit Dose Dispensing System and the effect on medication errors studied.

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Appendix A: Conversations with the Director of the Hospital Pharmacy

A Letter for the Educational Purpose in the December 2008

Dear Director ***,

I am writing this letter to ask for your help with my research. My dissertation research project is to evaluate the effect of a unit dose system on medication accuracy in Chinese hospitals. I am planning to send a questionnaire to ask about the current processes of dispensing medications in your hospital pharmacy, and information about unit dose systems in Chinese hospital pharmacies.

I am sending you this questionnaire in email for your review firstly, and then later I plan to call you on the phone for your answers to these questions.

You were selected to be part of this project because you are a highly respected member committee of the Chinese Hospital Pharmacy Association, which is also interested in medication errors. Your hospital was one of the famous hospitals in the People's Republic of China. I know that as the Director of Pharmacists you are very busy, but I hope that you will take the time to participate in helping me draft this national questionnaire.

Before drafting my questionnaire, I did a literature review of Chinese hospital pharmacies. I found very few published papers that displayed in detail the processes of dispensing medications in hospital pharmacy. The specific purpose of my study is to help me get a clear picture of the processes of dispensing medications in hospital pharmacy and the current status and usage of unit dose system.

Please try to answer the questions in detail and precisely as much as you can. Your answers will be completely confidential. Your response will be used for research purposes only. I will not release any information identifying your hospital pharmacy to a third party. If you feel uncomfortable about some questions, please let me know and I will change them.

Thank you in advance for your help in drafting this questionnaire. If you have any questions, please contact me at 334-275-1778 or dingqia@auburn.edu or Dr Barker at 334-844-5152 or BARKEKN@auburn.edu.

Sincerely,

Qian Ding
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Questions to the Director of Pharmacy

问题:

A. Those questions are focused on your hospital inpatient pharmacy

A. 以下问题是关于您所在的医院药房:

1. When prescribing, do the physicians use Electronic Physician Order Entry?

请问医生开药方的时候, 使用电子医生处方输入体系么?

2. Who transcribe the prescription orders, nurses or pharmacists?

请问由谁转录医生的处方? 护士还是药剂师?

3. What kind of orders do pharmacists receive, original physician orders, photo-copied orders or transcribed orders? When do pharmacists receive them after the orders are prescribed and how do pharmacists receive them, through fax, scanner or personnel delivery?

请问药房药师收到的是医生的原始处方, 复印件还是转录过的处方?

请问一般医生开好处方, 药房多久可以收到?

请问处方通过什么方式到达药房的? 传真, 扫描还是有专人运送?

4. Who dispense medications, pharmacists, technicians or others_____?

请问药房由谁发药? 药剂师, 技术人员(技工)还是其他? 如果是其他, 请说明。

5. Is the medication dispensed from the same pharmacy? Are there pharmacies on each floor?

请问住院病房和门诊所有的药都是从一个药房发出的么? 住院部每一个楼层还备有药房么?

6. How long will the pharmacy process the dispensing?

请问药房收到处方后何时摆药, 从收到处方到摆要完成需要多长时间?

7. How many doses and what kind of packages are dispensed to the nursing unit at one time?

请问每次送到各个住院部护士站的药物是每个病人几天的剂量, 包装材料是什么?

8. Please explain how the medications are delivered from pharmacy to the nursing units and how many times they deliver for each day?

请问药房摆好的药物是怎样运到各住院部护士站的? 并且每天送几次?

9. How do nurses check medications when they receive medications from pharmacy?

请问护士收到药物怎样核实药品和病人的?

10. When, where and how do nurses prepare medications before administration?

请问各住院部护士在什么时间, 什么地点, 怎样给病人准备服用的药品的?

B. Those questions are related to the workload:

以下问题关于工作量

1. How many beds in your hospital?

请问贵医院住院部有多少床位?

2. How many patient wards in your hospital?

请问贵医院一共有多少住院单元?

3. How many beds per patient ward and how many nurses per patient ward?

请问每个住院单元有多少床位, 多少护士?

4. How many pharmacists in the hospital pharmacy?

请问医院住院药房共有多少药剂师?

5. How many prescription orders dispensed per day minimum, average and maximum?

请问医院药房平均每天摆多少处方药, 最少和最多每天摆多少处方药?

C. Those questions are related to the attitude and knowledge of unit dose system:

以下问题关于您对单剂量发药体系的态度和知识

1. Are you familiar with the concept of unit dose system?

请问您了解单剂量发药体系概念么?

2. Has your hospital pharmacy installed the Unit Dose Dispensing System?

请问贵医院药房使用单剂量发药体系了么?

3. If not, would you like to install the Unit Dose Dispensing System?

如果上题回答没有, 请问您愿意使用单剂量发药体系么?

4. Do you know which hospital has installed unit dose system in hospital pharmacy in Mainland China?

请问您知道国内哪些医院安装了单剂量体系发药体系么?

5. Can you give me their contact information?

请问您知道他们的联系方式么?

D. Those two questions are related to the resource about hospital pharmacy information

以下问题关于医院药房信息资源

1. Is there an association, which is like ASHP in the US, in Mainland China?

请问您知道国内有没有相当于 ASHP 的组织?

2. Is there such a book published by government or Health Department gathering information of hospitals in China and where can I buy such a book?

请问您知道国内有没有权威出版社出版的医院名录，请问哪里有卖这本书的？

Script to the Observed Nurses

Subject: Protocol “The Effects of the Unit Dose Dispensing System on IV Medication Administration Accuracy in a Chinese Hospital: Inpatients”

Principal Investigator: Qian Ding

Key Personnel: Qian Ding, Kenneth N. Barker, and Elizabeth A. Flynn

Date research materials submitted to IRB: Feb 05, 2010

Name of Institutional Review Board: Hospital Clinical Research Ethical Review Board

Objective of the Study:

1. Explore the nature and frequency of IV medication errors among Chinese hospital inpatients.
2. Study the effect of a Unit Dose Dispensing System upon IV medication errors in Chinese hospital inpatients?

Research Methods:

Randomize Control Trial

Two patient units will be randomly selected to be the Control group or the Experimental group.

The Before intervention observations (Baseline) will run from June to September 2010. The traditional system is that the nurses prepare IV medications in the treatment room in the inpatient units.

The intervention to be introduced, Unit Dose Dispensing for IV drugs, is designed to be used the patient unit selected as the experimental group by random assignment from October 2010 to March 2011. The IV drugs are designed to be dispensed from the pharmacy in the ready-to-administer unit dose form, which means that the additives are added into the base solutions with labels on the base solutions. The pharmacists will check the IV drugs before they are dispensed to the patient units.

The After intervention observations will run from April to June 2011.

Outcome Measurement:

IV medication administration errors by the Direct Observation Method

The observer, Qian Ding, was trained by Dr. Flynn the direct observation method for one week in a U.S. hospital in the summer 2008 and certified in the proper use of observation method to detect medication errors.

The regular medications preparation and administration working processes will be observed and recorded on the standardized observational tools (Drug Pass Worksheet, Drug Order, and Medication Error Summary Worksheet) by the observer. The details are as follows. The observer will randomly select a nurse, follow this nurse, and observe the processes as she uses to prepare and administer the medicines, including any dosage form. The observer will write down what the nurse did, including the medication's name, dosage form, dose, strength, dose preparation and administration time, and administration rate if the medicine is an IV drug. Then the notes will be compared with the written interpretable

orders on the patients' charts to detect the IV medication administration errors. Once the errors are identified and addressed on the Medication Error Summary Worksheet, The observer will shred the worksheets of Drug Orders and Drug Pass with patients' names within 90 days.

Observation period for each patient ward will cover about 14 consecutive days from 7 AM to 3 PM. The consented nurses or the pharmacists for one patient ward have the same opportunities to be picked up for the observation during the observation period. The total observation periods will cover around 56 days for four patient wards.

Participants:

Medication nurses in the chosen patient wards

IV preparation pharmacists in the chosen experimental groups

Participants will be recruited by the script of the project description posted on the board in the patient wards, which was provided by the Principal Investigator. Before initiating the study, an AU IRB approved stamped consent form will be given to the medication nurses and IV preparation pharmacists. The Principal Investigator will describe the study to the nurses and pharmacists before they read the consent form. The participants have the opportunities to ask any questions to the Principal Investigator. The signed consent forms are returned to Qian Ding in the closed envelopes. The consent forms are confidential to their supervisors, colleagues or the third party. The nurses have the opportunities to withdraw the study at any time during the study without causing bad relationship with their employer hospital or bad effects on their job in the future.

Protection of the DATA:

The data collected with patients name will be shredded in 10 days when the observer detects the errors. Before shredding, the data are locked in the drawer in Qian Ding's apartment in Beijing.

Pictures and videos without any identifiable person's face are allowed. The hardcopies including the pictures and the Medication Error Summary Worksheet will be locked in the Qian Ding's personal cabinet in 205 Dunstan Hall in Auburn University. The electronic records of the pictures and videos are stored in Qian Ding's personal laptop locked by a private password. The Principal Investigator will shed the hardcopies and delete the electronic files from the laptop by June 1, 2013.

Appendix B: Official IRB Approval Letter from the Hospital



OFFICIAL IRB EQUIVALENT APPROVAL LETTER

March 22, 2010

Auburn University Institutional Review Board
The Office of Human Subjects
307 Samford Hall
Auburn, AL 36849

Dear IRB Committee Members in Auburn University,

I am one of the committee members of [redacted] Hospital Clinical Research Ethical Review Board. Qian Ding's application for "The Effects of a Unit Dose Dispensing System on I.V. Medication Administration Accuracy in a Chinese Hospital: Inpatient" doesn't fall under our regular IRB ethical reviewing process. The [redacted] Hospital Clinical Research Ethical Review Board only review studies involving patients as subjects such as with a new drug clinical trial, a new medical surgery technical trial, or a new medical device trial.

However, in response to the request of Qian Ding and her advisor Dr. Barker, we can offer this official IRB equivalent approval letter to allow her to conduct her doctoral research project here using observations of the medication nurses and pharmacists from June 1, 2010 to as late as June 30, 2011.

We have reviewed the details of her proposed study including the data collection method and the protection of the confidentiality of the data, which we summarize below. The observation will be conducted twice: before (June 1-September 1, 2010) and after (April 1-June 30, 2011) the intervention of a unit dose dispensing system on I.V. drugs. Four patient wards are going to be chosen for the observation by Qian Ding. The regular medications preparation and administration working process will be observed and recorded on the standardized observational tools (Drug Pass Worksheet, Drug Order, and Medication Error Summary Worksheet) by the observer. Once the errors are identified and addressed on the Medication Error Summary Worksheet, The observer will shred the worksheets of Drug Orders and Drug Pass with patients' identifiable information (patients' initials, room numbers and bed numbers) within 10 days. By June 2013, Qian Ding will shred all the research hardcopies which will be locked in the cabinet in Dunstan Hall in Auburn University and delete electronic files which will be protected by a private password from her

personal laptop. Observation period for each patient ward will cover about 14 consecutive days from 7AM to 3PM. The consented nurses or the pharmacists for one patient ward have the same opportunities to be picked up for the observation during the observation period. The total observation period will cover around 56 days for four patient wards.

Qian Ding has agreed to provide a copy of the Auburn University IRB approved, stamped consent document before she recruits the nurses and the pharmacists. Qian Ding will recruit the medication nurses or the pharmacists in chosen four patient wards by giving a 30 minutes meeting and handing out the Auburn IRB approved and stamped consent forms to them. The participations in the research are totally voluntary and the participants have the opportunity to withdraw at any time during the study without any harm in the relationship with their supervisors or the employer. The nurses and pharmacists will return the completed and signed consent forms in closed envelopes on the second day. The signed consent forms are not released to the supervisors of the participated nurses and the pharmacists. The hospital will not identify the connections between the errors and the medication nurses or the pharmacists and hence will not be able to identify and punish the individuals observed for any errors observed.

We agree to monitor the conduct of the study as it progresses and notify you of any changes or adverse events. If you have any question relating to the ethical subjects, please contact our Clinical Ethical Research Review Board through the E-mails: [redacted] or [redacted]

Best Regards,

[redacted]
[redacted] Director
Outpatient Department
[redacted] Hospital
[redacted]
Beijing, [redacted] China
Phone: 86-10-[redacted]
E-mail: [redacted]
Web Address: [redacted]

Appendix C: Informed Consent Letter (English and Chinese Versions)

DEPARTMENT
OF PHARMACY
CARE SYSTEMS

Consent Letter



AUBURN UNIVERSITY

HARRISON SCHOOL
OF PHARMACY

The Auburn University
Institutional Review Board
has approved this document for use
from 3/10/10 to 3/1/11
Protocol # 10-054 AK 1003

(NOTE: DO NOT SIGN THIS DOCUMENT UNLESS AN IRB APPROVAL STAMP WITH
CURRENT DATES HAS BEEN APPLIED TO THIS DOCUMENT.)

INFORMED CONSENT

for the Research Study of

"THE EFFECTS OF UNIT DOSE DISPENSING SYSTEMS ON MEDICATION
ADMINISTRATION ACCURACY IN INTRAVENOUS DRUGS IN A CHINESE HOSPITAL:
INPATIENTS"

You are invited to participate in a research study to investigate the effects of unit dose dispensing systems on I.V. medication administration accuracy. The study is being conducted by Qian Ding B.S., under the direction of Kenneth N. Barker Ph.D. in the Auburn University Department of Pharmacy Care Systems.

You may participate if you are a medication nurse or pharmacist who prepares medications, and you are age 19 or older. If you decide to participate in this research study, you will be asked not do anything different from what you normally do in working from 7AM to 3PM. This study has two observation periods from June to August 2010 and Mar to June 2011. Each observation period will cover 14 consecutive days. During each of the 14 observation days, you will be observed by me. I will follow you, observe, and write notes on what you have done when you are doing your normal work. But your name will not be recorded in the note. The risks associated with participating in this study are minimal. To minimize these risks, we will collect data anonymously. There are no direct benefits, compensation or costs for participating in this study. No information that could be connected to you will be shared with the hospital or your supervisor.

Your privacy will be protected. Any information obtained in connection with this study will be anonymous. There is no direct or indirect link between the records and the participants' information. Results obtained through your participation may be published in a professional journal or presented at a professional meeting without releasing any personal information.

Participant's initials _____

Page 1 of 2

If you have questions about this study, please ask me now or contact Qian Ding at 334-275-1778 or e-mail her at dingqia@auburn.edu. You can return your consent form (signed or not signed) to me tomorrow in a sealed envelop. The results of this consent forms are private to your colleagues and your employer. A copy of this signed document will be given to you to keep.

If you change your mind about participating, you can withdraw at any time during the study. Your participation is completely voluntary. If you choose to withdraw, your data can be withdrawn as long as it is identifiable. Your decision about whether or not to participate or to stop participating will not jeopardize your future relations with your employer, the [redacted] Hospital.

If you have questions about your rights as a research participant, you may contact the Auburn University Office of Human Subjects Research or the Institutional Review Board by phone (334)-844-5966 or e-mail at hsubjec@auburn.edu or IRBChair@auburn.edu.

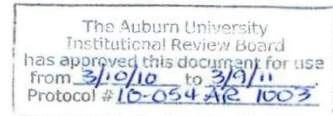
HAVING READ THE INFORMATION PROVIDED, YOU MUST DECIDE WHETHER OR NOT YOU WISH TO PARTICIPATE IN THIS RESEARCH STUDY. YOUR SIGNATURE INDICATES YOUR WILLINGNESS TO PARTICIPATE.

Participant's signature Date

Investigator obtaining consent Date

Printed Name

Printed Name



知情同意书

The Auburn University
Institutional Review Board
has approved this document for use
from 3/10/10 to 3/9/11
Protocol # 10-054 AR 1003

DEPARTMENT
OF PHARMACY
CARE SYSTEMS



AUBURN UNIVERSITY

HARRISON SCHOOL
OF PHARMACY

(注明: 在伦理委员会盖章并注明当前日期生效前请不要签署此文件)

知情同意书

研究项目

(单剂量发药系统对中国医院住院病人输液给药准确性效果的研究)

您被邀请参加本次关于单剂量发药系统对输液给药准确性效果的实验。本次实验由奥本大学药事管理系的丁倩学士在Kenneth N. Barker 博士的指导下设计与实施。

如果您是19岁以上并且配发药品的护士或者药师, 您将可以参加本次实验。如果您决定参加本次实验, 您将被请求在实验过程中不改变您任何的日常工作方式。本次实验包括两次观察阶段分别是2010年6月至9月和2011年3月至6月, 每次观察时间是连续14天从早上7点到下午3点。在每次连续14天的观察期间, 您有可能被随机抽到被观察。在您工作期间, 我将跟随您并将您的日常工作过程记录下来, 本次实验的数据采用匿名收集, 将对您的危害性降到最低。整个实验不对您提供任何直接性的补偿和报酬, 同样也不需要您作出花费。任何与您相关的信息将不会被医院或者您的主管获得。

对于您来说, 所有的信息将是保密的。如果您决定参加本项研究, 实验过程中数据收集采取匿名方式(保密)。数据与个人信息之间没有直接或间接联系。这项研究结果发表到专业期刊或会议时, 将不会披露您个人的任何资料。

参加试验者签名_____

页码 1 / 2

如果您对本研究有任何疑问，您可以首先向研究人员提出来。您可以通过电话334-275-1778或者电子邮件dingqian@auburn.edu直接联系本项目的研究人员丁倩。请于明天将签好或空白的知情同意书放在封好的信封中交给我，参加实验人员的名单将对您的同事和医院保密。在您将收到一份签过字的“知情同意书”副本。

您可以选择不参加本次实验，或者在任何时候通知研究者要求退出实验，您的数据将不纳入研究结果，您的任何参加或不参加本次实验的决定不会影响或危害您今后与 [redacted] 的关系。

如果您对参与本次实验的权利有问题，您可以通过电话 (334)-844-5966 或者电子邮件方式 hsubject@auburn.edu or IRBChair@auburn.edu 联系奥本大学人类研究对象保护办公室或机构审查委员会。

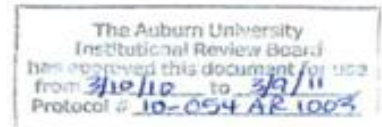
阅读完上述信息，请您决定是否参加本次实验，您的签名表示您愿意参加本次实验。

实验参加者签名 日期

研究者签名 日期

实验参加者姓名

研究者姓名



Appendix D: Renewed IRB Form

APPROVED

**AUBURN UNIVERSITY INSTITUTIONAL REVIEW BOARD for RESEARCH INVOLVING HUMAN SUBJECTS
REQUEST for PROTOCOL RENEWAL**

For information or help completing this form, contact: THE OFFICE OF HUMAN SUBJECTS RESEARCH, 307 Samford Hall
Phone: 334-844-5966 e-mail: hsubjec@auburn.edu Web Address: http://www.auburn.edu/research/vpr/ohs/index.htm

Complete this form using Adobe Acrobat Writer (versions 5.0 and greater). Hand written forms will not be accepted.

1. Protocol Number: 10-054 AR 1003
 2. Original IRB Approval Dates: From: March 10, 2010 To: March 9, 2011
 3. Requested ONE YEAR MAXIMUM Renewal Period: From: March 10, 2011 To: Mar 9, 2012
 4. PROJECT TITLE: THE EFFECTS OF UNIT DOSE DISPENSING SYSTEMS ON MEDICATION ADMINISTRATION ACCURACY IN INTRAVENOUS DRUGS IN A CHINESE HOSPITAL: INPATIENTS
- | | | | | |
|----------------------------------|--|------|------------------|--------------------|
| 5. Qian Ding | Ph.D. Candidate | PCS | 334-844-5152 | dingqia@auburn.edu |
| PRINCIPAL INVESTIGATOR | TITLE | DEPT | PHONE | AU E-MAIL |
| <i>(on file)</i> | 205 Dunstan Hall, Auburn University, AL, 36849 | | | qian1978@gmail.com |
| PI SIGNATURE | MAILING ADDRESS | | ALTERNATE E-MAIL | |
| Kenneth N. Barker, Ph.D. | <i>[Signature]</i> | PCS | 334-844-5152 | barkekn@auburn.edu |
| FACULTY ADVISOR | SIGNATURE | DEPT | PHONE | AU E-MAIL |
| Name of Current Department Head: | Richard A. Hansen, Ph.D. | | AU E-MAIL: | rah0019@auburn.edu |
6. Current External Funding Agency: None
 7. List any contractors, sub-contractors, or other entities or IRBs associated with this project:
None
 8. Briefly list (numbered or bulleted) the activities that occurred over the past year, particularly those that involved participants.
 1. Permission letter obtained from study site hospital.
 2. Travel to hospital in Beijing, China.
 3. Presentations to pharmacy and nursing leaders: permission obtained.
 4. Orientation to I.V. preparation/administration areas: work areas, work systems, personnel, jobs.,
 5. Selecting patient care areas, random assignment to control/experiment units
 6. Observing I.V. work by consented nurses: charts reviewed for errors.
 7. Errors detected tabulated and described.
 8. Work begun on defining process changes to Unit Dose concept.
 9. Explain why you are requesting additional time to complete this research project.
N.A.

The Auburn University Institutional Review Board has approved this document for use from 9/22/10 to 3/9/11 Protocol # 10-054 AR 1003

Appendix E: Data Collection Forms

Table 39: Drug Pass Worksheet

Observer _____		Date _____	Page _____
Patient Initial:		Room #:	Bed #:
OE#	Time	Med, Strength, Amount, Form, Route	Comments (e.g., prep. Technique, circumstances, interruptions)
	Prep		
	Admin		

Table 40: Drug Order Worksheet

Observer _____

Page _____

Date _____

Patient Initial:		Room #	Bed #					
OE#	Date, time of the order	Med, strength, amount, form, instructions	Time dose due					

Drug allergies: _____

Table 41: Medication Error Summary Worksheet

Observer _____ Date _____

Page _____

OE#	Med Error Description: Administered versus Ordered	Error Category								
		Omission	Unordered	Wrong Dose	Wrong Dosage Form	Wrong Route	Wrong Administration Rate	Wrong Time	Compatibility time	Wrong Administration Technique
Subtotal:										

Total Errors= _____

Total Opportunities for Error= _____ (_____ #Doses Given + _____ #Omission)

Accuracy Rate:

((Total Opportunities for Error)-(Total Errors)) divided by (Total Opportunities for Error)x100 = _____%

Accuracy Rate Excluding Wrong Time Errors:

((Total Opportunities for Error)-(Total Errors)+(Wrong Time Errors))divided by (Total Opportunities for Error)x100= _____%

Appendix F: SAS Codes

SAS Code 1: Analysis of Covariance (ANCOVA)

```

/*ANCOVA*/
ODS Graphics on;
ODS RTF;
options nodate;

Data Disser_ANCOVA;
Input Group Overall_Before Overall_After WrongDose_Before
WrongDose_After Omission_Before Omission_After;
/*
Adjusted=After(i)-Beta*[Before(i)-Before(mean)]
The coefficient Beta is a weighted average of the slopes of the linear
regression.
To obtain this coefficient, add the solution option to the Model
statement:
Model After = Group Before/solution
*/
Overall_Adjusted=Overall_After-(-0.137579664)*(Overall_Before-5.56);
WrongDose_Adjusted=WrongDose_After-(-0.179758520)*(WrongDose_Before-
3.83);
Omission_Adjusted=Omission_After-0.007073043*(Omission_Before-1.36);
Datalines;
1 30.77 3.70 7.69 0.00 15.38 3.70
1 9.09 14.29 9.09 0.00 0.00 9.52
1 3.23 2.56 3.23 0.00 0.00 2.56
1 5.26 8.00 5.26 4.00 0.00 4.00
1 4.35 8.00 4.35 8.00 0.00 0.00
1 10.00 11.36 0.00 2.27 10.00 9.09
1 0.00 15.00 0.00 7.50 0.00 7.50
1 6.67 3.03 6.67 3.03 0.00 0.00
1 6.67 19.44 6.67 2.78 0.00 16.67
1 0.00 8.57 0.00 2.86 0.00 2.86
1 0.00 . 0.00 . 0.00 .
2 0.00 0.00 0.00 0.00 0.00 0.00
2 12.00 2.04 12.00 0.00 0.00 2.04
2 4.00 0.00 4.00 0.00 0.00 0.00
2 3.45 0.00 3.45 0.00 0.00 0.00
2 2.86 2.63 2.86 0.00 0.00 2.63
2 3.23 0.00 0.00 0.00 3.23 0.00
2 3.23 0.00 3.23 0.00 0.00 0.00
2 4.55 5.26 4.55 0.00 0.00 5.26
2 3.70 2.27 3.70 0.00 0.00 2.27
2 3.70 0.00 3.70 0.00 0.00 0.00
;
run;

Proc Format;
Value Group 1='Control Group'
2='Experimental Group';
run;

/*Medication Error Rate Overall*/
/*Scatter Plot of the Slope between Pre and Post Test*/

```

```

Proc gplot;
PLOT Overall_Before *Overall_After = group;
Format group group.;
Title "Scatter Plot: Overall Error Rates Pre and Post";
RUN;

/*Descriptive Summary*/
proc Means mean STD Min Max;
Class group;
Var Overall_Before Overall_After;
Format group group.;
Title "Descriptive Means: Overall Error Rates";
RUN;

/*ANCOVA TEST*/
Proc GLM PLOT=Meanplot(cl) data=Disser_ANCOVA;
Class group;
Model Overall_After=Group Overall_Before/ss3 solution;
LSMeans group/stderr pdiff cl;
Format group group.;
Output out=Overall_After p=Pred r=Res;
Title "ANCOVA: Overall Error Rates";
run;

/*Assumption 1: Normality Test of Residual*/
Proc Univariate data=Overall_After normal;
var Res;
Histogram /normal;
Probplot /normal (mu=est sigma=est);
Title "Normality Test for Residuals: Overall Error Rate Post Test";
run;

/*Assumption 2: Homogeneity Levene's Test*/
Proc GLM data=Disser_ANCOVA;
Class group;
Model Overall_Adjusted = group;
Means group / hovtest = Levene;
Title "Homogeneity Levene's Test: Overall Error Rates";
run;

goptions reset=all;
/*Assumption 3: Hypothesis of Common slope between groups*/
Proc GLM data=Disser_ANCOVA;
Class group;
Model Overall_After=Group Overall_Before group*Overall_Before/ss3;
Format group group.;
Title "Hypothesis of Common Slope: Overall Error Rates Pre and Post";
run;

goptions reset=all;
/*Wrong Dose Error Rate*/
/*Scatter Plot of the Slope between Pre and Post Test*/

```

```

PROC gplot DATA = Disser_ANCOVA;
PLOT WrongDose_Before*WrongDose_After = group;
Format group group.;
Title "Scatter Plot: Wrong Dose Error Rates Pre and Post";
RUN;

/*Descriptive Summary*/
proc means mean STD Min Max DATA = Disser_ANCOVA;
Class group;
VAR WrongDose_Before WrongDose_After;
Format group group.;
Title "Descriptive Means: Wrong Dose Error Rates";
RUN;

/*ANCOVA Test*/
Proc GLM PLOT=Meanplot(cl) Data=Disser_ANCOVA;
class group;
Model WrongDose_After=group WrongDose_Before/ss3 solution;
format group group.;
LSMeans group/ stderr pdiff cl;
output out=WrongDose_After p=Pred r=Res;
Title "ANCOVA: Wrong Dose Error Rates Post Test";
run;

/*Assumption 1: Normality Test of Residual*/
Proc Univariate data=WrongDose_After normal;
Var Res;
Histogram /normal;
Probplot /normal (mu=est sigma=est);
Title "Normality Test for Residuals: Wrong Dose Error Rate Post Test";
run;;

/*Assumption 2: Homogeneity Levene's Test*/
Proc GLM data=Disser_ANCOVA;
Class group;
Model WrongDose_Adjusted = group;
Means group / hovtest = Levene;
Title "Homogeneity Levene's Test: Wrong Dose Error Rates";
run;

/*Assumption 3: Hypothesis of Common slope between groups*/
Proc GLM data=Disser_ANCOVA;
Class group;
Model WrongDose_After=Group WrongDose_Before
group*WrongDose_Before/ss3;
Format group group.;
Title "Hypothesis of Common Slope: Wrong Dose Error Rates Pre and
Post";
run;

goptions reset=all;
/*Omission Error Rate*/

```

```

/*Scatter Plot of the Slope between Pre and Post Test*/
PROC gplot DATA = Disser_ANCOVA;
Plot Omission_Before*Omission_After = group;
format group group.;
Title "Scatter Plot: Omission Error Rates Pre and Post";
RUN;

/*Descriptive Summary*/
proc means mean STD Min Max DATA = Disser_ANCOVA;
Class group;
VAR Omission_Before Omission_After;
Format group group.;
Title "Descriptive Means: Omission Error Rates";
RUN;

/*ANCOVA Test*/
Proc GLM PLOT=Meanplot(cl) Data=Disser_ANCOVA;
Class group;
Model Omission_After=group Omission_Before/ss3 solution;
format group group.;
LSMeans group/ stderr pdiff cl;
Output out=Omission_After p=Pred r=Res;
Title "ANCOVA: Omission Error Rates Post Test";
run;

/*Assumption 1: Normality Test of Residual*/
Proc Univariate data=Omission_After normal;
Var Res;
Histogram /normal;
Probplot /normal (mu=est sigma=est);
Title "Normality Test for Residuals: Omission Error Rate Post Test";
run;

/*Assumption 2: Homogeneity Levene's Test*/
Proc GLM data=Disser_ANCOVA;
Class group;
Model Omission_Adjusted = group;
Means group / hovtest = Levene;
Title "Homogeneity Levene's Test: Omission Error Rates";
run;

/*Assumption 3: Hypothesis of Common slope between groups*/
Proc GLM data=Disser_ANCOVA;
Class group;
Model Omission_After=Group Omission_Before group*Omission_Before/ss3;
Format group group.;
Title "Hypothesis of Common Slope: Omission Error Rates Pre and Post";
run;

ODS Graphics off;
ODS RTF close;

```

SAS Code 2: Analysis of Variance (ANOVA) of Group Mean Differences

```

/*One-Way ANOVA*/

ODS RTF;
ODS graphics on;
Options nodate;

Data Disser_ANOVA;
Input Group Overall_Before Overall_After WrongDose_Before
WrongDose_After Omission_Before Omission_After;
Datalines;
1      30.77 3.70  7.69  0.00  15.38 3.70
1      9.09  14.29 9.09  0.00  0.00  9.52
1      3.23  2.56  3.23  0.00  0.00  2.56
1      5.26  8.00  5.26  4.00  0.00  4.00
1      4.35  8.00  4.35  8.00  0.00  0.00
1      10.00 11.36 0.00  2.27  10.00 9.09
1      0.00  15.00 0.00  7.50  0.00  7.50
1      6.67  3.03  6.67  3.03  0.00  0.00
1      6.67  19.44 6.67  2.78  0.00  16.67
1      0.00  8.57  0.00  2.86  0.00  2.86
1      0.00  .      0.00  .      0.00  .
2      0.00  0.00  0.00  0.00  0.00  0.00
2      12.00 2.04  12.00 0.00  0.00  2.04
2      4.00  0.00  4.00  0.00  0.00  0.00
2      3.45  0.00  3.45  0.00  0.00  0.00
2      2.86  2.63  2.86  0.00  0.00  2.63
2      3.23  0.00  0.00  0.00  3.23  0.00
2      3.23  0.00  3.23  0.00  0.00  0.00
2      4.55  5.26  4.55  0.00  0.00  5.26
2      3.70  2.27  3.70  0.00  0.00  2.27
2      3.70  0.00  3.70  0.00  0.00  0.00
;
run;

Proc Format;
Value Group 1='Control Group'
           2='Experimental Group';
run;

/*Medication Error Rate Overall*/
/*Descriptive Summary*/
proc means mean STD Min Max;
Class group;
Var Overall_Before Overall_After;
Format group group.;
Title "Descriptive Means: Overall Error Rates";
RUN;

/*ANOVA Test of Mean Difference before unit dose between Control and
Expreimetal Group, GLM was used because of unbalanced sample size*/
Proc GLM PLOT=boxplot data=Disser_ANOVA;
class group;
Model Overall_Before=Group;

```

```

means group/cldiff hovtest = Levene;
format group group.;
output out=Overall_Before r=RES1 p=PRED1;
Title "One-Way ANOVA Mean Difference: Overall Error Rates Before Unit
Dose";
run;

/*ANOVA Test of Mean Difference after unit dose between Control and
Expreimetal Group*/
Proc GLM PLOT=boxplot data=Disser_ANOVA;
class group;
Model Overall_After=Group;
Means group/cldiff hovtest = Levene;
format group group.;
output out=Overall_After r=RES2 p=PRED2;
Title "One-Way ANOVA Mean Difference: Overall Error Rates After Unit
Dose";
run;

/*Assumptions : Normality Test of Residual*/
Proc Univariate data=Overall_Before normal;
var Res1;
Histogram /normal;
Probplot /normal (mu=est sigma=est);
Title "Normality Test for Residuals: Overall Error Rates Before Unit
Dose";
run;

Proc Univariate data=Overall_After normal;
var Res2;
Histogram /normal;
Probplot /normal (mu=est sigma=est);
Title "Normality Test for Residuals: Overall Error Rates After Unit
Dose";
run;

goptions reset=all;
/*Wrong Dose Error Rate*/
/*Descriptive Summary*/
proc means mean STD Min Max DATA = Disser_ANOVA;
Class group;
VAR WrongDose_Before WrongDose_After;
format group group.;
Title "Descriptive Means: Wrong Dose Error Rates";
RUN;

/*ANOVA Test of Mean Difference before unit dose between Control and
Expreimetal Group, GLM was used because of unbalanced sample size*/
Proc GLM PLOT=boxplot data=Disser_ANOVA;
class group;
Model WrongDose_Before=Group;
means group/cldiff hovtest=levене;
format group group.;
output out=WrongDose_Before r=RES1 p=PRED1;

```



```

Title "One-Way ANOVA of Mean Difference: Wrong Dose Error Rates Before
Unit Dose";
run;

/* ANOVA Test of Mean Difference after unit dose between Control and
Expreimetal Group */
Proc GLM PLOT=boxplot data=Disser_ANOVA;
class group;
Model WrongDose_After=Group;
Means group/cldiff hovtest=levne;
format group group.;
output out=WrongDose_After r=RES2 p=PRED2;
Title "One-Way ANOVA Mean Difference: Wrong Dose Error Rates After Unit
Dose";
run;

/*Assumptions: Normality Test of Residual*/
Proc Univariate data=WrongDose_Before normal;
var Res1;
Histogram /normal;
Probplot /normal (mu=est sigma=est);
Title "Normality Test for Residuals: Wrong Dose Error Rates Before Unit
Dose";
run;

Proc Univariate data=WrongDose_After normal;
var Res2;
Histogram /normal;
Probplot /normal (mu=est sigma=est);
Title "Normality Test for Residuals: Wrong Dose Error Rates After Unit
Dose";
run;

goptions reset=all;
/*Omission Error Rate*/
/*Descriptive Summary*/
proc means mean STD Min Max DATA = Disser_ANOVA;
Class group;
VAR Omission_Before Omission_After;
format group group.;
Title "Descriptive Means of the Omission Error Rates";
RUN;

/* ANOVA Test of Mean Difference before unit dose between Control and
Expreimetal Group, GLM was used because of unbalanced sample size*/
Proc GLM PLOT=boxplot data=Disser_ANOVA;
class group;
Model Omission_Before=Group;
means group/cldiff hovtest=levne;
format group group.;
output out=Omission_Before r=RES1 p=PRED1;
Title "One-Way ANOVA Mean Difference: Omission Error Rates Before Unit
Dose";
run;

```

```

/* ANOVA Test of Mean Difference after unit dose between Control and
Expreimetal Group*/
Proc GLM PLOT=boxplot data=Disser_ANOVA;
class group;
Model Omission_After=Group;
Means group/cldiff hovtest=levене;
format group group.;
output out=Omission_After r=RES2 p=PRED2;
Title "One-Way ANOVA Mean Difference: Omission Error Rates After Unit
Dose";
run;

/*Assumptions: Normality Test of Residual*/
Proc Univariate data=Omission_Before normal;
var Res1;
Histogram /normal;
Probplot /normal (mu=est sigma=est);
Title "Normality Test for Residuals: Omission Error Rates Before Unit
Dose";
run;

Proc Univariate data=Omission_After normal;
var Res2;
Histogram /normal;
Probplot /normal (mu=est sigma=est);
Title "Normality Test for Residuals: Omission Error Rates After Unit
Dose";
run;

ODS Graphics off;
ODS RTF close;

```

Appendix G: Medication Error Rates by Each Observational Day

Daily Error Rate in the Control Group

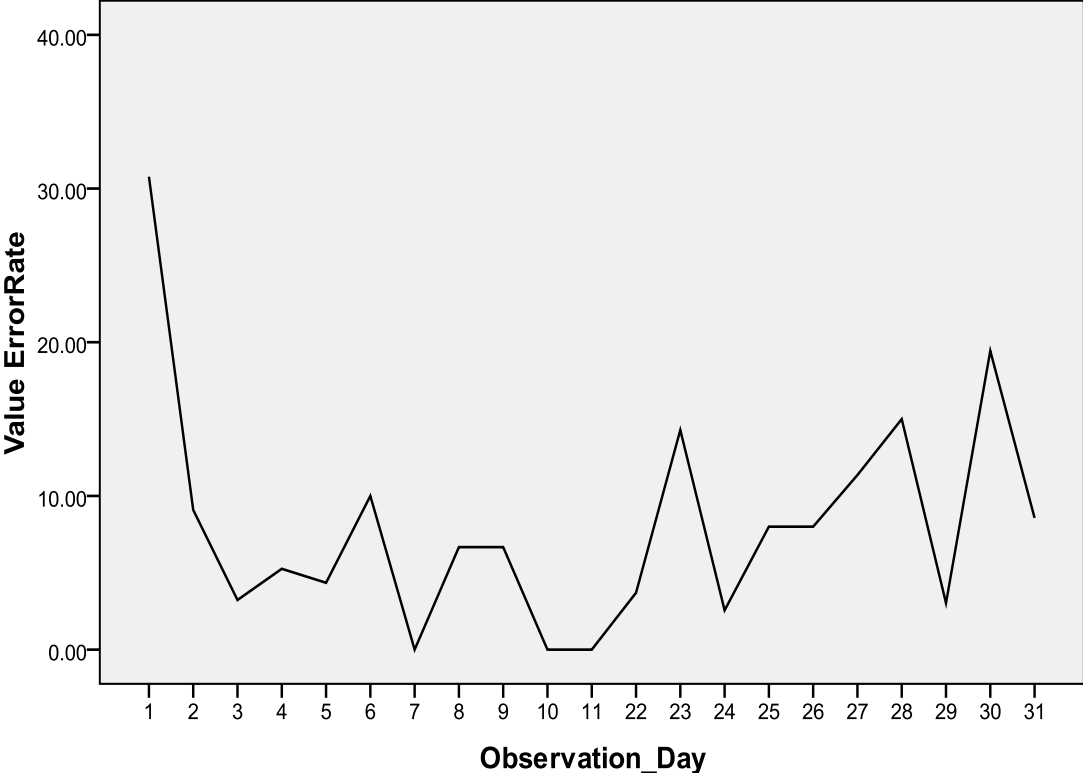


Figure 20: Error Rates in Each Observational Day: Control Group before-after

Daily Error Rate in the Experimental Group

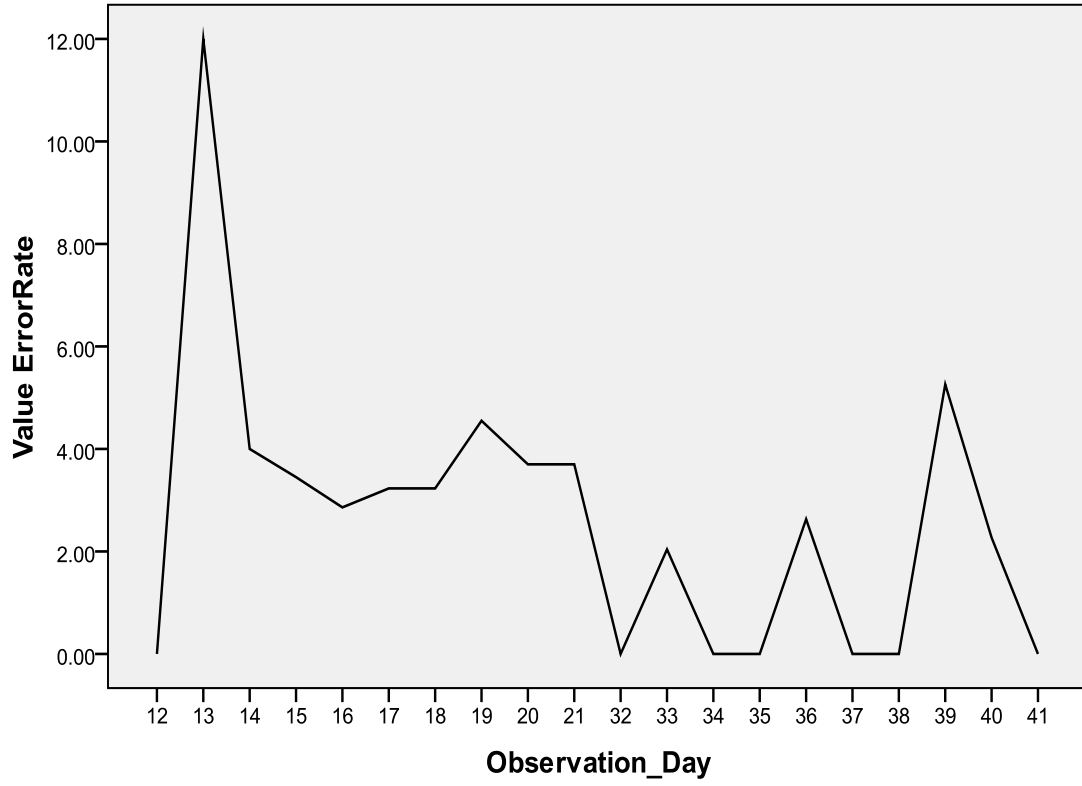


Figure 21: Error Rates in Each Observational Day: Experimental Group before-after

Appendix H: Figures in the Study

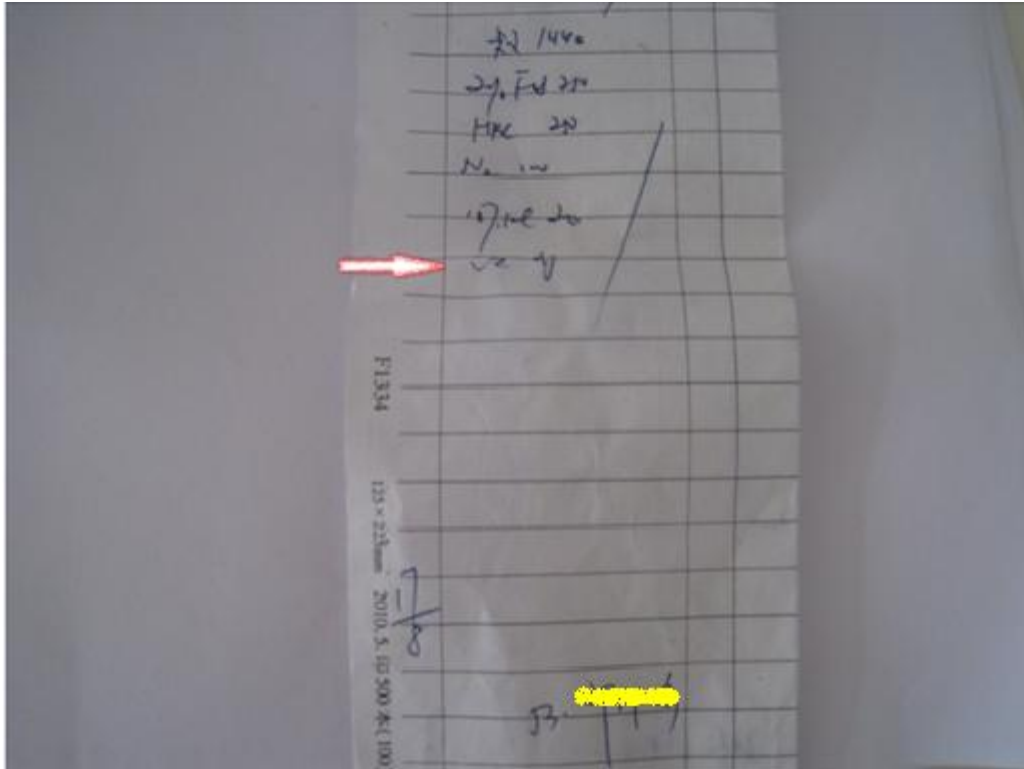


Figure 22: Error Example 1 -- Vitamin C 2 g or 3 g
(Vitamin C 2 g was mixed, while the prescription was Vitamin C 3 g)

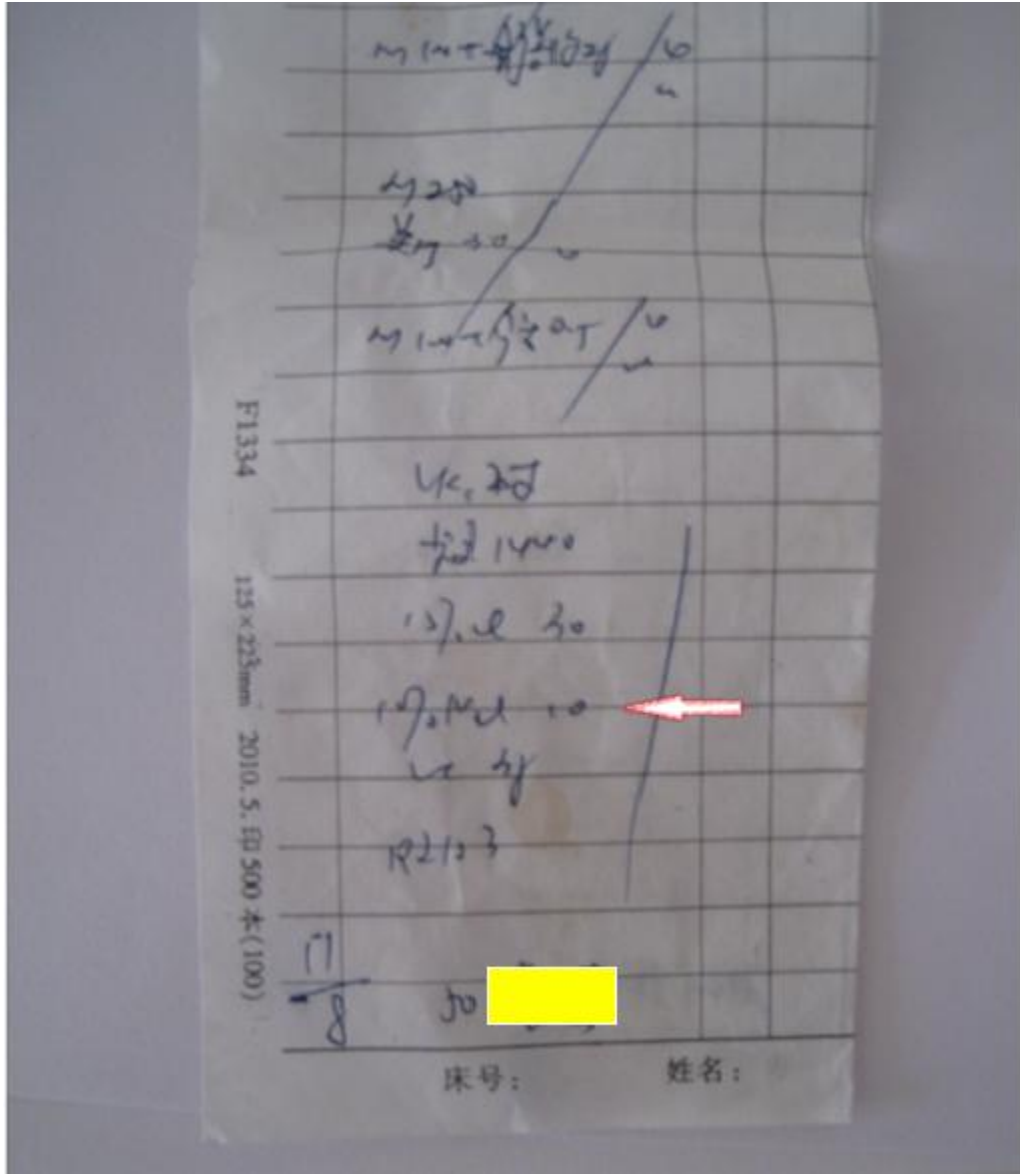


Figure 23: Error Example 2 -- 10% NaCl 10 ampoules or 10 ml
(10% NaCl 10 ml was mixed, while the prescription was 10% NaCl 100 ml)

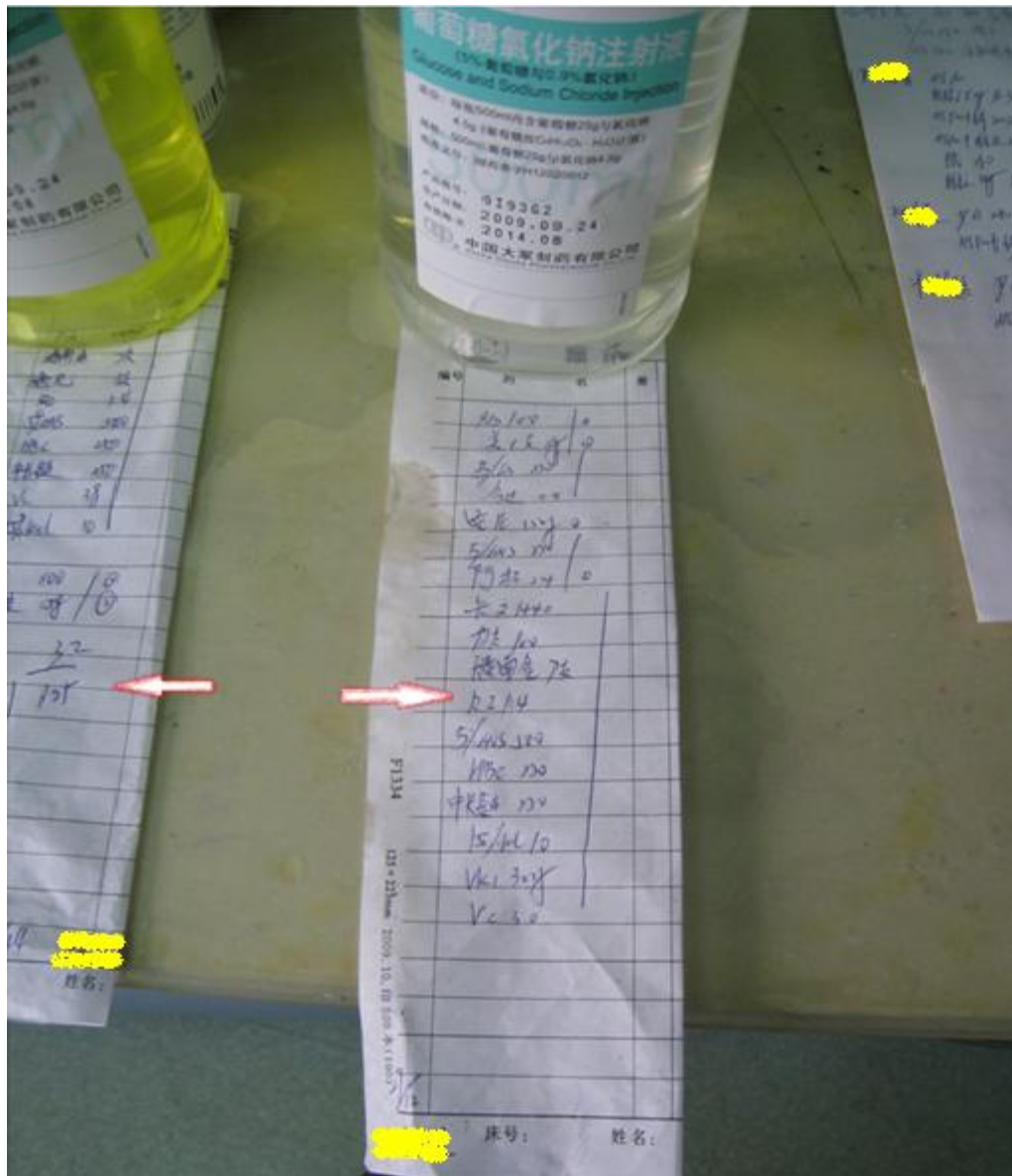


Figure 24: Source of Error involving the Volume of Insulin

(The transcribed order only had the ratio of insulin unit to the weight of the glucose. The medication nurses need calculate the insulin volume just at the time when they mixed the

TPNs)



Figure 25: Syringe (1 ml) for Insulin

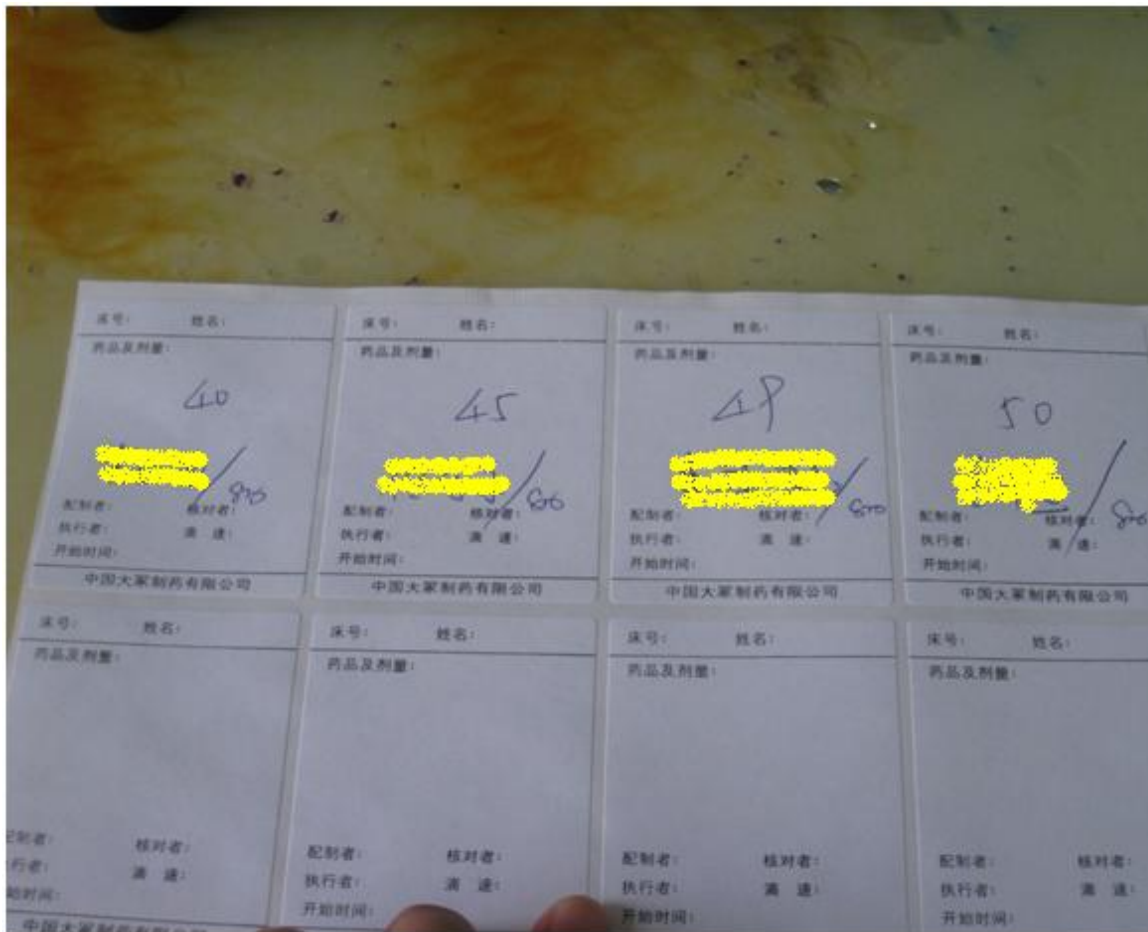


Figure 26: Old Label in the Existing System

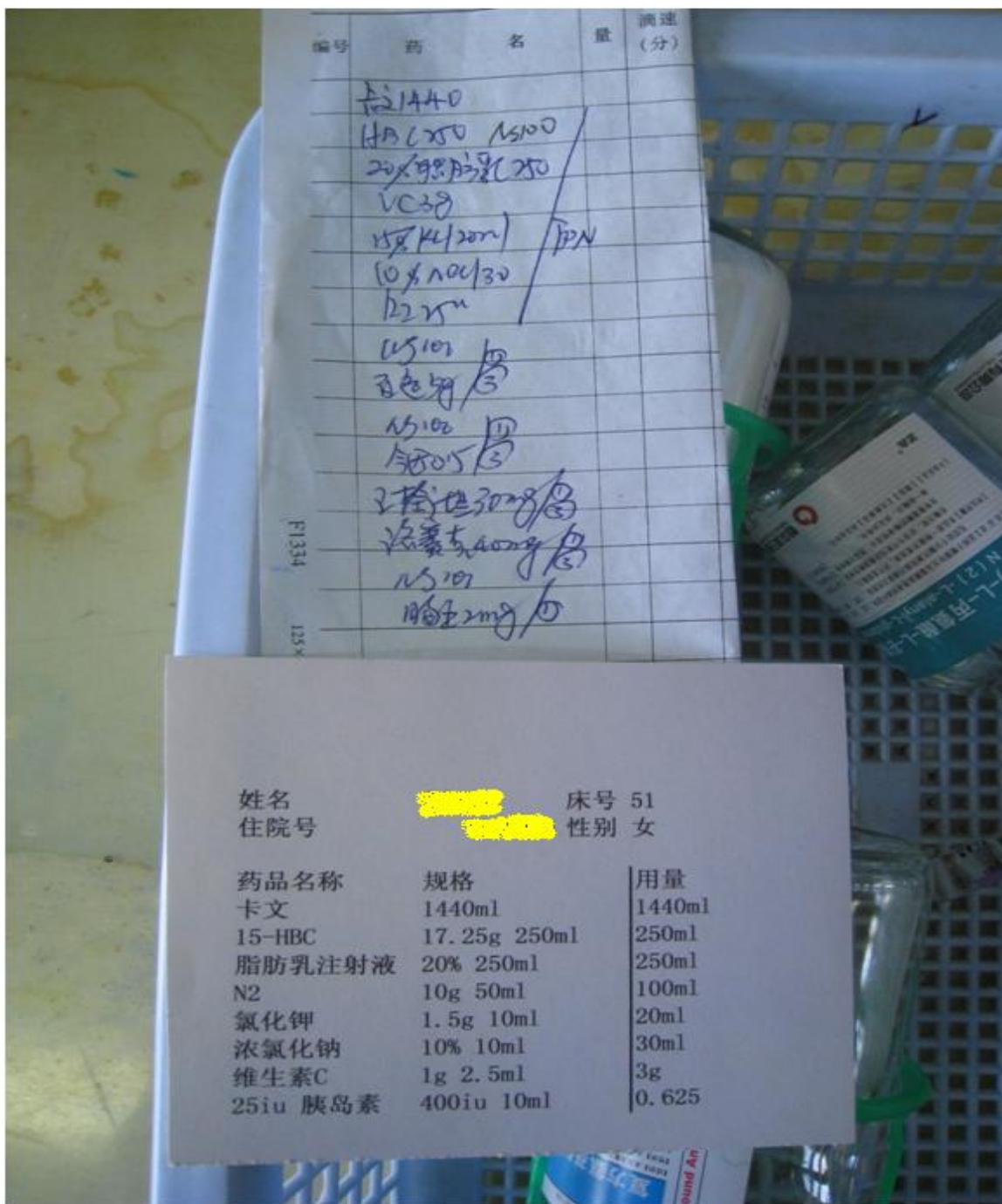


Figure 27: Printable Unit Dose Label of TPN for One Patient and Handwritten Label



Figure 28: Basket for the Unit Dose Dispensing



Figure 29: A Pharmacist Checked Doses before the TPN Preparation

Appendix I: Patients' TPN File in the Unit Dose System for the Experimental Group

Table 42: Patients' TPN Medication File in the Unit Dose System for the Experimental Group

姓名 Name	CHX	床号 Bed Number	33	住院号 ID	***0837
药品名称 Drug Name	规格 Strength	用量 Volume	途径 Route	频率 Fq.	给药时间 Time
脂肪乳氨基酸（17）葡萄糖（11%）注射液（卡文） Fat Emulsion, Amino Acids (17) and Glucose (11%) Injection (Kabiven™ PI)	1440 ml	1440 ml	TPN	每天 Once Daily	9 AM
多种微量元素注射液(II)(安达美注射液) Trace Elements for Injection (Addammel®N)	10 ml	10 ml			
注射用水溶性维生素(水乐维他粉针) Water-Soluble Vitamin for Injection (Soluvit®N)	Compound powder/ vial	1 vial			
脂溶性维生素注射液(II)(维他利匹特(成人)注射液) Fat-Soluble Vitamin Injection (II) (Vitalipid®N Adult)	10 ml	10 ml			
甘油磷酸钠注射液(格利福斯注射液) Sodium Glycerophosphate Injection (Glycophos®)	10 ml	10 ml			
丙氨酰谷氨酰胺注射液 N(2)-L-Alanyl-L-Glutamine Injection	20% 100 ml	100 ml			
葡萄糖酸钙注射液 Calcium Gluconate Injection	10% 10 ml	10 ml			
15%浓氯化钾注射液 Potassium Chloride Injection Concentrate (15%)	1.5 g: 10 ml	10 ml			
5% 葡萄糖氯化钠注射液 5% Glucose and 0.9% Sodium Chloride Solution	5% 500 ml	500 ml			
10% 葡萄糖注射液 10% Glucose Solution	10% 500 ml	500 ml			

姓名 Name	WXG	床号 Bed Number	34	住院号 ID	***4475
药品名称 Drug Name	规格 Strength	用量 Volume	途径 Route	频率 Fq.	给药时间 Time
脂肪乳氨基酸（17）葡萄糖（11%）注射液 Fat Emulsion, Amino Acids (17) and Glucose (11%) Injection (Kabiven™ PI)	1440 ml	1440 ml	TPN	每天 Once Daily	9 AM
中长链脂肪乳注射液（C8-24） Medium and Long Chain Fat Emulsion Injection(C8-24)	20% 250 ml	250 ml			
丙氨酰谷氨酰胺注射液 N(2)-L-Alanyl-L-Glutamine Injection	20% 100 ml	100 ml			
注射用水溶性维生素(水乐维他粉针) Water-Soluble Vitamin for Injection (Soluvit®N)	Compound powder/ vial	1 vial			
脂溶性维生素注射液(II)(维他利匹特(成人)注射液) Fat-Soluble Vitamin Injection (II) (Vitalipid®N Adult)	10 ml	10 ml			
多种微量元素注射液(II)(安达美注射液) Trace Elements for Injection (Addammel®N)	10 ml	10 ml			
甘油磷酸钠注射液(格利福斯注射液) Sodium Glycerophosphate Injection (Glycophos®)	10 ml	10 ml			
葡萄糖酸钙注射液 Calcium Gluconate Injection	10% 10 ml	10 ml			
复方氨基酸注射液（15-HBC） Compound Amino Acid Injection (15-HBC)	17.25 g: 250 ml	250 ml			
10% 葡萄糖注射液 10% Glucose Solution	10% 500 ml	500 ml			
15%浓氯化钾注射液 Potassium chloride injection concentrate (15%)	1.5 g: 10 ml	20 ml			
维生素 C 注射液 Vitamin C injection	1 g: 2.5 ml	2 g (5 ml)			
10%浓氯化钠注射液 Sodium chloride injection concentrate (10%)	10% 10 ml	50 ml			

姓名 Name	WXF	床号 Bed Number	36	住院号 ID	***2479	
药品名称 Drug Name	规格 Strength	用量 Volume	途径 Route	频率 Fq.	给药时间 Time	
脂肪乳氨基酸（17）葡萄糖（11%）注射液 Fat Emulsion, Amino Acids (17) and Glucose (11%) Injection (Kabiven™ PI)	1440 ml	1440 ml	TPN	每天 Once Daily	9 AM	
丙氨酰谷氨酰胺注射液 N(2)-L-Alanyl-L-Glutamine Injection	10 g: 50 ml	100 ml				
注射用水溶性维生素(水乐维他粉针) Water-Soluble Vitamin for Injection (Soluvit®N)	Compounded powder/ vial	1 vial				
多种微量元素注射液(II)(安达美注射液) Trace Elements for Injection (Addammel®N)	10 ml	10 ml				
甘油磷酸钠注射液(格利福斯注射液) Sodium Glycerophosphate Injection (Glycophos®)	10 ml	10 ml				
脂溶性维生素注射液(II)(维他利匹特(成人)注射液) Fat-Soluble Vitamin Injection (II) (Vitalipid®N Adult)	10 ml	10 ml				
注射用复合辅酶 Coenzyme Complex for Injection 200 IU	200 iu : 0.2 mg	200 iu (0.2 mg)				
15%浓氯化钾注射液 Potassium chloride injection concentrate (15%)	1.5 g: 10 ml	20 ml				
10%浓氯化钠注射液 Sodium chloride injection concentrate (10%)	10% 10 ml	20 ml				

姓名 Name	ZFD	床号 Bed Number	38	住院号 ID	***3050
药品名称 Drug Name	规格 Strength	用量 Volume	途径 Route	频率 Fq.	给药时间 Time
脂肪乳氨基酸（17）葡萄糖（11%）注射液 Fat Emulsion, Amino Acids (17) and Glucose (11%) Injection (Kabiven™ PI)	1440 ml	1440 ml	TPN	每天 Once Daily	9 AM
15%浓氯化钾注射液 Potassium chloride injection concentrate (15%)	1.5 g: 10 ml	20 ml			
注射用复合辅酶 Coenzyme Complex for Injection 200 IU	200 iu: 0.2 mg	200 iu (0.2 mg)			
注射用水溶性维生素(水乐维他粉针) Water-Soluble Vitamin for Injection (Soluvit®N)	Compounded powder/ vial	1 vial			
多种微量元素注射液(II)(安达美注射液) Trace Elements for Injection (Addammel®N)	10 ml	10 ml			
甘油磷酸钠注射液(格利福斯注射液) Sodium Glycerophosphate Injection (Glycophos®)	10 ml	10 ml			
脂溶性脂溶性维生素注射液(II)(维他利匹特(成人)注射液) Fat-Soluble Vitamin Injection (II) (Vitalipid®N Adult)	10 ml	10 ml			
胰岛素注射液 Insulin Injection	400 iu: 10 ml	0.5 ml (20 iu)			

姓名 Name	NFM	床号 Bed Number	42	住院号 ID	***3233	
药品名称 Drug Name		规格 Strength	用量 Volume	途径 Route	频率 Fq.	给药时间 Time
10% 葡萄糖注射液 10% Glucose Solution		10% 500 ml	500 ml	TPN	每天 Once Daily	9 AM
维生素 C 注射液 Vitamin C Injection		1 g: 2.5 ml	3 g (7.5 ml)			
维生素 K1 注射液 Vitamin K1 Injection		10 mg: 1 ml	2 ml			
10%浓氯化钠注射液 Sodium chloride injection concentrate (10%)		10% 10 ml	60 ml			
丙氨酰谷氨酰胺注射液 N(2)-L-Alanyl-L-Glutamine Injection		10 g: 50 ml	100 ml			
复方甘草酸苷注射液(美能注射液) Compound Glycyrrhizin Injection		40 mg: 20 ml	60 ml			
中长链脂肪乳注射液 (C8-24) Medium and Long Chain Fat Emulsion Injection(C8-24)		20% 250 ml	250 ml			
复方氨基酸注射液 (15-HBC) Compound Amino Acid Injection (15-HBC)		17.25 g: 250 ml	250 ml			
15%浓氯化钾注射液 Potassium chloride injection concentrate (15%)		1.5 g: 10 ml	20 ml			
5% 葡萄糖氯化钠注射液 5% Glucose and 0.9% Sodium Chloride Solution		5% 500 ml	500 ml			
胰岛素注射液 Insulin Injection		400 iu: 10 ml	1.05 ml (42 iu)			

姓名 Name	TCY	床号 Bed Number	45	住院号 ID	***3251
药品名称 Drug Name	规格 Strength	用量 Volume	途径 Route	频率 Fq.	给药时间 Time
脂肪乳氨基酸（17）葡萄糖（11%）注射液 Fat Emulsion, Amino Acids (17) and Glucose (11%) Injection (KabivenTM PI)	1440 ml	1440 ml	TPN	每天 Once Daily	9 AM
丙氨酰谷氨酰胺注射液 N(2)-L-Alanyl-L-Glutamine Injection	20% 100 ml	100 ml			
维生素 C 注射液 Vitamin C Injection	1 g: 2.5 ml	3 g (7.5 ml)			
维生素 K1 注射液 Vitamin K1 Injection	10 mg: 1 ml	2 ml			
胰岛素注射液 Insulin Injection	400 iu: 10 ml	0.625 ml (25 iu)			
15%浓氯化钾注射液 Potassium Chloride Injection Concentrate (15%)	1.5 g: 10 ml	10 ml			

姓名 Name	HYC	床号 Bed Number	49	住院号 ID	***3627
药品名称 Drug Name	规格 Strength	用量 Volume	途径 Route	频率 Fq.	给药时间 Time
脂肪乳氨基酸（17）葡萄糖（11%）注射液 Fat Emulsion, Amino Acids (17) and Glucose (11%) Injection (Kabiven™ PI)	1440 ml	1440 ml	TPN	每天 Once Daily	9 AM
复方氨基酸注射液（15-HBC） Compound Amino Acid Injection (15-HBC)	17.25 g: 250 ml	250 ml			
中长链脂肪乳注射液（C8-24） Medium and Long Chain Fat Emulsion Injection(C8-24)	20% 250 ml	250 ml			
维生素 C 注射液 Vitamin C Injection	1 g: 2.5 ml	3 g (7.5 ml)			
维生素 K1 注射液 Vitamin K1 Injection	10 mg: 1 ml	2 ml			
15%浓氯化钾注射液 Potassium Chloride Injection Concentrate (15%)	1.5 g: 10 ml	20 ml			
注射用复合辅酶 Coenzyme Complex for Injection 200 IU	200 iu: 0.2 mg	400 iu (0.4 mg)			
浓氯化钠注射液 Sodium Chloride Injection Concentrate (10%)	10% 10 ml	40 ml			

姓名 Name	FLS	床号 Bed Number	53	住院号 ID	***9743
药品名称 Drug Name	规格 Strength	用量 Volume	途径 Route	频率 Fq.	给药时间 Time
脂肪乳氨基酸（17）葡萄糖（11%）注射液 Fat Emulsion, Amino Acids (17) and Glucose (11%) Injection (Kabiven™ PI)	1440 ml	1440 ml	TPN	每天 Once Daily	9 AM
复方氨基酸注射液（15-HBC） Compound Amino Acid Injection (15-HBC)	17.25 g: 250 ml	250 ml			
丙氨酰谷氨酰胺注射液 N(2)-L-Alanyl-L-Glutamine Injection	10 g: 50 ml	100 ml			
15%浓氯化钾注射液 Potassium chloride injection concentrate (15%)	1.5 g: 10 ml	20 ml			
10%浓氯化钠注射液 Sodium chloride injection concentrate (10%)	10% 10 ml	60 ml			
维生素 C 注射液 Vitamin C Injection	1 g: 2.5 ml	2 g (5 ml)			
葡萄糖酸钙注射液 Calcium Gluconate Injection	10% 10 ml	10 ml			
甘油磷酸钠注射液(格利福斯注射液) Sodium Glycerophosphate Injection (Glycophos®)	10 ml	10 ml			
维生素 B1 注射液 Vitamin B1 Injection	100 mg: 2 ml	100 mg			
维生素 B6 注射液 Vitamin B6 Injection	50 mg: 1 ml	1 ml			
维生素 B12 注射液 Vitamin B12 Injection	0.5 mg: 1 ml	0.5 mg (1 ml)			

Appendix J: Pictures of the Unit Dose Dispensing System in Other Military Hospitals



Figure 30: Checking IV Label and Dispensing Unit Dose



Figure 31: Pharmacy Intravenous Admixture Center Service (PIVAS) Windows (In-Out)



Figure 32: IV Unit Dose Ready for Admixture