Engineering and Evaluating EZChemo:

An Electronic Chemotherapy Ordering System

By

Hari Krishna V. Rekapalli, M.S.

Master's Capstone Project

Presented to the Department of Medical Informatics and Clinical Epidemiology

and the Oregon Health & Science University

School of Medicine

in partial fulfillment of

the requirements for the degree of

Master of Biomedical Informatics

May 2008

School of Medicine

Oregon Health & Science University

Certificate of Approval

This is to certify that the Master's Capstone Project of

Hari Krishna V. Rekapalli

"Engineering and Evaluating EZChemo: An Electronic Chemotherapy Ordering System"

Has been approved

[redacted]

Thesis Advisor – Holly Jimison, Ph.D.

TABLE OF CONTENTS

List of Figures:

List of Exhibits:

List of Tables:

Dedicated to the most beautiful woman in the world, my wife, Denise Carmen Rekapalli, for her unwavering support and tireless efforts. Draga Denise, ***Te Iubesc, mereu!***

Acknowledgements

First and foremost, I would like to thank Dr. Benjamin Cho for the excellent mentorship and friendship extended and for going out of his way to help me complete this project study successfully. I am not sure how many physicians I would be able to go up to and ask for help with surveying the participants while I would be gone for my honeymoon, but he did it for me even before I had asked for it! I thoroughly enjoyed working with him.

I am very thankful to Dr.Holly Jimison, my project advisor for her excellent guidance and for helping me to think objectively about every aspect of study evaluation. Her voluntary help with IRB approval process and the flexibility she has shown in letting me progress at my own pace have been invaluable. I thank Dr. Tibor Kovacsovics for giving me the opportunity to work on EZChemo and Joseph Bubalo R.Ph. for being such a wonderful partner in the study. I would like to thank Dr. William Hersh, my supervisor, for financially supporting me throughout the course of my graduation. I would also like to extend my gratitude to Andrea Ilg, Lynne Schwabe, and last but not least, Diane Doctor for all the administrative and moral support.

I can never thank my parents and sister enough for their unconditional love.

Abstract

Background: *Chemotherapy, the prescription and administration of drugs to cancer patients, has traditionally been prescribed according to standard protocols through paper-based systems. Given the complexity of existing protocols, multiple errors can occur during the paper-based prescription leading to potentially serious consequences. To alleviate the problem, several recommendations have been published suggesting the use of computerized prescribing systems that have several advantages.*

***Objectives**: The goal of the proposed project is to create a safe and standardized chemotherapy prescription software and evaluate it for its effectiveness, efficiency and usability when compared to the current paper- based chemotherapy ordering system.*

***Design**: To compare EZChemo with the paper- based system with respect to efficiency and effectiveness, a hierarchical cross-over study design was employed. Usability of the system was evaluated by interviewing the participants for their perception on EZChemo. A combination of both quantitative and qualitative approaches was used to evaluate the electronic tool.*

***Participants**: A total of 20 study participants, 11 physicians, 4 nurse practitioners, 4 residents and 1 physician assistant, were recruited for the study from the Department of Hematology at Oregon Health Sciences University (OHSU). Evaluation of the participants' chemotherapy orders for their correctness and completeness was performed by a pharmacist affiliated to the Department of Hematology, while the clinical case studies required to prepare chemotherapy orders were compiled by a physician in the Department of Hematology.*

Study Setting: *Providers' computer room, Hematology floor (5-C), OHSU and Hematology residents' computer room, Multnomah Pavilion, OHSU.*

Results: *EZChemo has been found to be:*

- *more efficient because there is a significant difference in the time it takes to complete chemo orders using EZChemo when compared to paper-based system, the difference being in favor of EZChemo*
- *more effective than paper- based system because it has decreased error rate by 86%*
- *more usable than paper-based system because all twenty provider users have expressed interest in and are currently using EZChemo for reasons based on several objective and subjective parameters*

Conclusions: *Further developments guided by the comments from Providers could be used to improve the current version of EZChemo to make it more effective, efficient and usable. EZChemo in its current form, however, is much more effective, efficient and usable than the existing paper-based system. Future work should include further testing of the accuracy of the EZChemo orders.*

Background

Medication Errors – Prevalence and Consequences

Healthcare in United States (U.S) is not as safe as it can be or should be. This fact, highlighted and detailed by IOM report "To Err is human: Building a safer health system" published in 1999, runs against the philosophy of practice of medicine in U.S. and everywhere else, the familiar Hippocratic oath: "first, do no harm", although it is, in general, the motto of every healthcare provider to provide the patient with the very best care possible within the constraints. The quality of healthcare delivered in U.S. is not optimal despite the fact that U.S. spends more on health care, both as a proportion of gross domestic product (GDP) and on a per-capita basis, than any other nation in the world [1], a trend that is illustrated in figure 1. It has been estimated that U.S spends as much as 17% of its GDP, $2.6 trillion/year, in healthcare and yet, as many as 44,000-98,000 people die in hospitals a year due to preventable medical errors [2]. Evidence suggests that deaths resulting from medical errors far exceed the number of deaths that are caused by motor vehicle accidents (43,458), breast cancer (42,297), or AIDS (16,516), making medical errors the 8th leading causing of death in the country [2]. The World Health Organization (WHO) in 2000 ranked the U.S. health care system first in both responsiveness and expenditure, but 37th in overall performance and 72nd by overall level of health, among 191 member nations surveyed [3].

Medical errors could broadly be defined as adverse patient events, resulting in injuries that could have been prevented by current state of medical knowledge. These errors can occur in all phases of patient care, including prevention, diagnosis, treatment and phases that are not related to patient care such as administrative tasks. Apart from posing threat to the patients' health, such medical errors also have a significant financial impact on the healthcare provider organizations and it has also been estimated that they cost as much as $17 billion - $29 billion annually at the national level [3]. The chasm in healthcare quality has been widening despite the advances and innovations in all aspects of medical care, and a variety of factors that are more systemic and process related are to blame and in need of fix. The key to reducing medical errors is to focus on improving the systems of delivering care and not to blame individuals.

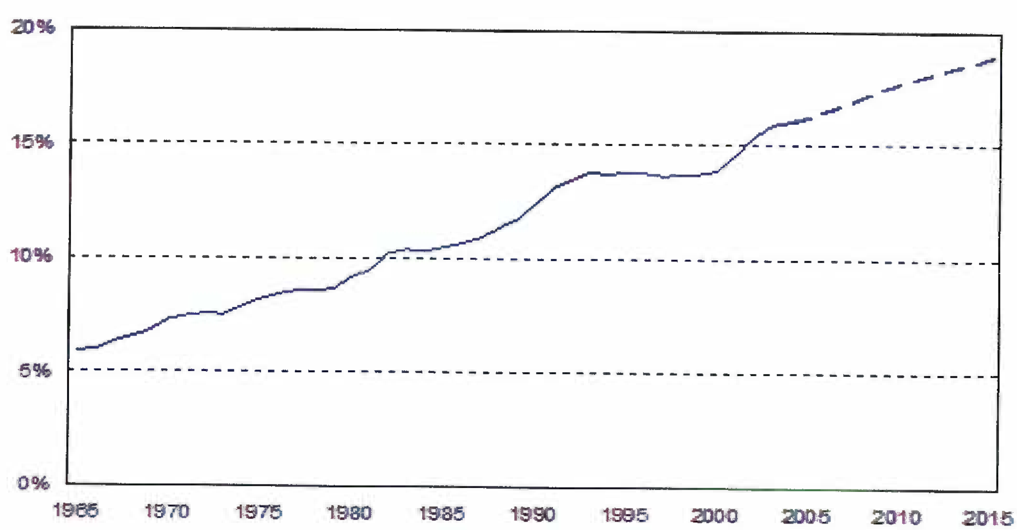

Figure 1: Growth in national health expenditure as a percentage of GDP.
Source: Centers for Medicare and Medicaid (CMS)

One of the several types of Medical Errors is Medication Errors (ME), which according to The National Coordinating Council for Medication Error and Prevention (NCCMEP) could be defined as ". . .any preventable event that may cause or lead to inappropriate medication use or patient harm, while the medication is in the control of the health care professional, patient, or consumer". Such events may be related to professional practice, health care products, procedures, and systems including: prescribing, order communication, product labeling, packaging and nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use.

Diagnostic:	• Mis-diagnosis • Failure to employ indicated tests • Use of outmoded tests • Failure to act on results of monitoring or testing
Treatment:	• Error in performance of an operation or test • Error in administering the treatment • Medication errors • Inappropriate care
Preventive:	• Failure to provide prophylactic treatment • Inadequate monitoring or follow-up of treatment
Other:	• Equipment failure • Other systems, such as software, failure

Exhibit 1: Examples of different types of errors [3]

Pharmaceutical treatment is an integral component of the healthcare process helping to cure and control diseases for millions. Almost everyone in the modern world takes medication at one time or another. Estimates suggest that, in any given week, almost 80% of U.S. adults will use prescription medicines, over-the-counter drugs or dietary supplements of some sort [4]. The percentage of drug consumption has been going up contributing to the increased spending on prescription drugs and as much as

9.4% of the net national healthcare expenditure has been channeled for this purpose, a trend that is illustrated in figure 2.

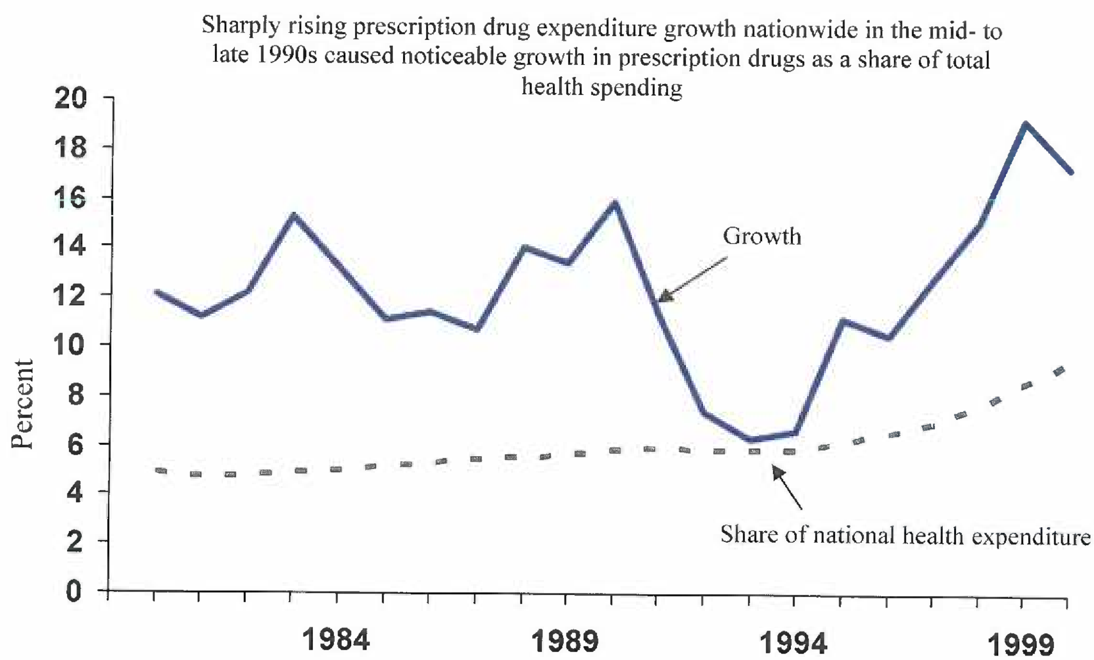

Figure 2: Prescription Drug Expenditure Growth and Share of National Health Expenditures. Source: Centers for Medicare & Medicaid

Given the high complexity in the healthcare delivery process and especially in the drug delivery process, medication errors are more common, both in ambulatory and in-patient settings, than it once was thought. These Medication Errors could further be classified as [5]:

- Adverse drug events (ADE, 2.2%): The ADEs are a type of medication error that can have harmful effects if allowed to reach the patient. Some of the most common reasons that lead to ADEs include:
    - Duplicate therapy : Same drug prescribed twice or 2 or more drugs from the same class with no evidence-based medicine to prove benefit from both

- Inappropriate dose: Drug dose amounts that is not evidence based
- Inappropriate route: Drug not available or not recommended to be given in the route ordered
- Inappropriate interval: Drugs administered in combination at wrong intervals
- Wrong drug : Wrong drug prescribed, most often due to similar sounding drug names
- Wrong unit : resulting from confusion with unit of the drug, such as ml, mg, µml etc.
- Drug interaction: documented drug interaction between 2 medications that deems drug ineffective or contraindicated (eg, beta-blocker with beta-agonist)
- Allergy : Patient has a documented allergy to the drug ordered

Injuries to patients could be caused because of any or a combination of the above mentioned reasons for ADEs or could be caused as "side-effects" of drugs that are properly prescribed, dispensed and administered. A split-up of prevalence of these two further classifications of ADEs is illustrated in figure 3.

- Medication prescription errors (MPE, 30%): These are errors made by the provider when inadequate or incomprehensible information is presented on the order requiring clarifications from the pharmacist. These errors could further be classified as follows:
    - Missing information: Missing route, interval, concentration, rate or dose that results in an incomplete order

- Inaccurate patient statistics: resulting from inaccurate recording of patient's height, weight, age and other statistics that are vital for deciding the drug concentration
- Illegible : Pharmacist is unable to read the prescription prepared by the provider, requiring further clarification

* Rule violations (RV, 6.8%): errors that were not compliant with hospital policies. An example RV is usage of abbreviations for drug names. Abbreviations are shortened or symbolized representation of drug names; dopa, epi, MSO_4 for example.

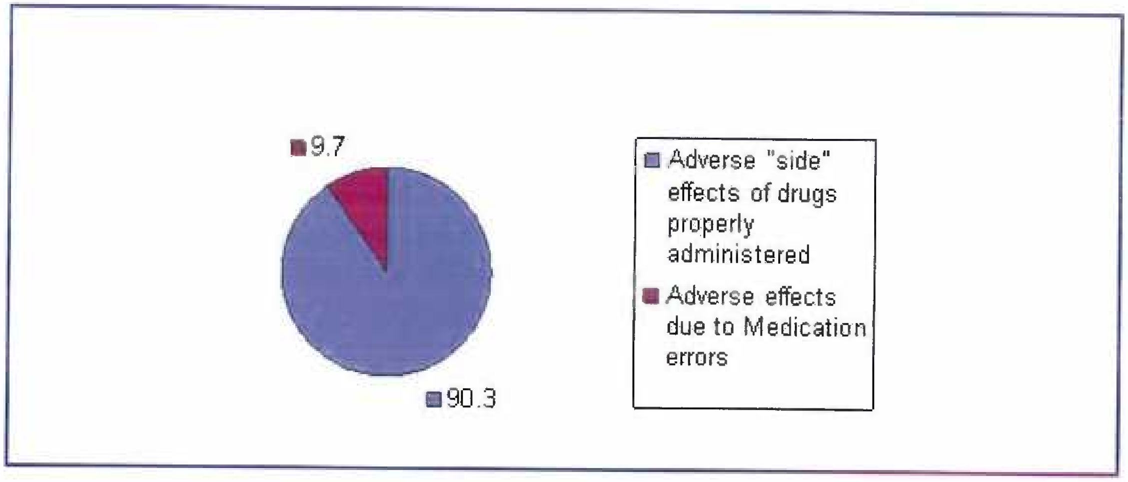

Figure 3: Split-up of types of adverse drug events (ADEs)*, expressed in percentage, in U.S. hospitals, by broad category, 2004 [6]

* Based on a total of 1,211,100 hospital stays with at least one ADE recorded.

Source: AHRQ, Center for Delivery, Organization, and Markets. Healthcare costs and Utilization Project, Nationwide sample, 2004

Further investigations made by Lesar et al [7] suggest that the major reasons contributing to mistakes made while preparing the prescription order include:

- knowledge and use of knowledge regarding drug and drug therapy factors (30%)
- knowledge and use of patient characteristics and patient history (29.2%)

- calculations and expression of rates and units (17.5%)
- nomenclature-related group (defined as use of incorrect drug names, dosage forms, or abbreviations, 13.4%)
- dosage form-related group (3.2%)
- administrative processes (defined as needing to rewrite orders when a patient is transferred from unit to unit or after surgery) group (2.6%)

Although most of these mistakes committed in the prescription process are rectified by the pharmacist, some do go un-caught potentially resulting in ADEs. Some of these ADEs might have no effect on the patient but some cause discomfort while some potentially cause harmful and irreversible injuries and in some extreme cases, death. Some of the more common symptoms of ADEs in patients include [8]:

- Rashes
- Change in respiratory rate, heart rate, hearing, or mental state
- Seizures
- Anaphylaxis
- Diarrhea
- Fever

An ADE arising from an error is considered preventable. Studies [6][10] have estimated that about 380,000-800,000 preventable ADEs occur nation wide in in-patient hospital settings while another study [6], has estimated that in 2004, ADEs that were both preventable and non-preventable were occurring in 1.2 million hospital stays in the U.S., about 3.1% of all stays. Several other studies that have surveyed in the local hospital settings have estimated that the prevalence of ADEs is about 6.5% [7][10][12]. It has been widely accepted though that the actual numbers might be much higher.

> ***Case #1:*** *Methotrexate is a powerful drug that is used as a treatment for cancer. However, doctors also prescribe methotrexate for the relief of arthritis and other disorders of the immune system. When methotrexate is used to treat immune disorders, it is taken only once or twice a week, unlike most medications. In December 2003, a physician inadvertently prescribed daily methotrexate for a 79-year-old woman with arthritis. The error was discovered after she had taken the drug for 9 days, but she subsequently died.*
>
> ***Case #2:*** *A patient was ordered Ondansetron (Zofran®) and Dexamethasone for prevention of nausea and vomiting associated with their chemotherapy regimen. A review of the patient's medication administration record by nursing staff the next day showed that these two medications had not been administered. Further investigation revealed that the night shift staff was unaware that dexamethasone was available from the unit's automated dispensing cabinet and pharmacy-prepared IV piggybacks for Ondansetron were stored in the unit's refrigerator. As a result, the patient suffered with nausea and vomiting throughout the night.*
>
> ***Case #3:*** *A daily IV infusion of cytarabine 200mg in 1 liter of sodium chloride 0.9% to be given for 7 days was prescribed for a patient with acute myeloid leukemia. After three days of treatment, the patient was transferred to a different patient care unit and the order was rewritten exactly as it was written initially for 7 days of therapy. Several days later, a pharmacist noticed that 10 doses had been billed despite the 7-day duration of therapy ordered. The pharmacist contacted the patient's nurse who determined that the dose currently infusing was indeed the tenth dose (i.e., it was the seventh dose given after the transfer, and three doses had been given prior to the transfer). The nurse immediately stopped the infusion and notified the attending physician. The patient experienced a worsening of sepsis, and the error may have contributed to this outcome.*

Exhibit 2: Example real world case studies illustrating the harmful effects of ADEs [9]

These ADEs, apart from causing injuries and discomforts on occasions to patients, do have a significant impact on the healthcare provider organizations. Bates D et al [10], have estimated that a hospital on average experiences a loss of about \$2.8million-\$5.6million per year mainly resulting from a patient's extended length of stay in the hospital. The same study has estimated that on average, a patient stays 2.2 days extra, costing the hospital on average \$3244, as a result of medication related injury that is preventable and 4.6 days extra, costing $5857 on average, as a result of ADE that is non-preventable. Assuming 400,000 such preventable events occur each year – the total annual cost of ADEs resulting from errors would be $3.5 billion in U.S [4]! This estimate, however, accounts only for extended stay in the hospitals and does not account for all the costs that result from an ADE, such as lost earnings, compensation for pain and suffering in liabilities, malpractice costs etc.

One of the main reasons contributing to ADEs has been identified as Medication Prescription Errors (MPEs) that account for 50-61% of the cases. Another study by Nebeker et al [13], suggests that MPEs account for 27% of ADEs, an estimate based on survey in the local hospital setting. Further, the relationship between the MPEs, MEs and ADEs, is illustrated in figure 6 [11].

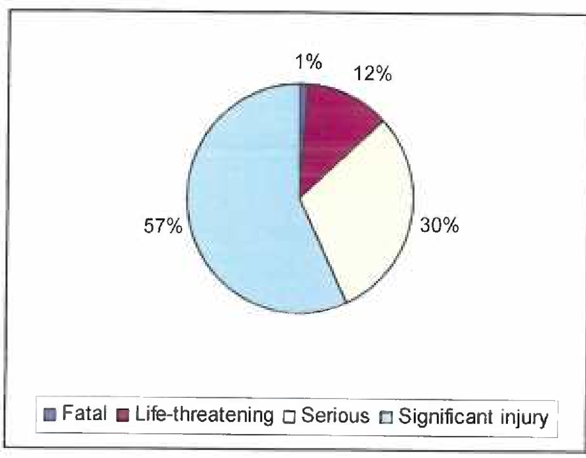

Figure 4: Consequences of ADEs [12]

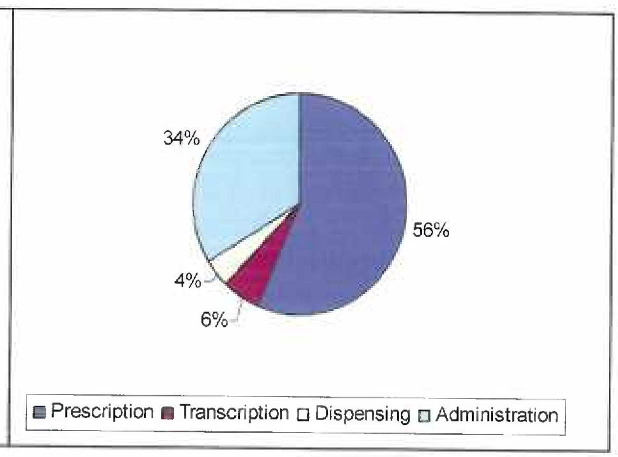

Figure 5: Phases of medical care processes leading to ADEs [12]

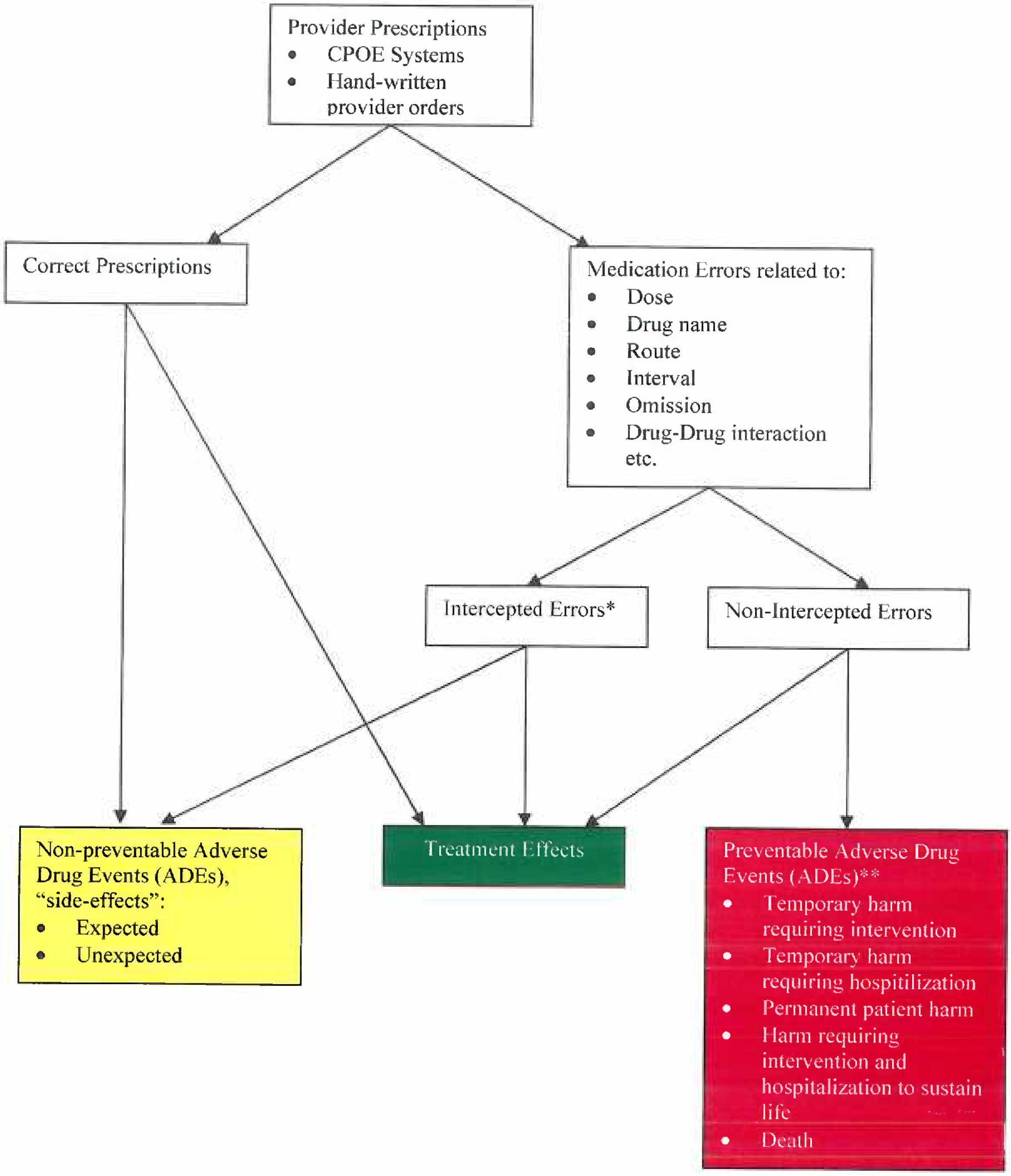

Figure 6: Conceptual model of the association between Healthcare Provider prescriptions, Medication Errors and Adverse Drug Events

* Intercepted medication errors are medication errors with significant potential to harm a patient that did not actually reach a patient. They may result in ADE not related to errors and therefore not preventable. Non-intercepted errors may result in treatment effects and preventable adverse events

** Adverse drug events are adverse patient injuries resulting from drug use. ADEs are associated with a medication error are considered preventable.

Use of Information Technology to Tackle Medication Errors:

To combat the ADEs problem, IOM report [4] recommends a series of steps that first involves patients' empowerment and improved patient-provider partnership. The report suggests that one of the most effective ways to reduce MEs and hence ADEs is to move toward a model of healthcare where there is more of a partnership between the providers and patients. The goal is to enable patients to understand medications better and take responsibility for monitoring the use of medications, while providers take steps to educate, consult with, and listen to the patients. As part of the care delivery process, the report suggests employing a more integrated systems model to enable better communication between various providers.

A second important step in mainly reducing MPEs and ADEs as a consequence, as recommended by the IOM report, is greater use of Information Technologies in prescribing and dispensing medications. Health care experts, policymakers, payers, and consumers consider health information technologies, such as Electronic Health Records (EHRs), Computerized Provider Order Entry (CPOE) systems and Electronic Prescribing Systems (eRx), to be critical to transforming the health care industry [2][4][14]. Information management is fundamental to health care delivery. Given the fragmented nature of health care, the large volume of transactions in the system, the need to integrate new scientific evidence into practice, and other complex information management activities, the limitations of paper-based information management are intuitively apparent. While the benefits of health information technology are clear in theory, adapting new information systems to health care has proven difficult and rates of use have been limited [15][16], for several reasons that are less technology related and more domain related.

Potts et al [5], have reported that use of WizOrder, a CPOE system has resulted in the reduction of MPEs in a Pediatric Critical Care Unit (PCCU) considerably. In effect, they have reported that introduction of CPOE system has reduced the error rate by 95.9% as compared to the times when paper-based system was in use. Bates et al [12] have reported that the use of CPOE systems, when implemented with proper care, have reduced the non-missed-dose medication error rate fell by 81% and non-intercepted MEs fell by 86%.

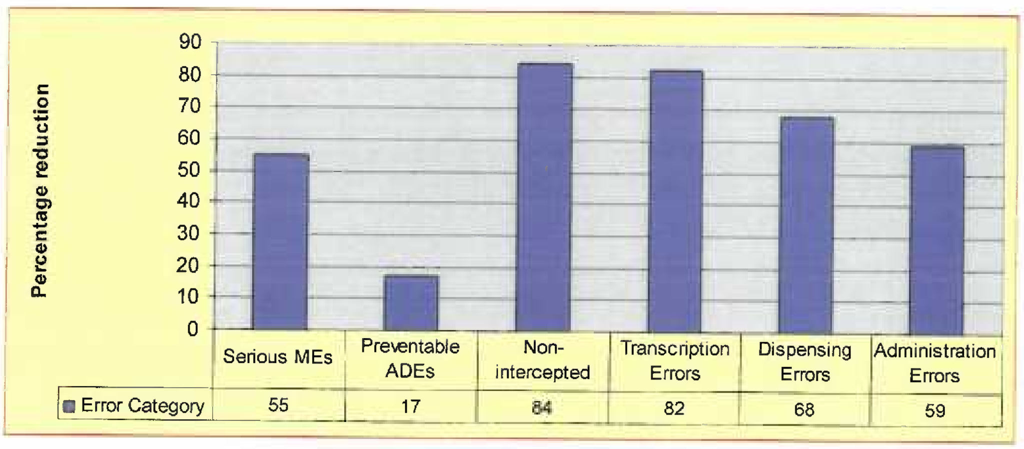

Figure 7: Percent reduction in Medication related errors in a local hospital setting, as reported by Bates et al [17], as a result of use of CPOE

This huge reduction in MPEs, MEs and ADEs as a consequence due to use of CPOE systems stems from the following specific advantages facilitated by CPOE, when compared to a paper-based system, as reported by Koppel et al [18]:

- Elimination of legibility problem
- Faster to reach the pharmacy

- Less subject to error associated with similar drug names
- More easily integrated into medical records and decision-support systems
- Less subject to errors caused by use of apothecary measures
- Easily linked to drug-drug interaction warnings
- More likely to identify the prescribing physician
- Ability to link to ADE reporting systems
- Ability avoid specification errors, such as trailing zeros
- Available and appropriate for training and education
- Available for immediate data analysis, including post-marketing reporting
- Claimed to generate significant economic savings
- With online prompts, CPOE systems can Link to algorithms to emphasize cost-effective medications
- Reduce under-prescribing and over-prescribing
- Reduce incorrect drug choices

However, blind introduction of CPOE has set in new problems that were analyzed by quantitative methods and qualitative analysis. Problems reported as those facilitated by introduction of a CPOE system that was in use include [18]:

- Information errors resulting from fragmentation and systems integration failure
    - Assumed dose information; as a result of over reliance on default values provided by the CPOE

- Medication discontinuation failures, resulting from not seeing patients' complete medication records, reported by 51%
- Procedure-Linked Medication Discontinuation Faults. Procedures and certain tests are often accompanied by medications. If procedures are canceled or postponed, no software link automatically cancels medications
- Immediate Orders and Give-as-Needed Medication discontinuation faults
- Antibiotic Renewal Failure: To maximize appropriate antibiotic prescribing, house staff are required to obtain approval by infectious disease fellows or specialist pharmacists. Lack of coordination among information systems, however, can produce gaps in therapy because antibiotics are generally approved for 3 days.
- Diluent options and errors
- Allergy information delay
- Conflicting and duplicated medication orders

- Human-Computer Interaction (HCI) design flaws in the CPOE Systems:
    - Wrong patient selection due to font problems
    - Wrong medication selection
    - Unclear log-on and log-off
    - Failure to provide medications after surgery
    - Post surgery suspended medications

- Loss of data, time and focus when CPOE is non-functional
- Inflexible ordering screens

Top 5 reasons for errors with CPOE medication system: • Improper dose/quantity 30.5% • Prescribing error 20.3% • Omission error 16.3% • Unauthorized drug 10.6% • Wrong time 8% • Wrong patient 6.8%	Top 5 reasons why CPOE increases pressure on users: • Distractions 56.5% • Workload increase 20.4% • Staff inexperienced 17% • Staffing insufficient 10% • System down 4%
Top 5 causes of CPOE errors related to screen display: • Abbreviations 21.6% • Dosage form confusion 5.89% • Non-metric units user 1.7% • Decimal point 1.3% • Brand/generic names look alike 1.2%	Top 5 causes of CPOE errors related to Programming/Rules: • Calculation error 20.9% • Computer software 2.2% • Contraindicated in disease 0.8% • Contraindicated drug/food 0.7% • Contraindicated drug allergy 0.2%
Top 5 challenges related to CPOE implementation: • Organizational cultural hindrances • Quality of clinical rules/decision support • Number of warnings/alerts • Connectivity between key information systems: CPOE with pharmacy, lab, Medical Administration Record (MAR)	Top 5 reasons for errors in medication ordering: • Performance deficit 52.2% • Transcription errors 28.1% • Knowledge deficit 27.7% • Procedure not followed 15.9% • CPOE 12% • Documentation 11.3%

Exhibit 3: Challenges in implementation of Medication Orders within CPOE system [19]

These new breed of problems introduced by CPOE systems result essentially from poor implementation strategies in the local settings. The challenges that a successful implementation of a CPOE system in a healthcare setting is illustrated in exhibit 3.

To minimize the number of mistakes that creep in into the care delivery process due to use of CPOE systems, studies have recommended the following [18][19]:

- Focus on work-flow, not technology alone
- Aggressively test the technology for errors

- Aggressively fix the errors introduced by technology
- Plan for continuous revisions and quality improvement
- Incorporate human factors engineering into planning process
- Pharmacy specific IT specialist
- Integration of various modules with CPOE system

Well implemented CPOE systems are reported to have, not only improved patient safety as previously discussed, but also have had significant financial impact saving the healthcare provider organizations enormous amounts of money basically by improving the efficiency and quality. Systematic reviews [20] by Agency for Healthcare Research and Quality (AHRQ) suggest that anywhere from 28 percent to 95 percent of ADEs can be prevented by reducing medication errors through computerized monitoring systems while saving the hospital that has invested in it as much as $500,000 in direct costs. RAND corp. estimates in their study [21] that at a national level, implementation of CPOE systems to combat ME, MPE and ADE problems could save the healthcare provider organizations $77 billion or more and could cost around $8 billion per year, assuming adoption by 90% of provider organizations, over a period of 15years. The study predicts that the health and safety benefits could double the savings while reducing illness and prolonging life.

Apart from full fledged CPOE systems that are more generic in nature, there exist Electronic Prescribing (eRx) systems that are more specific to a streamlined drug delivery process and do not necessarily concern the other aspects of CPOE such as lab-test orders etc. More specifically, Electronic Prescribing systems (E-Prescribing or eRx) could be defined as the use of an automated data entry system to generate a prescription, rather than writing it on paper. Electronic prescribing systems, in addition to transferring prescriptions electronically between various healthcare providers, typically offer many more features of value including secure real time electronic delivery of prescriptions to providers and pharmacists of patient specific information on eligibility, benefits, drug interactions, warnings, dose adjustments, medication history and the availability of generics. Automation of the outpatients prescribing process has many potential benefits to different healthcare stakeholders. Patients and physicians benefit from a) Improved patient safety through generation of legible prescriptions that have been checked by the computer for possible harmful interactions b) Better formulary adherence c) Streamlined communication between different healthcare providers d) Improved patient satisfaction, through rapid prescription fulfillment and fewer errors [21]. Pharmacists benefit from the electronic prescribing systems heavily specifically due to improvements facilitated in quality of care and reduced call-backs to the physicians for clarifications. Payers benefit from these systems mainly due to the improvements in utilization of cost-effective drugs, such as generic, therapeutic alternatives and step-therapy resulting from use of electronic prescribing systems.

eRx is growing in popularity but is still only found in a relatively small minority of U.S. practices, and even where it is used, available systems have many, but not all, of the most basic essential decision support features; advanced, higher value features are found in only a minority of commercially available systems. Thus, a majority of U.S. patients are not yet reaping the safety and quality benefits that can come from eRx. Studies [22] conducted nation wide suggest that while as much 36% of physicians said eRx improved efficiency, 45% of them said it improved compliance with formularies and 33% of them said it had a major impact on the quality of care, only 20% of them have adopted the eRx systems due to barriers that mainly are beyond the realm of practice of care and technology, some of which include a) high costs of purchasing, implementation and operation b) workflow impact c) lack of systems thinking d) poor reimbursement plans d) confusion about availability, standards, and management of best-practice knowledge. e) Lack of trust among some of the physicians in the quality of information provided by the eRx systems. Physicians in more than half of the practices did not have access to formulary data electronically, and those who did questioned the data's reliability. More importantly, none of the physicians were able to access comprehensive lists of patients' medications prescribed outside their practices and relied on patients to complete medication lists.

Some of the recommendations that have been made by the experts in the field to make e-prescribing systems work and help all the stakeholders reap benefits include a) clear plan for incentivizing the early adopters b) continuing progress towards better designed and more usable systems c) infrastructure for a knowledge management structure in the Clinical Decision Support Systems (CDSS) integrated into the eRx systems so both the developers and users are provided with a sense of ownership of the final quality of the product. d) Integration of e-prescribing systems with an overall health record system e) One-on-One training and support upon initial development. [21]

Given that more than 3 billion prescriptions are written annually, studies [22] suggest that the national savings from universal adoption of electronic prescribing systems could total as much as $27 billion, some from the prevention of medication errors and the majority from better drug utilization, guided by these systems.

Computerized solutions, such as CPOE and eRx are more effective when alternative strategies, such as the following are used in conjunction to minimize the medication errors [20]:

- Using the FDA's MedWatch program to report serious adverse drug reactions.
- Improving incident reporting systems. The process of incident reporting can be streamlined to accommodate the health care provider's busy schedule and can offer feedback indicating that reported information is being used.
- Creating a better atmosphere for health care providers to report ADEs where the person reporting the error does not fear repercussions or punishment.
- Relying more on pharmacists to advise physicians in prescribing medications, and promoting health care provider education on medications.
- Improving the nursing medication administration and monitoring systems. These changes might include bar coding medications, along with additional warnings on medications with higher potential for harm, such as insulin, opiates, narcotics, potassium chloride, and anticoagulants

Medical prescription is the result of a complex cognitive process [23]. As such, it must integrate several elements – namely, patient's characteristics and medical conditions, treatment goals and particulars, institutional rules and regulations, and the preferences of medical and nursing staff and of the patient. Medical order sheets are an essential way of communication between physicians, nurses and pharmacists. Medication errors refer to errors in the process of ordering, transcribing, dispensing, administering or monitoring drugs. They can lead to adverse drug events, some of which are preventable and some of which can lead to adverse patient events. In a study specifically on ordering of drugs, about 20% of orders were found to be poorly legible and 24% were incomplete [24].

Chemotherapy Prescription Ordering Systems:

Chemotherapy, the prescription and administration of cytotoxic drugs to cancer patients, has traditionally been prescribed according to standard protocols through paper-based systems. It is given according to protocols and for repeated cycles. Potent and potentially toxic drugs are used, usually given with infusion solutions. The dosage is commonly adapted to the patient's body surface area (BSA) and/or renal function. Given the complexity of existing protocols, multiple errors can occur during the paper-based prescription leading to potentially serious consequences.

To alleviate the problem, several recommendations have been published suggesting the use of computerized prescribing systems that have several advantages. In the context of chemotherapy orders, Voeffray et al [26] have reported the effect of a chemotherapy ordering software, developed in-house, on drug prescription errors committed by the providers. The assessment was conducted at an 850 bed university hospital in Lausanne, Switzerland. Handwritten paper-based system was used as the base line and errors committed using this system were recorded over a period of 15 months and after-effects of introduction of a computerized chemo ordering software were studied over a period of 36 months. In effect, they have reported a decrease of 92% of prescription errors as a result of use of chemo ordering software. According to the study, the main reasons for the effective minimization of prescription errors using electronic chemo orders include:

- Electronic orders are legible
- They automatically calculate standard dosages
- They provide a control over effective administration of drugs as tracking of prescriptions becomes much easier.

Materials and Methods

Need for EZChemo:

Due to the overwhelming evidence of improvements in efficiency and minimization of prescription errors made possible by electronic ordering systems, such as CPOE, and due to inherent problems in the current paper-based system, a team comprising of a pharmacist and two physicians from the department of Hematology at Oregon Health & Sciences University (OHSU) have proposed an in-house implementation of a safe, reproducible, standardized method of electronic order generation available to multiple sites for multiple different cancer types. To address this need, EZChemo (www.ezchemo.com), an electronic chemo ordering system has been implemented with the following specific goals:

- A software tool that is more effective. The software is said to be effective if:

    - It makes accurate calculation of doses allowing dose changes as required to individualize doses for specific patients.
    - There are safeguards put in place to minimize order entry errors in patient heights and weights.
    - The number of errors or calls for order clarification by pharmacy and nursing decreases when using the system created orders vs. those that were handwritten.
- A software tool that is more efficient. The tool is said to be more efficient if it decreases the amount of time it takes to complete a chemo order vs. the hand made chemo orders.
- A software tool that is more usable. The tool is said to be more usable if the users perceive it to be more:
    - Satisfactory
    - Worth recommending to colleagues
    - Easy to use

Keeping in view the growing evidence of the importance of workflow as a factor in adoption of computer software in clinical settings, the tool was envisaged to be a good fit with the current workflow process in the Hematology department at OHSU. In an effort to develop software that would fit well into the workflow, a site visit to the Hematology floor has been conducted and the workflow sequence in the local settings has thus been investigated:

Workflow Analysis

- A nurse typically takes care of editing the electronic template orders, currently in the MS-Word format, before it is filled in either by the NP or the Attending or the fellow/resident. The order that is prepared, typically in 5 minutes (per estimate given by a fellow in the department), by an authorized provider is finally verified and signed by the attending physician.
- A chemo order thus prepared is then put in a folder and flagged for verification by a pharmacist. The pharmacist visits the department floor couple of times a day typically, before 3pm, and checks for abnormalities in the prescription orders marked for verification by the physician. If the order looks questionable, the pharmacist makes appropriate comments on the same order for later physician review. If the order looks free of errors, then the pharmacist signs it off and leaves an "ok" note on the same paper.
- A chemo order that has been signed off by the pharmacist is then scanned and faxed by the nurse to the pharmacy floor for order fulfillment and dispensing
- Orders received on the pharmacy floor are then reviewed by the pharmacist for any drug interactions, patient allergy interactions, abnormalities in doses and infusion rates. Other drugs that interact with chemo regimen are simply discontinued and appropriate anti-emetics are prescribed to patients to alleviate the allergy problems but otherwise, no dose adjustment is made.
- Another pharmacist makes a final review of the order that has been reviewed previously first by a physician, next by a pharmacist on the floor and then by a pharmacist at the pharmacy. Unless errors are found, the pharmacist prepares a Medication Administration Record (MAR), the order that has the list of medications,

corresponding doses and the dates when they need to be administered to the patient, for the nurse electronically

- The MAR and order are given to a pharmacist technician for actually preparing the drug who then tags a sticker both onto the drug and the order for identification purposes. Drugs thus dispensed, along with the MAR, are picked up by the nurses who then cross compare it with the original order to verify that there are no mismatches.
- Nurses then administer the drugs per the instruction on the MAR to the appropriate patients and signs off the MAR to indicate that the order administration is complete

Within this context, the software that is intended to minimize the prescription errors operates in the milieu of Provider prescription process. The inefficiencies in the remaining phases of the drug delivery process, namely drug dispensing and administration are not addressed by EZChemo. The only change that has been introduced by EZChemo in the entire chemo ordering work flow has been in the prescription process and more specifically, in the retrieval of the chemo orders which are made accessible from EZChemo's homepage (www.ezchemo.com), while rest of the processes and sub-processes remain the same. In effect, the new workflow in the prescription process of chemo orders involves the following steps:

- Go to website: www.EZchemo.com
- Go to Malignancy type
- Download PDF and save to patient folder
- Fill in appropriate fields
- Hit Validate/Calculate then save

- When orders printed, data will also be sent to database

Architecture of EZChemo

The term EZChemo refers to standardized chemo orders, which have been carefully planned and prepared by the EZChemo team comprising of three physicians and a pharmacist, in Portable Document Format (PDF) format with scripts embedded within to make appropriate validations and calculations. These electronic chemo orders are made accessible from the EZChemo's homepage to the authorized users. One of the main reasons for choosing Adobe Acrobat [26] as the underlying platform for implementation of chemo orders in PDF form was that the files thus generated were platform and OS independent. The other reason was that PDF files accommodate JavaScript that can be used to make calculations and validations.

Each of the chemo orders standardized by the EZChemo team were used as the basis for developing PDF forms that essentially calculate the drug doses and the dates when they need to be administered using the patient's height, weight and first day when the patient receives chemotherapy as the parameters. The drug dose calculations also can be adjusted based on the patient's renal function, which the provider inputs as percentage reduction in standardized dose, and the CNS prophylaxis status. Apart from making calculations, scripts in the PDF files have been implemented to ensure that the providers do not forget to fill in important information in the chemo orders such as allergies, data of birth of the patient, name of the attending physician etc. Each of these chemo orders that are thus filled in are further saved into the shared network drive, referred to as L:/ locally for future reference. Completed and signed orders are then printed out and flagged for further verification from the pharmacist.

So far, twenty five chemo orders have been implemented in Adobe PDF format and each of these are hosted on EZChemo's homepage and topically organized into the following categories:

- IT Chemotherapy
- APL
- Myeloma/Lymphoma
- AML/ALL

The EZChemo website itself is currently being hosted on a third party server machine and was built using Joomla [27], a free, open source content management system for publishing content on the world wide web and intranets. A web database for tracking the chemo medication use and other kinds of analysis has also been envisaged. The architecture of the database was prepared, as illustrated in figure 9, but not implemented and integrated yet into EZChemo because the EZChemo team did not feel comfortable, rightfully so, in storing sensitive patient data on a third party server machine. Planning is under progress, however, to host EZChemo and the database on OHSU's intranet servers.

Evaluation of EZChemo

EZChemo was evaluated by interviewing twenty healthcare providers from the department of Hematology at OHSU for its effectiveness, efficiency and usability when compared to the paper-based system. The study, with ID IRB00004162, was approved by the Institute of Review Board (IRB) at OHSU.

The EZChemo team has come to the consensus that the tool is effective if it reduces the number of mistakes made in the prescription chemo order by the provider, efficient if it reduces the time it takes to complete an order, and usable if it is perceived so subjectively by the provider user. To compare EZChemo with the paper-based system with respect to efficiency and effectiveness, a hierarchical cross-over study design was set up, as illustrated in figure 11. Each of the twenty subjects were asked to prepare the chemo orders using both systems, EZChemo and paper-based, for given clinical chemotherapy case studies that were tailor made specifically for two kinds of orders namely "HyperCVAD-cycle-A" and "3+7 IdaCytarabine" orders. These two orders specifically were selected as they, per consensus, were known to be the one among the most frequently used on a daily basis on the Hematology department floor at OHSU and represented orders of opposite extremes with respect to difficulty levels. On average, using paper-based systems it was estimated that completion of a HyperCVAD order took around 7 minutes while 3+7 IdaCytarabine order took around 2 minutes for a provider with intermediate levels of experience in writing chemo orders.

To minimize the carry-over effect, which refers to the phenomenon of a provider remembering calculations performed in one particular order using one system (paper or EZChemo) and re-using them when making calculations using the other system, two sets of HyperCVAD and 3+7IdaCytarabine clinical cases were prepared in advance and handed over to the providers in a pseudo-random fashion. In effect, each provider was asked to complete four orders, one set of HyperCVAD and 3+7IdaCytarabine using EZChemo and the second set using paper-based system.

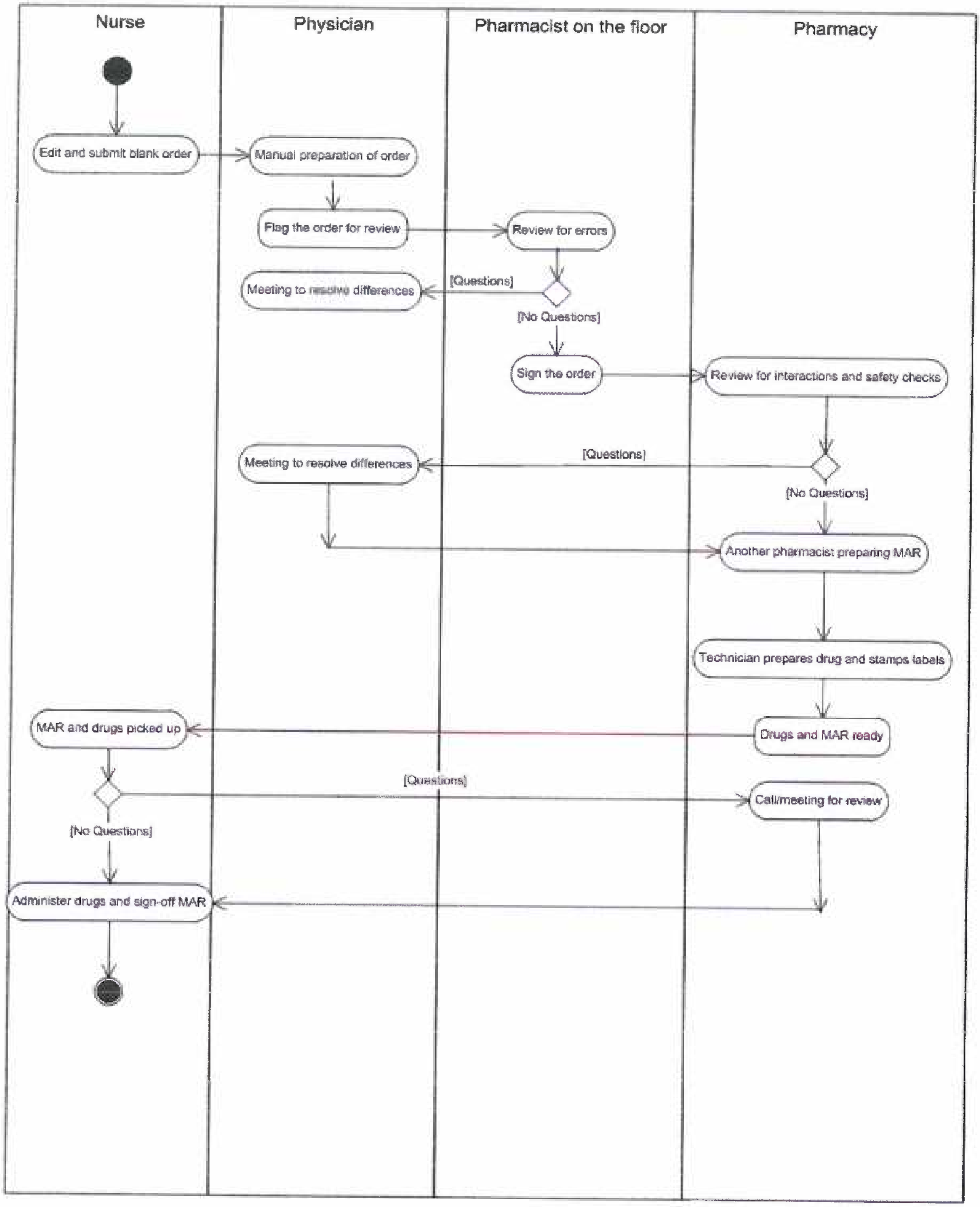

Figure 8: Activity diagram of workflow sequence followed in the Medication prescription, dispensing and administration process in the department of Hematology, OHSU using paper-based system

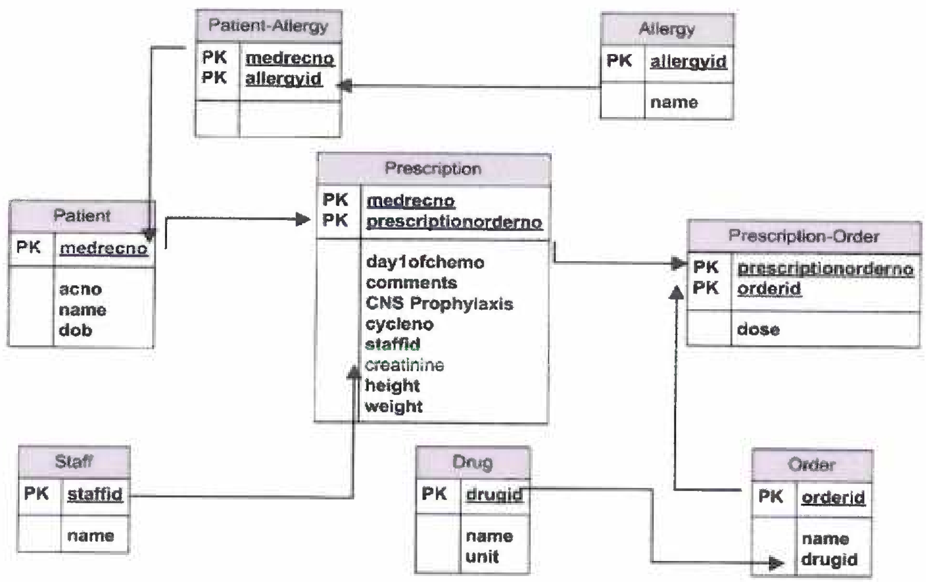

Fig 9: Class diagram illustrating the logical schema for the proposed EZChemo database

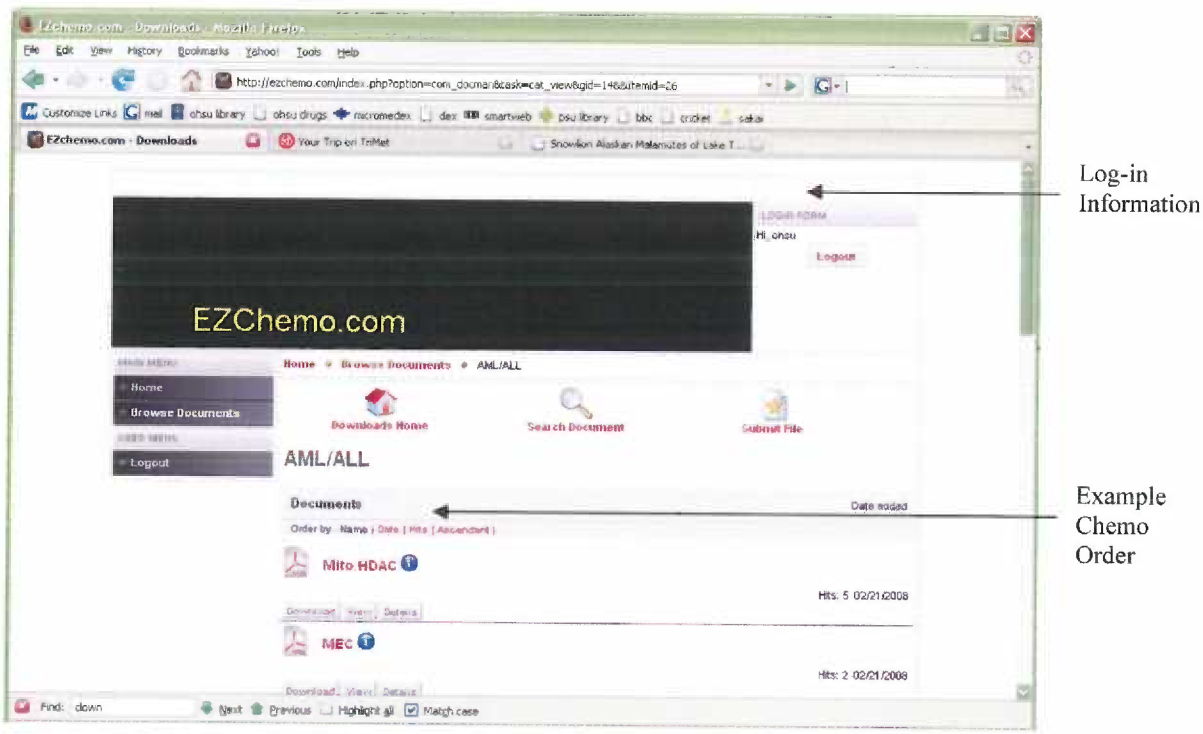

Fig 10: Screenshot of a webpage from www.EZChemo.com

In addition, to minimize the order bias, which refers to the phenomenon of a provider getting familiar with the chemo ordering process with one system and using that experience (remembering the way doses and dates are calculated) to prepare orders using the second system, providers were assigned EZChemo and paper-based systems in a pseudo-random fashion.

The experiments were conducted in the providers' computer room on the Hematology floor and residents' computer lab in Multnomah pavilion, where providers typically prepare their chemo orders for patients undergoing chemotherapy and these places were chosen to imitate the real-world settings, and thus to minimize any location bias. Each provider, prior to the experiment, was briefed about the process and any questions regarding EZChemo's use (login information for example) were clarified to minimize any negative impacts on the study. The providers were then handed over the clinical case studies and the order preparation methodology (paper/EZChemo) in a pseudo-random order that's planned in advance and the time it took for them to complete each of the orders was measured using a well calibrated stop-watch. Chemo order completion process was divided into two phases, namely chemo order retrieval and order preparation, and each of these phases were timed separately to check if the difference in order completion using each system was made significant by one of the phases.

Order retrieval in paper-based system is defined as the process of locating the appropriate order (HyperCVAD-Cycle-A or 3+7IdaCytarabine) from the local shared network drive and in case of EZChemo, it is defined as the process of logging into EZChemo's homepage, locating the appropriate order and opening it using Adobe

Acrobat Reader. The second phase of order preparation is defined, in the case of paper-based system, as the process of filling-in the order with patient's demographic information, dose calculations for each drug and determining the dates when each of these drugs were to be administered. It is defined, in the case of EZChemo, as the process of typing in patient's demographic information, locating the "Validate & Calculate" button within the electronic order, and pushing it to let the script make all the validations and calculations. If the order was found to be incomplete, script embedded within the PDF document popped-up an alert prompting the providers to address the appropriate incomplete information. However, these alerts could be by-passed by the provider and the logic behind this implementation step was to allow the provider to take full responsibility to the order while letting the software play only a supporting role and remain as un-intrusive as possible to the care delivery process. Finally, the order completion process is said to be complete when the provider verifies for the accuracy and completeness of the order and signs it indicating that the order is thorough.

At the end of order completion, the providers were handed over a survey form and asked to fill-in to express their satisfaction/dissatisfaction/concerns with EZChemo when compared to the current paper-based system. The providers were also asked to fill in some of their demographic information that was non-identifying such as their levels of experience in writing chemo orders and experience in general with computers. These survey forms, along with timing information and complete orders were further analyzed for EZChemo's effectiveness, efficiency and usability. Filled in chemo orders were then sent for evaluation of effectiveness to a pharmacist who was involved in the planning and development process of EZChemo and who was routinely involved in verifying for the accuracy of orders prepared by physicians before they were dispensed by the in-patient pharmacy division of OHSU. Copies of filled-in orders and survey forms are retained by the researchers for further evaluation purposes.

Evaluation of efficiency, measured in terms of the time it took for completing an order using EZChemo when compared to the paper-based system, was performed using a paired sample t-test. The data points did not quite follow a normal distribution, given only 20 samples, but the difference between the two distributions did and this justifies use of t-tests. Besides, t-tests are known to be more robust to assumptions about normality of distributions and unequal variances, as long as the number of data points in the two distributions are equal – a condition that is satisfied in the current data analysis [28]. In the first phase, paired sample t-test was performed to check if there is significant difference between the time it took to retrieve a chemo order using paper-based system and EZChemo and in the next phase, the same test was performed to check if there is difference between the times it took to prepare an order using paper and EZChemo. Finally, paired t-test was performed to check if there is significant, statistically speaking, difference between the total time it took for the order completion process using paper and EZChemo.

Total time is calculated as the gross amount of time it took for providers to complete both HyperCVAD and 3+7 IdaCytarabine orders and although separate conclusions could have been made for these two orders, comparison of total time that it takes to complete chemo orders using paper and EZChemo was of more interest to the EZChemo team and hence was the only quantitative analysis that was performed.

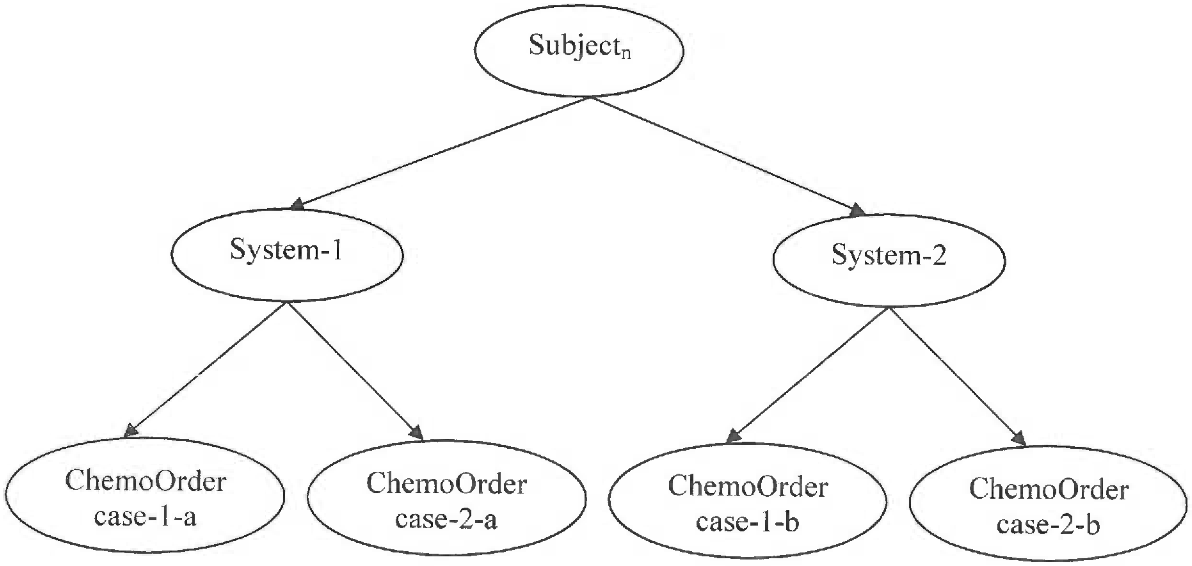

Figure 11: Study set-up. 'System' here refers to the methodology used to complete the chemo order, EZChemo or Paper. Chemotherapy clinical cases refer to the case studies prepared for HyperCVAD and 3+7 IdaCytarabine orders.

An evaluation of the usability of EZChemo when compared to the paper-based system was performed using mixed-methods qualitative data analysis techniques. Survey forms that were filled in at the end of experiments were analyzed for clusters of patterns in the users' opinions regarding their perception on EZChemo based on the following parameters:

- Ease of use
- Levels of trust with calculations
- Levels of willingness to recommend EZChemo to peers as opposed to paper-based systems
- Overall levels of satisfaction
- Areas for improvement in EZChemo

- Readiness of EZChemo to fit into their workflow
- Concerns with Human Computer Interaction (HCI) issues in the electronic system

These clusters of opinions represented the distinct opinions of provider users on their perception of usability of EZChemo when compared to paper-based system.

Results

Efficiency

With respect to efficiency, the null hypothesis that was postulated was that statistically speaking there is no significant difference in the average total time it took to complete a chemotherapy order using EZChemo and paper-based system. The total time is calculated as the net amount of time it took for providers to complete both HyperCVAD and 3+7IdaCytarabine orders and the average total time is calculated as the average of the total times for all subjects. Each of these orders could have been analyzed separately for the difference in their amounts of time for order completion but it was of no interest to the EZChemo team and hence is beyond the scope of current analysis.

Considering: $\mu_{EZChemo} - \mu_{Paper} = \delta$

Null hypothesis H_0 : $\delta = 0$ and

Alternate hypothesis H_a : $\delta \neq 0$

A paired sample t-test was performed because each provider was subjected to both paper-based system and EZChemo and measurements were taken in both cases. This self-pairing is actually advantageous because it eliminates distortions that might be introduced by comparing subjects who differ on the basis of demographics such as levels of experience in writing chemo orders etc. Statistical tests were performed using SPSS [29].

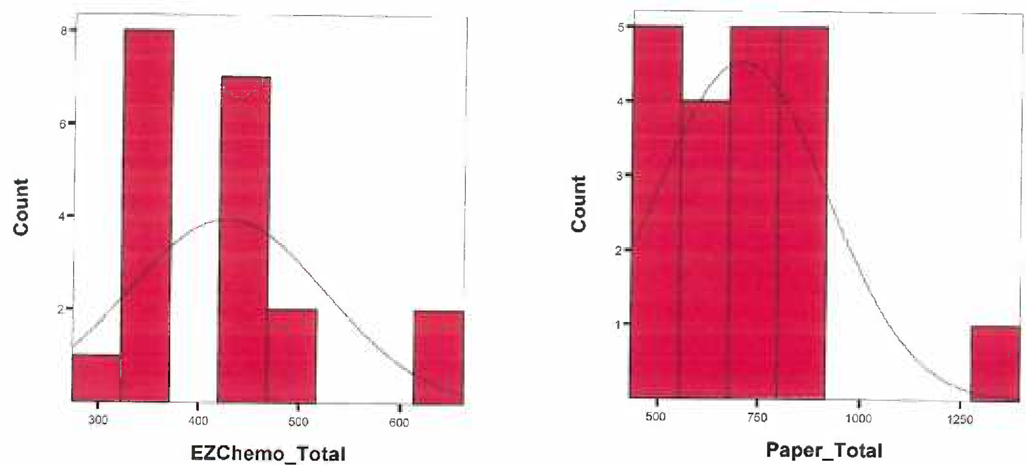

Fig 12 : A Histograms plot of distributions of total time in seconds the providers took to complete both chemo orders

Since normality of data is not apparent in the distributions from the above graphs in figure 12, a Q-Q plot analysis was further performed and results are illustrated in figure 13.

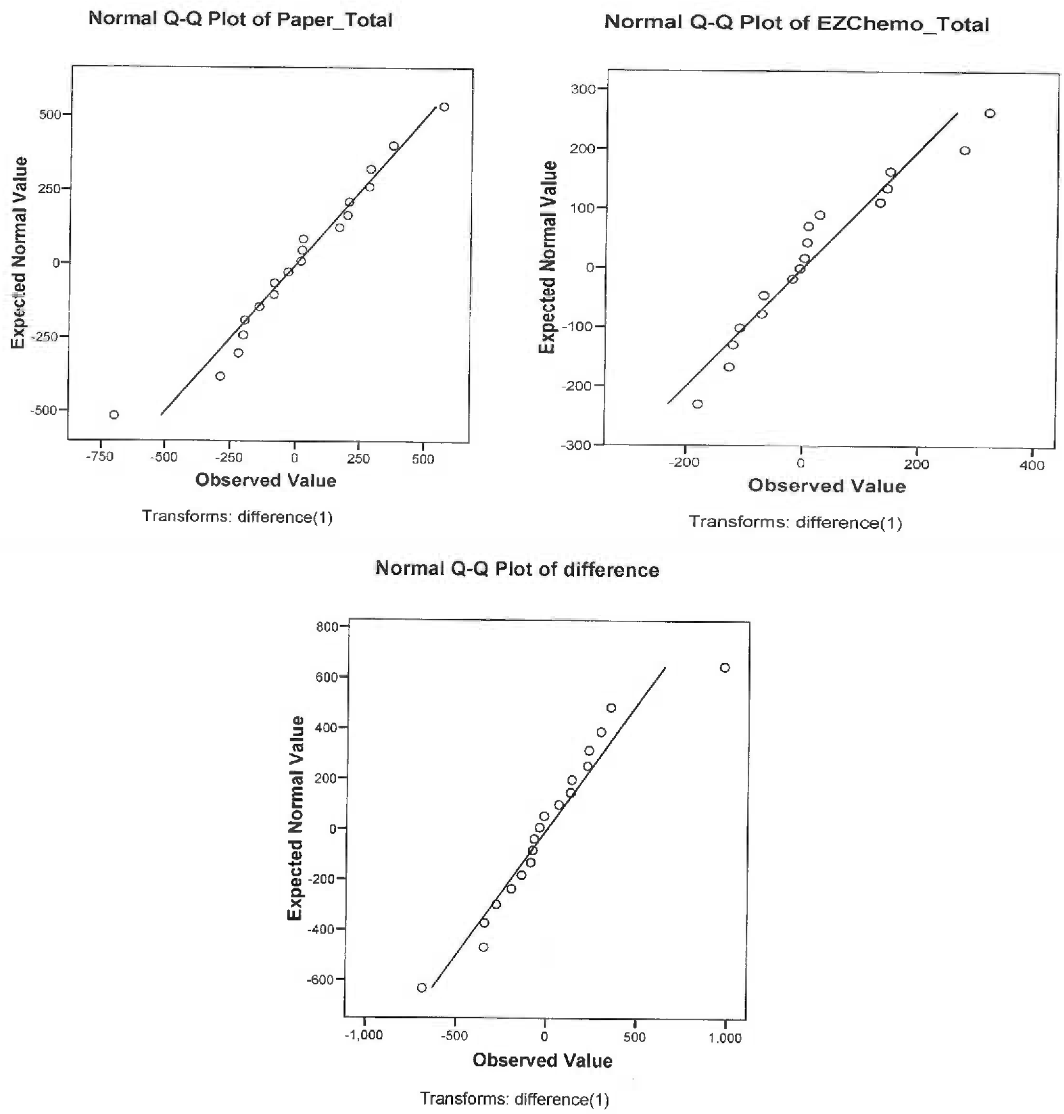

Fig 13: Q-Q plots of time distributions for paper-based and EZChemo systems and the "difference" distribution calculated as the difference between the paired samples of paper and EZChemo time distributions

From these plots, although it is not clear whether or not the distributions of the total time it took for providers using EZChemo and paper followed a Gaussian pattern, the difference between these two distributions seems to be following Gaussian except for one data point that seems to be an outlier. Paired sample t-test is however robust to assumptions of normality of underlying distributions and is especially safe to perform, given that there are equal number of data points in both paper and EZChemo distributions. A raw comparison of these two distributions is apparent from figure 14 indicating that there is a possible statistical difference between these two distributions.

The results generated by SPSS and displayed in Table 1, suggest that the p-value is <<0.0001 for the two-tailed test. So, we reject the null hypothesis and state that there exists statistically significant difference between the time it takes to complete a chemo order using EZChemo when compared to paper- based system at 0.05 level of significance. In other words, the false positive rate, which is the probability for rejecting the null hypothesis that there exists no difference between the time it takes to complete an order using EZChemo and paper when it actually is true, is far less than 0.00001 in the current case.

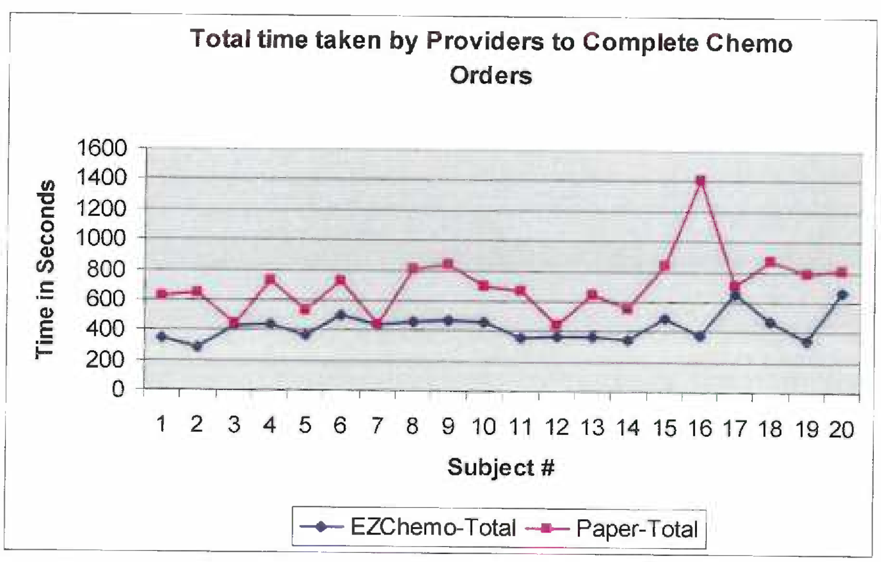

Fig 14: Comparison of the total time it took for the providers to complete the two chemo orders using EZChemo and paper-based system

We also analyze and check if there is significant difference in the time it takes to retrieve a chemo order using paper-based system and EZChemo. SPSS is used again to perform similar paired sample t-test and the results are presented in table 2.

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	EZChemo_Total	427.15	20	98.111	21.938
	Paper_Total	705.15	20	212.775	47.578

Paired Samples Correlations

		N	Correlation	Sig.
Pair 1	EZChemo_Total & Paper_Total	20	.171	.470

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	EZChemo_Total - Paper_Total	-278.000	218.505	48.859	-380.263	-175.737	-5.690	19	.000

Table 1: SPSS output for paired sample t-test comparing the time providers took to complete chemo orders using paper-based system and EZChemo

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Paper_Retrieval	227.10	20	163.934	36.657
	EZChemo_Retrieval	115.25	20	45.163	10.099

Paired Samples Correlations

		N	Correlation	Sig.
Pair 1	Paper_Retrieval & EZChemo_Retrieval	20	.113	.636

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	Paper_Retrieval - EZChemo_Retrieval	111.850	165.052	36.907	34.603	189.097	3.031	19	.007

Table 2: SPSS output for paired sample t-test comparing the time providers took to retrieve chemo orders using paper-based system and EZChemo

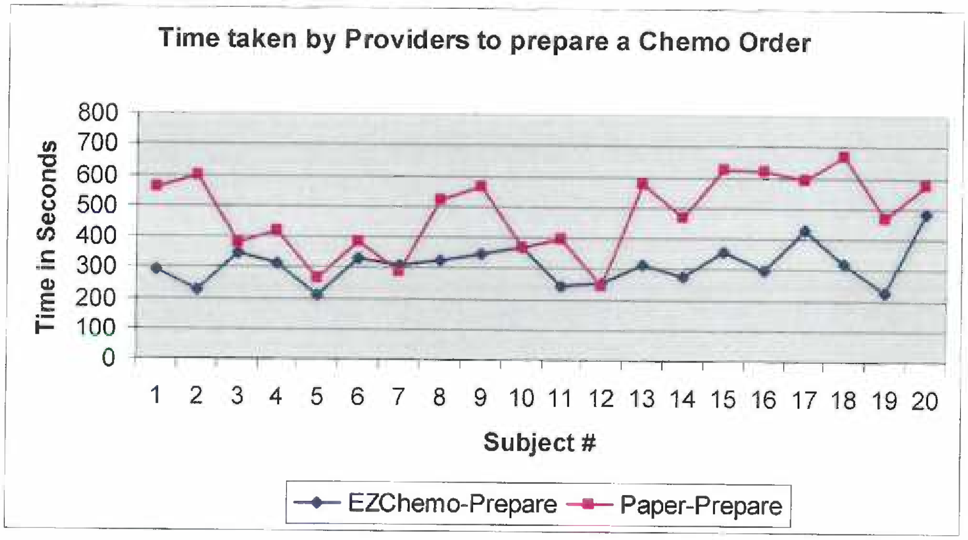

Fig 15: Comparison of the total time it took for the providers to retrieve the two chemo orders using EZChemo and paper-based systems

The results generated by SPSS and displayed in Table 2, suggest that the p-value is <<0.0001 for the two-tailed test. So, we reject the null hypothesis and state that there exists statistically significant difference between the time it takes to retrieve a chemo order using EZChemo when compared to paper- based system at 0.05 level of significance.

We further analyze and check if there is a significant difference in the time it takes to prepare a chemo order using paper-based system and EZChemo. Preparation of the chemo order is defined as the process of filling in the chemo order, once it is retrieved, making appropriate validations and calculations and signing the order in the end. SPSS is used again to perform similar paired sample t-test and the results are presented in table 3.

The results generated by SPSS and displayed in Table 3, suggest that the p-value is <<0.0001 for the two-tailed test. So, we reject the null hypothesis and state that there exists statistically significant difference between the time it takes to retrieve a chemo order using EZChemo when compared to paper- based system at 0.05 level of significance.

To summarize, there is significant difference in the amount of time it takes to retrieve, prepare and hence the total time it takes to complete a chemo order using EZChemo and paper- based systems. Thus it is readily evident EZChemo is more efficient that paper- based system because it takes less time to complete chemo orders using EZChemo.

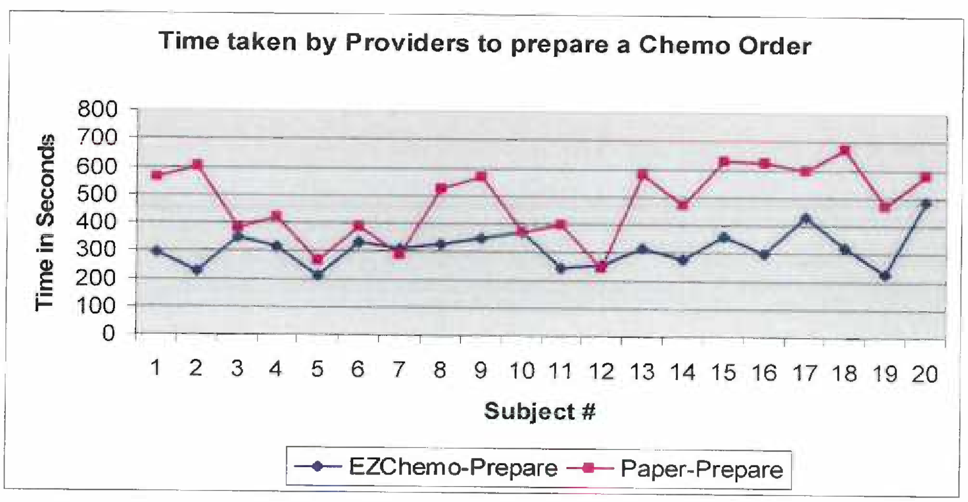

Fig 16: Comparison of the total time it took for the providers to prepare the two chemo orders using EZChemo and paper-based systems

Effectiveness

Evaluation of effectiveness of EZChemo in minimizing medication errors was performed by a pharmacist who was involved in the planning and development process of EZChemo and who was routinely involved in verifying for the accuracy of orders prepared by physicians before they were dispensed by the in-patient pharmacy division of OHSU.

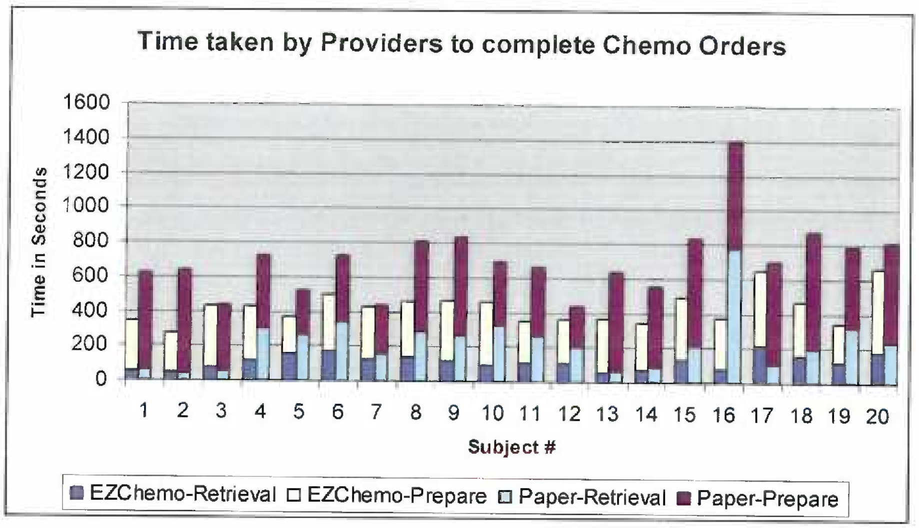

Fig 17: Comparison of the total time it took for the providers to complete the two chemo orders using EZChemo and paper-based systems: split-up of the phases

The pharmacist was given the completed chemo orders and after thorough evaluation, it has been found that ***7 out of 20 (35%)*** of the handwritten orders had errors that would have required a call from a pharmacist. These errors mainly comprised primarily of missing patient identifiers. All most all had at least one cross out of other blot on them. In contrast only 1 person's EZchemo forms had an error, ***1 out of 20, (0.05%)*** because they left the patient name off . This has probably happened because EZChemo currently lets the Provider complete the order without requiring him/her to enter the patient name and this validation needs to be enforced in the next version of EZChemo.

So, in effect EZChemo has brought down the error rate from 7 to 1 in a given set of 20 chemotherapy orders, a difference of 86%. Taking these findings into consideration it could be deduced that EZChemo has significantly decreased the error rate and hence is more effective than paper- based system.

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	EZChemo_Prepare	311.90	20	67.513	15.096
	Paper_Prepare	478.05	20	130.320	29.140

Paired Samples Correlations

		N	Correlation	Sig.
Pair 1	EZChemo_Prepare & Paper_Prepare	20	.353	.126

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	EZChemo_Prepare - Paper_Prepare	-166.150	123.782	27.678	-224.082	-108.218	-6.003	19	.000

Table 3: SPSS output for paired sample t-test comparing the time providers took to prepare chemo orders using paper-based system and EZChemo

Usability

Analyzing the survey forms filled in by the provider users, the following clusters of opinions have been deduced in the following categories:

Suggestions for improvements in EZChemo, recurring themes

(1) Additional parameters could be included for dose calculation purposes:

a. Some of the participants have suggested that EZChemo should allow chemo order preparation in non-standardized cases, as an extension to the current capabilities. Suggestions included use of "ideal" body weight, as opposed to actual body weight, in determining BSA and hence dose calculation and also the ability to adjust dose per the bilirubin values and . In essence, while most participants were happy with what EZChemo offers, some participants were interested to see some flexibility in the way they prepared orders using EZChemo by letting them do orders in "un-standardized" ways.

(2) Documentation needed:

a. Some of the participants did not quite understand whether to "view" or "save" the PDF files because the current tutorial does not make this aspect quite clear. Some of the participants did not know that scripts could be embedded within PDFs and so hence weren't sure how to fill-in the dose values. Most participants weren't sure how to name the file either. So, a brief tutorial that makes these aspects quite clear needs to be prepared and distributed.

b. Also, a brief mention that only "Print" button at the bottom of the order should be used and not the "Print" button from "File" menu of Adobe acrobat should be made in the tutorial. This is because "Print" button from the file menu does not run the script that's important for internal validations.

(3) Human-Computer Interaction (HCI) issues:

a. Ability to convert measurement values, lbs to kgs and cms to inches, back and forth. This will save the provider some time so he/she won't have to refer to a third-party tool for converting measurements.
b. Balloon tip help to indicate what "Validate & Calculate" buttons are exactly doing. Some of the providers were confused as what exactly is the kind of validation that the script is doing.
c. Ability to see the code that runs behind screens for making dose calculations. The idea is to put the provider in context of logic being used in the script for making calculations
d. Add "Validate & Calculate" button at the end of each page to un-necessitate "too much of scrolling"

Recurring themes in workflow issues

All the twenty participants that were interviewed agreed that EZChemo would fit into their work flow. The main reason most participants mentioned for this is that they have been used to accessing chemo templates using computers and accessing orders via EZChemo doesn't require them to follow a different protocol (The url and the login information has been made clear to the participants in advance with the help of a tutorial).

They report that EZChemo fits well into their workflow also because (a) it allows them to access the orders from anywhere using the Internet and (b) it doesn't require them to print the orders on special papers, thus saving them additional time that otherwise would be spent in retrieving them, either on their own or with the help of colleagues and staff (an estimated time of 5 additional minutes). There is also a participant who took exceptionally long time in finding chemo orders on the network drive (paper-based system) because he is not used to writing chemo orders on a regular basis and is glad that EZChemo makes access so much easier (this participant is an MD PhD who is more concerned with research than with everyday patient care).

All participants are mainly happy, in essence, because they have the information (chemo orders) that they need when they need it and no special protocols are required for them to learn to access and use EZChemo.

Reasons why participants would or wouldn't use EZChemo: Recurring themes

All the participants mentioned that they would use EZChemo, and none of them said they wouldn't, mainly for the following reasons:

- EZChemo is more faster and saves time
- EZChemo is more accurate because calculations are standardized. Although, there is one participant who is unsure about the accuracy and had to do manual calculations in addition to verify the dose values tallied. This problem could be

alleviated and more trust with EZChemo's calculations could be established when a provider is experienced with EZChemo.

- EZChemo is more comprehensive. Some of the participants mentioned that it is good that EZChemo also takes a patient's CNS Prophylaxis parameter values into consideration for making dose adjustments in HyperCVAD orders. This was a feature that was not included in the paper-based chemo order templates system.
- EZChemo makes internal validations in that it alerts the provider the specific information (the parameter values such as Patient ID, Date of Birth, Allergy information etc.) that he/she has forgotten to include. EZChemo, however, only functions as a supporting tool and lets the provider by pass the alert at his/her discretion. Thus, participants think that EZChemo leaves less room for transcribing errors.
- Legibility issues found in paper-based systems are eliminated as chemo orders made using EZChemo do not involve hand written transcriptions.

From this analysis, it could be concluded that provider participants have found EZChemo to be highly usable in that all of them have expressed interest to use EZChemo on a daily basis and as a matter of fact, it has been reported that most provider users in the Hematology department at OHSU are currently using EZChemo. Suggestions have been made for improvements and all these findings have been reported to the EZChemo team to be used as guidelines for the implementation of next version of EZChemo.

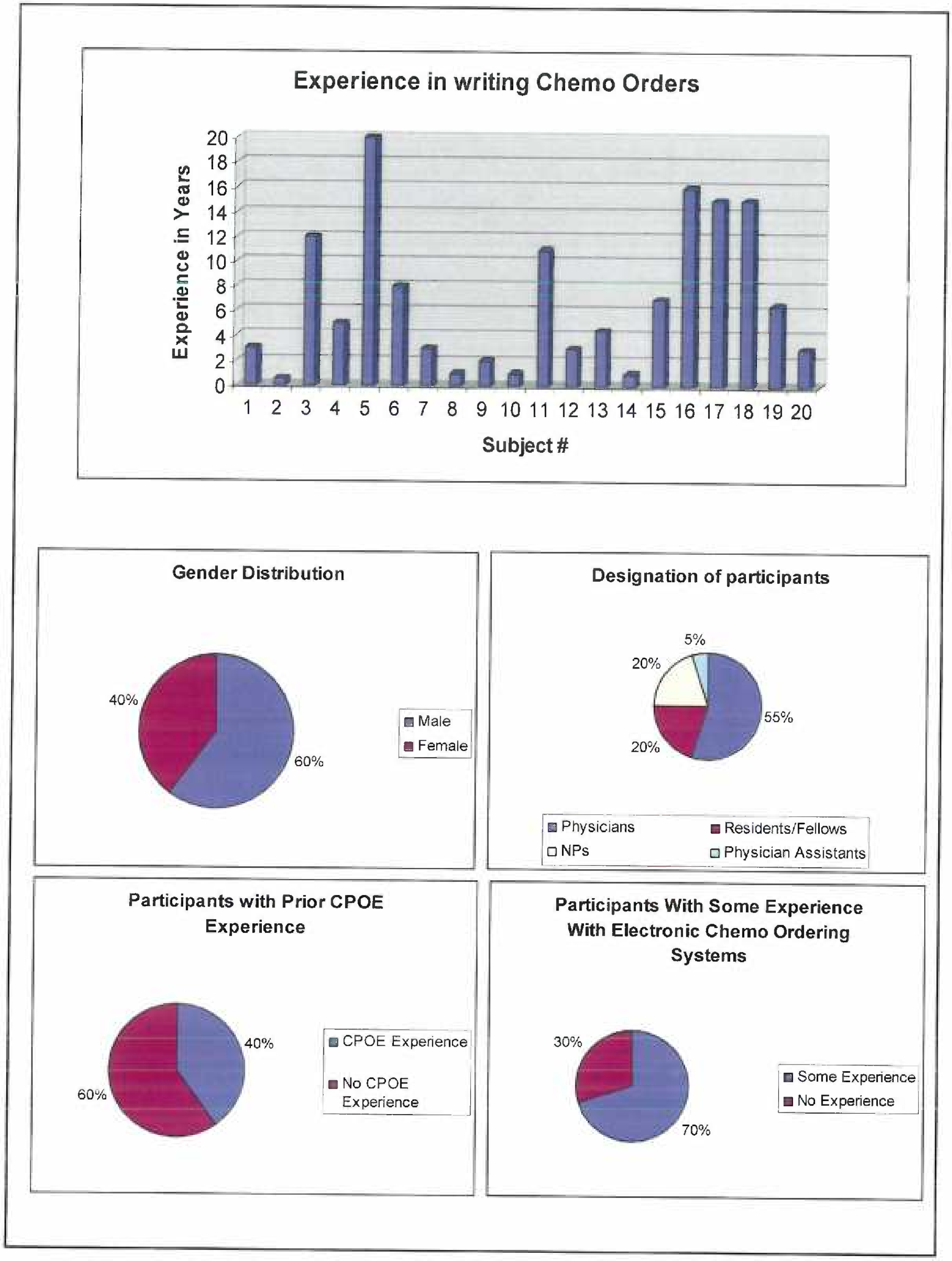

Fig 18: Demographics of provider subjects

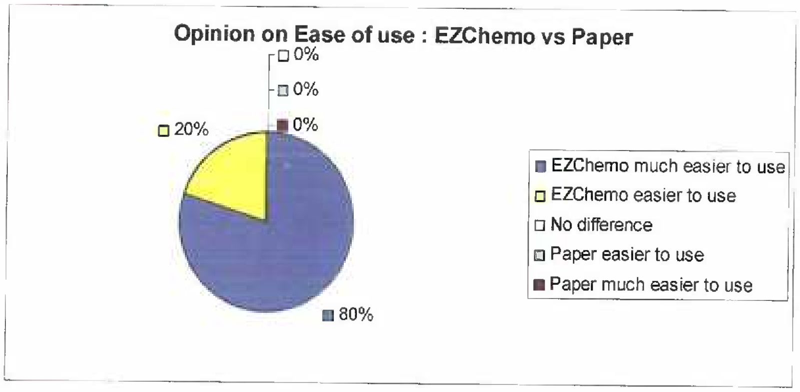

Fig 19: Participants' opinion on ease of use: comparison between EZChemo and Paper

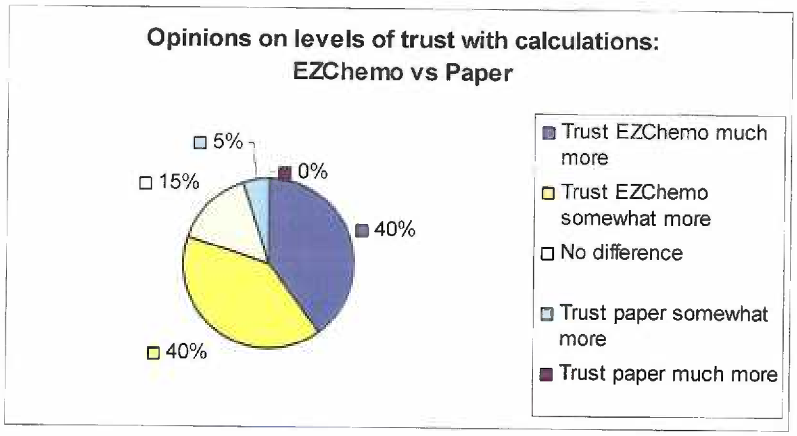

Fig 20: Comparison of trust levels with calculations made by EZChemo when compared to trust with manual calculations

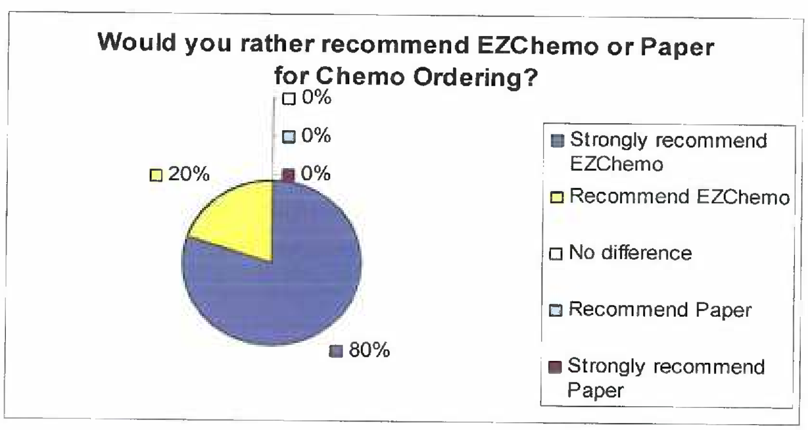

Fig 21 : Comparison of comfort levels of Providers in recommending EZChemo to peers when compared to paper-based system

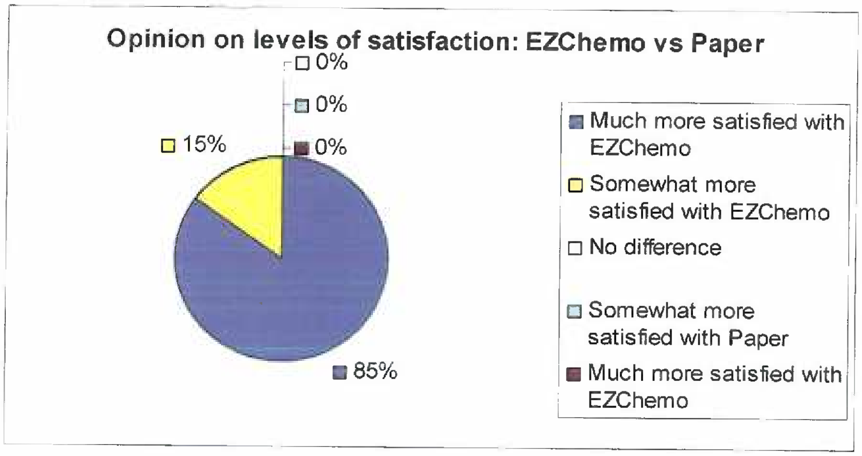

Fig 22: Comparison of satisfaction levels of Providers with EZChemo compared to paper -based system

Conclusion

In effect, it could be concluded that EZChemo is:

- *more efficient because there is a significant difference in the time it takes to complete chemo orders using EZChemo when compared to paper-based system, the difference being in favor of EZChemo*
- *more effective than paper-based system because it has decreased error rate by 86%*
- *more usable than paper-based system because all twenty provider users have expressed interest and are currently using EZChemo for reasons based on several objective and subjective parameters*

Further developments guided by the comments from Providers could be used to improve the current version of EZChemo to make it more effective, efficient and usable. EZChemo in its current form, however, is much more effective, efficient and usable than *the existing paper-based system. Future work should include further testing of the accuracy of the EZChemo orders.*

Bibliography

1. World Health Organization Statistical Information Systems [homepage on the Internet]. Geneva, Switzerland: World Health Organization©; c1998. Accessed on 04/10/2008 and available from: http://www.who.int/whosis/database/core/core_select_process.cfm?countries=all&indicators=nha

2. Kohn L, Corrigan J, Donaldson M, eds. Institute of Medicine (Ed.). To Err Is Human: Building a Safer Health System. Washington, DC: Committee on Quality of Health Care in America, Institute of Medicine. National Academy Press; 2000.

3 World Health Organization assess the world's health system. Press Release WHO/44 21 June 2000.World Health Organization assess the world's health system. Press Release WHO/44 21 June 2000.

4. Burke JP. Preventing Medication Errors; Medication Errors N Engl J Med 2007 357: 624-625 Preventing Medication Errors. IOM report

5. Potts AL, Barr FE, et al. Computerized physician order entry and medication errors in a pediatric critical care unit. Pediatrics 2004 Jan; 113(1 Pt 1):59-63

6. Elixhauser A, Owens P. Adverse Drug Events in U.S. Hospitals, 2004. Healthcare Cost and Utilization Project (HCUP). Statistical Briefs. Statistical Brief # 29. April 2007. Agency for Healthcare Research and Quality, Rockville, MD. Available from: www.hcup-us.ahrq.gov/reports/statbriefs.jsp

7 Lesar TS, Briceland L, et al. Factors related to errors in medication prescribing. JAMA 1997; 277(4): 312-7.

8. Reducing and Preventing Adverse Drug Events To Decrease Hospital Costs. Research in Action, Issue 1. AHRQ Publication Number 01-0020, March 2001. Agency for Healthcare Research and Quality, Rockville, MD. Accessed on 03/28/2008 and available from http://www.ahrq.gov/qual/aderia/aderia.htm. AHRQ report.

9. U.S. Pharmacopeia © [home page on the Internet]. Rockville, MD. United States Pharmacopeial Convention ©. Oncolytic Therapy Requires Special Vigilance: CapsLink April 2004. Accessed on 04/02/2008 and available from: http://www.usp.org/hqi/practitionerPrograms/newsletters/capsLink/

10. Bates D, Spell WN, et al. The costs of adverse drug events in hospitalized patients. Adverse Drug Events Prevention Study Group. JAMA January 1997; 277(4): 307-11.

11. Shamliyan TA, Duval S, Du J, Kane RL: Just what the doctor ordered: Review of the evidence of the impact of computerized physician order entry system on medication errors. Health Serv Res 2008, 43(1 Pt 1):32-53.

12. Bates DW, Cullen DJ, et al. Incidence of adverse drug events and potential adverse drug events. Implications for prevention. ADE Prevention Study Group. JAMA 1995; 274(1): 29-34

13. Nebeker JR, Hoffman JM, et al. High rates of adverse drug events in a highly computerized hospital. Arch Intern Med 2005; 165(10): 1111-6.

14. Asch SM, McGlynn EA, Hogan MM, Hayward RA, Shekelle P, Rubenstein L, et al. Comparison of quality of care for patients in the Veterans Health Administration and patients in a national sample. Ann Intern Med. 2004;141:938-45

15. Ash JS, Gorman PN, Seshadri V, Hersh WR. Perspectives on CPOE and patient care. J Am Med Inform Assoc. 2004;11:207-216.

16. Ash JS, Stavri PZ, Kuperman GJ. A consensus statement on considerations for a successful CPOE implementation. J Am Med Inform Assoc. 2003;10:229-34

17. Bates DW, Leape LL, Cullen DJ, Laird N, Petersen LA, Teich JM, et al. Effect of computerized physician order entry and a team intervention on prevention of serious medication errors. J Am Med Assoc 1998;280(15):1311-6.

18. Koppel R, Metlay JP, et al. Role of Computerized Physician Order Entry Systems in Facilitating Medication Errors. JAMA. 2005;293:1197-1203

19. Han YY, et al. Unexpected Increased Mortality After Implementation of a Commercially Sold Computerized Physician Order Entry System. Pediatrics 2005 116: 1506-1512

20. Eisenberg JM. The best offense is a good defense against medical errors: Putting the full-court press on medical errors. Speech given by Director, Agency for Healthcare Research and Quality, at the Duke University Clinical Research Institute; 2000 Jan 2. URL: http://www.ahrq.gov/news/spch012000.htm

21. Teich JM et al. Clinical Decision Support in Electronic Prescribing: Recommendations and an Action Plan. J Am Med Inform Assoc. 2005 Jul–Aug; 12(4): 365–376

22. eHealth Initiative. "Executive Summary--Electronic Prescribing: Toward Maximum Value and Rapid Adoption." Washington: eHealth Initiative, 2004. Accessed from: http://www.ehealthinitiative.org/initiatives/erx/ on 04/21/2008.

23. Roish DW. A model of methods for influencing prescribing. A review of educational methods, theories of human reference, and delineation of the model. DICP 1990; 24; 537-42

24. Winslow E, Nestor V, Davidoff S, et al. Legibility and completeness of physician's handwritten medication orders. Heart and Lung 1997; 26: 158-64

25. Fisher DS et al. Improving the cancer chemotherapy use process. J Clin Oncol 1996; 14: 3148-55

26. Adobe © [home page on the Internet]. Acrobat JavaScript Scripting Reference. Copyright © 2008 Adobe Systems Incorporated. Accessed on 04/14/2008, available from: partners.adobe.com/public/developer/en/acrobat/sdk/AcroJS.pdf

27. Rahmel, Dan (2007). Beginning Joomla: From Novice to Professional. Apress. ISBN 1590598482.

28. PROPHET StatGuide: Do your data violate t test assumptions? [home page on the Internet]. Northwestern University, Chicago IL. Last updated on March 17, 1997, accessed on 04/14/2008 and available from: http://www.basic.northwestern.edu/statguidefiles/ttest_unpaired_ass_viol.html#Non-normality

29. Levesque R. SPSS Programming and Data Management: A Guide for SPSS and SAS Users, Fourth Edition (2007), SPSS Inc., Chicago Ill. SPSS

Appendix-A

Javascript used to make calculations and validations for chemo order HyperCVAD cycle-A, an example case:

```
var risk = (this.getField("risk")).value;


var day1 = this.getField("day1").value;

var dayinc = new Date(day1);

dayinc.setDate(dayinc.getDate() + 1);

var day2 = util.printd("mm/dd/yy", dayinc);


dayinc = new Date(day1);

dayinc.setDate(dayinc.getDate() + 7);

var day8 = util.printd("mm/dd/yy", dayinc);


var line = "Intrathecal Chemotherapy due on day2 ("+day2+") and day8 ("+day8+"). (See
Intrathecal Chemotherapy orders. Cytarabine on day2 and Methotrexate on day8)";


if(risk=="1") {

var cycle = this.getField("cycle").value;

        if(cycle<3) {

                this.getField("risktext").value = "Low risk cycles A + B 1 and 2\n\n\n"+
line;

        }

        else {
```

```
            this.getField("risktext").value = "no intrathecal chemotherapy this cycle";
        }
} else if(risk == "0") {
        this.getField("risktext").value = "High risk! Intrathecal chemotherapy due cycles
A + B 1 through 4\n\n\n"+line;
}

var BSA = (this.getField("BSA")).value;
var weight = (this.getField("weight")).value;
var drdoxorubicin = (this.getField("drdoxorubicin")).value * 0.01;
var res = parseFloat(BSA) * parseFloat(drdoxorubicin);

(this.getField("doxorubicin")).value = Math.round(50.00 * parseFloat(res));

var drcyclophosphamide = (this.getField("drcyclophosphamide")).value * 0.01;
var res = parseFloat(BSA) * parseFloat(drcyclophosphamide);
(this.getField("cyclophosphamide")).value = Math.round(300.00*parseFloat(res));

var drmesna = (this.getField("drmesna")).value * 0.01;
var res = parseFloat(BSA) * parseFloat(drmesna);
(this.getField("mesna")).value = Math.round(600.00 * parseFloat(res));

var acnumber = this.getField("acnumber").value;
var mrnumber = this.getField("mrnumber").value;
```

```
var name = this.getField("name").value;
var dob = this.getField("dob").value;
var cycle = this.getField("cycle").value;
var day1 = this.getField("day1").value;
var staff = this.getField("staff").value;
var allergies = this.getField("allergies").value;


if(mrnumber=="" || name == "" || dob == "" || staff == "" || allergies == "" || day1 ==
"01/01/99" || cycle== "" || risk== "Off"){
var err = "";
if(mrnumber==""){ err = "\n<Medical Record Number>"; }
if(name == "") { err = err+"\n<Patient Name>"; }
if(dob == "") { err = err+"\n<Date of Birth>"; }
if(cycle == "") { err = err+"\n<Cycle Number>"; }
if(day1 == "01/01/99") { err = err + "\n<Day1 of Chemotherapy>"; }
if(staff == "") { err = err+"\n<Attending Staff>"; }
if(allergies== "") { err = err+"\n<Allergies>"; }
if(risk=="Off") { err = err+"\n<CNS Prophylaxis> (High Risk/ Low Risk)"; }
app.alert("Please fill in the values for the following required fields:\n-------------------------
-------------------------------------------"+err);
}


if(weight<75)
{
```

```
(this.getField("fil")).value = 300;
}
else
{
(this.getField("fil")).value = 480;
}

if(drdoxorubicin<1 || drmesna<1 || drcyclophosphamide<1){
app.alert("Please note in the comments the reason for dose adjustments");
}
```

Javascript used to make calculations and validations for chemo order 3+7 IdaCytarabine, an example case:

```
var BSA= (this.getField("BSA")).value;


var drcytarabine= (this.getField("drcytarabine")).value * 0.01;

var res = parseFloat(BSA) * parseFloat(drcytarabine);

(this.getField("cytarabine")).value = Math.round(100.00*parseFloat(res));


var dridarubicin= (this.getField("dridarubicin")).value * 0.01;

var res = parseFloat(BSA) * parseFloat(dridarubicin);

(this.getField("idarubicin")).value = Math.round(12.00*parseFloat(res));



var mrnumber = this.getField("mrnumber").value;

var name = this.getField("name").value;

var dob = this.getField("dob").value;

var day1 = this.getField("day1").value;

var staff = this.getField("staff").value;

var allergies = this.getField("allergies").value;


if(mrnumber=="" || name == "" || dob == "" || staff == "" || allergies == "" || day1 ==
"01/01/99"){

var err = "";

if(mrnumber==""){ err = "\n<Medical Record Number>"; }
```

```
if(name == "") { err = err+"\n<Patient Name>"; }

if(dob == "") { err = err+"\n<Date of Birth>"; }

if(day1 == "01/01/99") { err = err + "\n<Day1 of Chemotherapy>"; }

if(staff == "") { err = err+"\n<Attending Staff>"; }

if(allergies== "") { err = err+"\n<Allergies>"; }


app.alert("Please fill in the values for the following required fields:\n-------------------------
-----------------------------------------"+err);

}


if(drcytarabine<1 || dridarubicin<1){

app.alert("Please note in the comments section the reason for dose adjustments");

}
```

Appendix – B

Notes from shadowing Healthcare providers in the Hematology Department, OHSU

- The chemotherapy orders corresponding to each patient are stored on a password protected shared network drive in a folder that is named after the patient's name
- Patients are admitted through 2 different routes: emergency department when the patient is in urgent need of care and admission as an inpatient in the department after consultation from a regular oncologist. Orders prepared for patients who are first admitted in the emergency department are sometimes not easy to track and those orders follow a different template
- The emergency department also uses an electronic system for preparing prescription orders but it is specific department and is not integrated with the rest of the department that are dependent on this system for documentation on the details of the patient's visit.
- Pharmacist disagrees or is confused (for several reasons including poor legibility) with the order prepared by a physician, on average, 5-10% of the time. When there is a disagreement between the pharmacist and the physician:
    - It takes 1 hr to resolve the differences
    - Sign-off overhead: 15mins to 1hr
- A patient typically gets a 24hr supply of medication and no more than 4hr supply of IV medications. This is to minimize the chances that drugs are dispensed even after they have been canceled by the physician

- Pyxis, an automated electronic drug dispensing system, is capable of showing the queue of scanned orders that are under review, that are approved by the pharmacy and those that are ready for dispensing to the nurses.
- One advantage that the physicians see in using paper-based systems is the free flow in making an order and the flexibility it offers to easily make edits.

- Some of the disadvantages of using paper-based system, as perceived by the physicians include:
    - Legibility issues. Hand written notes made by other physicians or pharmacists is sometimes hard to read
    - No integrated view of the condition of the patient as the information is distributed in several other papers
    - Lost paper records!
    - Difficulty experienced sometimes in locating the appropriate paper-based records
    - Paper-based records obtained from other healthcare centers that describe patient's history are especially hard to interpret. Creating a consolidated record is especially difficult.
    - Distribution of the orders is not easy. Other departments who might need access to the patients' orders need to send someone to physically come collect the appropriate paper work
    - Using a paper-based system, there is actually no way to ensure that a nurse administers the drugs that are prescribed in the order to the intended patient. Such errors are not unheard of!

    - Using paper-based systems, there is no guarantee that the drugs were administered at the time they were due

- Some of the disadvantages of using paper-based system, as perceived by the pharmacists include:
    - Legibility issues
    - Lack of an integrated view of the patient's condition, including his/her lab reports, medications: current and past, allergies, height, weight and progress notes
    - With a paper-based system, nurses do not have a way to know if the pharmacist got a chance to work on the order for dispensing and so, they occasionally make calls to the pharmacy to find out the status, much to the inconvenience of the pharmacist who is already overloaded with work
    - Using paper-based systems, pharmacists do not get to know if the order that has been dispensed has actually been administered properly by the nurse
    - Pharmacists sometimes get into a situation when they are required to authorize a prescription order although some of the lab values are missing or pending, which could affect the final decision whether or not to dispense a drug in the prescribed portions. This is mainly because the pharmacists do not get to review the order until the last minute resulting from physician's delayed order preparation. Using a paper-based system, it is rather a daunting task to keep track of such records that are missing in

lab values and hence need to be re-reviewed. Often times, such records once signed off by the pharmacist do not get re-reviewed

- Advantages of using an electronic prescribing system, as perceived by physicians and pharmacists:
    - No more legibility issues
    - Automated calculations can decrease the effort and improve the accuracy
    - Integrated view of patient information: current and past that helps in making better and timely decisions
    - Possible drug-reconciliation, highly valued
    - Occasional reminders and alerts integrated into the electronic prescribing system that might be of value
    - Easy storage and access to documentation of procedures performed to the patients
    - Easy for the healthcare provider involved to track the life cycle of the prescription order. A nurse can electronically check to see whether or not a drug has been dispensed or is in suspended status due to pharmacy specific reasons or other miscellaneous reasons. A pharmacist and a physician can electronically check to see whether or not a nurse has actually administered the drugs to the appropriate patients in the right portions at the right points of time
    - A pharmacist can immediately get to know when and if a drug or an entire order has been marked as discontinued by a physician for a patient and so he/she will get a chance to hold the drug that is ready to be dispensed.

Reasons for discontinuation can easily be communicated between the physicians and pharmacists

- Improved sense of involvement in the care delivery process could be felt by the pharmacists

- Disadvantages of using electronic prescribing systems, as perceived by both the physicians and pharmacists:
    - CDSS systems tied up with prescribing systems inundate users with alerts and reminders which often get over-ridden
    - As much as 99% of the alerts are over ridden by the pharmacists as they fail to see the value in the information provided by them
    - Physician users also find the quality of information provided by the alerts to be "variable"
    - Physician users do not like to be "told by a computer" how to practice better
    - Alerts that most often get over ridden are the ones that are either too long and/or are too "dense"
    - Suggestions made by alerts and reminders sometimes are not specific to the conditions and preferences of the patients

- <u>Recommendations for future electronic prescribing systems:</u>
    - An electronic chemotherapy order system would be highly beneficial if it could heavily prompt the physician user to complete the order at least a day prior to the date of drug dispensing

- An electronic system that immediately indicates whether or not any lab values are still pending for the related order would be helpful
- A system that suggests to the physician user to enter the reason for dose adjustments, if any, made in the order. Reasons could include certain lab report values, reduced renal function of the patient etc.
- Extra notes that accompanies the order for free communication between different providers would be very useful
- A system would be largely helpful if it could instantaneously indicate when a chemotherapy order has been canceled or modified along with the documented reasons
- System also needs to lay out the order in which the drugs could be administered, along with the details of any flexibility that is there in administration, for the benefit of inexperienced pharmacists who otherwise have no idea often times and for the benefit of nurses who can "squeeze in" administration of certain drugs between others for efficiency and time saving reasons

Appendix – C

Clinical Case Studies

ALL case 1

(Code: H-a)

Mr. David Schmidt is a 45 year old male patient, who has a history of pre-B ALL diagnosed 4 months ago. He has high-risk disease for CNS involvement. He is admitted for consolidation with cycle 3A of hyper-CVAD.

He has normal renal and hepatic functions.

He measures 170 cm and weighs 81 kg.

Med Rec # : 12345
DOB : 12/12/62

ALL case 2

(Code: H-b)

Elisabeth Nguyen is a 22 year old female patient, with a history of pre-B ALL diagnosed 6 months ago. She has low-risk disease for CNS involvement. She is admitted for consolidation with cycle 5A of hyper-CVAD.

She has normal renal and hepatic functions.

She measures 153 cm and weighs 60 kg.

Medical Record # : 98765
DOB : 10/08/85

AML case 1

(Code: 37 a)

Mr. John Smyth is a 27 year old male patient, who has just been diagnosed with AML. He has no co-morbidities.

His renal and liver function are normal.

He measures 182 cm and weighs 87 kg.

Medical Record # : 55555
DOB : 08/06/80

AML case 2

(Code: 37 b)

Mrs Cynthia Patersonis a 35 year old female patient, who has just been diagnosed with AML. She has no co-morbidities.

Her renal and liver function are normal.

She measures 165 cm and weighs 75 kg.

Medical Record # : 77777
DOB : 03/28/72

Appendix – D

EZChemo Protocol

Subject ID	Modality	Order Name	Clinical Case ID
1	E	37	37-b
		H	H-a
	P		37-a
			H-b
2	E	37	37-b
		H	H-b
	P		37-a
			H-a
3	E	H	H-a
		37	37-a
	P		H-b
			37-b
4	P	H	H-b
		37	37-b
	E		H-a
			37-a
5	P	H	H-a
		37	37-a
	E		H-b
			37-b
6	E	H	H-b

		37	37-b
	P		H-a
			37-a
7	P	37	37-a
		H	H-a
	E		37-b
			H-b
8	P	H	H-b
		37	37-b
	E		H-a
			37-a
9	P	37	37-a
		H	H-b
	E		37-b
			H-a
10	E	37	37-a
		H	H-a
	P		37-b
			H-b
11	P	37	37-b
		H	H-b
	E		37-a
			H-a
12	E	H	H-a
		37	37-b
	P		H-b
			37-a

13	E	37	37-a
		H	H-a
	P		37-b
			H-b
14	P	H	H-b
		37	37-b
	E		H-a
			37-a
15	P	37	37-a
		H	H-b
	E		37-b
			H-a
16	E	H	H-b
		37	37-b
	P		H-a
			37-a
17	P	H	H-a
		37	37-b
	E		H-b
			37-a
18	E	37	37-a
		H	H-a
	P		37-b
			H-b
19	E	H	H-b
		37	37-b
	P		H-a

			37-a
20	P	H	H-a
		37	37-b
	E		H-b
			37-a

Table A: Pseudo randomization at the Modality and the clinical case study level to minimize bias. Note that the order was preserved for the second system in each case to minimize the carry over effect. To eliminate redundancy, the order of chemotherapy Orders as assigned to providers was not listed twice in the above table.

Legend:

"P" = Paper-based system

"E" = EZChemo

"H" = Chemo Order HyperCVAD Cycle A

"37" = Chemo Order 3+7 IdaCytarabine

a/b = Code as detailed in Appendix-III

Appendix – E

Sample Chemotherapy Order : HyperCVAD - Cycle A

Oregon Health & Science University
Hospitals and Clinics

PO1500

PHYSICIANS' ORDERS

Account.No :
Med.Rec.No :
Name :
Birth Date :

Chemotherapy Orders
Hyper CVAD Cycle [ ] A for ALL
(Kantarjian HM, JCO 2000; 18(3):547-61)

Height (cms)	:
Weight (kgs)	:
BSA (m^2)	: 0.00
% of original Doxorubicin dose	: 100
% of original Cyclophosphamide dose	: 100
% of original Mesna dose	: 100

1. Patient on Hematologic Malignancies Team
2. Day 1 of chemotherapy is : (01/01/99) [mm/dd/yy]
3. Dx : Acute Lymphoblastic Leukemia
4. CNS Prophylaxis : (High Risk ◯ / Low Risk ◯)
5. Staff :
6. Allergies :

Meds:
1. Bactrim DS- one tab PO BID Q Mon & Thurs.
2. Allopurinol 600 mg PO now, then 300 mg PO daily X 6 days total.

Antiemetics:
1. Ondansetron 24mg PO / 8mg IV 60 minutes before first chemotherapy dose each day with Lorazepam 1 mg PO X 4 days. Give with each day's dexamethasone dose.

PRN Antiemetics:
1. Lorazepam 0.5-1 mg IV/PO q 4hours PRN N/V
2. Diphenhydramine 25 mg IV/PO q 4 hours PRN EPS symptoms or N/V
3. Droperidol 0.625 mg IV q 2 hours PRN N/V
4. Prochlorperazine 5-10 mg PO/IV every 4 hours PRN N/V
5. Haloperidol 0.5-2 mg IV/PO Q 4 hours PRN N/V

IV FLUIDS:
D5W NS infuse at 250 mL/hour for 4 hours then 150 mL/hour

Signature: ______________________

Oregon Health & Science University
Hospitals and Clinics

PO1500

PHYSICIANS' ORDERS

Account.No :
Med.Rec.No :
Name :
Birth Date :

Chemotherapy Treatment schedule

1. **Doxorubicin** 50 mg/m^2 x 100 % = **mg** IV Push on day 4 (01/04/99)
2. **Vincristine** 2 mg IV Push on Day 4 (01/04/99) and day 11 (01/11/99)
3. **Dexamethasone** 40 mg PO Daily on day 1 (01/01/99) through Day 4 (01/04/99) and day 11 (01/11/99) through day 14 (01/14/99). **On day 1 (** 01/01/99 **) through day 4 (** 01/04/99 **), give each day's dose 60 minutes before first chemotherapy dose with ondansetron.**
4. **Cyclophosphamide** 300mg/m^2 x 100 % = **mg** in 250 mL NS IV over 2 hours every 12 hours for 6 doses. Begin Day 1 (01/01/99). Dose is based on actual body weight. Mesna & Cyclophosphamide can infuse through same side of catheter.
5. **Mesna** 600 mg/m^2 x 100 % = **mg** in 1000 mL NS IV as a continuous infusion at 44 mL/hr for 3 days. Begin with first Cyclophosphamide dose on day 1 (01/01/99)
6. **Filgrastim** 5mcg/kg = **mcg** sub cutaneous over 30mins daily beginning on day 5 (01/05/99) until ANC > 1500 for 2 consecutive days (**Pegfilgrastim** 6mg SQ if outpatient)
7.

Signature: ______________________________

03/19/08

Oregon Health & Science University
Hospitals and Clinics

PO1500

PHYSICIANS' ORDERS

Account.No :
Med.Rec.No :
Name :
Birth Date :

Comments:

Signature: ______________________________

Appendix – F

Sample Chemotherapy Order : 3+7 IdaCytarabine

Oregon Health & Science University
Hospitals and Clinics

PO1500

PHYSICIANS' ORDERS

Account.No :
Med.Rec.No :
Name :
Birth Date :

Idarubicin & Cytarabine (3 + 7) Chemotherapy for AML
(Wiernik PH, et al; Blood 1992: 79:313)

Height (cms)	:	
Weight (kgs)	:	
BSA (m^2)	:	0.00
% of original Cytarabine dose	:	100
% of original Idarubicin dose	:	100

1. Patient on Hematologic Malignancies Team
2. Day 1 of chemotherapy is : (01/01/99) [mm/dd/yy]
3. Dx : AML
4. Staff :
5. Allergies :

Meds
1. Allopurinol 600 mg PO now, then 300 mg PO daily X 6 days total.

Antiemetics
1. Ondansetron 24mg PO / 8mg IV, dexamethasone 8 mg PO, and Lorazepam 1 mg PO 60 minutes prior to Idarubicin dose on Day 1 (01/01/99) through Day 3 (01/03/99)

PRN Antiemetics:
1. Lorazepam 0.5-1 mg IV/PO q 4 hours PRN N/V
2. Diphenhydramine 25 mg IV/PO q 4 hours PRN extrapyramidal symptoms or nausea
3. Prochlorperazine 5-10 mg IV/PO every 4 hours PRN N/V
4. Droperidol 0.625 mg IV q 2 hours PRN N/V
5. Haloperidol 0.5-2 mg IV/PO Q4 hours PRN N/V

Signature: ______________________________

Oregon Health & Science University
Hospitals and Clinics

PO1500

PHYSICIANS' ORDERS

Account.No :
Med.Rec.No :
Name :
Birth Date :

Chemotherapy Treatment schedule

1. IVF during chemotherapy:
   IV fluids D5 .45 NS @ 150mL/hr
2. **Cytarabine** 100 mg/m^2/day x 100 % = mg IV in 500 mL NS by continuous infusion daily for Day 1 (01/01/99) through Day 7 (01/07/99)
3. **Idarubicin** 12mg/m^2/day x 100 % = mg IV over 30 minutes in 100 mL D5W on Day 1 (01/01/99) through Day 3 (01/03/99) through central catheter

Comments:

Signature: ______________________

Appendix – G

Sample Survey Form

OREGON HEALTH & SCIENCE UNIVERSITY

Engineering and Evaluating EZChemo: An Electronic Chemotherapy Order System

Subject: 10 Date: 4/7/08

Timings (in seconds):

	EZChemo-37 a	EZChemo-Hb	Paper-37 b	Paper – Ha
Getting document	:26	1:05	2:40	2:45
Filling it out	3:05	3:00	3:34	4:31
Total	3:31	4:08	6:14	9:16

Questionnaire

Demographic Information

- Experience in writing chemotherapy orders: 1 years
- Gender : ○ M ● F
- Designation : ○ Physician ○ NP ● Fellow/Resident
- How would you rate your computer skills on a scale of 1-5 (1 = never used, 5 = expert)?

  3

- What kind of tasks do you use computers for? Check all that apply:
  - [ ] Computerized provider order entry (CPOE) for medication ordering
  - [x] Reviewing patient results
  - [x] Entering patient notes
  - [x] Literature Review
  - [x] Research
  - [x] E-mail
  - [x] Leisure activities

❖ Do you have prior experience with any electronic chemo ordering system(s) ?

◉ yes ○ no

If yes, where and which system(s)?

a) used ez chemo once

b) ______________________

c) ______________________

Usability of EZChemo:

❖ How would you rate EZChemo when compared to the current paper based system, with respect to ease of use ?

Paper much easier to use	Paper easier to use	No Difference	EZChemo easier to use	EZChemo much easier to use

❖ Would you trust EZChemo's automated calculations or would you rather trust your own manual calculations ?

Trust paper much more	Trust paper somewhat more	No difference	Trust EZChemo somewhat more	Trust EZChemo much more

❖ Would you recommend EZChemo or the current paper based system to your colleagues for use on a daily basis?

Strongly recommend paper	Recommend paper	No difference	Recommend EZChemo	Strongly recommend EZChemo

- When compared to current paper based system, what are your overall satisfaction levels with using EZChemo ?

Much more satisfied with paper	Somewhat more satisfied with paper	No difference	Somewhat more satisfied EZChemo	Much more satisfied with EZChemo
				(circled)

General comments on EZChemo:

- Please tell us what we could do to improve EZChemo to better fit your needs.

- Will this software fit into your work flow? Why or why not?

yes, easy to use from any computer, can print out on any paper

- List few reasons why you would and wouldn't use EZChemo software on a daily basis.

AML case 1
(37 a)

Mr. John Smyth is a 27 year old male patient, who has just been diagnosed with AML. He has no comorbidities.

His renal and liver function are normal.

He measures 182 cm and weighs 87 kg.

Medical Record # : 55555
DOB : 08/06/80

Oregon Health & Science University
Hospitals and Clinics

PO1800

PHYSICIANS' ORDERS

Account.No	:	
Med.Rec.No	:	55555
Name	:	Smythe, Jason
Birth Date	:	08/06/80

Idarubicin & Cytarabine (3 + 7) Chemotherapy for AML
(Wiernik PH, et al; Blood 1992: 79:313)

Height (cms)	:	182.0
Weight (kgs)	:	87.0
BSA (m^2)	:	2.09
% of original Cytarabine dose	:	100
% of original Idarubicin dose	:	100

1. Patient on Hematologic Malignancies Team
2. Day 1 of chemotherapy is : (04/07/08) [mm/dd/yy]
3. Dx : AML
4. Staff : Deininger
5. Allergies : NKDA

Meds
1. Allopurinol 600 mg PO now, then 300 mg PO daily X 6 days total.

Antiemetics
1. Ondansetron 24mg PO / 8mg IV, dexamethasone 8 mg PO, and Lorazepam 1 mg PO 60 minutes prior to Idarubicin dose on Day 1 (04/07/08) through Day 3 (04/09/08)

PRN Antiemetics:
1. Lorazepam 0.5-1 mg IV/PO q 4 hours PRN N/V
2. Diphenhydramine 25 mg IV/PO q 4 hours PRN extrapyramidal symptoms or nausea
3. Prochlorperazine 5-10 mg IV/PO every 4 hours PRN N/V
4. Droperidol 0.625 mg IV q 2 hours PRN N/V
5. Haloperidol 0.5-2 mg IV/PO Q4 hours PRN N/V

Signature: Fleischman 13333

Oregon Health & Science University
Hospitals and Clinics

PO1500

PHYSICIANS' ORDERS

Account.No :
Med.Rec.No : 55555
Name : Smythe, Jason
Birth Date : 08/06/80

Chemotherapy Treatment schedule

1. IVF during chemotherapy:
   IV fluids D5 .45 NS @ 150mL/hr

2. **Cytarabine** 100 mg/m^2/day x 100 % = **209 mg** IV in 500 mL NS by continuous infusion daily for Day 1 (04/07/08) through Day 7 (04/13/08)

3. **Idarubicin** 12mg/m^2/day x 100 % = **25 mg** IV over 30 minutes in 100 mL D5W on Day 1 (04/07/08) through Day 3 (04/09/08) through central catheter

Comments:

Signature: Fleischman 13333

ALL case 2
(H-b)

Elisabeth Nguyen is a 22 year old female patient, with a history of pre-B ALL diagnosed 6 months ago. She has low-risk disease for CNS involvement. She is admitted for consolidation with cycle 5A of hyper-CVAD.

She has normal renal and hepatic functions.

She measures 153 cm and weighs 60 kg.

Medical Record # : 98765
DOB : 10/08/85

04/07/08

Oregon Health & Science University
Hospitals and Clinics

PO1500

PHYSICIANS' ORDERS

Account.No :	
Med.Rec.No :	98765
Name :	Nguyen, Elisabeth
Birth Date :	10/08/85

Chemotherapy Orders
Hyper CVAD Cycle 5 A for ALL
(Kantarjian HM, JCO 2000; 18(3):547-61)

Height (cms)	: 153.0
Weight (kgs)	: 60.0
BSA (m^2)	: 1.57
% of original Doxorubicin dose	: 100
% of original Cyclophosphamide dose	: 100
% of original Mesna dose	: 100

1. Patient on Hematologic Malignancies Team
2. Day 1 of chemotherapy is : (04/07/08) [mm/dd/yy]
3. Dx : Acute Lymphoblastic Leukemia
4. CNS Prophylaxis : (High Risk ○ / Low Risk ◉)
5. Staff : Deininger
6. Allergies : NKDA

Meds:

1. Bactrim DS- one tab PO BID Q Mon & Thurs.
2. Allopurinol 600 mg PO now, then 300 mg PO daily X 6 days total.

Antiemetics:

Ondansetron 24mg PO / 8mg IV 60 minutes before first chemotherapy dose each day with Lorazepam 1 mg PO X 4 days. Give with each day's dexamethasone dose.

PRN Antiemetics:

Lorazepam 0.5-1 mg IV/PO q 4hours PRN N/V
Diphenhydramine 25 mg IV/PO q 4 hours PRN EPS symptoms or N/V
Droperidol 0.625 mg IV q 2 hours PRN N/V
Prochlorperazine 5-10 mg PO/IV every 4 hours PRN N/V
Haloperidol 0.5-2 mg IV/PO Q 4 hours PRN N/V

FLUIDS:

NS infuse at 250 mL/hour for 4 hours then 150 mL/hour

Signature Fleischman 13333

04/07/08

Oregon Health & Science University
Hospitals and Clinics

PO1500

PHYSICIANS' ORDERS

Account.No :
Med.Rec.No : 98765
Name : Nguyen, Elisabeth
Birth Date : 10/08/85

Chemotherapy Treatment schedule

1. **Doxorubicin** 50 mg/m^2 x 100 % = **79 mg** IV Push on day 4 (04/10/08)
2. **Vincristine** 2 mg IV Push on Day 4 (04/10/08) and day 11 (04/17/08)
3. **Dexamethasone** 40 mg PO Daily on day 1 (04/07/08) through Day 4 (04/10/08) and day 11 (04/17/08) through day 14 (04/20/08). **On day 1 (04/07/08) through day 4 (04/10/08), give each day's dose 60 minutes before first chemotherapy dose with ondansetron.**
4. **Cyclophosphamide** 300mg/m^2 x 100 % = **471 mg** in 250 mL NS IV over 2 hours every 12 hours for 6 doses. Begin Day 1 (04/07/08). Dose is based on actual body weight. Mesna & Cyclophosphamide can infuse through same side of catheter.
5. **Mesna** 600 mg/m^2 x 100 % = **942 mg** in 1000 mL NS IV as a continuous infusion at 44 mL/hr for 3 days. Begin with first Cyclophosphamide dose on day 1 (04/07/08)
6. **Filgrastim** 5mcg/kg = **300 mcg** sub cutaneous over 30mins daily beginning on day 5 (04/11/08) until ANC > 1500 for 2 consecutive days (**Pegfilgrastim** 6mg SQ if outpatient)
7. no intrathecal chemotherapy this cycle

Signature: Fleischman 13333

Oregon Health & Science University
Hospitals and Clinics

PO1500

PHYSICIANS' ORDERS

Account.No :
Med.Rec.No :98765
Name :Nguyen, Elisabeth
Birth Date :10/08/85

Comments:

Signature: ______________________________

AML case 2
(37 b)

Mrs Cynthia Patersonis a 35 year old female patient, who has just been diagnosed with AML. She has no comorbidities.

Her renal and liver function are normal.

She measures 165 cm and weighs 75 kg.

Medical Record # : 77777
DOB : 03/28/72

Oregon Health & Science University
Hospitals and Clinics

PO1500

PHYSICIANS' ORDERS

Page 1 of 1

Patient Name
MR#

ACCOUNT NO
MED REC NO 77777
NAME Patersonis, Cynthia
BIRTHDATE 03/28/1972

Patient Identification

PATIENT DRUG ALLERGIES:

Pt. Weight: Kg

Attending has changed to: Pager #:

DATE MO	Day	Year	Hour	All verbal or telephone orders require a "READ BACK" to prescribing practitioner to verify accuracy.
4/7/08 1700				

CHEMOTHERAPY ORDERS
Idarubicin & Cytarabine for AML Induction

1. **Day 1 of chemotherapy for AML is** (4/07/08)
2. **Allergies:** NKDA
3. **Attending physician:** Deininger
4. Allopurinol 600 mg PO Now and 300 mg PO Daily x 4 days.

IVF during chemotherapy:
D5. 45 NS at 150 mL/hr, send on arrival. Chemotherapy may start as soon as patient ready on (4/7/08).

Antiemetics

Chemotherapy Premedication:
1) Ondansetron 24 mg PO, dexamethasone 8 mg PO, and Lorazepam 1 mg PO 60 minutes prior to Idarubicin dose on Day 1 (4/7/08) Day 2 (4/8/08), and Day 3 (4/9/08).
2) Haloperidol 0.5-2 mg IV every 4 hrs PRN N/V.
3) Lorazepam 0.5-1 mg IV/PO q 4 hrs PRN N/V/restlessness
4) Prochlorperazine 5-10 mg IV/PO every 4 hrs PRN N/V.

Chemotherapy Treatment schedule

Ht 165cm ~~inches~~ BSA 1.82 m^2

Wt 75 kg ~~lbs~~

1. **Cytarabine** 100 mg/m^2/day= 182 mg in 500 mL NS IV continuous infusion at 23 mL/hr daily for 7 days (Days 1-7) (4/7/08) through (4/13/08).

2. **Idarubicin** 12mg/m^2/day= 21.84 mg in 100 mL NS IV over 30 minutes through a central catheter on Day 1(4/7/08), Day 2 (4/8/08), and Day 3 (4/9/08).

Fleischman 13333

Signature

ALL case 1
(H-a)

Mr. David Schmidt is a 45 year old male patient, who has a history of pre-B ALL diagnosed 4 months ago. He has high-risk disease for CNS involvement. He is admitted for consolidation with cycle 3A of hyper-CVAD.

He has normal renal and hepatic functions.

He measures 170 cm and weighs 81 kg.

Med Rec # : 12345
DOB : 12/12/62

Oregon Health & Science University
Hospitals and Clinics

PO1500

PHYSICIANS' ORDERS

Page 1 of 1

Name
MR#

ACCOUNT NO
MED REC NO ~~50~~
NAME Schmidt, David
12345
BIRTHDATE 12/12/1962

Patient Identification

PATIENT DRUG ALLERGIES:

Pt. Weight: Kg

Attending has changed to: Pager #:

DATE				All verbal or telephone orders require a "READ BACK" to prescribing practitioner to verify accuracy.
MO	Day	Year	Hour	
4/7/08				
1700				

Chemotherapy Orders

~~**Hyper CVAD Cycle A (JCO 2000;18(3):547-61)**~~

1. Bone Marrow Transplant Team
2. Day 1 of chemotherapy is (4/7/08).
3. Dx: Acute Lymphoblastic Leukemia
4. Staff: Deininger
5. Allergies:
NKDA

Meds:

1) Bactrim DS- one tab PO BID Q Mon & Thurs.
2) Allopurinol 600 mg PO now, then 300 mg PO daily X 6 days total.

Antiemetics

Antiemetics:

1) Ondansetron 24 mg PO 60 minutes before first chemotherapy dose each day with Lorazepam 1 mg PO X 4 days. Give with each day's dexamethasone dose.

PRN Antiemetics

1. Lorazepam 0.5-1 mg IV/PO q 4hrs PRN N/V.
2. Diphenhydramine 25 mg IV/PO q 4 hrs PRN EPS symptoms or N/V.
3. Droperidol 0.625 mg IV q 2 hrs PRN N/V.
4. Prochlorperazine 5-10 mg PO/IV every 4 hrs PRN nausea.
5. Haloperidol 0.5-2 mg IV/PO Q 4 hrs PRN N/V

IV FLUIDS:

D5W NS infuse at 250 mL/hr for 4 hours then 150 mL/hr.

Chemotherapy Treatment schedule

Ht 170 cm ~~inches~~ BSA 1.9 m^2

Wt 81kg ~~lbs~~

1. **Doxorubicin** 50 mg/m^2 = 95 mg IV Push on day 4 (4/10/08).

2. **Vincristine** 2 mg IV Push on Day 4 (4/10/08) and 11 (4/17/08)

13333

Signature [signature] - Fleischman

Oregon Health & Science University
Hospitals and Clinics

PO1500

PHYSICIANS' ORDERS

Name
MR#

ACCOUNT NO
MED REC NO
NAME
BIRTHDATE

Schmidt, David
12345
12/12/1962

Patient Identification

PATIENT DRUG ALLERGIES:

Pt. Weight: Kg

Attending has changed to: Pager #:

DATE				All verbal or telephone orders require a "READ BACK" to prescribing practitioner to verify accuracy.
MO	Day	Year	Hour	
4/7/08 1700		3.		~~Dexamethasone~~ 40 mg PO Daily on days 1-4 (4/7/08—4/10/08) and days 11-14 (4/17/08-4/20/08). On days 1-4 give each day's dose 60 minutes before first chemotherapy dose with ondansetron.
		4.		~~Cyclophosphamide~~ 300mg/m² = 570 mg in 250 mL NS IV over 2 hrs every 12 hours for 6 doses. Begin Day 1 (4/7/08). Dose is based on actual body weight. Mesna & Cyclophosphamide can infuse through same side of catheter.
		5.		**Mesna** 600 mg/m² = 1140 mg in 1000 mL NS IV as a continuous infusion at 44 mL/hr for 3 days. Begin with first Cyclophosphamide dose on (4/7/08).

Signature Fleischman 13333

Appendix – H

Results in Raw Format

Subject #	EZChemo-Retrieval	EZChemo-Prepare	EZChemo-Total	Paper-Retrieval	Paper-Prepare	Paper-Total
1	55	290	345	60	560	620
2	50	225	275	42	595	637
3	78	346	424	55	380	435
4	118	313	431	301	419	720
5	154	210	364	262	262	524
6	169	327	496	342	384	726
7	124	305	429	153	285	438
8	136	321	457	288	521	809
9	119	345	464	265	566	831
10	91	368	459	325	365	690
11	108	243	351	261	397	658
12	106	254	360	199	239	438
13	53	310	363	62	573	635
14	70	275	345	85	467	552
15	133	356	489	210	623	833
16	75	295	370	780	620	1400
17	218	429	647	107	594	701
18	152	316	468	196	671	867
19	117	226	343	316	466	782
20	179	484	663	233	574	807

Table B : Time in seconds each subject took to retrieve, prepare and hence complete a Chemo order using EZChemo and paper-based system

Appendix – I

SQL Statements for implementing EZChemo Database Schema

```
CREATE TABLE allergy (
 allergyid varchar(50) NOT NULL,
 name varchar(50),
 PRIMARY KEY  (allergyid)
);
CREATE TABLE drug (
 drugid integer NOT NULL,
 unit varchar(10),
 name varchar(50),
 PRIMARY KEY  (drugid)
);
CREATE TABLE staff (
 staffid varchar(50) NOT NULL,
 name varchar(50),
 PRIMARY KEY  (staffid)
);
CREATE TABLE patient (
 medrecno varchar(50) NOT NULL,
 accountno varchar(50) default NULL,
```

```
  name varchar(50),
  dob datetime,
  height integer,
  PRIMARY KEY (medrecno)
);
CREATE TABLE patient_allergy (
  medrecno varchar(50) NOT NULL,
  allergyid varchar(50) NOT NULL,
  PRIMARY KEY  (medrecno, allergyid),
  FOREIGN KEY(allergyid) REFERENCES allergy(allergyid),
  FOREIGN KEY (medrecno) REFERENCES patient(medrecno)
);
CREATE TABLE chemoorder (
  orderid varchar(50),
  name varchar(50),
  drugid integer,
  PRIMARY KEY  (orderid),
  FOREIGN KEY(drugid) REFERENCES drug(drugid)
);
CREATE TABLE prescription (
  medrecno varchar(50) NOT NULL,
  prescriptionorderno varchar(50) NOT NULL,
  day1ofchemo datetime,
  weight float,
```

```
  cnsprophylaxis varchar(50),
  cycleno int(11),
  staffid varchar(50),
  comments varchar(50),
  PRIMARY KEY  (medrecno,prescriptionorderno),
  FOREIGN KEY (medrecno) REFERENCES patient(medrecno),
  FOREIGN KEY(staffid) REFERENCES staff(staffid)
);
CREATE TABLE prescription_chemoorder (
  prescriptionorderno varchar(50) NOT NULL,
  orderid varchar(50),
  dose int(11),
  PRIMARY KEY  (prescriptionorderno),
  FOREIGN KEY (orderid) REFERENCES chemoorder(orderid),
  FOREIGN KEY (prescriptionorderno) REFERENCES
prescription(prescriptionorderno)
);
```