

MEASURING THE HEALTH OF MEDICATION PROCESS
USING AN EHR DATA REPOSITORY

By

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Dissertation

Submitted to the Faculty of the
Graduate School of Vanderbilt University
in partial fulfillment of the requirements

for the degree of

DOCTOR OF PHILOSOPHY

in

Biomedical Informatics

August, 2015

Nashville, Tennessee

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ACKNOWLEDGEMENTS

First, I would like to thank Dr. Christoph Lehmann. I appreciate his patience with my questions and his effort to help me improve my writing styles. He advised me on the appropriate actions to achieve desired goals. He was always available to review and discuss the outcome of my analyses and research.

I would also like to thank my committee members for their time and advice towards shaping the outcome of my research. Their input helped whetting the initial hypothesis and specific goals of this dissertation research. Their encouragement and continued support was valuable in achieving the desired goals of this research.

I would like to extend my thanks to the department secretaries, Rischelle Jenkins in the department of Biomedical Informatics, and Angela Peek, Lynn Booker, Marten Roos, and Mette Smith in the department of Pediatrics, for all their help in arranging the meeting rooms and time with faculty members.

I want to extend my gratitude towards Amy Frye-Anderson, Johniene Doran, and Matt Marshall who provided valuable input on the enterprise data warehouse (EDW) data objects. Their guidance was helpful in wading through the complex web of unknown data in the EDW.

Going would have been too tedious without some individuals. However, I had a wonderful company of my fellow students Josh Smith, Jacob VanHouten, and Ravi Atreya, who helped create lighter side whenever the going got tough.

Throughout the ambitious and demanding times of my graduate school, my wife Parneeta and daughter Karishma have always been on my side. I attribute my success to their support, encouragement, and their patience with me.

This dissertation research was made possible through the National Library of Medicine Training Grant T15LM 007450.

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LIST OF ABBREVIATIONS

Abbreviation	Definition
ARRA	American Recovery and Reinvestment Act
BIDEV	Development instance of Enterprise Data Warehouse
BIPROD	Production instance of Enterprise Data Warehouse
CDR	Clinical Data Repository
CDS.....	Clinical Decision Support
CPOE	Computerized Provider Order Entry
DB	Database
DBMI	Department of Biomedical Informatics
EDW	Enterprise Data Warehouse
EHR.....	Electronic Health Records
eMAR.....	electronic Medication Administration Records
EoL.....	End of Life
GB	gigabyte
HED	Horizon Expert Documentation
HITECH.....	Health Information Technology for Economic and Clinical Health
IRB	Institutional Review Board
IT.....	Information Technology
MeSH	Medical Subject Headings
MU	Meaningful Use
NICU.....	Neonatal Intensive Care Unit (or Neonatal ICU)
QI	Quality Improvement
SHRINE	Shared Health Research Information Network
TB	terabyte
VCH	Vanderbilt Children's Hospital or Vanderbilt's Monroe Carrel Jr. Children's Hospital
VTE.....	Venous Thromboembolism
VUMC.....	Vanderbilt University Medical Center
WHO.....	World Health Organization

Organization of the Dissertation Document

This document, *the Dissertation work by Haresh Bhatia towards his Doctor of Philosophy (PhD) degree in Biomedical Informatics*, is organized around the research papers already published, submitted for publication, or intended to subsequently submit for publication.

Chapter 1 provides the introduction and background of the dissertation project. It describes the context and importance of the research, the (re)use of EHR data and related history, hypothesis and specific aims of the project, IRB approvals obtained, challenges faced, and the resulting documentation.

Chapter 2 is adapted from the manuscript titled “**Pediatric Inpatient Medication Compliance – What are we Missing?**”, and is ready for submission to a reputed peer-reviewed journal. The manuscript is a culmination of the Aim1 described under the “Hypothesis and Specific Aims” in Chapter 1. It describes the importance of the medication compliance and focusses on the ordered medication doses that were deemed not administered either because the corresponding documentation indicates so or no such documentation exists. The missed or non-administered doses are analyzed by medication class and the documented non-administered doses are analyzed by the documented reasons. The chapter concludes with inferences and corresponding discussion about the reasons for missed or non-administered doses.

Chapter 3 is adapted from the manuscript titled “**Medication Process Compliance in Pediatric Inpatients – Time to the First Dose**”. This chapter is culmination of the Aims 2 and 3 described under “Hypothesis and Specific Aims” in Chapter 1. It captures the three time points in the medication process – Order-time, Schedule-time, and Administration-time – and maps the interval between these times to the corresponding pharmacy and nursing functions. Analysis of

the variations of these times across various dimensions – e.g., patient demographics, NICU or other units, medication class, and scheduled-hour of medication – informs about the medication process efficiency and bottlenecks thereof. The chapter concludes with the discussion about inferences drawn from the distribution and variance of respective time-intervals across the studied dimensions, and related scope of improvements.

Chapter 4 is adapted from the manuscript titled “**Detecting Quality Improvement Signals in an Enterprise Data Warehouse**”. While analyzing the medication process time-intervals (detailed in chapter 3), unexpected deviations in the efficiency of pharmacy delivery times were noticed for some medication types. Further analysis clarified that the deviations were not a measurement error but the result of a quality improvement (QI) effort launched around the same timeframe when this dissertation project was initiated. This analysis corroborated the improvements resulting from the QI effort. The chapter concludes with a discussion about the use of Information Technology (IT) methods to successfully assess the status of healthcare processes, given a reliable data source.

Chapter 5 summarizes the doctoral research project components, discussing its significance, the overall findings of the medication process analyses, and importance of establishing a base-line compliance levels for a healthcare facility.

During the course of this dissertation research I encountered some challenges with the EHR data repository and the data contained therein. Appendix – A briefly describes those challenges.

While waiting for the resolution of those challenges I conducted a study on the Code Status documentation. In an era of widespread use of EHR systems most healthcare facilities and hospitals still document the admitted patients’ end-of-life (EoL) care options – termed as Code

Status – on a paper based system, which is not conducive to patient hand-offs and transition of care. Appendix – B is adapted from the published manuscript of Code Status data analysis titled **“Code Status and Resuscitation options in the electronic health record”**, which describes the context of EoL decisions by patients, importance of electronic documentation thereof, and the ease of accessing it in an event of the patient having cardio-pulmonary arrest. The manuscript subsequently provides the descriptive statistics and association of patient demographics with the corresponding Code Status documentation. Appendix – B is relatively independent of the **“Medication Compliance Study”** and documents a manuscript that is already published.

After the data issues and challenges were resolved, I documented some suggestions to improve the DB design and expedite the usage of the data repository in a whitepaper titled **“Recommendations for Database Design and Documentation Procedures”**, which is listed in Appendix – C.

Appendix – D lists the supplementary figures that are referenced by the manuscripts in Chapter 3 (titled **“Medication Process Compliance in Pediatric Inpatients – Time to the First Dose”**) and Chapter 4 (titled **“Detecting Quality Improvement Signals in an Enterprise Data Warehouse”**).

CHAPTER 1

Introduction

Research Statement

Response to a disease process and the related outcome in a patient are dependent on the appropriate medical care and adhering to the treatment plan including the medication regimen prescribed by the healthcare provider. Medication compliance is critical for both acute and chronic conditions.

The terms *adherence* and *compliance* have context based implications. PubMed considers *adherence* to be synonymous with *compliance*¹, which is defined as the degree of conformity to the treatment recommendations by healthcare providers. However, *compliance* may also refer to the degree to which healthcare providers follow the stipulated guidelines, rules, or policies and procedures – as implied by the World Health Organization’s (WHO) High5 report², and the newsletter from the Institute for Safe Medication Practices (ISMP)³.

For the purpose of this dissertation, the term ‘*Adherence*’ is defined to imply a patient following the provider’s advice and signifies the patient’s active role in achieving a common goal of disease treatment⁴, for example, by taking the prescribed medications. Also for the purpose of this dissertation, the term ‘*Compliance*’ is defined to indicate a passive role by the patient and an active role of the healthcare staff (e.g., nurses and pharmacists), for example, by following the instructions stipulated in a medication order issued by the provider and abiding by the institutional rules, policies, and procedures. Both these definitions are with reference to medication treatment as used in this dissertation research. Following these definitions, *Adherence* would be critical in outpatient settings as patient is responsible for following the

medication regimen, while *compliance* would be important in inpatient settings wherein the healthcare staff is responsible for medication administration.

Adherence is affected by patient factors⁴ such as socio-economic status and affordability of medication, ability to refill the prescription, ability to comprehend complex medication regimens, recollection to take medications, or proper storage of medication, etc.⁵ Compliance in the inpatient settings is influenced by the healthcare setup, policies, and staff^{2,3}. Due to the structured and supervised patient care environments of a hospital medication compliance rates in inpatient settings are expected to be significantly higher than adherence rates observed in outpatient settings⁶. In surgical environments compliance has been shown to be higher than in internal medicine settings⁷. Non-compliance, attributable to healthcare staff, indicates deviance from the regimen including delayed or missed medications⁶.

My PubMed queries revealed several studies that investigate compliance subsequent to implementation of a new system^{8,9} or for a specific medication regimen¹⁰. However, none of the queries returned any study that performed a systematic and extensive institution-wide investigation for medication compliance. I surmise that a top-down approach with a broader scope may uncover previously unknown or unsuspected lacunae in the medication use processes that may otherwise be missed by individual ad-hoc studies with narrower focus.

This dissertation research is aimed at evaluating the *status* of the medication process and to study the medication compliance at Monroe Carell Jr. Children's Hospital at Vanderbilt (VCH) – a major tertiary pediatric hospital and part of Vanderbilt University Medical Center (VUMC). This research considers medication administration and related timings with respect to the corresponding medication orders placed for pediatric inpatients admitted to VCH. Akin to

assessing the human body's condition, and thus extending the terminology, the title of this dissertation uses the phrase "Measuring the *'health'* of the medication process". To briefly extend on this analogy: The human body uses interdependent processes to regulate complex functions like a steady body temperature. Medicine measures axillary or rectal temperature to determine the *'health'* of these processes or to detect any abnormality. The approach of using administration success and timing similarly uses proxy measures to determine the proper functioning of the complex underlying system of ordering, dispensing, delivering, and administering medications and to detect flaws in the process. Using that terminology seems appropriate because this research innovatively explores the functioning of the medication process with respect to its timing, efficiency, and malfunctions. The outcome of this research may prompt further exploration for the probable causes and factors associated with any observable aberrance with process improvements as the ultimate goal.

Research Context

According to a report published by the World Health Organization (WHO)⁴, on average only half of the patients in developed countries adhere to their medication regimen. As succinctly stated by former US Surgeon General Dr. C. Everett Koop, it would be logical to conclude that "Drugs don't work in patients who don't take them"¹¹. Literature reviews suggest that a significant adherence gap is still prevalent^{12,13}. While promising interventions may show improvements in adherence rates, the clinical outcomes were inconsistent at best^{12,14}. Other studies have also indicated association among adherence rates and race^{15,16} and health-literacy¹⁷.

Multiple documented factors influence medication adherence in outpatient environments, including medication cost and patient's economic status¹⁸. However, less is known about factors influencing medication compliance in supervised inpatient settings, where the medication

process is driven by a different set of actors including the ordering providers, hospital pharmacists, and nursing staff^{2,3}. Although medication compliance rates in an inpatient setting may be expected to be much higher, studies demonstrate the existence of compliance gaps in inpatient settings as well. A study by Shermock et al. indicated significant compliance gaps of up to 27% for the ordered doses of venous thromboembolism (VTE) prophylaxis in inpatient environments⁷. The study also suggests that understanding the patterns of variation in compliance would be useful in devising effective and efficient interventions.

The factors influencing medication compliance in the inpatient environments involve the hospital's financial and staffing states, complexity of patients' care, as well as policies and procedures^{2,3}. Much of the inpatient medication compliance literature focusses on a limited set of patients, for specific medications¹⁹ or disease conditions²⁰, and concentrates on patient factors. The study by Fanikos et al. indicated '*patient refusal*' as the most frequent cause of missing the thromboembolism prophylactic dose and recommended patient education to improve compliance¹⁹. The Shermock study was conducted at a different institution and confirmed a similar pattern of missing the ordered thromboembolism prophylactic doses albeit for a larger patient population⁷. A qualitative study by Elder et al., however, revealed a previously unrecognized *nursing perception of assessing individual patient risks and benefits* of the pharmacologic prophylaxis medication to the patients⁶. The Elder et al. study therefore indicates that the compliance by the nursing staff also plays an important role in the medication process that culminates in administration of the ordered doses.

Regardless of the contributing factor, missing an ordered dose of medication ultimately has the potential to harm the patient. Pediatric inpatients, in particular, often rely on the nursing staff (or their parents) to have the ordered medication administered^{21,22} and thus have lesser control over

this process. It is therefore important to explore the current state of medication compliance with the pediatric inpatient environment.

Opportunity

Though there have been numerous studies on medication adherence in outpatient environments, there are limited studies on medication compliance for inpatients. A PubMed search for (("medication adherence"[MeSH Major Topic]) AND "inpatients"[MeSH Terms]) returned 17 articles, a majority of which were for outpatients. The literature search thus revealed only a handful of studies conducted on medication compliance in inpatient settings, and each of those focused on specific medication or disease condition. Additionally, none of those studies investigated medication process for *pediatric inpatients* with respect to compliance.

In a majority of pediatric cases the potential communication barriers with their caregivers are of particular concern since children depend on others for appropriate medication administration²³. Parents in most cases act as proxy for the pediatric patient and may often defer the decision about the treatment or medication administration to the nursing staff at the hospital.

The qualitative study by Elder⁶ opened a new dimension to the medication compliance by suggesting that nursing bias may play a role in medication administration for inpatients. The Elder study was subsequent to the Shermock study⁷ at the same institution, which in turn was prompted by the Faniko's study¹⁹ on a similar medication treatment at another institution. Given the fact that the medication compliance gap is observed for a specific treatment, there may be similar inconsistencies and lacunae in other treatments or the overall medication process itself.

In summary, the observations with respect to measuring the medication compliance gap are – 1) there are very limited studies conducted for inpatients and very few of those focus on pediatrics,

2) most of the documented inpatient studies focus on the from patients' perspective rather than from the perspective of the healthcare staff, and 3) if there are measurable compliance gaps in the medication administration process for a specific treatment, similar discrepancies may exist in the overall medication process.

Therefore, I decided to study the medication processes using electronic health records (EHR) and assess the medication compliance gaps retrospectively. Most of the retrospective studies use the data collected by the EHR system components such as computerized provider order entry systems (CPOE) and electronic medication administration record (eMAR) systems. By capturing routine healthcare input, the EHR systems collect valuable patient, provider, and treatment information, and therefore can act as great data sources for these research studies²⁴.

Since the early developments of EHRs in the 1960s²⁵ research groups have been investigating methods for storage and use of patient treatment data²⁶. Even in its simplest form, the documentation in computerized EHRs is transmittable, persistent, and legible. EHR systems functionality can be further extended by adopting modularization and following Dr. Octo Barnett's 10 commandments²⁷. Specialized components of an EHR cater to specific needs of the provider workflow and patient care. CPOE is one of the most studied EHR components. A meta-analysis of multiple studies for CPOE systems indicated their effectiveness in improving patient treatment²⁸ by reducing medication errors and preventable adverse drug events. Integrating clinical decision support (CDS) to the EHRs further improves patient care and outcomes, allows better disease status monitoring, and keeps healthcare providers informed^{29,30}.

This dissertation research, titled "Measuring the Health of Medication Process Using an EHR Data Repository" (Medication Compliance study) was proposed to examine the medication

process and to establish medication compliance rates for the pediatric patients admitted to VCH. This research study is not limited to a specific subset of pediatric patients, medications, or disease conditions. The time-period of the medication order data was limited to orders initiated between July 1, 2010 and December 31, 2013.

This Study used the Enterprise Data Warehouse (EDW) as a source for the medication process data. The EDW at VUMC facilitates financial, billing, and administrative functions. The EDW receives daily data feeds from Vanderbilt's CPOE (Horizon Expert Order), eMAR, and other operational systems. Given the rich healthcare data residing in the EDW, it is often used as a source for healthcare research efforts. EDW is a relational database management system using Oracle 11g as its engine, has over 12 terabytes (TB) of allocated space, and resides behind a firewall. [More details relevant to EDW instances are covered in Appendix – A.]

Hypothesis and Specific Aims

Considering that the earlier studies on medication adherence and compliance suggested significant gaps in outpatient and inpatient environments, and that none of those involved pediatric inpatients, one may not assume the medication compliance in pediatric inpatients to be perfect. I hypothesized that there are measurable gaps in the medication compliance for pediatric inpatients.

To study medication compliance, this research addressed the following specific aims.

Aim 1: To measure the proportion of medication orders for which the corresponding administration record either indicated dose not-administered or was missing.

Aim 2: To measure the time intervals from ordering to dispensing, scheduling, and administration of medications.

Aim 3: To analyze the time intervals from aim-2 and interpret the underlying causes of deviations.

IRB Approvals

The Vanderbilt Institutional Review Board (IRB) Committee for human research protection program issued its approval for the Medication Compliance Study on April 1, 2013 (approval #130400), which was valid for one year. The approval has since been renewed annually (renewals approved on February 26, 2014 and January 16, 2015).

IRB approval #130400..... April 1, 2013

IRB Renewal February 26, 2014

IRB Renewal..... January 16, 2015

Methodology Overview

The “Medication Compliance Study” extracted the medication ordering, dispensing, and administration data from Vanderbilt’s EDW. A set of patient demographics for the pediatric inpatients was isolated using the encounters and patient datasets. Based on this dataset of pediatric patients corresponding medication orders dated between July 1, 2010 and December 31, 2013 were isolated. The starting date of July 1, 2010 was selected to ensure that most of the pediatric units, including neonatal ICUs (NICUs), had an operational eMAR system. Pediatric emergency department (ED) did not have the eMAR implemented by that starting date; the medication orders issued for patients in that unit were therefore excluded from the study. Though the dissertation proposal was finalized and pilot study was done in 2013, the full-blown study started in early 2014. The end-date of December 31, 2013 was thus assigned to the medication orders’ date range.

The schematic in Figure 1-1 describes the data selection and filtration process. For the order records thus collected, the data selection process gathered the matching pharmacy dispense data and corresponding administration data for the ordered medications. The final set was further filtered to exclude “as needed” (PRN) and total parenteral nutrition (TPN) orders, because the former are not scheduled medications and the latter are documented as fluids rather than medications by the nurses.

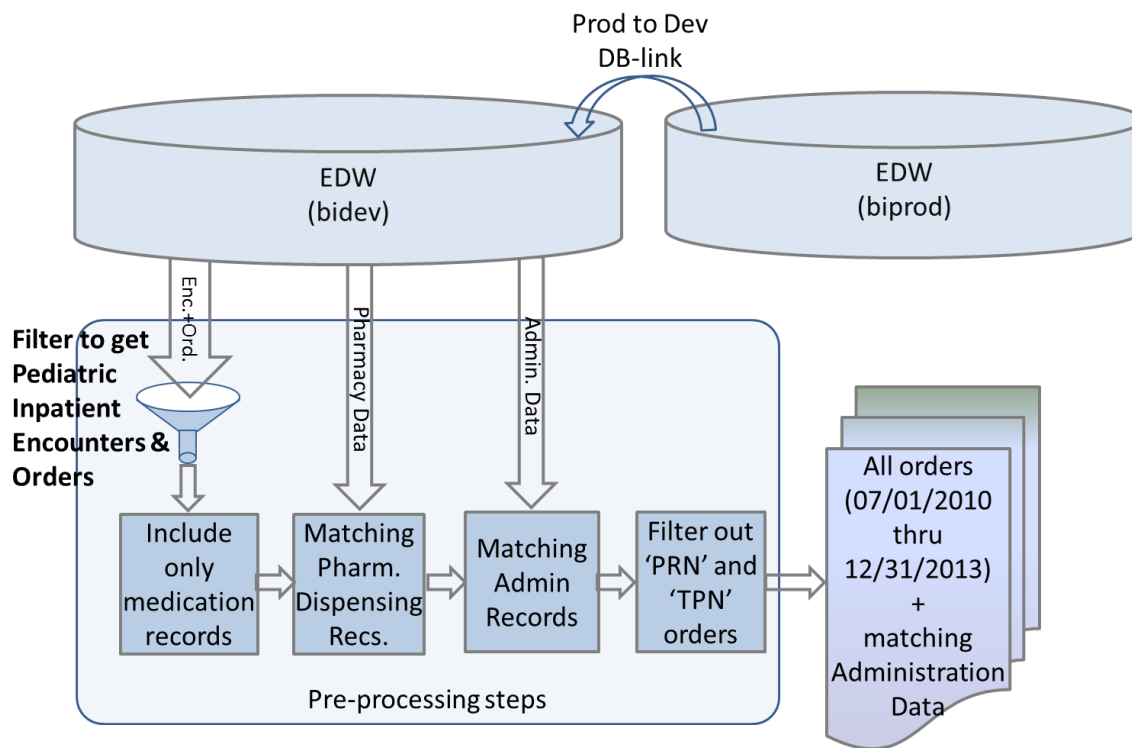


Figure 1-1: Schematic showing the data extraction from the EDW objects for ordering, dispensing, and administration data, and related data filtration.

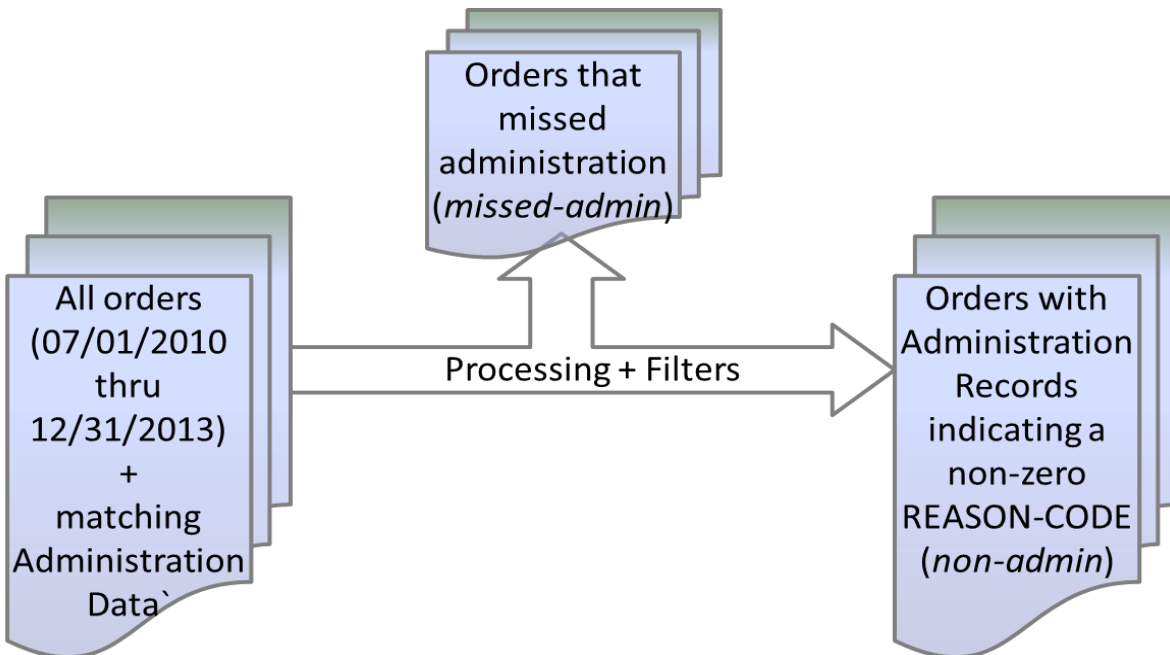


Figure 1-2: Schematic showing the processing and segregating the *missed-admin* and *non-admin* data sets.

This set of ordering, dispensing, and administration data was processed and filtered to generate two separate sets of orders, one that did not have any matching administration records (termed as *missed-admin* order subset) and the other set of orders where the matching administration records had a REASON-CODE indicating that the ordered medication was not administered (termed as *non-admin* order subset). Schematic in Figure 1-2 describes this step to analyze data for Aim 1 (described under “Hypothesis and Specific Aims” section).

The remaining set of orders with corresponding valid administration data was further processed to collect the values for the order-time, scheduled-time, and administration-time for the respective first doses. This data was analyzed in aims 2 and 3 (described under “Hypothesis and Specific Aims” section). There were over 11,000 administration records with default schedule-time (of 01/01/1800); those records were filtered out. Including those records for the analysis of the medication process time-intervals would have skewed the results.

Results and papers

The detailed effort, results, and analysis of those results are described in the following three chapters (2, 3, and 4). These chapters are adapted from the manuscripts that are intended to be published in reputed peer-reviewed journals.

Challenges

The medication process data (including medication orders, pharmacy dispensing, and medication administration records), patient demographics, and patient units at VUMC reside in the EDW. Gaining access to the relevant database (DB) objects in the EDW is not sufficient, however. I met several challenges before obtaining the requisite data and related resources for this study.

Appendix–A describes those challenges.

CHAPTER 2

Pediatric Inpatient Medication Compliance – What are we missing?

Introduction

Healthcare providers prescribe medications with the goal of treating disease or maintaining the health of their patients. Health or disease is influenced by the patient's adherence to the medication regimen prescribed by the provider. The term 'Adherence', frequently used in outpatient settings, indicates a patient following providers' advice (on medication or health-behavior) and signifies the patient's active role in achieving a common goal of disease treatment. 'Compliance', often used in inpatient settings, indicates a passive role by patient and an active role of the medical staff (e.g., nurses and pharmacists). Non-compliance indicates deviance from the regimen including delayed, inappropriate, or missed medication administration. Ho et al.¹¹ explored various associations between medication non-adherence and disease outcome quoting former Surgeon General Dr. C. Everett Koop with "Drugs do not work in patients who don't take them".

Medication compliance is critical for both acute and chronic conditions. According to a report published by World Health Organization⁴, only half of the patients in the developed countries adhere to their medication regimen. Outpatient studies for disease outcomes in domains like cardiovascular¹¹, pediatrics³¹, and psychiatry³² have attempted to establish the reasons for non-compliance. In pediatric outpatient settings, adherence has been described as low: Talley³³ showed that only 56% of pediatric patients filled prescriptions after a psychiatric stay and of those only 76% reported to be compliant.

Background and Significance

This study determines the state of medication compliance focusing on missed doses for the pediatric inpatient population of a major tertiary pediatric hospital.

Medication compliance rates in an inpatient setting are expected to be much higher than adherence rates observed in an outpatient setting due to the structured and supervised patient care environments of a hospital. However, Janssen et al. showed for a cohort of psychotic disorder patients³⁴ that the average medication compliance was below 50%. This study also demonstrated that patient compliance is influenced by factors like education level, profession, admission status, etc., in addition to other comorbid conditions. Other recent studies also indicated significant compliance gaps in the inpatient medication process^{35,36}. Experiences in adult patients have shown that compliance with inpatient Venous Thromboembolism prophylaxis orders can vary significantly between nursing units. For subcutaneous Heparin orders, Elder et al. found a compliance rate of only 80% in certain nursing units at a major academic medical center⁶.

In pediatric inpatient settings, medication is generally administered by nursing staff and occasionally by parents. Compliance for pediatric inpatient settings is therefore more dependent on the integrity of the medication dispensing and administration process³⁷. Medication management for pediatric patients is more complex and poses higher safety risks due to the developmental gradient of children and their inability to buffer errors due to limited internal reserves^{21,22}. It is therefore important that every medication ordered for a pediatric patient is delivered and administered as intended by the provider. Further, it is in the interest of a healthcare institution to periodically assess the robustness of medication compliance to ensure quality of the care. A PubMed search for (“Inpatient” [Mesh]) and (“Medication Compliance” [Major]) did not discover any studies conducted on medication compliance for a pediatric

inpatient cohort. There has been some limited work done in examining the medication process in general, after relocation of a children's hospital at an academic medical center³⁷. Thus, we decided to perform the first study of medication compliance for pediatric inpatients. This paper focuses on the medication orders that were not administered to pediatric patients at a major tertiary pediatric hospital.

Methods

The Enterprise Data Warehouse (EDW) at the Vanderbilt University Medical Center (VUMC) receives daily feeds from Vanderbilt's operational systems, such as Vanderbilt's order entry system (Horizon Order Entry and WizOrder) and the electronic Medication Administration Record (eMAR) System. The data in the EDW is maintained for longer periods to facilitate data analytics and research. We queried datasets that contain data on medication orders, dispensing, administration, patient encounters, and demographics.

We isolated the pediatric patients based on their inpatient encounters (including admissions and observational stays) and extracted their demographic information. For this pediatric patient dataset, we collected all orders from July 01, 2010 through December 31, 2013 (42 months). To identify the medication orders, we included only orders serviced by pharmacy, and applied filters to exclude orders for pharmacy consultations. We also excluded orders where the administration was not mandatory (e.g., PRN orders) or was not routinely recorded in the medication administration record (e.g., TPN orders were recorded by nurses as fluids and not medications). For the medication orders collected, we isolated the corresponding pharmacy dispense data, medication administration data, and the patients' unit location at the time of the order.

In the next step, we identified medication orders that did not have a corresponding matching administration record – we labeled this set of order records the “*missed-admin*” subset. Orders not explicitly for a medication (e.g., orders named ‘PHARMACY MESSAGE’) or for discontinuation of medications were also excluded. We further excluded the orders for patients who were not in a pediatric unit and the orders from the pediatric emergency department since it used a paper-based MAR process.

At VUMC, nurses may select a REASON (from a predefined list) to indicate why a medication was not administered or delayed. The presence of a (non-zero) REASON-CODE indicates a deviation from the order. Some non-zero REASON-CODEs indicate that medication was ‘not administered’ – others refer to deviation in timing or route. We labeled the set of orders with the corresponding administration records indicating ‘not administered’ REASON-CODEs as ‘*non-admin*’ subset.

We further analyzed the orders in the *missed-admin* or *non-admin* subsets with respect to the medication class. Because of the nature of the data stored, the medication details (name, dose, frequency) etc. are contained in a free-text attribute. We used MedEx³⁸ to extract the medication details from the text attribute and Anatomical Therapeutic Chemical (ATC) Classification³⁹ to classify the medications.

Vanderbilt EDW uses Oracle 11g database engine and is located behind a firewall. This data collection and analysis effort was part of a larger effort to study Medication Compliance for pediatric inpatients at VUMC. We obtained the Vanderbilt IRB approval for this Medication Compliance Study. We used statistical package R [64-bit version 2.15.2 (2012-10-26)] for statistical analyses and plots.

Results

We isolated the demographic data for 56,428 distinct pediatric patients (26,006 Females), who were inpatients or observation patients, with 110,435 encounters. Over half of the patients admitted (30,442 or ~54%) were less than 3 years old (of which 18,360 were neonates) with 51,443 (~47%) encounters. We recognized 1,570,994 medication order records corresponding to these patients. There were 3,742,013 matching administration records for these orders. Only 596 distinct medication order records did not have a valid matching administration record (the *missed-admin set*). **Table 1** summarizes these results.

Table 1: Overview of Pediatric Medication Administration Data

Parameter	Value
Period of Study [Order Entry Date]	July 1, 2010 – December 31, 2013
Distinct Pediatric Inpatients	56,428
Encounters	110,435
Distinct number of Medication Orders	1,570,994
Matching Administration Records	3,742,013
Missing administration records	596
Administration records with REASON-CODE indicating non-administration (Table 3)	69,614
Distinct medication orders corresponding to the administration with a REASON-CODE indicating non-administration (Table 3)	40,999

Medication class distribution

Of the 596 “*missed-admin*” orders, half (50%) were for the “Alimentary Tract and Metabolism Drugs” (e.g., antiemetic medications like Ondansetron, steroids like Prednisolone, etc.), 14.4% were for the “Nervous system Drugs” (e.g., pain medications like Morphine), and 10.9% were for the “Antiinfectives for Systemic Use” (Influenza Virus Vaccine, Ampicillin, etc.). **Table 2** shows the distribution of the “*missed-admin*” orders by (ATC) drug-class.

Table 2: Medication Class (ATC) Distribution for “*missed-admin*” Orders

Anatomical Therapeutic Chemical (ATC) Class	Count	Prop. %
ALIMENTARY TRACT AND METABOLISM DRUGS	298	50.0
NERVOUS SYSTEM DRUGS	86	14.4
ANTIINFECTIVES FOR SYSTEMIC USE	65	10.9
CARDIOVASCULAR SYSTEM DRUGS	52	8.7
DERMATOLOGICALS	45	7.6
BLOOD AND BLOOD FORMING ORGAN DRUGS	20	3.4
MUSCULO-SKELETAL SYSTEM DRUGS	12	2.0
RESPIRATORY SYSTEM DRUGS	8	1.3
VARIOUS DRUG CLASSES IN ATC	4	0.7
SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS	3	0.5
ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS	3	0.5

The distribution of administration records with non-zero REASON-CODEs is shown in **Table 3**. We grouped the non-zero REASON-CODEs into three categories: “Administered per Protocol”, “Permitted Deviations”, and “*Not Administered*”. “Administered per Protocol” indicates that the medication was given in a modified manner, for example, delayed when the patient was off the unit; and “Permitted Deviations” indicates that the medication was not administered for valid ‘circumstantial reasons’. The remaining REASON-CODEs were categorized as “*Not Administered*”. 101,688 administration records had REASON-CODEs indicating that the respective medications were *not administered*, which corresponded to 40,999 distinct medication orders (**Table 1**). A quarter (26.1%) of the administration records with non-zero REASON-CODEs corresponded to the “**Not Administered**” category. Of all the medication orders in the “Not Administered” category almost half of the administrations missed (20,455 out of 40,999 or 49.9%) were the first doses.

Table 3: The Medication Administration Records with a Non-Zero REASON-CODE (indicating Non-Administration or Deviation from the Stipulations of the Order)

Description	Category	Administration Count	Proportion (%)	Category Prop. (%)
Already given	Administered per Protocol	92,530	35.50	52.5
Given by Other		21,676	8.32	
Schedule Change		18,510	7.10	
See Procedure/Code rec		1,540	0.59	
See alt route		1,443	0.55	
See MAR		745	0.29	
Given Off Unit		226	0.09	
Med/Patch Removed		85	0.03	
Given by MD		25	0.01	
Med Discontinued		Permitted Deviations	18,429	
Per MD order	10,919		4.19	
NPO	10,782		4.14	
Per Parameter	3,631		1.39	
Sleeping	3,398		1.30	
No insulin required	2,288		0.88	
No IV access	2,176		0.83	
Nauseated/Vomiting	1,973		0.76	
Sedated	272		0.10	
Unable to swallow	216		0.08	
Not on Unit	121	0.05	26.7	
VPH Partial Patient	66	0.03		
Other- annotate	Not Administered	39,111		15.00
Patient / Family refused		29,587		11.35
Acknowledged		573		0.22
REASON NOT GIVEN		290	0.11	
Med not available		53	0.02	
All		260,665	100.0	

Table 4 shows the cross-tabulation of select REASON-CODEs (NPO, Sleeping, No-IV Access, and Sedated) by drug-class. For the overall count of doses with these four REASON-CODEs, almost half of them (46.1%) were for the “Alimentary Tract and Metabolism Drugs” (e.g., electrolytes like Potassium Chloride, pancreatic enzymes like Creon, laxatives like Docusate Sodium, H2-blockers like Famotidine), over 12% of them were for the “Nervous

System Drugs” (e.g., pain medications like Acetaminophen and Methadone), and almost 9% of them were “Genito-Urinary System and Sex Hormones” (e.g., vitamins like Poly-VI-Sol w/Fe, Cholecalciferol, and Ascorbic Acid).

Table 4: Medication Class (ATC) Distribution in Administrations with Select Reasons in “Permitted Deviations” Category

Anatomical Therapeutic Chemical (ATC) Class	Reason in Permitted Category				Sum of 4 Select Reasons	All Orders ^a	Prop. by ATC (%) ^b
	NPO	Sleeping	No-IV Access	Sedated			
ALIMENTARY TRACT AND METABOLISM DRUGS	3,490	900	479	38	4,907	213,903	2.3
NERVOUS SYSTEM DRUGS	667	405	116	128	1,316	189,643	0.7
GENITO URINARY SYSTEM AND SEX HORMONES	904	27	3	5	939	14,118	6.7
DERMATOLOGICALS	251	309	299	15	874	82,102	1.1
CARDIOVASCULAR SYSTEM DRUGS	619	103	58	36	816	84,475	1.0
ANTIINFECTIVES FOR SYSTEMIC USE	165	30	609	1	805	67,624	1.2
RESPIRATORY SYSTEM DRUGS	212	143	5	10	370	39,879	0.9
BLOOD AND BLOOD FORMING ORGAN DRUGS	119	46	117	4	286	46,922	0.6
MUSCULO-SKELETAL SYSTEM DRUGS	56	12	142	9	219	14,072	1.6
SENSORY ORGAN DRUGS	6	37	2	3	48	12,656	0.4
VARIOUS DRUG CLASSES IN ATC	44	0	2	0	46	1,203	3.8
ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS	9	0	2	1	12	9,824	0.1
SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS	6	0	2	0	8	2,109	0.4
ANTIPARASITIC PRODUCTS, INSECTICIDES AND REPELLENTS	1	0	0	0	1	320	0.3

^a This is count of all medication orders with the indicated Anatomical Therapeutic Chemical (ATC) Class (left-most column) of the ordered medication.

^b This indicates the proportion of orders of Select Reason with respect to all orders in respective ATC (for each row).

The χ^2 analysis indicated that the non-administration in these four Permitted Deviations was significantly associated with the ATC drug class ($P < 0.01$). Certain drugs that are considered more critical and time sensitive (such as antimicrobials, cardiac medication, anti-neoplastic

medications, or hormones accounted for a small proportion in these categories suggesting that nurses were less likely to override administration instructions for critical drugs using these specific reason codes.

Table 5: Medication Class (ATC) distribution for *non-admin* orders (corresponding to the administration REASON-CODEs indicating non-administration).

Anatomical Therapeutic Chemical (ATC) Class	Non-Admin orders	All Orders ^a	Prop. by ATC (%) ^b
ALIMENTARY TRACT AND METABOLISM DRUGS	13,665	172,888	7.9
NERVOUS SYSTEM DRUGS	6,900	173,344	4.0
CARDIOVASCULAR SYSTEM DRUGS	4,235	72,578	5.9
DERMATOLOGICALS	3,960	68,090	5.8
RESPIRATORY SYSTEM DRUGS	3,323	28,871	11.5
ANTIINFECTIVES FOR SYSTEMIC USE	3,245	55,500	5.9
BLOOD AND BLOOD FORMING ORGAN DRUGS	2,568	42,882	6.0
SENSORY ORGAN DRUGS	1,196	8,169	14.6
GENITO URINARY SYSTEM AND SEX HORMONES	1,022	9,900	10.3
MUSCULO-SKELETAL SYSTEM DRUGS	716	11,515	6.2
ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS	138	9,301	1.5
VARIOUS DRUG CLASSES IN ATC	126	984	12.8
SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS	123	1,893	6.5
ANTIPARASITIC PRODUCTS, INSECTICIDES AND REPELLENTS	11	289	3.8

^a This is count of all medication orders with the indicated Anatomical Therapeutic Chemical (ATC) Class (left-most column) of the ordered medication.

^b This indicates the proportion of orders of Select Reason with respect to all orders in respective ATC (for each row).

Of the 40,999 distinct *non-admin* order records, a third (33.1%) were for the “Alimentary Tract and Metabolism Drugs” (e.g., Docusate Sodium, Pancrelipase, etc.), a sixth (16.7%) of those orders were for pain management labeled “Nervous System Drugs” (e.g., Morphine, Fentanyl, etc.), and over a tenth (10.3) were for what ATC labeled as “Cardiovascular System Drugs” but also included medications to manage pain (e.g., Emla Cream, Ibuprofen, Lidocaine, etc.). **Table 5** shows the distribution of the *non-admin* medication orders by drug-class (ATC). The χ^2 test

between the non-admin orders and all orders showed that that certain medication classes are more likely not to be administered ($p < 0.01$).

Because a few medications were categorized into multiple medication classes, the total sum of numbers in the 'Counts' column of **Table 5** is slightly larger than the number of distinct non-admin orders (40,999).

Discussion

The medication process (ordering, dispensing, and administration) is one of the most complex processes in pediatric care^{40,41}. Health information technology can help measure the quality status of the medication process at various levels^{42,43}. Hospital leadership is entrusted to ensure that health care processes work in a sufficiently reliable manner at both macro and micro levels thus assuring safety for patients and quality of care. Among various aspects of the medication process, medication compliance is a quality measure that one would want to control for a given health-care facility. However, to our knowledge the reliability of the medication process is not routinely assessed and no studies have evaluated medication compliance in a pediatric hospital.

The small number of missing administration records (596 of the total 1,570,994 orders – $< 0.05\%$) shows robustness of the Vanderbilt eMAR, which reminds nurses to document every scheduled dose. This small gap could reflect truly not administered and undocumented doses. Or these could have been a loss due to the validation phase of the processes that transfer data from the operational healthcare systems (CPOE, MAR, Pharmacy Information Systems) into the EDW. At the micro level the missing administration records may well be a tolerable error of the EDW. Further analysis revealed that most (75.3% or 449) of the missed-admin orders were for

‘Alimentary tract and metabolic drugs’, ‘Nervous system drugs’, and ‘Antiinfectives for systemic Use’.

The *non-admin* orders corresponded to < 3% (40,999 distinct orders) of the total 1,570, 994. As an overall proportion this may be tolerable. Though the corresponding absolute number of over 40,000 may seem concerning, the breakdown of the REASONS suggests a high level of hospital protocol use, implying an active decision making process explaining missed medication administration. Further, the distribution of medication classes demonstrates that certain classes are more likely not to be administered. Almost a half (49.8% or 20,565) of these non-administered doses consisted of the ‘Alimentary tract and metabolic drugs’ and medications associated with pain management. Similar medications also seemed to be missed for the missed doses under “Permitted Deviations” reason category. Certain critical and time sensitive medications such as anti-infective medications and pain medications have a lower rate of non-administration, suggesting that nurses, and perhaps parents, consider medication class in decision making about medication administration. However, further research is needed to explore why certain medication classes are less likely to be administered.

Limitations:

When ordered, the pharmacy also dispenses items that are not medications (e.g., bags of saline or emergency kits). Excluding such records would have been too complicated. However, serendipitously those records were automatically excluded from the medication class distribution – since such items were not classified into any particular ATC class.

Further, this analysis was done only on a high-level and did not delve into the administration details of individual medications. Exploring further into time from ordering to dispensing and administration might provide more detail on the health of the medication process.

Conclusion

To our knowledge, this is the first study of its kind conducted at a sizable pediatric healthcare institution. We discovered that the medication process in the organization is robust and were able to establish a baseline performance. Studies of this nature help to understand the status of the medication process in pediatric care, may serve to be the means to unravel other unknown gaps in the process, and may spawn further detailed studies of sub-processes and locales within the institution. Such studies may potentially allow comparison between organizations.

Our findings indicated that the medication process in pediatric practice at Vanderbilt is quite robust. There were virtually no indications of missing administration records. Deviations from the orders were appropriately logged in the administration records with corresponding REASONS. Nurses appear to use their discretion in non-administration based on medication class. A detailed analysis of the orders with REASON-CODEs of ‘Patient / Family refused’ could also shed more light on the reasons of refusal.

Acknowledgements

Joshua C. Smith, a fellow student in the Department of Biomedical Informatics, Vanderbilt University Medical School, helped to obtain the medication classes for the given attributes of medication (name, form, route, etc.) using MedEx³⁸.

CHAPTER 3

Medication Process Compliance in Pediatric Inpatients – Time to the First Dose

Introduction

Medication compliance is critical for both acute and chronic conditions. In a pediatric inpatient setting, medications are generally administered by the nursing staff (or occasionally by parents). Compliance is therefore less dependent on patients and more dependent on the ‘health’ of the medication dispensing and administration process³⁷. Compliance in the medication process involves dispensing, delivering, and administering the treatment as (dose, form, route, etc.) and when it was intended by the provider⁴⁴.

There is limited literature on compliance in pediatric inpatient settings⁴⁵. However, there have been some studies on the related topic of medication errors. Kaushal et al.²¹ pointed out that the medication ‘errors with potential for harm occurred most often in the youngest, most vulnerable patients cared for in the NICU’ and described contributory factors that included delivery systems, human interactions (with the system and other individuals), and work environment⁴². These factors also have influence on the elapsed time for steps in the medication process.

Background and Significance

The medication process for inpatients involves scheduling, preparation, and actual administration. Medication scheduling is a function performed by pharmacists and is conducted in conference with the nursing staff responsible for administration. A pharmacist reviews medication orders entered by providers and schedules the administration of the respective medications based on the urgency of the individual orders. For STAT and NOW orders the pharmacist confers with the involved nursing staff on scheduling and arranges to deliver the medication doses at the required time, while doses for the ROUTINE orders are dispensed with

the next scheduled batch delivery to the patients' respective units and are scheduled at the unit's routine administration times based on the medication frequency.

The medication preparation step is handled either by the pharmacy or by the nursing staff member responsible for administering the dose, or both, depending on the requirements for the specific medication and the order. In many instances, the nurse may have to carry out essential preparation just before administering the medication like priming an infusion line. In addition to the medication preparation, nurses may also spend time on essential checks to ensure a proper process and the accuracy of the dose^{46,47}. Medication administration by itself is a complex process that may be interrupted multiple times due to distractions, workflow issues, emergencies, or other interruptions, while requiring close collaborations, multiple handoffs, and redundant checking^{22,48-50}.

The medication process in pediatric care carries increased safety risks due to the patient's continuously changing physiology, the need for weight based dosing, and the limited internal reserves to buffer the impact of disease and medication errors^{21,22}. For certain diseases (e.g., serious infections) reducing the time between intent to treat and actual treatment has been shown to improve patient outcome and reduce readmissions⁵¹. The medication process therefore requires balancing the opposing pressures of urgency and the required thoroughness to assure the seven rights⁵² (right patient, medication, dose, route, form, time and, documentation). The dichotomy becomes especially relevant for the STAT and NOW orders.

We studied the time-interval between medication order and corresponding administration of the first-dose as a proxy for the complete medication process from order to administration. As part of a larger medication compliance study, we analyzed the times to medication scheduling (Ord-

Sched interval) and medication administration (Ord-Adm interval) for medication orders of pediatric inpatients at Vanderbilt University Medical Center (VUMC).

In this paper we focus on a high-level analysis and demonstrate the possibility of reasoning, inferences, and interpretation at various levels, using medication process data from computerized provider order entry (CPOE) and electronic medical administration record (eMAR) systems.

Methods

We used the Enterprise Data Warehouse (EDW) at the Vanderbilt University Medical Center (VUMC) to gather data for this study. The EDW receives daily feeds from the VUMCs operational systems, such as Vanderbilt's order entry system (Horizon Order Entry) and the electronic Medication administration Record (eMAR) system. The data in the EDW is retained to support data analytics and research efforts. We used the datasets and objects that store patient demographics, encounters, medication orders, dispensing, and administration details.

We first isolated the patient dataset based on the encounters for pediatric inpatients, including admissions and observational stays. We then extracted the medication orders for this set of patients during the period of the study – from July 1, 2010 through December 31, 2015. We filtered orders to include only those served by pharmacy, excluding most of the non-medication orders. Orders not explicitly for medications (e.g., orders named 'PHARMACY MESSAGE') or for discontinuation of medications were also excluded. Additional filters were applied to exclude PRN and total parenteral nutrition orders.

The EDW also stores data pertaining to the location (hospital unit) for admitted patients at VUMC. We linked each medication order with the corresponding patient location at the time when the order was issued (order time). Any orders with the location other than pediatric inpatient units were excluded.

The order records contained ‘PRIORITY’ descriptors that indicated the urgency of the order. Order records with the ‘PRIORITY’ descriptor of ‘STAT’ or ‘NOW’ were considered urgent; otherwise the order was termed as the ‘ROUTINE’ type.

For the resulting medication orders, we collected the corresponding administration data from the eMAR system. We identified the first administered dose for each medication order by linking the administration record with the earliest administration time. For each pair of order and corresponding first-dose administration record, we collected three timestamps (date-time): order-time, schedule-time, and administration-time. Using these three time-points we computed time-to-medication-administration (Ord-Adm) as the interval between order-time and corresponding administration-time, time-to-medication-schedule (Ord-Sched) as the interval between medication order-time and corresponding schedule-time, and schedule-to-administration (Sched-Adm) as the interval between schedule-time and administration-time. These intervals satisfy the equation $\text{Ord-Adm} = \text{Ord-Sched} + \text{Sched-Adm}$. For the purpose of this study, we shall call this the “medication process equation”.

The Ord-Sched interval represents the time taken by the pharmacy to formulate and dispense the medication at the scheduled time, which is assigned by the pharmacy in conference with the nursing staff. The Sched-Adm interval is the time for the nursing staff to retrieve and prepare the medication and administer it to the patient. All time-gaps are measured in hours and on a continuous scale. Though the ‘medication process equation’ holds true for individual medication order instances, it may not hold up for respective statistical parameters. For example, the medians of Ord-Adm, Ord-Sched, and Sched-Adm may not follow the ‘medication process equation’. However the statistical parameters are used to examine the underlying trends of the medication process from different angles and to draw indicative inferences.

The EDW uses an Oracle 11g database engine and is located behind a firewall. This research analysis was part of a larger effort to study medication compliance for pediatric inpatients at the VUMC, which was approved by the Vanderbilt IRB. We used statistical package R [64-bit version 2.15.2 (2012-10-26)] for statistical analyses and plots.

Results

We isolated the demographic data for 56,428 distinct pediatric inpatients or observation patients (26,006 - 46% females), who had a total of 110,435 encounters. We analyzed 509,304 distinct order records, along with associated unit and patient demographic information, and corresponding first-dose administrations.

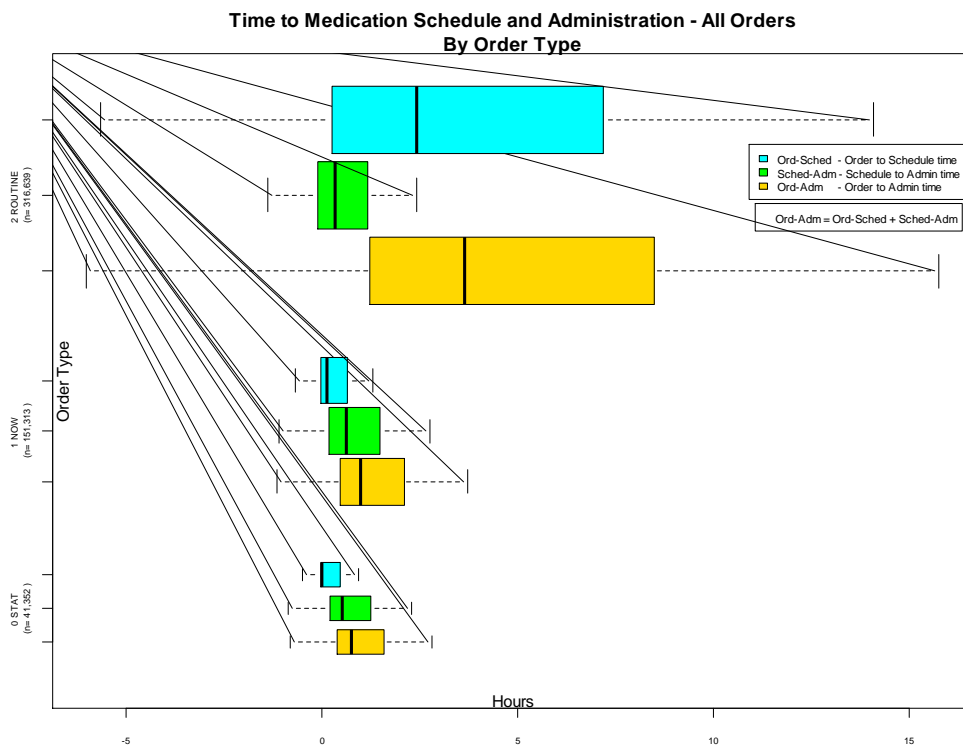


Figure 1: Ord-Adm, Ord-Sched, and Sched-Adm intervals (see the legend on the plot for details) for all medication orders pertaining to the pediatric inpatients admitted at the VUMC, **by Order-Type**. The box-thickness is proportional to the number of medication orders (shown in the parentheses).

Figure 1 shows the box-plots of Ord-Adm, Ord-Sched, and Sched-Adm intervals for all the medication orders segregated by order-type: STAT, NOW, and ROUTINE. The plots for STAT

and NOW orders show a narrower distribution for all three intervals – Ord-Adm, Ord-Sched, and Sched-Adm. For ROUTINE orders, Ord-Adm and Ord-Sched intervals have higher median and variance while the Sched-Adm interval seems comparable to those of NOW or STAT orders.

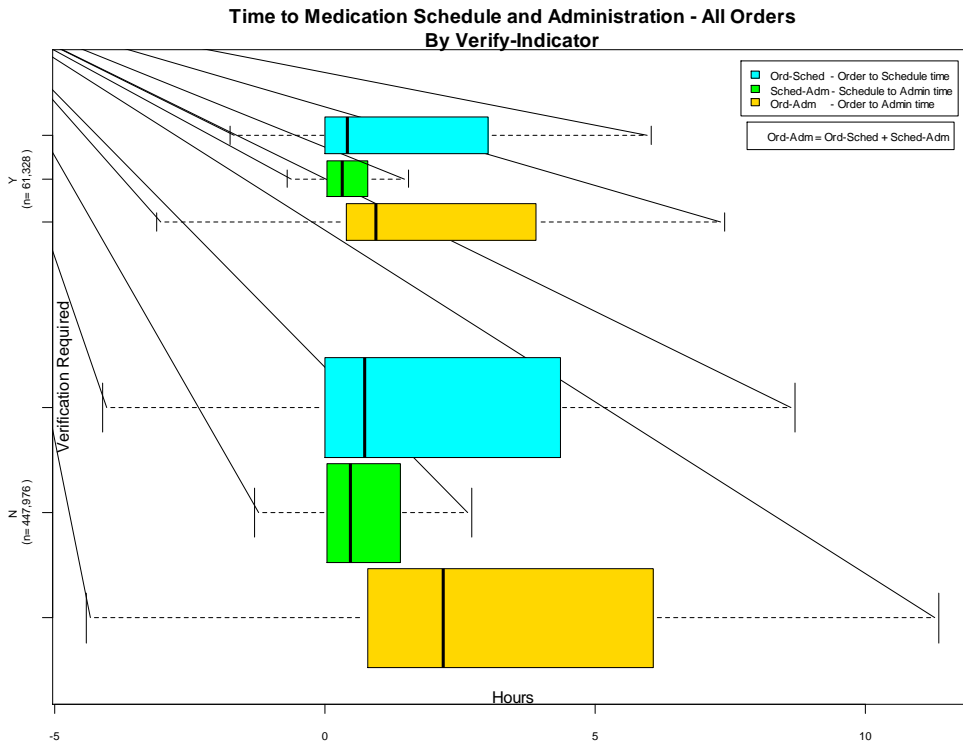


Figure 2: Ord-Adm, Ord-Sched, and Sched-Adm intervals (see the legend on the plot for details) for all medication orders pertaining to the pediatric inpatients admitted at the VUMC, **by Verify-Indicator**. The box-thickness is proportional to the number of medication orders (shown in the parentheses).

Figure 2 shows the box-plots for Ord-Adm, Ord-Sched, and Sched-Adm intervals for all medication orders arranged by administration verification status. A medication requiring verification demands checking of the medication and its dose by a second nurse prior to administration to assure safety and accuracy⁵³. The plots suggest that medications requiring verification have shorter Ord-Adm, Ord-Sched, and Sched-Adm intervals, with narrower variations. Interval averages for medications requiring verifications were about an hour shorter than those that did not require verification. Ord-Adm, Ord-Sched, and Sched-Adm intervals by order type are shown in supplementary **Figures 2-A, 2-B, and 2-C** (Appendix – D). All intervals

consistently show smaller variation for orders requiring verification compared to those that do not except for the Ord-Sched interval for ROUTINE orders.

Figure 3 shows the Ord-Adm, Ord-Sched, and Sched-Adm interval box-plots for orders comparing NICU locations with all other locations. At Vanderbilt most NICU beds are collocated with the pediatric pharmacy. Ord-Sched intervals for NICU patients are shorter and have less variation, especially for STAT and NOW orders, compared to patients in other units, suggesting faster delivery of medications. Sched-Adm and consequently Ord-Adm intervals for NICU orders have wider variations with higher medians. Ord-Adm, Ord-Sched, and Sched-Adm intervals, for NICU and other units, segregated by order-type are shown in supplementary **Figures 3-A, 3-B, and 3-C** (Appendix – D).

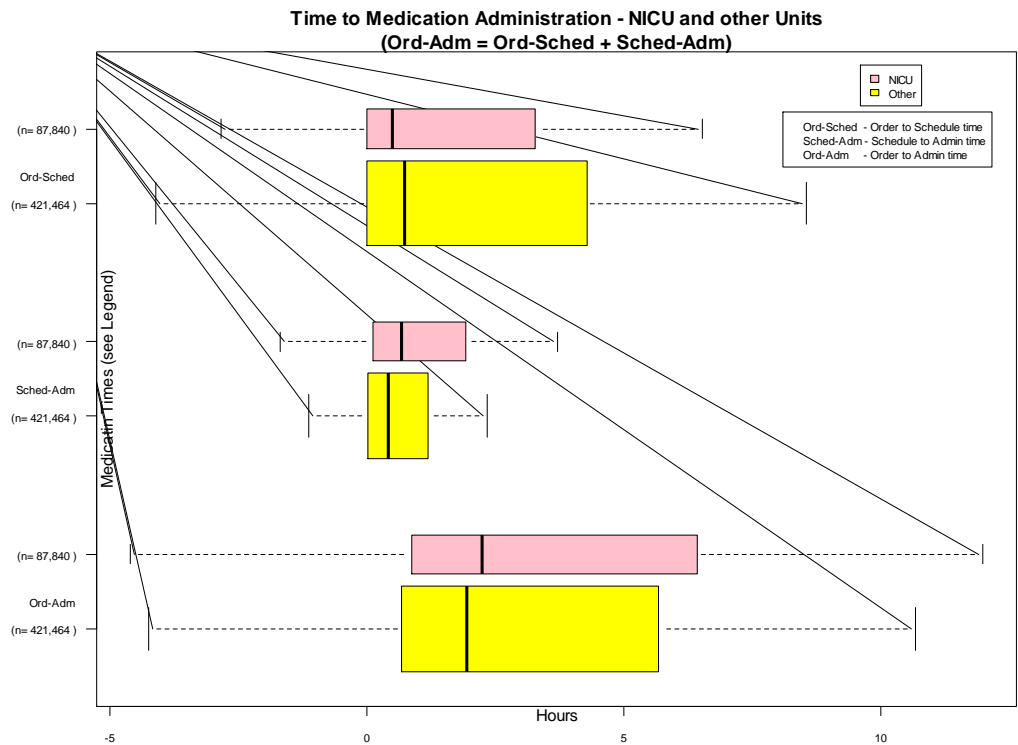


Figure 3: Ord-Adm, Ord-Sched, and Sched-Adm intervals (legend on the plot for details) for all medication orders segregated by patient unit – NICU or Other. The box-thickness is proportional to the number of medication orders (shown in the parentheses).

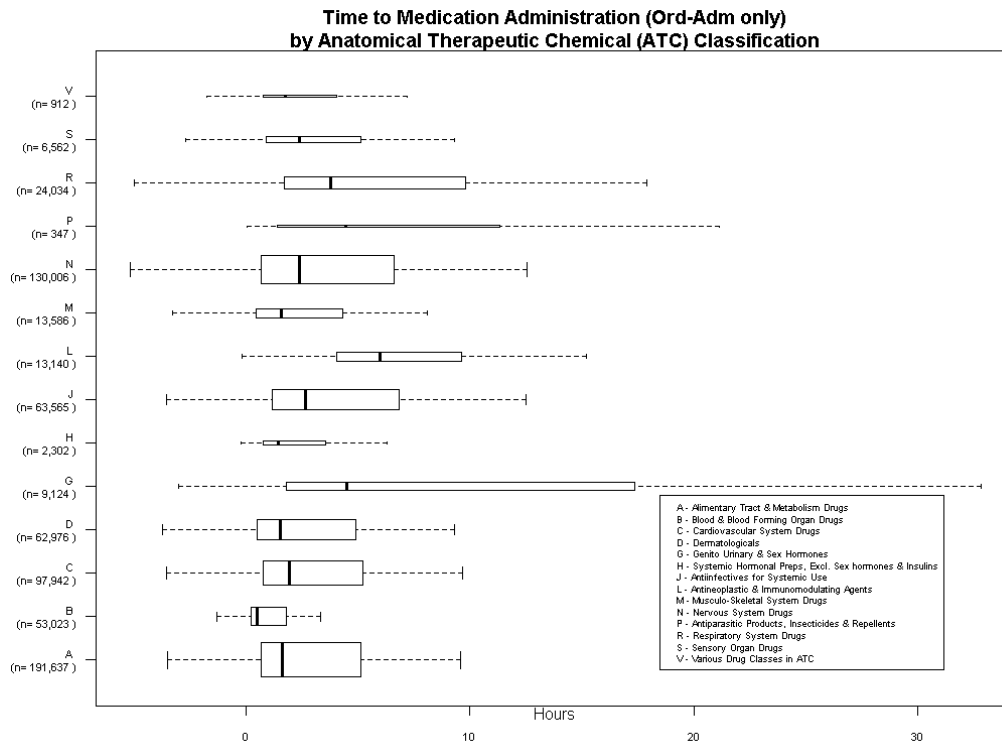


Figure 4: Ord-Adm intervals for all medication orders pertaining to the pediatric inpatients admitted at the VUMC, by Anatomical Therapeutic Chemical (ATC) class of medicines. The box-thickness is proportional to the number of medication orders (shown in the parentheses).

Figure 4 shows the box-plots for Ord-Adm intervals by Anatomical Therapeutic Chemical (ATC) class³⁹ of the ordered medications. The oncology drugs (“Antineoplastic and Immunomodulating Agents – ATC class ‘L’”) have the largest Ord-Adm median, which would be expected due to the complexity associated with dispensing. The median Ord-Sched interval for this class is also the largest of all medication classes and the administration – Sched-Adm interval has one of the largest medians and the highest variance, with third quartile extending beyond 2 hours compared to ~1 hour for other classes (supplementary **Figures 4-A and 4-B**, Appendix – D).

Figure 5 displays Ord-Adm intervals by the hour of the day the medication was scheduled for administration. The variations and medians of the Ord-Adm interval for hours 6 am, 8 am and 10 am (and in a mirroring fashion also for 6 pm, 8 pm, and 22 pm) are higher. A similar pattern is

shown by the Ord-Sched intervals for these hours (supplementary **Figure 5-A**, Appendix – D) suggesting a slower turnaround in pharmacy from 6 to 10 (am and pm) hours. The Sched-Adm had highest medians and variances at 7am, 9am, and 11am (supplementary **Figure 5-B**, Appendix – D).

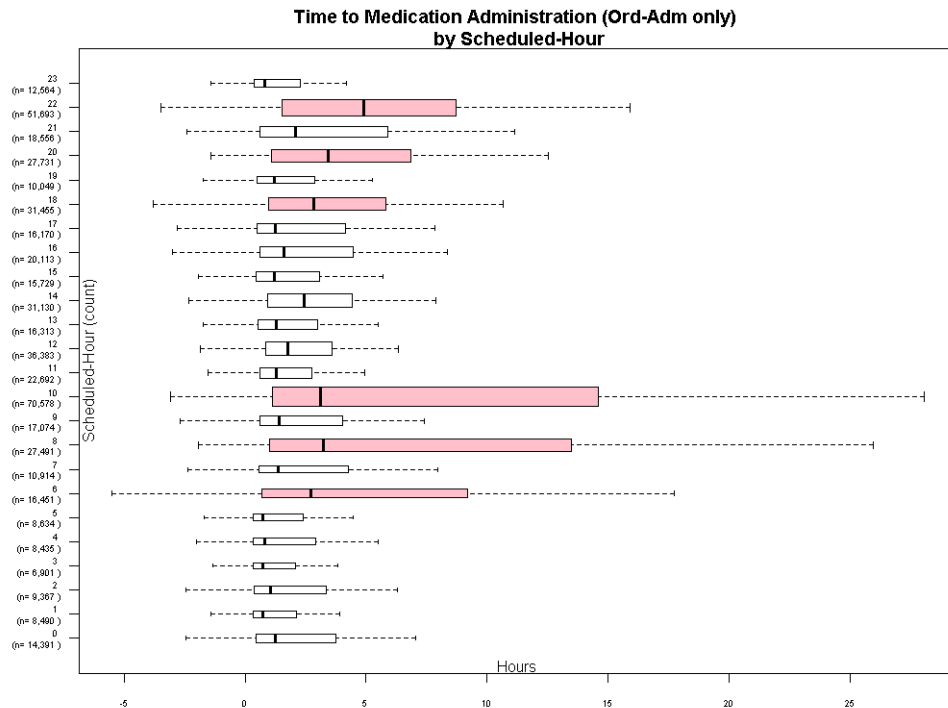


Figure 5: Ord-Adm intervals for all medication orders pertaining to the pediatric inpatients admitted at the VUMC, **by scheduled-hour** of the ordered medication. The box-thickness is proportional to the number of medication orders (shown in the parentheses) for the respective scheduled hours.

Figure 6 shows the Ord-Adm intervals by patient age. The median intervals and the variations increase with the patients’ age. Supplementary **Figures 6-A** and **6-B** (Appendix – D) show that the Ord-Sched intervals for neonates (age < 31 days) are near 0 with very narrow variation, while the Sched-Adm intervals show widest variation for this age-group.

Discussion

The medication process for inpatients is a collaborative effort between providers, pharmacists, and nurses. After receiving an order from a provider, a pharmacist interprets a provider’s intent,

confirms the availability in the formulary, and dispenses the dose based on patient parameters. If necessary, the pharmacist consults with the ordering provider for substitutions (e.g., the specific ordered medication is not available). The pharmacist then schedules the medication delivery after conferring with the responsible nurse who then administers the medication as per the order.

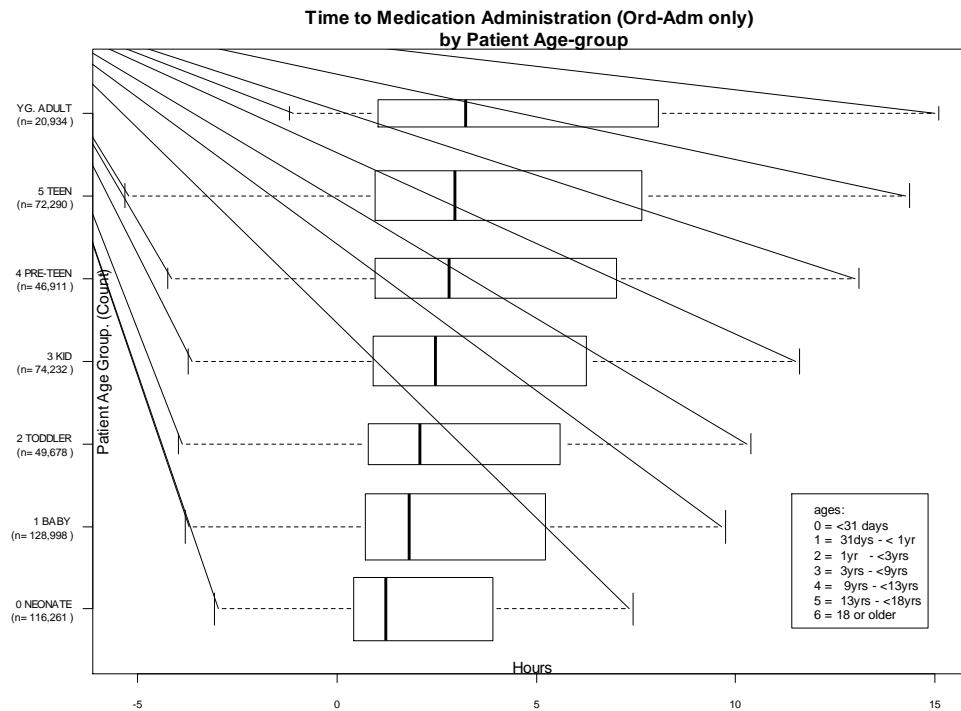


Figure 6: Ord-Adm intervals for all medication orders pertaining to the pediatric inpatients admitted at the VUMC, **by patient age-group**. The box-thickness is proportional to the number of medication orders (shown in the parentheses) for the respective age groups.

Effective team work is important to assure appropriate medication delivery and administration as intended by the ordering provider. The analysis of medication process intervals, showing the variations in durations of medication dispensing and administration, can generate pointers leading to further investigation of the underlying causes of observed delays. We analyzed the order-to-administration (Ord-Adm) time interval by dissecting it into two components – order-to-schedule (Ord-Sched) and schedule-to-admin (Sched-Adm) intervals. The Ord-Sched interval reflects pharmacy actions including dispensing and scheduling of the medication, and Sched-

Adm reflects nursing actions including preparing and administering medications. For the first medication doses, the relationship $\text{Ord-Adm} = \text{Ord-Sched} + \text{Sched-Adm}$, which we call “medication process equation”, holds true.

Overall the medication process at Vanderbilt’s Children’s hospital appears to be healthy based on the intervals of Ord-Sched and Sched-Adm. From the box-plots of medication administration intervals by order-type (**Figure 1**), we can infer that a bulk of Ord-Adm time is contributed by Ord-Sched interval for ROUTINE orders. Given that all ROUTINE orders are scheduled to be delivered with the ‘next-batch’ medication delivery, a sizable padding to the scheduling may add time to the earliest orders resulting in a wide spread. For routine orders, such a delay to optimize pharmacy delivery processes appears to be acceptable. Also, the Sched-Adm interval median and variance is comparable across all order-types, unlike those for the Ord-Sched intervals. This indicates that the nursing workflow does not change considerably for STAT and NOW medications, but workflow for pharmacists does.

The Sched-Adm intervals are similar for all the order types (STAT, NOW, or ROUTINE), suggesting that the administration processes are very similar irrespective of the order-type. Relatively shorter Sched-Adm intervals for ROUTINE orders also indicate medication availability and managing a known and expected event. Relatively longer Sched-Adm intervals for STAT and NOW orders may reflect the need to scramble for the medication (run to pharmacy), and an unforeseen and unanticipated event requiring additional processing time.

Surprisingly, the box-plots of the Ord-Adm, Ord-Sched, and Sched-Adm, by Verify status in **Figure 2**, suggest that the respective intervals for the orders requiring verification by another nurse are shorter than those without – as apparent from the respective medians and variance.

Empirically, any order requiring verification (by a fellow nurse) before administration is expected to take longer than if no verification was needed. Plots in **Figure 2**, however indicate otherwise. We observe (supplementary **Figures 2-A, 2-B, and 2-C**, Appendix – D) that the respective median intervals are still shorter for the orders with verify compared to those without (except the Ord-Sched for the ROUTINE orders – **Figure 2-B**). A significant difference is observed for the Sched-Adm intervals (**Figure 2-C**), specifically for the NOW and STAT orders, indicated by wider variance. One reason for the reduced intervals for the doses with ‘verify-indicator’ could be that these orders are given priority by the nurses and pharmacists. However, this finding will require further research.

Medication process intervals for patients in NICU and other units (**Figure 3**) show that Ord-Sched intervals have a marginally shorter median time with narrower variance, indicating a more efficient pharmacy process for NICU patients. The fact that, at VUMC, a majority of the NICU beds are co-located with the pediatric pharmacy may play a role. Each of the three intervals are further analyzed by order-type (Supplementary figures **3-A, 3-B, and 3-C**, Appendix – D), which show patterns consistent with the plots in **Figure 3** Sched-Adm in the NICU are longer, which seems to be explained by the complexity of the NICU patients and their treatments and the complicated tasks to be performed for the administration of medications in critically ill neonates.

We observed that the oncology drugs (class ‘L’ – Antineoplastic and Immunomodulating agents) have the largest median Ord-Adm interval. The Ord-Sched plots by ATC class (supplementary **Figure 4-A**, Appendix – D) show a similar pattern. The Sched-Adm interval plots reflecting nurse administration (supplementary **Figure 4-B**, Appendix – D) indicate a uniform median time of less than half-hour, albeit showing a much wider variation for oncology drugs. This observation suggests a greater variability for nurses to prepare and administer oncology drugs⁵⁴,

which may reflect the increased safety measures required. The wider variations in the Ord-Sched intervals of some other ATC classes may require further investigation.

The distribution of the Ord-Adm intervals by scheduled hour of the medication can show bottlenecks in the medication process. The median Ord-Adm intervals in **Figure 5** are measurably longer, with much wider variations, for orders scheduled during 6th, 8th, and 10th hours on the clock (thus likewise for 18th, 20th and 22nd hours). Though the generation of orders during periodic rounding is logical explanation for 10th and 22nd hours (also apparent in the volume of orders expressed in the thickness of the bar), the rationale for a similar pattern during 6th, 8th, 18th, and 20th hour is unclear. The corresponding Ord-Sched interval plots show similar patterns (supplementary **Figure 5-A**, Appendix – D). Exploration with pharmacy personnel revealed that the pharmacy is short-handed during these hours of the day and, the repetition schedules of medications (q8, q12, etc.) fall during these hours.

The Sched-Adm interval plots by scheduled hour (supplementary **Figure 5-B**, Appendix – D) indicate that the variation in administration is quite steady across all the ‘waking’ hours. However, the Sched-Adm intervals are longer for 7th, 9th, and 11th hours (as suggested by respective medians and variance). The shift-change during the 7th and 19th hour explains the lengthening of Sched-Adm time during those hours, but further investigation may be needed for the 9th and 11th hours.

Ord-Adm by patient age-group (**Figure 6**) show the median and the variation marginally increase with the patients’ age. Further analysis shows that Ord-Sched (supplementary **Figure 6-A**, Appendix – D) intervals are shortest for the neonates (age < 31days), while they vary widely for older patients. The smaller Ord-Sched interval for the neonates can be explained by the fact

that most of the NICU beds are co-located with the Pharmacy (neonates account for many patient-days in the NICU), which may influence the medication dispense and delivery times favorably. The longer Sched-Adm time for neonates (supplementary **Figure 6-B**, Appendix – D) can be explained by the extra care and the related complexity involved in medication administration for the very young and fragile patients. The median Sched-Adm time of half-hour or less for all ages indicates an efficient administration process. Performance of nurses appears consistent across all the age-groups.

Apparently, **Figure 6** box-plots may not reconcile well with those for Ord-Adm plots by patient unit (NICU vs. other Units) shown in **Figure 3**, since Figure 3 suggests that the Ord-Adm interval for NICUs is longer. However, not all the neonates admitted to VCH are in the NICU – as corroborated by the respective counts of the medication orders (Figure 3 has NICU count of 87,840 vs. 116,261 for neonates).

We plotted the Ord-Adm, Ord-Sched, and Sched-Adm across other dimensions like patient demographics (Gender, Race, and Ethnicity), Nursing Staff Status, and Provider Privileges (Attending, Referring, and Surgical) (Data not shown). We did not notice any discernible association of those with the medication process intervals.

We have demonstrated the utility of the health data repository to assess the health of medication process in a healthcare institution. Given a widespread adoption of the electronic health record (EHR) systems⁵⁵ due to the incentives offered through the American Recovery and Reinvestment Act⁵⁶, this approach should be available to most institutions. We demonstrated the value of healthcare data that already exists within current system. We were able to identify challenges in the medication process (e.g., a bottleneck in the medication process between 6AM and 10AM; or

medications of a specific class take longer to prepare, dispense, and administer) that will be used to take appropriate steps and improve the processes. In order to improve hospital processes, outcome measures have to be observed and measured. We demonstrated a series of outcome measures for the medication process that are easy to obtain and can be compared across hospital locations and even institutions.

Limitations:

Considering the data bulk, and the number of dimensions, we limited our analysis to a very high-level. Our study provided us with an understanding of delays and bottlenecks in the medication process. From our data, we cannot draw direct conclusions to the origins and causes for these findings. Our results will require further observational studies and interviews with stakeholders.

A detailed analysis at varying depths could reveal additional signals and may either address some of the unexplainable observations (e.g. longer Sched-Adm times for medications of ATC class ‘G’, ‘M’, or ‘S’) of observed variations or spur additional questions to investigate further.

Conclusion

It is critical for a health care institution to assure the effectiveness and safety of the medication process and ensure that the medication orders result in medication administration. It has been shown that for certain disease conditions, reducing the time between intent to treat and actual treatment can influence the patient outcome⁵¹. We have demonstrated that rich information can be obtained from the analysis of medication process timings at various steps. Analyzing the medication process intervals from various perspectives can provide clues to the scope for improvements along different dimensions.

One of the purposes of this paper was to demonstrate the use of health care data to enable institution-wide analytics at various levels. The EDW provided the widest possible breadth of patient data for an institution (VUMC). We conclude that research analytics for the medication process are possible at various levels of depths. To our knowledge this is the first study to analyze the medication process at an institution wide level for patients and medications.

CHAPTER 4

Detecting Quality Improvement Signals in an Enterprise Data Warehouse

Introduction

The medication process for inpatients follows the path of ordering a medication, counter-checking and dispensing of the medication by the pharmacy, and administration by the nursing staff caring for the patient. Medication management in pediatrics, however, poses distinctive challenges. Limited reserves of the pediatric patients to absorb the impact of the disease and the medication's side effects, the specifics of pediatric medications based on (gestational) age, weight, and disease indications, and rapidly fluctuating physiologic aspects, place children at a higher risk of incorrect dosing^{21,22}. This is particularly true for treating infections in neonates⁵⁷. Considering the immature immune system of neonates, immediate and appropriate actions must be taken to control infections^{51,58}.

Pharmacists verify the details of the ordered medication and create an appropriate dose for the ordered medication, given the patient parameters⁴⁴. The step of medication administration by itself is complex; it requires preparation of the dose, close interactions, multiple handoffs, as well as redundant checking, which can be interrupted at many points in the process⁴⁹.

These complexities could result in delays between ordering a medication and subsequent administration of the medication to the patient. However, for serious infections reducing the time between the intent to treat and the actual treatment has been shown to alter the patient outcome and patient readmissions⁵⁹. The medication process, therefore, should be well tuned and successfully navigated to assure timed delivery and administration as intended by the provider.

Background

As part of a medication compliance study in 2014, we conducted an evaluation of medication process at the Monroe Carell Jr. Children’s Hospital (VCH) at the Vanderbilt University Medical Center (VUMC). We extracted and analyzed ordering, scheduling, and administration data from the Enterprise Data Warehouse (EDW). While exploring the ordering to administration times of anti-infective medications by location we noticed the administration times were noticeably shorter in one Neonatal ICU (NICU). Further, the variance of administration times in the same NICU was much narrower compared to the other NICUs. The faster administration times for a specific NICU appeared more of an anomaly, given the fact that this NICU was located farther from the pharmacy.

The Pediatric Pharmacy for the VUMC is located in the VCH building. The NICUs, however, are scattered across the medical campus of the VUMC. Some of the NICUs are collocated at the VCH, while others are at a distance of up to a quarter of a mile (~0.4 KM) from the VCH building. This geographical separation between the units should result in some delay due to the longer delivery time for medications by the pharmacy (See **Table 1**).

Initially suspecting a documentation flaw, we investigated the cause of the anomaly.

Table 1: NICU grouping (map in supplementary **Figure 7-A, Appendix – D**)

Group	Units	Comments
7S	Neonatal 7 South	This unit is located ~0.25 miles (0.4 KM) from the pediatric pharmacy
4NIB-I	NICU Pods B – I (Critically ill patients)	These units are co-located with the pediatric pharmacy.
4NIA&J	NICU Pod A & J (Step down Units)	
4NI	Stahlman NICUs 1, 2, and 5	Unit where “Golden Hour” effort was initiated. This unit is located at ~0.25 miles from the pediatric pharmacy.

Methods

We isolated the pediatric patient cohort based on their inpatient encounters (including observation patients). For this pediatric patient cohort we collected the ordering, scheduling, and

administration data from the EDW for the medication process evaluation. The order data included only medication order records serviced by Pharmacy, and we filtered out medication discontinuation and other non-medication orders. Corresponding to these orders we obtained the pharmacy dispensing and nurse administration data-subsets from the EDW. We also associated this data with the corresponding unit location for patients for the respective medication order-times.

For all medication orders, we computed the order-to-administration interval (Ord-Adm) as the difference between order-time and the corresponding administration time for the first dose. Likewise we computed the order-to-schedule interval for the medication (Ord-Sched) as the difference between the order-time and the corresponding schedule-time for the first dose. We then derived the schedule-to-administration time (Sched-Adm) by subtracting Ord-Sched from Ord-Adm ($\text{Ord-Adm} = \text{Ord-Sched} + \text{Sched-Adm}$). For first doses of medications, for the most part, the Ord-Sched can be expected to represent the time taken by the pharmacy to prepare and dispense the medication, while the Sched-Adm represents mainly the time taken by the nursing staff to administer the medication to the patient. All intervals are measured in hours on a continuous scale. For the purpose and scope of this case-report, we focused on the orders of antibiotics ampicillin and gentamicin (amp-gent orders).

EDW uses Oracle 11g database engine and is behind a firewall. We used statistical package R [64-bit version 2.15.2 (2012-10-26)] for statistical analyses and plots. We had obtained the Vanderbilt IRB clearance for the aforementioned study with wider scope (the Medication Compliance Study).

Results

As part of medication process evaluation effort, narrowing in on the anti-infective medication orders for ampicillin and gentamicin in the NICUs, we isolated 8,394 ampicillin or gentamicin orders pertaining to 3,263 distinct pediatric patients admitted to the NICUs at the VUMC (as listed in methods section). We plotted the order-to-administration (Ord-Adm) times of the amp-gent orders for the patients in NICUs, as shown in **Figure 1**.

We observed that administration times for Stahlman NICU were shorter, with narrower variance (**Figure 1**). Given the fact that Stahlman NICU is located at a quarter of a mile from the Pediatric Pharmacy, this observation was in contrast to our intuition. We investigated further to confirm whether this was an anomaly or there was an underlying cause for this shorter administration time.

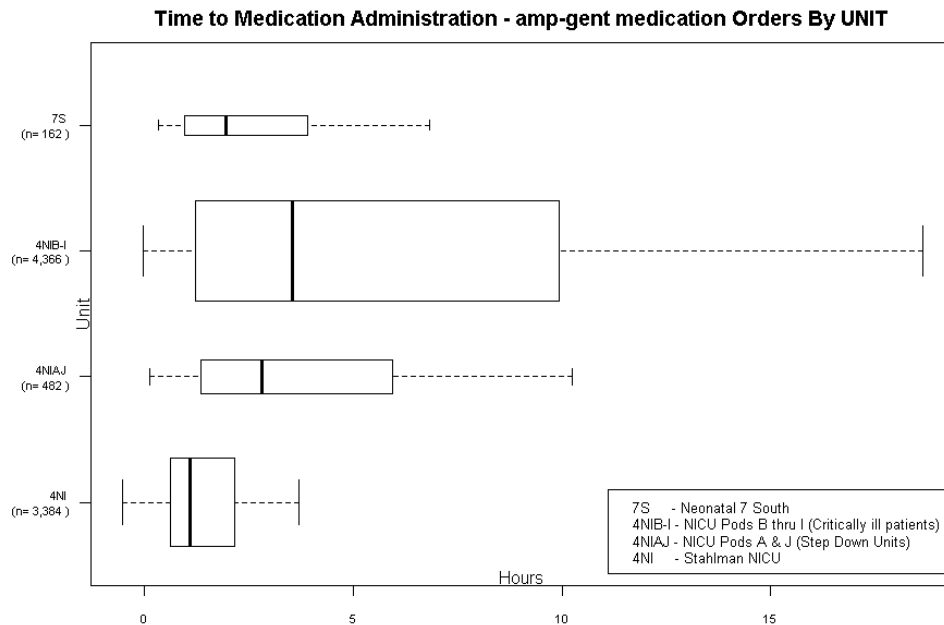


Figure 1: The order-to-administration (Ord-Adm) intervals of ampicillin and gentamicin orders for patients in the NICUs.

Interviewing the providers we learned that a quality improvement (QI) effort titled “Golden Hour” had been started in 2012. One of the aims of this QI effort was to improve the timing for the first dose of ampicillin and gentamicin after delivery for neonates. To achieve this goal, dispensing of ampicillin and gentamicin was done directly in the Stahlman NICU by nurses and not in the pharmacy and nurses had been educated on the importance of an early antimicrobial coverage. The effect of the “Golden Hour” intervention had been measured using paper-based forms with manual data collection.

We further analyzed the Order-to-administration (Ord-Adm) time by splitting it into two parts – Order-to- schedule (Ord-Sched), and schedule-to-administration (Sched-Adm) times. We plotted the Ord-Sched and Sched-Adm for the NICUs, as shown in **Figures 2** and **3**, respectively.

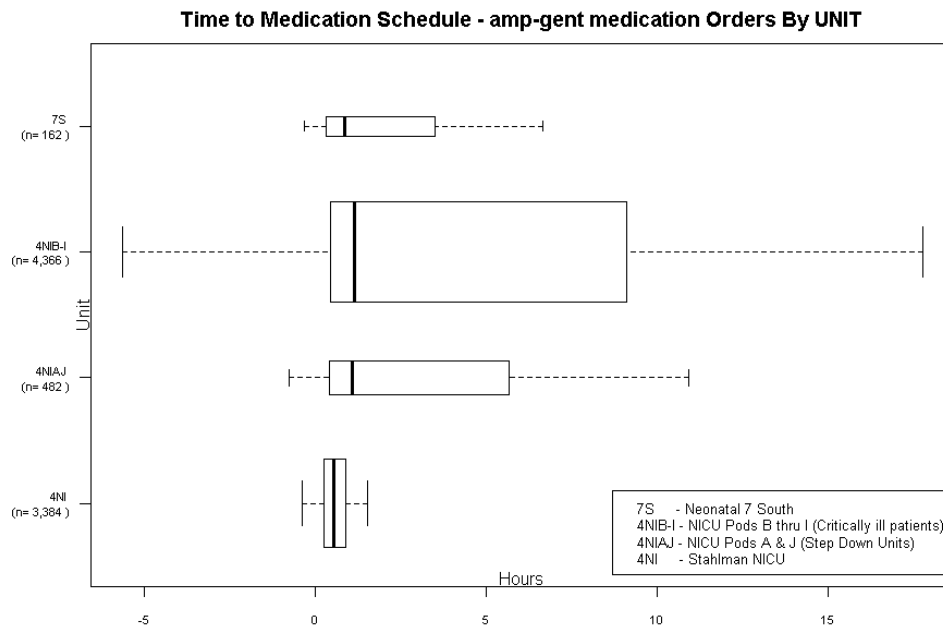


Figure 2: The Order-to-schedule (Ord-Sched) intervals of ampicillin and gentamicin orders for patients in the NICUs.

Figure 2 plots shows that the Ord-Sched medians and spreads were similar to the plots of Ord-Adm in **Figure 1**. However, the respective plots of Sched-Adm in **Figure 3** show medians in a

narrow range of about half-an-hour, and similar variance across all the NICUs suggesting that gains in Ord-Adm intervals were secondary to the local dispensing.

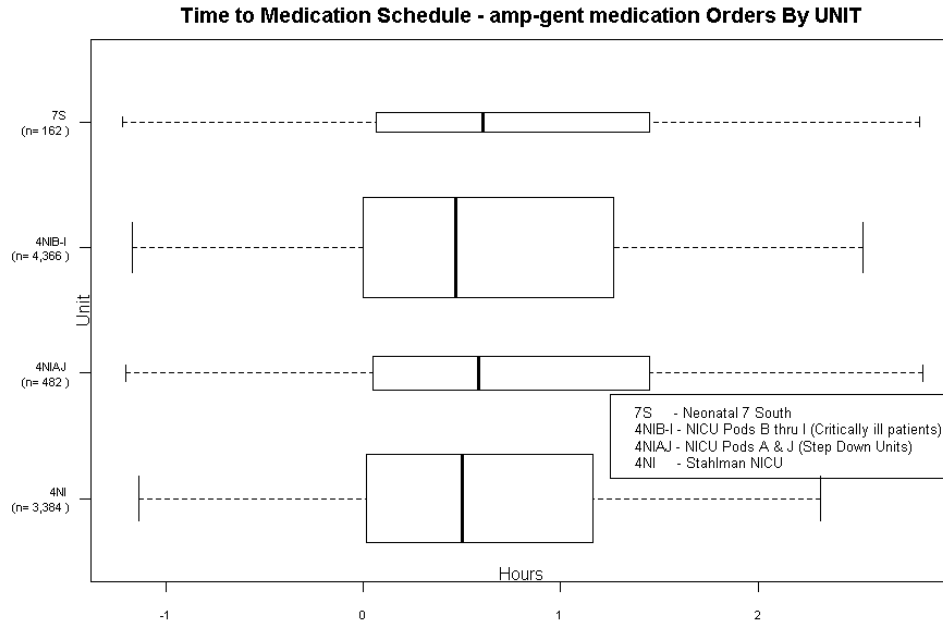


Figure 3: The schedule-to-administration (Sched-Adm) intervals of ampicillin and gentamicin orders for patients in the NICUs.

Discussion

The process of medication ordering, dispensing, and administration involves team work. After a medication is ordered by a provider, a pharmacist checks the availability of the corresponding formulary and other patient parameters to verify and dispense the dose. The pharmacist then assigns the schedule-time when the medication dose is available to the nursing staff. For the first dose of an antibiotic that needs to be administered immediately, the gap between the order-time and schedule-time (Ord-Sched interval) can be interpreted as the time taken by the pharmacy staff to dispense the medication. This is specifically true for the STAT and NOW orders, and mostly true for the first dose of any order. Further, the nursing staff takes time to prepare and

administer the medication after receiving it from the pharmacy – this is the gap between schedule-time and administration-time.

We observed that the Ord-Adm variation is bound to a tighter range for Stahlman NICU than other NICUs (**Figure 1**). After learning about the QI effort to improve the efficiency of dispensing ampicillin and gentamicin doses, we created additional plots for the Ord-Sched intervals and Sched-Adm intervals separately for the respective NICUs.

The Ord-Sched plots display a pattern similar to the Ord-Adm plots, with a shorter median time and a narrower spread for Stahlman NICU compared to the other NICUs. This suggests that the QI intervention positively impacted the dispensing of the ampicillin and gentamicin doses, as intended by the QI effort – thus improving the median time almost by a half-hour and decreasing the spread by several hours. With pharmacy making the ampicillin and gentamicin dispensing available directly in the Stahlman NICU, the dispensing time was significantly shortened.

The Sched-Adm plots, however, show the median for Stahlman NICU only slightly improved, with nominal narrowing of the spread. Though the “Golden Hour” effort did have a component for the nurses’ awareness of the importance of the early antimicrobial coverage, the scope of Sched-Adm improvement due to the QI effort was marginal. Rationale for this observation could be given by a couple of reasons. Educational interventions lose their effectiveness after several months and the education has to be repeated to maintain effect. Further any effect would be seen in other NICUs as well since staff rotates among the varying units. Switching to dispensing of ampicillin and gentamicin did not require education and thus became a self-sustaining effort.

The important point of this case-report is that the effects of QI effort were detected in a routine data analysis of a medication process evaluation study, which was independent of the “Golden

Hour” QI effort. The medication process evaluation effort used larger data sets and still noticed the signal of an anomaly that let us to detect the presence of a sustained QI effort.

We conclude that quality improvement activities or local performance improvement activities may be detected when exploring enterprise data sets. These “anomalies” may be used to explore why processes are better or worse in certain locales, proving opportunities to improve quality, safety, and effectiveness of hospital processes.

Conclusion

To our knowledge, this is the first time that a routine medication process analysis inadvertently captured the effectiveness of an ongoing QI project. The QI effort measured their performance using paper-based forms with manual data entries. We demonstrated the same effect using the EDW data. Though independent of the “Golden Hour” QI effort, and processing data at a larger scale with wider dimensions, our medication process evaluation effort was able to detect the QI signal. This case study corroborates that, given a robust and reliable data repository, information technology (IT) methods and related tools can be used to assess sustained QI projects and may replace the manual methods of measuring the intervention outcomes.

CHAPTER 5

Summary and Conclusion

Summary

The medication administration process in pediatric care is more complex and prone to errors than in adult populations^{60,61}. Proactive measures, policies, and procedures are needed to minimize the risk of errors, which may result due to the gaps in medication compliance and may adversely affect the hospital patients. Important metrics to appraise the quality of the medication administration process in a hospital setting include an assessment of medication compliance and the determination of whether the patients received their medication as prescribed, and in a timely manner. However, except for narrowly focused QI processes, healthcare facilities generally do not conduct an organization wide evaluation of the overall inpatient medication compliance and timeliness. Recognizing a research gap on this subject matter⁴⁵ I initiated this study to assess the ‘health’ of the medication process at Monroe Carell Jr. Children’s Hospital at Vanderbilt (VCH), a major tertiary pediatric hospital in Nashville, TN.

The medication process for inpatients is a collaborative and finely choreographed effort between providers, pharmacists, nurses, and patients (and patients’ families). The information flow concerning medication ordering, dispensing, delivery, and ultimate administration requires a controlled, precise, and expeditious handling. Given the involvement of various personnel and systems, it is important to optimally tune this process for smooth and efficient flow that culminates in the desired patient treatment. A system with streamlined processes and procedures does not strain the thought process of the nursing staff⁶², leaving them to concentrate on the wellbeing of the patients, thus improving the treatment outcome.

The aims of this Medication Compliance study divided the approach to first explore the true gaps in the medication process and then analyze if there are any processing weaknesses. A true gap in the medication process was defined as any dose of a medication order not culminating into the corresponding administration to the patient. The analysis of processing weaknesses involved collection of the proxy time-intervals of medication process steps and inspection of their relativity along various dimensions. Though the comprehensive analysis did not reveal any gaping chasms or voids, it did reveal some indications of inconsistencies and disparities.

One of the findings of the first aim indicated a small proportion ($< 0.05\%$) of missing administration records, which suggests that the medication administration systems and processes at VCH are robust. Such a small gap could even be attributed to a loss due to the processes that transfer data from the operational systems – e.g., WizOrder, Horizon Expert Documentation (HED), and Pharmacy Information Systems – into the EDW. The proportion of orders that indicated non-administration in the HED corresponded to $< 3\%$. The corresponding absolute number of over 40,000 non-administered orders may seem concerning. However, the breakdown of the REASONS for non-administration indicated an effective use of hospital protocols and active decision making by the staff members to explain the non-administration (e.g., the ordered pain medication would not need to be administered while the patient is off the floor and is undergoing a surgery). The non-administration was also associated with the ATC class of medication ordered. . Chapter 2 discussed these findings.

The time intervals associated with the medication process components, and variations thereof, provide important information about the ‘health’ of the medication process compliance. The analyses of time intervals from order to schedule and administration provided insights into the pharmacy and nursing actions including preparing, dispensing, and administering medications.

Investigation of these intervals along various dimensions, and their relative measures with respect to the corresponding interacting steps, provided awareness of the information that would have been missed otherwise – e.g., elongated order-to-schedule time intervals during the scheduled-hours of 6AM through 10AM. These analyses also flagged some observations that are not normally considered for a detailed analysis (e.g., the oncology drugs take longer to process by pharmacy and to administer by nurses, or much wider variations exist in dispensing and administration times of the genito-urinary and sex hormone drugs).

While conducting the time-interval analyses of medication process, the interval patterns signaled much shorter times, with narrower variations, for the medications ordered for patients in specific NICU beds. Further investigation discovered the variation to be the result of a QI effort (named “Golden-Hour”, described in chapter 4), rather than a documentation error. Therefore, this focused analysis provides an example of using IT methods and related tools to assess QI efforts. The general medication process interval analyses and the focused case-study to assess the effectiveness of QI efforts were covered in chapters 3 and 4 respectively.

This Medication Compliance study substantiates the existence of a robust and healthy medication administration process at VCH. Additionally it provides high-level indications towards the need for further investigation and observation into certain functional aspects (e.g., bottlenecks of nursing function during certain hours of a day). Studies like this are necessary to establish the baseline functioning of healthcare processes rather than making any assumptions about their current operating status.

The Medication Compliance study sourced the medication process data from the EDW, which acts as a clinical data repository (CDR) for VUMC and receives EHR feeds from the operational

systems. This study is another example of using EHR data to research *operational health* of a healthcare facility³⁷.

Discussion

Effective communication and team work are crucial for medication delivery and administration as intended by the ordering provider. The medication administration is itself a compound and complex process that may be interrupted, while requiring close collaborations, multiple handoffs, and redundant checking^{48–50}. In certain cases, such as severe infections, however, the time interval between intent to treat and actual treatment has been shown to influence the patient outcome⁵¹. Nurses therefore have to balance the opposing pressures of urgency and thoroughness to ensure appropriate compliance towards medication process.

Health information technology (HIT) can facilitate the qualitative and quantitative assessment of the healthcare data in the CDR from various aspects⁴². Medication compliance is one such quality measure that the hospital leadership should assess, and perhaps improve, at a given healthcare facility. However, the reliability of the medication administration process is not routinely assessed. To my knowledge this is the first study to evaluate the inpatient medication administration compliance in a pediatric hospital at the aggregate level, and from different perspectives – e.g., breakup of non-administrations by reasons and medication class (ATC), and analyses of process times for the first dose of medications along different dimensions (order type, patient age group, scheduled-hour, medication class, etc.)

This study demonstrated that the medication administration process is relatively consistent. However, the data, when analyzed from various perspectives, indicated some non-intuitive patterns that were otherwise not perceptible. For example, the medication administrations that

required verification by a fellow nurse were more expeditious. If certain workflow patterns can make the ‘VERIFY’ administrations more efficient, could those be adopted for ‘NON-VERIFY’ administrations as well? Other indications offered by the data analysis were the variations in the administration process times based on the ATC class of the drug being administered and a less efficient administration process during certain hours of the day. The latter could be due to the dependence of the medication administration process on factors related to the availability of nursing staff and interdependence of the administration process on pharmacy delivery practices (the study illustrated that the pharmacy process itself shows such inefficiencies in the preceding hours). The individual QI projects have specific and narrower focus, and those projects attempt to resolve the known problems in the processes. This broad study elicited the patterns that would not have been discovered otherwise. It also provided a *bird’s-eye-view* of the status of medication process.

This study discovered that the medication administration process at VCH is sound, which was unknown before conducting the study. The extremely small number of missing administration records suggests that the the Vanderbilt eMAR system (the HED) feature that reminds the nurses to document every scheduled medication dose is effective. The non-administration rate represented a small proportion (< 3%) of all the medication orders for this population. Requiring the nurses to provide a reason for each non-administration documents the rationale for the deviation from orders and illustrates a high level of discretion used by nurses based on the application of hospital protocols. The medication class distribution for *non-admin* orders suggests that they are associated with the ATC class of medication (based on the χ^2 test between the non-admin orders and all orders detailed in chapter 2). Nurses might be considering the medication type and its effect in the instances when a medication is not administered as ordered.

. Such deviations may be in the patient’s best interest; however, further research may be needed to explore the repercussions of missing medications in specific classes and the corresponding patient outcome.

This study also illustrated an elegant example of applying HIT techniques to discern the quality improvement cues in the CDR data (as described in chapter 4), rather than evaluating the QI efforts using manual data collection process – as it was done for “Golden Hour”. The ‘perturbations’ detected by the HIT techniques can be explored further to analyze whether the processes are better or worse in certain locales, providing the opportunity to improve quality, safety, and effectiveness of hospital processes. Appropriate planning of a QI effort in conjunction with a quality CDR can make the evaluation of the QI implementation much more efficient, leaving the resources (especially the clinical staff) for more important tasks – such as caring for the patients.

In part due to the 2009 HITECH Act’s financial incentives^{56,63}, EHR system usage has penetrated to varying degrees in healthcare practices of various sizes⁵⁵. These EHR systems collect and create healthcare data by virtue of their operational use. Unlike the old paper-based systems, the EHR systems not only increase the availability of the rich healthcare data but also facilitate its secondary use making it conducive to healthcare research and analytics^{64–66}. Recognizing this utility institutions accumulate the healthcare data in CDRs⁶⁷ that enable research across diverse dimensions^{42–44}. However, the quality of the research outcome is dependent on the merit, integrity, and constitution of the source CDR (more on this in limitations).

Limitations:

This research was a comprehensive study of medication process at VCH without focus on any specific aspect. The purpose of the study was to conduct a top-down assessment to establish the baseline performance of the medication administration process and to gather signs that indicated anomalies, oddities, or non-intuitive patterns to spur further investigation. Though this study provided some indications of inefficiencies, anomalies, and disparities in the medication processes (as indicated in chapters 2 and 3), additional investigative studies would be needed to provide any direct or conclusive causes for those findings.

The segregation of the medication orders from an all-inclusive dataset of orders was not perfect. However, it was sufficiently accurate for the high-level analysis. Matching with the ATC class also helped to filter out the non-medication orders.

There were challenges and impediments in ‘reaching’ and accessing the medication process data. However, once those barriers were tackled, the quality and consistency of the data in the EDW (the Vanderbilt CDR) was found to be sufficiently good. In the process of extracting and analyzing the medication process data, numerous tests and cross querying were conducted to ensure the data consistency.

It is important to call attention to the fact that I do not have any formal qualification in the medical or clinical practice and patient care. However, the necessary supervision and oversight with respect to the clinical practice and patient care was provided by the dissertation committee chairman and members of the committee. I also participated in observational rounds with the clinicians for several weeks to understand the medication administration process.

Future Directions

I would like to extend the medication compliance study beyond just the missing doses and administration times. In the future studies I plan to include the dose-amount, time, form, route, etc., and explore the compliance across the 7 rights of the nursing practice⁵². Additional worthwhile work would be an attempt to link data from the Vanderbilt adverse outcome reporting database ‘Veritas’ related to medication errors to data from the administration study to explore whether associations can be extrapolated.

The future research would consist of well-designed mix of qualitative and quantitative studies. The quantitative studies would be based on data analysis and focus on specific aspects starting with a lead from this comprehensive analysis. Such qualitative studies might include observational studies of medication dispensing and administration processes during specific scheduled hours or for the medications of specific ATC class(es).

The outcomes of the missing doses and medication process time-interval analyses provided various pointers to conduct focused studies. For example, the missed and non-administered doses analysis indicated that the non-administration is somehow associated with the medication type (ATC class). Further investigation is needed to determine and assess the specific reasons for this association. The non-administration analysis also indicated the association of patient conditions (sleeping, sedated, no-IV access, etc.). These factors must be investigated further to determine the consequences and significance thereof. Such investigations may address questions such as ‘do the administrations of certain class involve work-around due to specific additional steps required?’ or ‘are their certain procedures / steps that abruptly end or must be retraced because of specific situation (patient sleeping or sedated).

The qualitative research may involve observational studies. For example, the outcomes of the time-interval analyses revealed some unanswered questions (e.g., why are the administration times for medications of ATC class ‘G’ – Genito-urinary and Sex hormones – longer and widely varying compared to those for the medications of other classes, or why are there administration bottlenecks for medications scheduled during hours 7, 9, and 11). Appropriately designed observational studies that understand the workflow of nurses, and analyze various process components of the medication administration for those specific orders or hours of the day, can address those questions. The findings of the qualitative observational studies may be further resolved or explored by conducting surveys among the nursing staff, which will help to understand the reasons for specific observations.

It is necessary to indicate that any subsequent studies should be conducted by teams that include clinicians. Clinicians provide the required knowledge and perspective to study the medication processes including the ordering, dispensing, and administration. It is not feasible to conduct proper analytical studies (qualitative or quantitative) of the medication processes without a thorough knowledge about the clinical practice, which can be provided by a practicing clinician.

Conclusion

This study demonstrates that rich information can be obtained from the analysis of medication administration process data contained in a CDR. This study was able to establish a baseline performance for the medication administration process at the VCH. Studying the missing or non-administered doses and the time-intervals from various perspectives can provide clues to the constituent components of the medication processes and indications to the scope of improvements in the medication processes.

This study also provided a high level understanding of the delays and bottlenecks in the medication administration process (e.g., longer median times with wider variations for certain scheduled hours). From the outcome of this analysis, however, it is not feasible to draw direct conclusions with respect to the origins and causes of the observed process behaviors. These outcomes will require further observational studies and interviews with the staff and stakeholders.

I hope to continue working towards studying the quality metrics for medication process and plan to conduct focused studies based on the outcomes of this primary or comprehensive study. I also hope to push towards improving the quality of data, and storage thereof, in the EDW along with creation of appropriate metadata to cater to the research community.

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APPENDIX – A

Challenges

The data required for Medication Compliance Study resides in EDW. However, just obtaining access to relevant DB objects in the EDW was not sufficient. This section describes the challenges I faced before obtaining required data resources to execute my dissertation project.

The EDW has two main instances (**Figure 1-1, Chapter 1**) – the production instance BIPROD and the development instance BIDEV. The BIPROD instance has over 12 terabytes (TB) of allocated space, of which about 2.5 TB is occupied by numerous DB objects in hundreds of schemas, storing the most up-to-date data from the operational systems. The EDW supports diverse applications, including billing, finance, administration, and Quality Improvement (QI), among others. Individuals pursuing research projects, after gaining the IRB approval for their research, are granted access to the relevant objects in BIPROD with an appropriate user role. The instance BIDEV is used for development and working storage purposes.

The Medication Compliance Study was granted the usual access to BIPROD and BIDEV instances after its IRB approval. However, processing a significant bulk of medication data required a substantial working storage space to store and process intermediate objects. An independent access to BIPROD, distinct from BIDEV, did not meet the data processing needs of the study and the EDW usage policy did not allow for working storage allocation in BIPROD.

A successful execution of the project required the ability to use production data in conjunction with the intermediate objects stored in the working storage in BIDEV. Additionally, the working storage available in BIDEV had limited free space and consisted of a common pool shared by the 100s of other EDW users. The EDW team had indicated that the BIPROD data is replicated into

BIDEV instance periodically, and can be practically treated as the production data. However, the comparisons of the query results from BIDEV & BIPROD indicated significant mismatches. After several months I convincingly established that the BIDEV data was not a representative of the production data in BIPROD.

I informed the dissertation committee of the three crucial requirements for a successful execution of the Study – the need for a working storage of about 10 gigabytes (GB), access to production data, and an ability to use the production data in conjunction with the intermediate objects in the working storage. With the help of the dissertation committee chair Dr. Christoph Lehmann and the Department of Biomedical Informatics (DBMI) Chairman Dr. Kevin Johnson, the EDW team assured its support for the DB needs of the study. In February 2014 the EDW team granted a dedicated working storage of 10GB and a DB link from BIDEV to BIPROD. The DB link enabled usage of the production data in conjunction with intermediate objects stored in the BIDEV working storage.

Another challenge in meandering through the DB schemas and corresponding data objects in the EDW is to understand the kind of data stored in those objects. There is no known and consistent source of metadata, or any other documentation, to inform users about the DB schemas and objects therein. The data objects' and attributes' nomenclature is inconsistent and does not indicate the nature of data contained in the objects. The only other resource of this knowledge would be the individuals who have had a long association with the EDW, and know the EDW data objects and their respective functions. Alternatively, Dr. Lehmann helped to confirm that data extracted from a table in the database actually reflected the documentation for a particular patient by using clinical systems like StarPanel or HEO. Knowing, for example, that a patient

had a specific medication ordered from within HEO indicated that I was indeed looking at the correct table in the EDW.

Whitepaper

I compiled a list of known issues and hindrances (commonly faced by other users and students as well) and informed the dissertation committee of these concerns and associated risks during a meeting in April, 2014. A copy this list was also forwarded to the DBMI chairman Dr. Kevin Johnson by a committee member. Subsequently, Dr. Johnson indicated that list of hindrances should be accompanied by appropriate recommendations to fix the associated problems. A whitepaper draft titled “**Recommendations for Database Design and Documentation Procedures**” was sent to Dr. Johnson after finalizing it with the committee chair Dr. Lehmann. The whitepaper is listed in **Appendix–C**.

The Medication Compliance study faced various issues while sourcing data from the EDW. Apparently every fellow student at DBMI has been facing similar problems related to the lack of documentation, data quality, and ability to access data from EDW or other CDRs at VUMC. The recommendations and practices suggested in the whitepaper for a good DB design, if adopted, may help future users of the CDRs at VUMC.

The “Code Status” Study

The EDW team granted the working storage space and production data access needs after about a year of negotiations in March 2014. During this time, apart from establishing the incongruence of BIDEV and BIPROD and substantiating the technical aspects of the requirements, I worked on several other data analyses and studies. One such study was that of the “**Code Status**” data, which was collected after introduction of a tool with the same name to create electronic documentation of the end-of-life (EoL) care directives of the patients admitted to VUMC

hospitals. Code Status data analysis is another good example of using EHR data from EDW. Subsequently this analysis was published as the paper⁷¹ titled “**Code Status and Resuscitation options in the electronic health record**” in “*Resuscitation*”, an Elsevier Journal. This paper is listed in **Appendix – B**.

APPENDIX – B

Code Status and Resuscitation Options in the Electronic Health Record⁷¹

Introduction

Resuscitation management in hospitals is driven by the patient's code-status. Discussing the end of life (EoL) decisions prior to clinical deterioration is labor intensive and potentially stressful for both patients and providers; however, it can improve care and quality of life, lead to the end-of-life experience desired by the patient,^{72,73} and decrease the cost of care.⁷⁴ A recent study showed that the patients who had prepared advance directives received care that was strongly associated with their preferences.⁷⁵ While patients may have advance directives for EoL care prepared prior to hospitalization, operationalizing these instructions requires translating them into a code-status. The establishment of code-status requires first a discussion between a provider and a patient or his designee, exploring the patient's preferences in the case of a cardiopulmonary arrest. The Code-status document is subsequently created to describe and share the patients' desires for EoL care in and is important in preventing undesired resuscitation.⁷⁶ It provides a predictable environment for patients, families, and providers.⁷⁷ Rates of code-status documentation remain low even among terminally ill patients,⁷⁸ and racial disparities in the implementation of advanced EoL directives have been observed.⁷⁹

A code-status is only useful if it can be easily located when needed. At Vanderbilt University Medical Center (VUMC), documentation of code-status was previously done on paper and remained elusive for decision-making purposes. Capturing code-status in the hospital electronic health record was anticipated to facilitate better distribution of information and improved decision making.

Pediatric CODE STATUS Form

Date 05/13/2014 Time 15:44

PREVIOUS CODE STATUS:

ESTABLISH CODE STATUS AS:

[Link to policy](#)

[Link to provider education handout](#)

- FULL CODE: In the event of a pulseless cardiac arrest, resuscitative measures are initiated.
- DO NOT RESUSCITATE (DNR): In the event of impending failure, provide all medically appropriate care not refused by the patient/surrogate/family (which may include intubation). In the event of a pulseless cardiac arrest, resuscitative measures, including endotracheal intubation, are not attempted.
- LIMITED RESUSCITATION (LIMITED): In the event of an acute deterioration in a s status, some or all of the emergent management is limited as below:
 - Withhold Antiarrhythmics
 - Withhold Intravenous Vasoactive Drugs
 - Withhold Defibrillation/ Cardioversion
 - Withhold Chest Compression
 - Withhold Ventilation by Mask
 - Withhold Endotracheal Intubation
 - Withhold Mechanical Ventilation
 - Withhold Other CPR Measures(specify): _____

1. REASONS FOR CODE STATUS ORDER (check all that apply):

- Patient's condition irreversible, death imminent/limited life expectancy
- Requested by Patient/Parent/Legal Guardian
- Designated Power of Attorney (POA) or surrogate consistent with patient wishes and best interests.
- Advance Directive (specify): _____
- Other (specify): _____

2. PATIENT'S DECISION MAKING CAPACITY: Present Absent Variable

3. DISCUSSION OF CODE STATUS HAS OCCURED WITH (check all that apply):

- Patient/Parent/Legal Guardian
 - Power of Attorney for Health Care Decisions
 - Other (specify): _____
- Name if not patient: _____

4. DISCUSSION OF CODE STATUS WAS PERFORMED BY:

- Primary Attending Physician
- Consulting Physician (specify) : _____
- Fellow (specify) : _____
- Resident (specify) : _____
- APN Nurse Practitioner / Physician's Assistant (specify) : _____
- Other (specify) : _____

I am an attending physician

Attending M.D. to approve: _____

Note: Please contact the Help Desk if the attending to approve can not be found in the autocompleter.

Comments

(clear)

(insert time)

Save As Final

Cancel and Exit

Figure 1: Code Status Documentation Form lists the five questions that are addressed when provider discusses Code Status options with a patient.

In 2012, VUMC introduced a tool for electronic documentation of code-status for patients admitted to the hospital. Providers place code-status orders in the Computerized Provider Order Entry system after documenting answers to five questions (**Figure 1**). The tool provides links to

a user-friendly reference guide and the hospital policy within the body of the documentation form. Completion of the code-status form populates the corresponding code-status field in the electronic health records, indicating the (un)desired interventions in the header of the patient's chart. Completion of the form is optional; if not completed, the code-status field in the electronic health record remains undocumented. Electronic storage enables automatic display of the code-status in handover tools, provider communication, or other documentation. At the time of readmission, a patient's code-status from the previous encounter automatically populates the field with the prior date and a reminder for verification. The patient may change or re-affirm the status at this time.

The new code-status field offered the opportunity to assess its documentation. Earlier code-status studies have focused on smaller subsets of patient populations,^{79,80} often constrained to terminally ill patients.⁷³ This descriptive study considers the complete inpatient population for a 909-bed university teaching hospital over a period of one year. The study design allows understanding of the factors influencing the code-status documentation and explores the utilization of the code-status tool. The study was approved by the Vanderbilt IRB after an expedited review.

Methods

In this retrospective study, we analyze the existing code-status data in the VUMC electronic health records with respect to patient age, gender, race, length of stay (LoS), severity of illness as measured by days in an ICU (ICU-days), death during the visit, proximity of primary residence to the hospital, and code-status updates during the hospital encounter.

We collected encounter data for patients admitted to the Vanderbilt University Hospital (VUH) and Monroe Carrel Jr. Children’s Hospital at Vanderbilt (VCH) for 12 months (01-APR-2012 – 31-MAR-2013). For each encounter, we tracked the code-status attribute (**Table 1**). In the design of the tool, adult and pediatric providers expressed different needs for code-status states. While adults had the status DNR_DNI (do not resuscitate, do not intubate), the pediatric providers had the option to document a LIMITED status where interventions could be individually declined by patients and families. An undocumented (NULL value) code-status attribute in the patient record indicated that the code-status was not recorded for the patient. VUMC policy treats an undocumented code-status as a desire for the standard of care, which is full resuscitation (FULL_CODE). With a documented FULL_CODE, however, a team knows that a discussion took place and that resuscitation is desired. This understanding is missing for an undocumented code-status.

Table 1: Description of the end-of-life care code (Code Status) used for this study for respective patient population

Code	Description	Adult Patient	Pediatric Patient
Undocumented	Not provided by patient. [Would default to “FULL_CODE”.]	X	X
FULL_CODE	Take every measure to resuscitate the patient	X	X
DNR	Do not resuscitate	X	X
DNR_DNI	Do not resuscitate and for impending respiratory failure, do not Intubate	X	
LIMITED	The DNR is limited NOT to take one or more of the following steps / actions as requested by patient. <ul style="list-style-type: none"> - WITHHOLD Antiarrhythmics - WITHHOLD IV Vasoactive Drugs - WITHHOLD Defibrillation / Cardioversion - WITHHOLD Chest Compression - WITHHOLD Ventilation by Mask - WITHHOLD Endotracheal Intubation - WITHHOLD Mechanical Ventilation - WITHHOLD Other CPR measures 		X

The adult and pediatric patients' data were analyzed separately. Encounter records for patients admitted before their 18th birthday were included in the pediatric set, the remainder in the adult set.

Some anomalies in the data records required data cleaning:

- Some patients had multiple notes by different providers (resident, attending) documenting the death. Since notes are written after the fact, the time-stamp of the earliest note was taken as the time of death.
- A small proportion (476 of 213,037) of encounter records with duplicate encounter numbers were discarded

Patients were categorized by code-status, which was then compared to age, number of encounters, LoS, and ICU-days during the 12 months study period. The LoS and ICU-days were summed over all the encounters of an individual patient. Chi-square analysis was used for parameters such as gender, race, ethnicity, etc., while T-test was used for the continuous variables like number of encounters, LoS, and ICU-days. We used statistical package R [64-bit version 2.15.2 (2012-10-26)] for statistical analyses and a p-value of 0.05 as the threshold for statistical significance.

Results

There were 83,248 distinct adult patients with **131,399** encounters (average 1.6 per adult patient) and 55,656 distinct pediatric patients with **80,778** encounters (average 1.5 per pediatric patient).

Table 2 shows the code-status distribution and survival status at the end of the study for adult and pediatric populations along with the respective proportions.

Table 2: Survival status and Code Status categories

Cohort	Survival Status (% of all Patients)	Code Status [% of patients with given Survival Status]				
		Undocumented	FULL_CODE	DNR	DNR_DNI	LIMITED
Adult	All (100) 83,248	78,823 [94.7]	2,052 [2.5]	494 [0.6]	1,879 [2.3]	N/A
	Death (1.56) 1,300	374 [28.8]	34 [2.6]	322 [24.8]	570 [43.8]	N/A
	Survival (98.44) 81,948	78,449 [95.7]	2,018 [2.5]	172 [0.2]	1,309 [1.6]	N/A
Pediatric	All (100) 55,656	55,567 [99.8]	9 [0.02]	66 [0.12]	N/A	14 [0.03]
	Death (0.35) 195	137 [70.3]	1 [0.52]	49 [25.1]	N/A	8 [4.1]
	Survival (99.65) 55,461	55,430 [99.9]	8 [0.01]	17 [0.03]	N/A	6 [0.01]

Adult patients – Code Status

Adult patients with documented code-status were older. Patients with a recorded FULL_CODE status were younger than those with a DNR (DNR / DNR_DNI). The average age of adult patients with a documented code-status was 15 years higher than those without one (**Table 3**). Among the patients with a code-status, those with FULL_CODE were almost 11 years older than those with a DNR code (DNR / DNR_DNI).

During the study period, the adult patients with a documented code-status had more encounters (2.6) compared to those without code-status (1.5). Among the adult patients with a code-status, those with FULL_CODE had more encounters (3.1) than those with a DNR code (2.2).

Adult patients with a code-status had over 4 times the LoS compared to those without (13.2 vs. 2.9). Among the adult patients with a code-status, those with FULL_CODE had a mean LoS of 13.9 days compared to 12.8 days for those with a DNR (DNR / DNR_DNI). Adult ICU patients without a code-status (n=8,873) had a mean ICU stay of 5.8 days compared to 8.2 days for those

admitted to an ICU with a code-status (n=2,486). Among the adult patients with a code-status, those with FULL_CODE and admitted to an ICU (n= 898) had a mean ICU stay of 8.4 days compared to 8.1 days for patients with a DNR code (n=1,588).

Table 3: Age, Encounters, LoS, and ICU-days for different Code Status categories [Adult (n=83,248) and pediatric patients (n=55,656)]

Parameter	No Code Status	Some Code Status	FULL_CODE	*DNR/ DNR_DNI	p-value
Adult Patients					
Avg. Age (Years)	47.0 ¹	62.2 ²			< 0.01
	47.0 ¹		56.4 ²		< 0.01
			56.4 ²	67.2 ²	< 0.01
Encounters	1.5	2.6			< 0.01
	1.5		3.1		< 0.01
			3.1	2.2	< 0.01
Length of Stay (days)	2.9 ³	13.3 ³			< 0.01
	2.9 ³		13.9 ³		< 0.01
			13.9 ³	12.8 ³	< 0.05
ICU (days)	5.8 ³	8.2 ³			< 0.01
	5.8 ³		8.4 ³		< 0.01
			8.4 ³	8.1 ³	0.47
Pediatric Patients					
Avg. Age (Years)	6.1 ¹	5.8 ²			0.67
	6.1 ¹		10.2 ²		0.14
			10.2 ²	5.3 ²	0.09
Encounters	1.4	3.4			< 0.01
	1.4		3.2		0.19
			3.2	3.5	0.86
Length of Stay (days)	2.5 ³	39.9 ³			< 0.05
	2.5 ³		17.6 ³		< 0.05
			17.6 ³	42.4 ³	< 0.01
ICU (days)	11.9 ³	33.1 ³			< 0.01
	11.9 ³		13.2 ³		0.75
			13.2 ³	34.9 ³	< 0.05

* DNR / LIMITED for pediatric patients

¹ Age calculated at the earliest encounter

² Age calculated at the earliest code-status recorded

³ Days indicating Avg. of sum over all encounters of individual patients

Survival Status: Among the adult patients who died during the study period, over two thirds (892 of 1,300) had a DNR (DNR / DNR_DNI) code documented. About a third of the adult patients (892 of 2,373) with a DNR code died during the study period, compared to less than 2% (34 of 2,052) of those with a FULL_CODE (**Table 2**).

Table 4: Chi-Square test for association with demographics for adult and pediatric patients

The counts exclude – 53 adult (20 pediatric) patients with unknown gender, 3 adult (1 pediatric) patients with race attribute unpopulated, and 147 adult (60 pediatric) patients with ethnicity attribute unpopulated. [These numbers may not be mutually exclusive.]

Parameter	Value	With Code Status [count (%)]	Without Code Status [count (%)]	p-value for Chi-Sq. comparing distributions (with & without CS)
Adult Patients				
Gender	M	2,308 (6.2)	34,892 (93.8)	< 0.01
	F	2,117 (4.6)	43,878 (95.4)	
Race	ALASKAN/INDIAN	14 (5.2)	256 (94.8)	< 0.01
	ASIAN / PACIFIC ISLAND	37 (2.7)	1,345 (97.3)	
	BLACK	624 (4.6)	13,004 (95.4)	
	UNKNOWN / DECLINED	212 (6.7)	2,952 (93.3)	
	WHITE	3,538 (5.5)	61,263 (94.5)	
Ethnicity	HISPANIC/LATINO	75 (2.7)	2,740 (97.3)	< 0.01
	NOT HISPANIC/LATINO	3,642 (5.1)	68,333 (94.9)	
	DECLINED / UNKNOWN	708 (8.5)	7,603 (91.5)	
Dist. From Hospital	Within 25 Miles	2,103 (4.3)	46,538 (95.7)	< 0.01
	> 25 Miles	2,322 (6.7)	32,285 (93.3)	
Pediatric Patients				
Gender	M	54 (0.2)	30,321 (99.8)	0.31
	F	35 (0.1)	25,226 (99.9)	
Race	ALASKAN/INDIAN	0 (0)	222 (100)	0.11
	ASIAN / PACIFIC ISLAND	2 (0.2)	1,313 (99.8)	
	BLACK	13 (0.1)	13,576 (99.9)	
	UNKNOWN / DECLINED	4 (0.1)	4,413 (99.9)	
	WHITE	70 (0.2)	36,042 (99.8)	
Ethnicity	HISPANIC/LATINO	4 (0.1)	6,695 (99.9)	< 0.01
	NOT HISPANIC/LATINO	69 (0.2)	45,526 (99.8)	
	DECLINED / UNKNOWN	16 (0.5)	3,286 (99.5)	
Dist. From Hospital	Within 25 Miles (40.2 KM)	37 (0.1)	40,713 (83.7)	< 0.01
	> 25 Miles (> 40.2 KM)	52 (0.2)	14,854 (42.9)	

Adult patients – Demographic distributions

Table 4 shows the association of gender, race, ethnicity, and distance of residence from hospital to the documentation of code-status for adult patients. Men were more likely than women to have a code-status documented, Hispanics were less likely to have a code-status documented, and those living farther away from hospital were more likely to have a code-status.

Adult patients – code-changes

There were 1,901 distinct adult patients, who had a change in code-status during the study period with a total of 2,015 changes – this includes those who changed from previously undocumented status. The number of encounters, LoS and ICU-days were 3.9, 18.3 days, and 9.4 days, respectively, for the patients who had a changed code-status during the study; the respective values for those with no code-status change were 1.5, 3.1 days, and 6 days. **Table 5** provides the comparison of the number of encounters, LoS and ICU days for the adult patients with and without a change in the code-status – along with respective p-values.

Table 5: LoS and ICU-days for adult and pediatric patients who did / did-not change the Code Status during the study period

³ Days indicating avg. of sum over all encounters for individual patient

⁴ Code Status change including the change from previous undocumented status

⁵ Avg. number of encounters

Parameter	Code Status Changed ⁴	Code Status Not Changed ⁴	p-value
Adult Patients			
Number of Encounters	3.9 ⁵	1.5 ⁵	< 0.01
Length of Stay (days)	18.3 ³	3.1 ³	< 0.01
ICU (days)	9.4 ³	6.0 ³	< 0.01
Adult Patients			
Number of Encounters	6.2 ⁵	1.4 ⁵	< 0.01
Length of Stay (days)	33.1 ³	2.5 ³	< 0.01
ICU (days)	15.7 ³	12.3 ³	0.30

Pediatric patients – Code Status

The average age of pediatric patients with a code-status was 5.8 years as compared to 6.1 years for those without (**Table 3**). Among the pediatric patients with a code-status, those with a FULL_CODE had an average age of 10.2 years and those with a DNR (DNR / LIMITED) code 5.3 years.

Pediatric patients with a documented code-status had more number of encounters (3.4) compared to those without (1.4). Among the pediatric patients with a code-status, those with a FULL_CODE had fewer encounters (3.2) compared to those with a DNR code (3.5) – but this difference was insignificant.

Pediatric patients with a code-status had almost 16 times the LoS compared to those without (39.9 vs. 2.5 days). The longer LoS for the pediatric patients with a code-status is mainly attributable to those with a DNR (DNR / LIMITED) since the mean LoS for them was significantly longer (42.4 days) compared to those with a FULL_CODE (17.6 days). Pediatric patients without a code-status, who were admitted to an ICU (n=3,589), had a mean ICU stay of 11.9 days compared to 33.1 days for those ICU patients with a code-status (n=75). Among the pediatric patients with a code-status, those with a DNR (DNR / LIMITED) code (n=69) had a mean ICU stay of 34.9 days compared to that of 13.2 days for those with a FULL_CODE.

Survival Status: Among the pediatric patients who died during the study period, over a quarter (57 of 195) had a DNR (DNR / LIMITED) code documented. Of all pediatric patients with a DNR code, ~71% (57 of 80) died during the study period, compared to ~ 11% (1 of 9) of those with a FULL_CODE (**Table 2**).

Pediatric patients – Demographic distributions

Table 4 gives the p-values for association of gender, race, ethnicity, and distance of the primary residence from hospital to the recording of code-status for pediatric patients. Similar to the adult population, Hispanics were less likely to have code-status documented, while those living farther away from hospital appear more likely to have a documented code-status. The association of gender and race was not statistically significant.

Pediatric patients – code-changes

There were 42 pediatric patients, whose code-status changed during the study period with a total of 44 changes – this includes those who changed from previously undocumented status. The number of encounters, LoS and ICU-days were 6.2, 33.1 days, and 15.7 days, respectively, for the patients who had changed their code-status during the study; the respective values for those who had no change were 1.5, 2.5 days, and 12.3 days. The comparison for ICU-days between the two groups was not statistically significant (p-value > 0.05). **Table 5** provides the comparison of the number of encounters, LoS, and ICU-days for the pediatric patients with and without a change in the code-status – along with respective p-values.

Discussion

End of life care decisions are frequently made for individuals with a critical health condition and are often prompted by health care providers, who approach the patient or her kin.

Although screening for advance directives is performed for every patient during the admission process, the additional step of establishing a code-status can be quite time consuming and may not be feasible for every admitted patient. Establishing a code-status during the admission may not be possible for patients admitted with altered mental status or inability to communicate.

Moreover, establishing a code-status on every patient could add unnecessary emotional distress to patients who are admitted for a minor illness or procedure. Therefore, the tool is available for widespread use but the discussion is optional.

Despite the limitations on when a code-status can or should be documented, we saw excellent adoption of the new code-status tool. Moreover, because the new tool was tied to attending verification, all code-status documented were guaranteed to have been reviewed by an attending physician. Further, the information is easily accessible and available for use automatically in handoff tools, white boards, or other documentation forms.

For the adult patient cohort, the age at which a patient (or the kin) opts to limit EoL care, and provides DNR choices, tends to be higher. This finding may reflect a provider preference to initiate EoL discussions for older patients. Younger patients tend to opt for FULL_CODE, while DNR is preferred by/for the older individuals.

Number of encounters, LoS, and ICU-days indicate a patient's health status. Sicker patients spend longer time in hospital and the ICU. Additionally, these patients may have more hospital visits (indicated by higher number of encounters and longer LoS). Our study shows that adult patients with a recorded code-status have higher number of encounters, longer LoS, and more ICU-days (**Table 3**). This indicates that a patient's health condition may also influence the EoL care decisions. Patients with FULL_CODE have a longer LoS and ICU-days compared to those with a DNR (DNR / DNR_DNI) status. This may be because of more aggressive treatment of patients with FULL_CODE. A similar (though statistically non-significant) trend is observed for the pediatric patient cohort (**Table 3**). For pediatric patients, therefore, the EoL care decisions appear to be influenced more by the severity of illness than by the age.

The health status of a patient influencing the EoL care decisions is also evident from the number of changes in the code-status by individuals in the adult patient cohort when number of encounters, LoS, and ICU-days are used as proxy for severity of illness. A statistically significant trend of higher number of encounters, LoS, and ICU-days was observed for those who had a change in code-status (**Table 5**). A similar behavior is observed for pediatric patient cohort as well.

Analysis of survival status (**Table 2**) indicated that the death rate among those with a DNR (DNR / DNR_DNI / LIMITED) code is higher compared to those with a FULL_CODE or no documented code. The proportion of death is higher for pediatric patients with a DNR code.

Aggressive medical treatment may not necessarily ease a patient's suffering.⁸¹ Lack of a code-status in the final moments of life may mean unnecessary interventions and procedures, associated with prolonged pain, suffering, and increased avoidable costs. With the introduction of this tool, more than 71% of adult patients who died during the admission had a documented code-status, which reduced uncertainty at the time of cardiopulmonary arrest. This study provides the first measure of the presence of code-status in hospitalized patients. Further studies will explore how we can increase the percentage of patients with code-status in the group of patients that expire during their stay.

Usually a code-status is preceded by a discussion between the patient or her kin and the initiating physician. EoL discussions are difficult and stressful for providers, and the utility of a code-status must overcome the provider's inhibition and discomfort to initiate the discussion. Successful EoL decision making may vary based on gender, race, or ethnicity of both patient and provider. Gender,⁸² race, and ethnic⁸³ biases have been reported in the past. An implicit ethnic

bias could be the language barrier. In both the adult and pediatric patient cohorts, Hispanic patients were less likely to have a code-status documented (**Table 4**).

Distance of residence from the hospital was associated with documented code-status. We suspect that the utility for providers to initiate discussions for patients whose next of kin would have to travel longer distances in the event of an arrest may be higher, thus leading to more provider initiated discussions (**Table 4**). A selection bias is another possibility. Patients traveling longer distances may have higher severity of illness, necessitating a referral to a tertiary medical center.

In our study, gender, race, and ethnicity were significantly associated with the presence of a code-status (**Table 4**) in adult patients. This was not the case in pediatric patients. However, analysis of a limited subset of pediatric patients with only ‘Black’ and ‘White’ race attributes indicated statistically significant association of race with the outcome.

Limitations:

For the 12 months’ study period, the proportion of pediatric patients with a documented code-status was relatively small compared to the adult population. The small numbers may have affected statistical significance of some comparisons.

We limited the scope of this study to the basic analysis of the code-status by patient demographics, preventing a complex cross-section of multiple attributes such as nature of illness. Subsequent studies may be planned for specific combination of attributes of interest, including multivariate logistic models.

The ease of accessibility during the handovers of an electronic code-status, rather than in paper format, is an empirical observation and a logical deduction from the experience with the other electronic health data. With no means to assess the paper-based code-status documentation prior

to the introduction of the electronic tool the before-after comparison of the code-status use was not feasible.

An important demographic attribute, the ‘Guardianship Status’, was not available. Guardianship Status may influence the decision to have code-status recorded especially in the case of very old and pediatric patients. Additionally, we did not analyze LIMITED code-status at individual levels due to the small number of pediatric patients with this status. Another attribute not analyzed was the ‘Hospital Service’, because it was not available for over 60% of adult (70% for pediatric) patients.

Conclusion

Availability of advance directives and code-status can be elusive, which can complicate the care delivered to patients during the final moments of life. Absence of a recorded code-status may result in unnecessary interventions. Documenting code-status in electronic records helps to create a ready reference for care providers and facilitates smoother transition of patient care.

To our knowledge, this is the first study attempting to determine the code-status documentation prevalence in electronic health records of a large university hospital system. Reviewing the code-status for all inpatient admissions to our adult and children’s hospitals for a year, we observed that for adult patients, age, severity of illness, gender, race, and ethnicity were associated with documented code-status. For the pediatric patients the decision to provide a code-status was associated with the severity of illness and not significantly associated with age.

With the introduction of the code-status tool, 71% of adult patients and 30% of pediatric patients who died had a documented code-status reducing uncertainty and potentially reducing pain,

suffering, and cost. Continued efforts are underway to identify measures that will increase documentation of code-status in populations at highest mortality risk.

Reference to Publication

Details of this project are covered in the following manuscript.

Bhatia, H. L. *et al.* Code status and resuscitation options in the electronic health record.

Resuscitation **87**, 14–20 (2015).

APPENDIX – C

Recommendations for Database Design and Documentation Proceduresⁱ **Haresh Bhatia**

The purpose of the hurdles document was to explore obstacles encountered in the preparation of Haresh's dissertation project. Thus this report is organized around the needs of that specific project. Further thoughts that went into the structure of this paper were the desire to organize around the needs of any general user of a database (DB) at the Vanderbilt University Medical Center (VUMC) – be it Enterprise Data Warehouse (EDW), Synthetic Derivative (SD), or other operational databases. General users include students, staff, new faculty members, and anyone who is granted access to use the database for a given task. Though this document is written with the DBs at the VUMC in mind, it may address similar issues at any other institution. Recommendations other than 'Visibility and Comprehension' apply mostly to the relational DB management systems (RDBMS). Also, some of the points discussed here may not apply to the SD (esp. data structure and maintenance), which uses Netezza, a highly optimized and tuned data warehouse (DW) platform.

1. Visibility and Comprehension

The access to the DBs at the VUMC must be strictly controlled to secure the patient data. However, once an individual is approved and permitted to access a DB, its content should be easily accessible and comprehensible. The DB structures should be lucid, intelligible, and coherent. Some of the aspects that must be considered are listed below.

a. *Documentation of the DB objects and attributes:*

Data needs for various departments and groups often overlap. However, absence of documentation in the data warehouse makes it difficult for individuals from different groups or departments to know the availability, location, and sources of required data. Without such documentation data may often be recreated to satisfy immediate needs, and invariably such recreated 'data silos' continue their life longer than expected because they are easier, and *apparently* efficient, in satisfying immediate needs. Continuing to use data silos can result in data-divergence, which may produce incongruent and inconsistent results. Data silos may also give rise to unwanted redundancies.

The importance of maintaining documentation and a data dictionary, as well as a corresponding web-publication with a single point of entry, would benefit institutions like VUMC. With every new research effort in biomedical informatics, there is a corresponding increase in the implementation of DB objects. At the same time, there is a churn of students every year resulting in substantial loss of institutional memory garnered by them. Given the fact that students are involved in a significant proportion of these projects, locating the relevant information would be easier and less time consuming with

ⁱ The recommendations for "Database procedures and documentation" (DB recommendations paper) is prepared by Haresh Bhatia, subsequent to the document describing "[Hurdles faced by Haresh Bhatia in the process of accessing EDW data](#)" (hurdles document) also prepared by Haresh, at the behest of his committee members during the formal committee meeting for his dissertation project (on April 10, 2014).

online (hyperlinked) documentation rather than approaching the faculty or staff for the details.

Suggestions:

- *Data Models:* [Prevailing data modeling tools](#) are very advanced and quite powerful. These tools provide the concept, context, and relationship of data objects in a model. Additionally, they provide means to create standards, establish terminology, create (hyper-linked) documentation and dictionaries at various levels, post them on the web with appropriate security, and generate (SQL) code for implementation. The web-posting of the model and documentation should be on the secure intranet, unless intended to be open to public.
- *Table and column comments:* This is the most basic method of documenting individual objects and attributes in the databases. Most of the DB management systems (DBMSs) – e.g. Oracle, MySQL, MS-SQL Server, etc. – allow users to add comments for individual tables and columns. Users may document the original purpose, use, processing, and any other details of individual DB objects and the corresponding elements (ample size – up to several KB – is allowed for individual comment).

Creating and maintaining DB documentation is an investment, rather than an expenditure, that saves time on every next generation of individuals using the data without prior knowledge of the information contained in the DB.

b. ***Standard and Consistent vocabulary:***

Almost every language, including English, has polysemantic and synonymous terms for concepts. Having a consistent vocabulary for attributes helps to maintain coherence of the data contained in a DB. If any given concept is defined by multiple terms, the resulting data can diverge. Data silos often give rise to this condition.

Consistent vocabulary practice involves use of standard and consistent terms, acronyms, suffixes, and prefixes for objects' and attributes' names. Controlled vocabulary helps to clarify hierarchy and relationship among objects. It also makes documentation precise, concise, and easy to maintain.

There may be occasions for the vocabulary to deviate from these principles (e.g., to accommodate object naming constraints for specific DBMS, or, on rare occasions, when another DB is merged with an existing one). Such instances / exceptions are appropriately clarified in documentation (another importance of the documentation).

Suggestions:

- *Data stewardship:* A group of individuals may be assigned the task of data stewardship (this group may be part of the DB administration / architecture group). Any structural changes for the DB (that the group is responsible for) will have to be routed through this group. The individuals in the group not only insure vocabulary, but also handle the creation and maintenance of the documentation and all the data architectural aspects of the DB.

Data Stewards may also be assigned the task of discouraging the creation of any data silos and assimilating the existing silos into the common (enterprise) data pools that follow standard conventions of creation and maintenance.

- *Percolate the culture of importance of data:* Data is an asset. Inconsistent data will produce inconsistent and erroneous results or information. Every individual must understand the importance of consistency and accuracy of processes. Data should be given similar consideration, given that data persist longer than any process or procedure.

2. Data Structure and Maintenance

There are several aspects to data structure and maintenance. For the purpose of this document, only indexes (keys) and table partitioning is covered. Other important aspects, like backups and disaster recovery procedures and drills, must be considered by the DB administration group.

a. *Indexes:*

For the DBs used mostly for read purposes (e.g., EDW), indexes help with querying the data. Apart from occupying physical memory, unnecessary indexes use additional resources for maintenance and processing (in terms of optimizer statistics and index rebuild after data load). Following facts about indexes may help creating / maintaining indexes.

Redundant Indexes: Multiple indexes with the same leading column(s) are redundant. For example, if a compound index I1 is defined on columns PAT_SEQ + PERFORM_DT + CHART_DT of a table then another index I2 on columns PAT_SEQ + PERFORM_DT would be redundant. Also, in most instances, multiple compound indexes on the same set of columns with different column sequence may not be required. For example, if an index I1 is defined on columns CLASSID + CONCEPTID + CONCEPTTYPE of a table then additional index on columns CONCEPTID + CLASSID + CONCEPTTYPE (first and second columns of index I1 are switched for index I2) is not be required. [In case of Oracle DBMS, the ‘skip scan’ feature uses the index even if the leading column of index is not used in the where clause. Other DBMSs may have similar features.]

Index read is not always faster: If the proportion of data read from a relational table is > 10%, a full table-scan is faster. In DW applications, aggregating queries reading bigger chunks of data from the DB may not use indexes at all. In DBMSs optimizers help select the most efficient execution path for a given query. If the optimizer detects that the aggregating query is using $\geq 10\%$ of data from a given table, it formulates an execution path that bypasses the use of indexes. An index on a table expedites querying data from the table only if the fetched set of data is 2% or less of the table content.

Cardinality: A candidate column (or a group of columns – when considering compound index) considered for index must have a cardinality of 50 or more (so that each individual value may represent an average of 2% of the table records). Candidates with a cardinality of less than 50 must be carefully examined because corresponding indexes may actually hamper the query performance (or make the index redundant – because the optimizer will bypass the index). More details can be found at “[Index read is not always faster](#)”.

Suggestions:

- *For existing DBs:* Compound indexes may be reexamined and redundant indexes may be dropped without any impact on the DB performance. Any index with cardinality of less than 20 may not add to any performance gains from queries and can be considered

to either be dropped or replaced with another appropriate compound index. Indexes with cardinality between 20 and 50 may be examined carefully to confirm if they help any specific set of queries.

- *For new DBs:* The DB index concepts listed above may be followed to create compound indexes with appropriate column order and avoidance of redundancy. Every candidate indexes must have cardinality of 50 or more (candidates with cardinality of < 50 may be thoroughly examined or not be considered index candidates).

b. *Partitioning of tables:*

Partitioning of the tables helps in data maintenance and querying by virtue of partition pruning. Creation of sub-partitions for huge tables extends this feature and helps to maintain data across multiple volumes. Though this feature has existed for more than 10 years, DBs either use it inappropriately or do not use it efficiently. EDW uses a partitioning feature, but it can be more efficient by using sub-partitions. For example, tables in EDW spanning several GBs or several 10s of GBs may be good candidates for sub-partitioning. Also partitioning / sub-partitioning helps in availability of the database (More details can be found at “[Availability of \(access to\) Data](#)”).

3. Availability of (access to) Data

The availability of database is often restricted, citing the maintenance processes that run on the DB – given the overall size of the DB and the intensity of the maintenance or update processes. [For example, I was told that availability of EDW is between 12:00PM and 8:00PM – I have seen it being available at other times but I was discouraged from using it, and I was told that the processes may be killed]. However, we have come a long way from the technological constraints of the early 90’s, when the DBs were blocked from access overnight while the data-feeds were processed. Often DWs get daily / periodic data feeds. The operational DBs may be affected by such processes as rebuilding of indexes or other routine / periodic maintenance. The current business needs call for continuous availability and most of the existing DBMSs incorporate technology to provide it.

For the DWs the periodic incremental data bulk to be loaded is relatively small – and virtually inconsequential to the regular querying of the DW. The periodic loads can be done in a staging area to make sure that the incremental data is clean. The subsequent augmentation of the (clean) incremental bulk to the DW should be transparent to the user-community. As to the other general maintenance of indexes, optimizer statistics etc. (for DW as well as any other DBs), the current DBMS technology provides for the background processes and other features that enable the high-availability of the DB systems.

Suggestions: [Most of this applies to DWs (EDW).]

- *Replication:* Data replication helps with the high-availability of the DBs. While (one of) the replicated instance(s) is available to the users, the master instance can be worked on for required updates.

Replication also allows for creation of a sandbox DBs that contain real data. The sandbox DBs can be used for development, testing, or any other appropriate purposes in research environment.

➤ *Partition switching*: Tactical object (table) partitioning helps with data updates or incremental loads. This technique is highly useful for fact or operational data that are created or updated frequently. The incremental data are loaded into a working copy of appropriate object (table) partition. After a successful load, the working object is switched with the corresponding object partition. This operation is quick, independent of the partition bulk, and does not affect the users. Most of the DBMSs provide this feature.

4. Following data principles may further help

- a. Data are the basis of informatics.
- b. Data are an asset (more so in the current era of informatics).
- c. Procedures and processes change with policy, but data outlive them all.
- d. Research data deserve a robust DB design with standardized vocabulary, terminology, and data-dictionary, rather than ad-hoc data structures with inconsistent terminology.
- e. Existence of data is questionable if it cannot be located or retrieved.

This document describes hurdles faced by Haresh Bhatia in the process of obtaining access to the EDW for his dissertation project titled “*Medication Compliance for Pediatric Inpatients*”. To ensure the brevity of this document the problems are listed as enumerated points.

Background:

- **IRB approval** for the project **received** by **April 2013**. [**Last revision** done in **March 2014**.]
- Haresh had access to production and development instances of EDW, but no ability to access production data from development (this need is explained later, in the list of hurdles).
- Haresh and Chris were given to understand that data in development instance of EDW was essentially a replica of production – albeit lagging in time by a week.

Hurdles:

1. The development instance data of EDW is not a copy of the production data – Several of the crucial data tables (or major partitions thereof) were missing.
2. Because the development data was not workable, it necessitated the use of data in production instance. However, a direct access to production data was not useful since it did not allow any working storage and creation of intermediate objects (necessary for data analyses) in production instance.
3. Though working storage (to create intermediate objects) was available in development instance, it was not useful due to following reasons
 - The working storage requirements for the dissertation project (~10 GB) were higher than the available space (~2GB). [Also, the working storage in the development instance was a common pool; thus the amount of available space was not guaranteed and varied between a few 100 MB to a couple of GB.]
 - The production data was not accessible from the development instance (to enable creation of intermediate data objects in working storage of the development instance).
4. There is no documentation about EDW database with respect to the following –
 - Data models that describe relationship between different data objects / tables. [Data model can also document description about the purpose of individual data tables and attributes.]
 - [Indexes of the EDW objects cannot be relied on to indicate any purpose of, or relationship between, the objects. Additionally, DWs, like EDW, normally do not have any foreign keys to aid discernment of relationships.]
 - Comments in the data dictionary that detail the purpose of individual objects / attributes. [EDW uses DBMS engine by Oracle – which facilitates comments in the data dictionary.]
 - Meta-data reference library (either online or off-line) documenting the DB objects.
5. The knowledge and know-how about the EDW workings and purpose of individual data objects is relatively scattered among the individual working groups (Finance, Pharmacy, data-warehouse maintenance group, etc.)

By the end of March 2014, problems 1 through 3 were resolved by providing a separate working storage of 10GB for Haresh’s dissertation project, and a DB link from development instance to production instance. However, the issues with respect to the problems # 4 and 5 still exist. To be able to conduct a meaningful data analysis, Haresh now relies on obtaining advice from, and discussing with, individual personnel who are knowledgeable about the database.

APPENDIX – D

Supplementary Figures

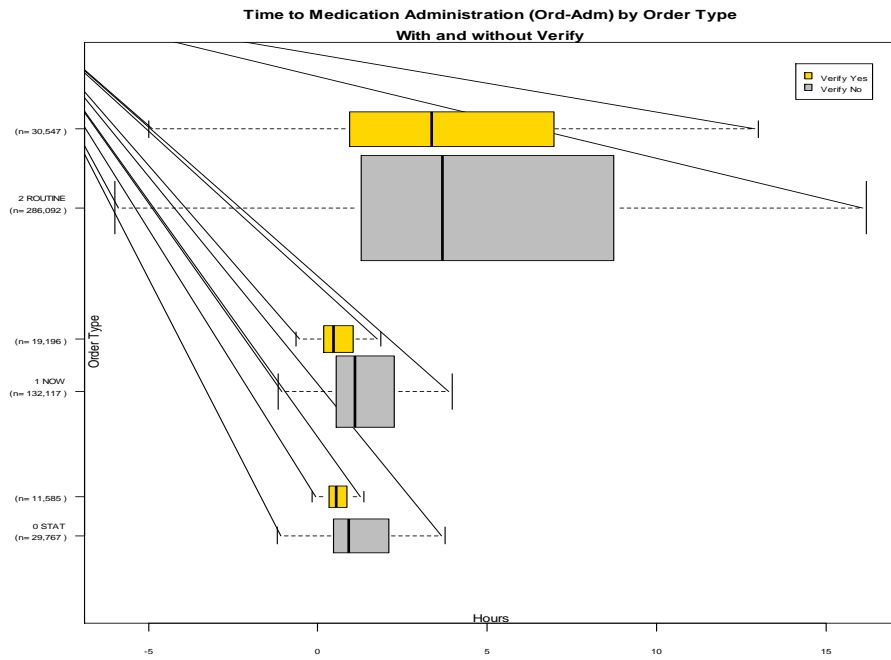


Figure 2-A: Ord-Adm intervals by order type and verify flag. The box-thickness is proportional to, and thus reflects, the number of medication orders (shown in the parentheses) for the respective order types and verify flag values.

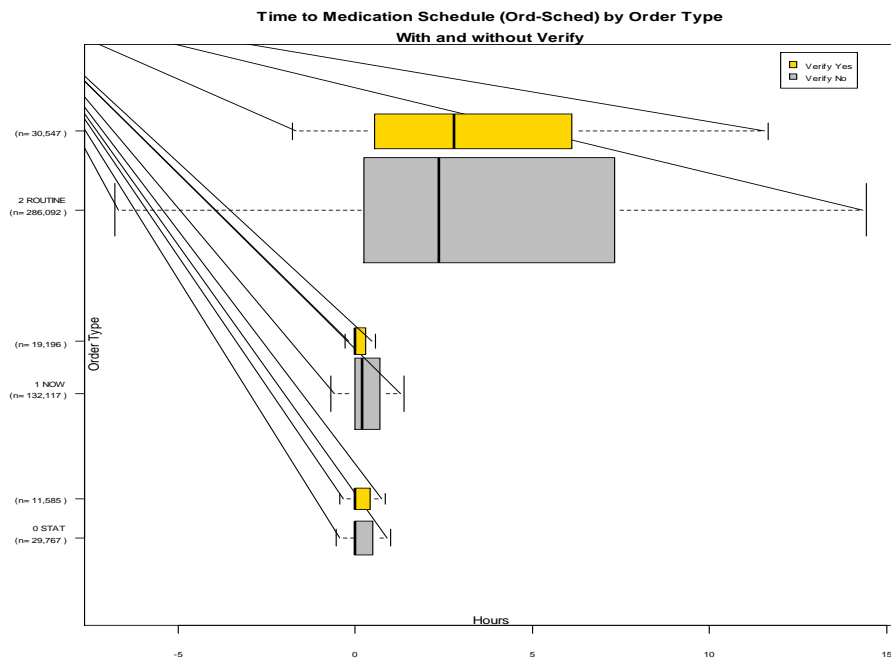


Figure 2-B: Ord-Sched intervals by order type and verify flag. The box-thickness is proportional to, and thus reflects, the number of medication orders (shown in the parentheses) for the respective order types and verify flag values.

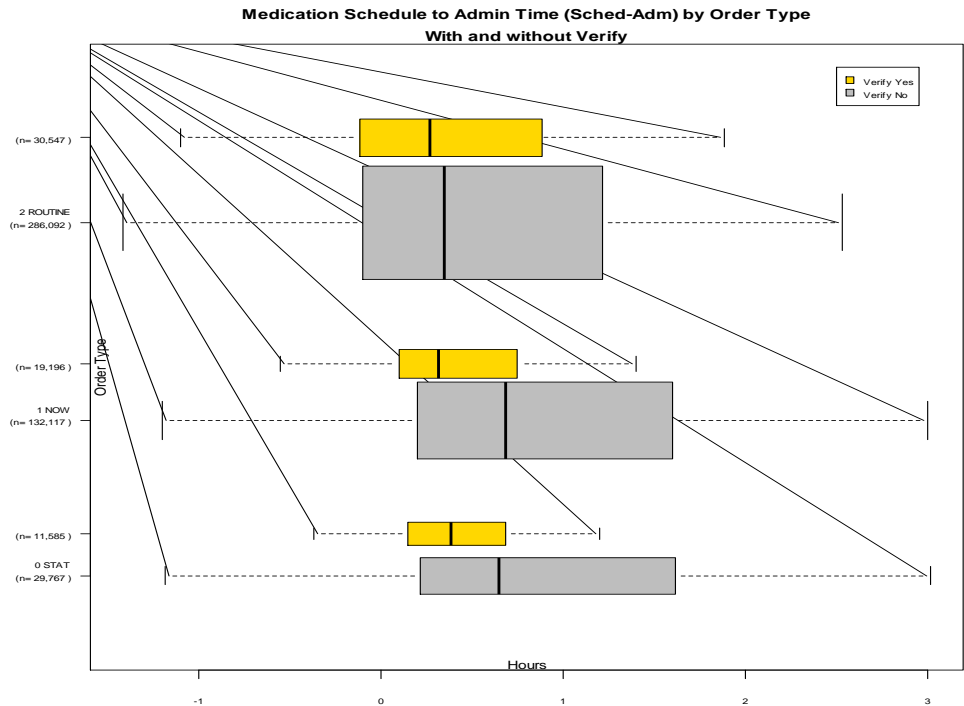


Figure 2-C: Sched-Adm intervals by order type and verify flag. The box-thickness is proportional to, and thus reflects, the number of medication orders (shown in the parentheses) for the respective order types and verify flag values.

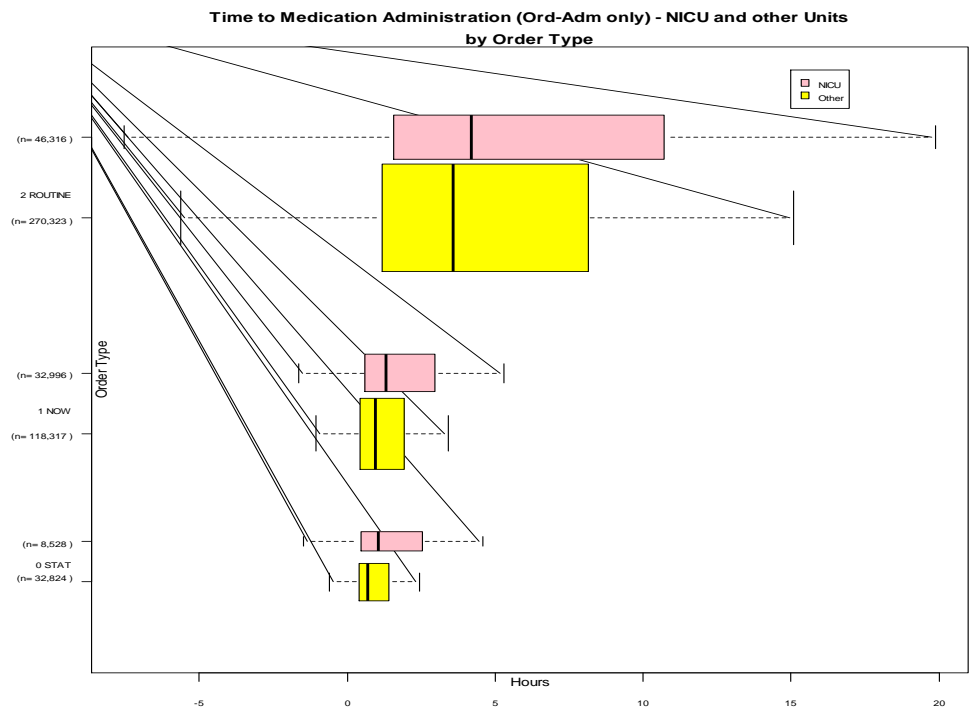


Figure 3-A: Ord-Adm intervals by order and unit type. The box-thickness is proportional to, and thus reflects, the number of medication orders (shown in the parentheses) for the respective order and unit types.

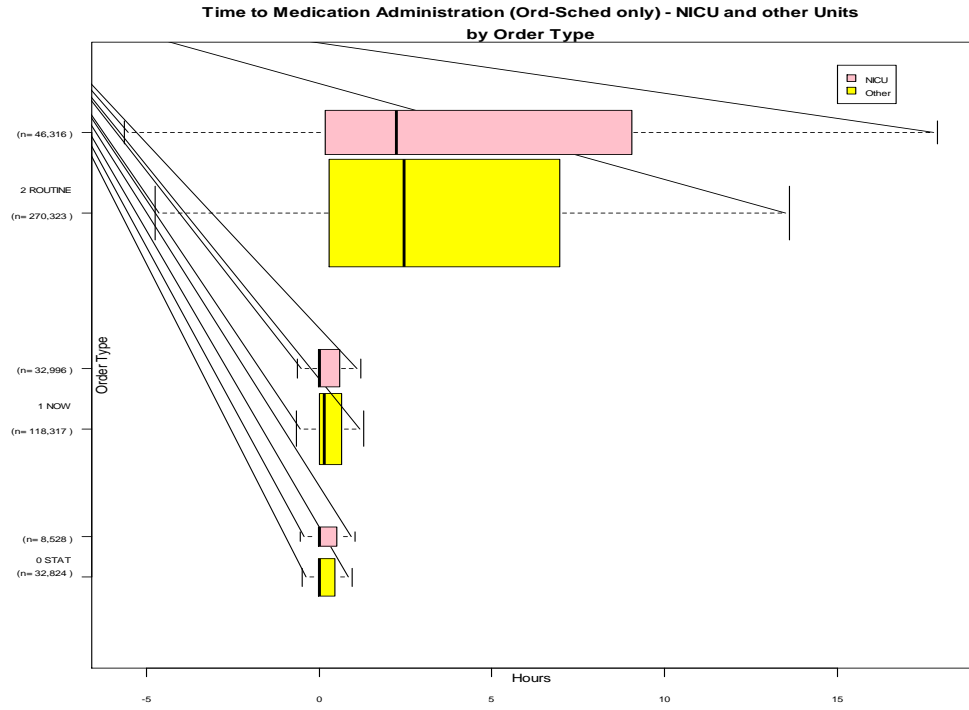


Figure 3-B: Ord-Sched intervals by order and unit type. The box-thickness is proportional to, and thus reflects, the number of medication orders (shown in the parentheses) for the respective order and unit types.

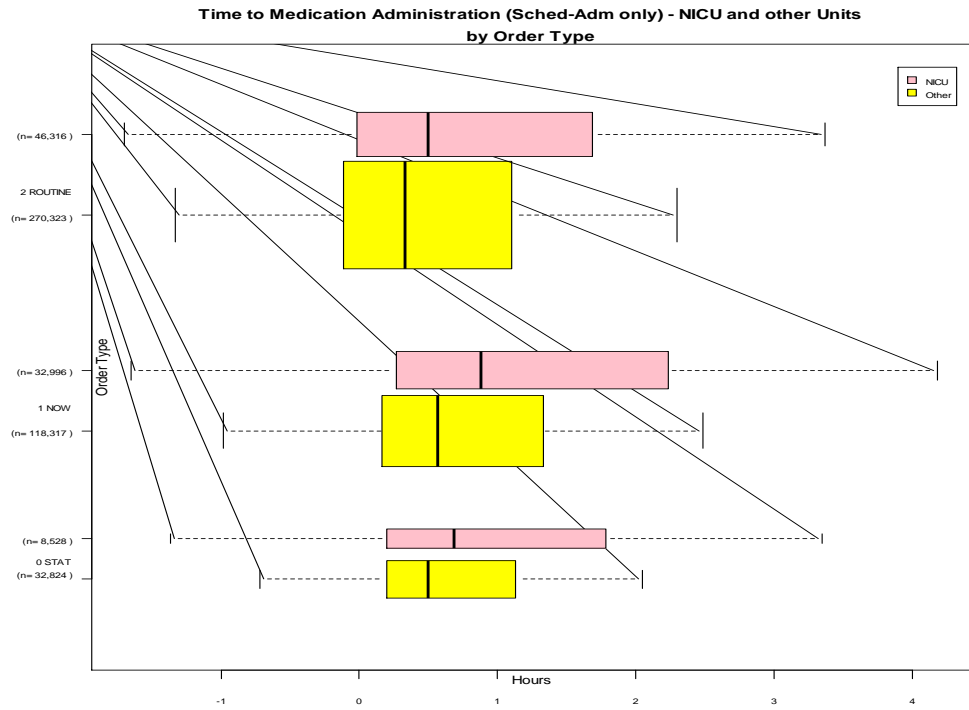


Figure 3-C: Sched-Adm intervals by order and unit type. The box-thickness is proportional to, and thus reflects, the number of medication orders (shown in the parentheses) for the respective order and unit types.

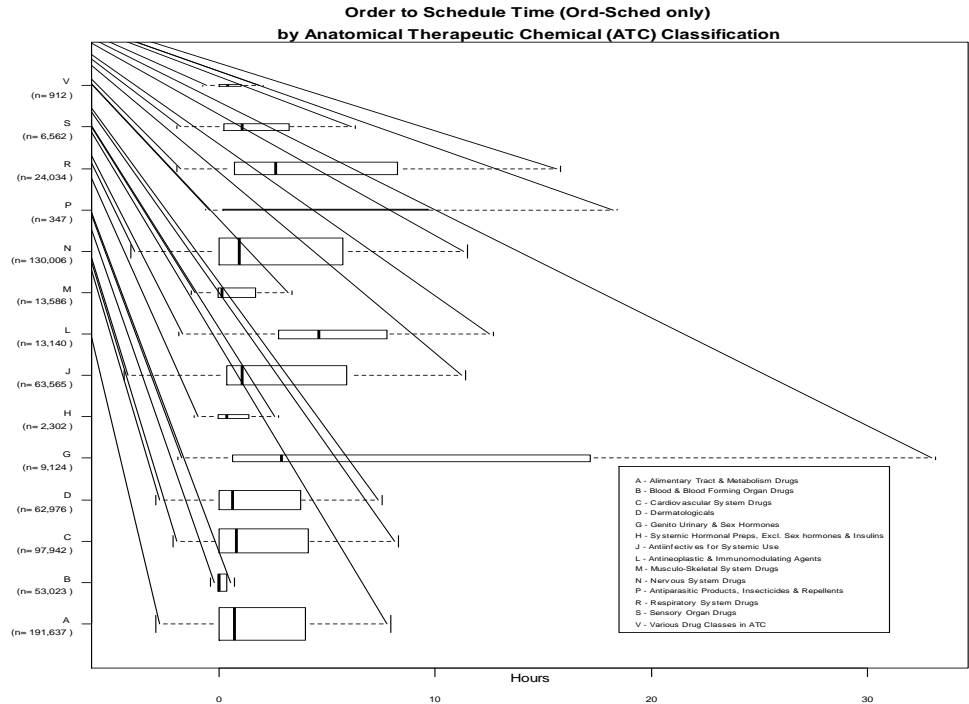


Figure 4-A: Ord-Sched intervals by ATC Class of medication. The box-thickness is proportional to, and thus reflects, the number of medication orders (shown in the parentheses) for the respective ATC classes.

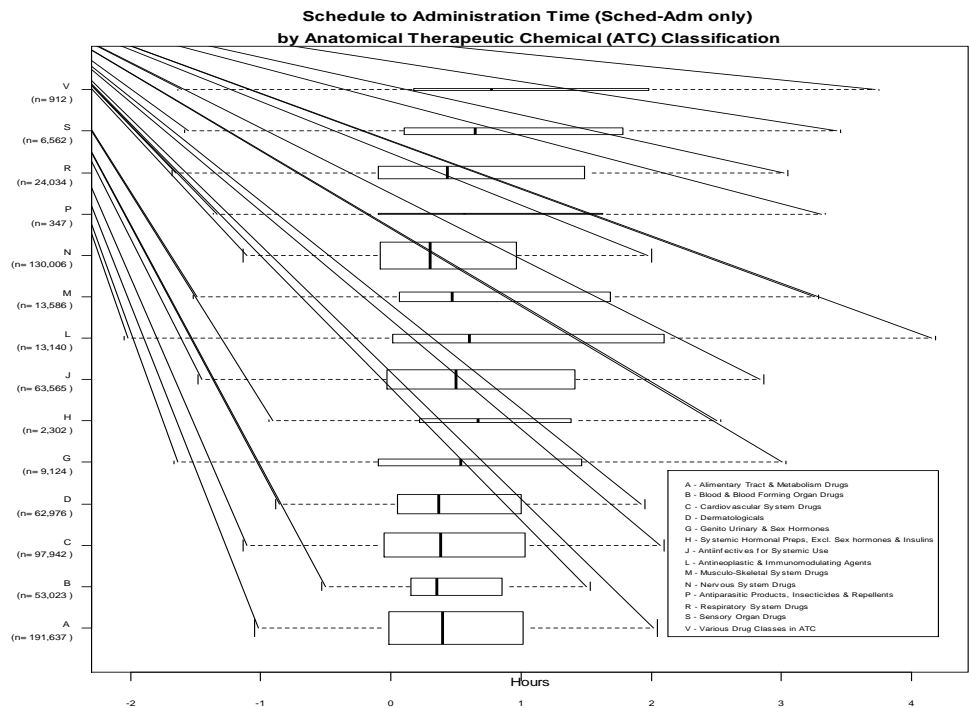


Figure 4-B: Sched-Adm intervals by ATC Class of medication. The box-thickness is proportional to, and thus reflects, the number of medication orders (shown in the parentheses) for the respective ATC classes.

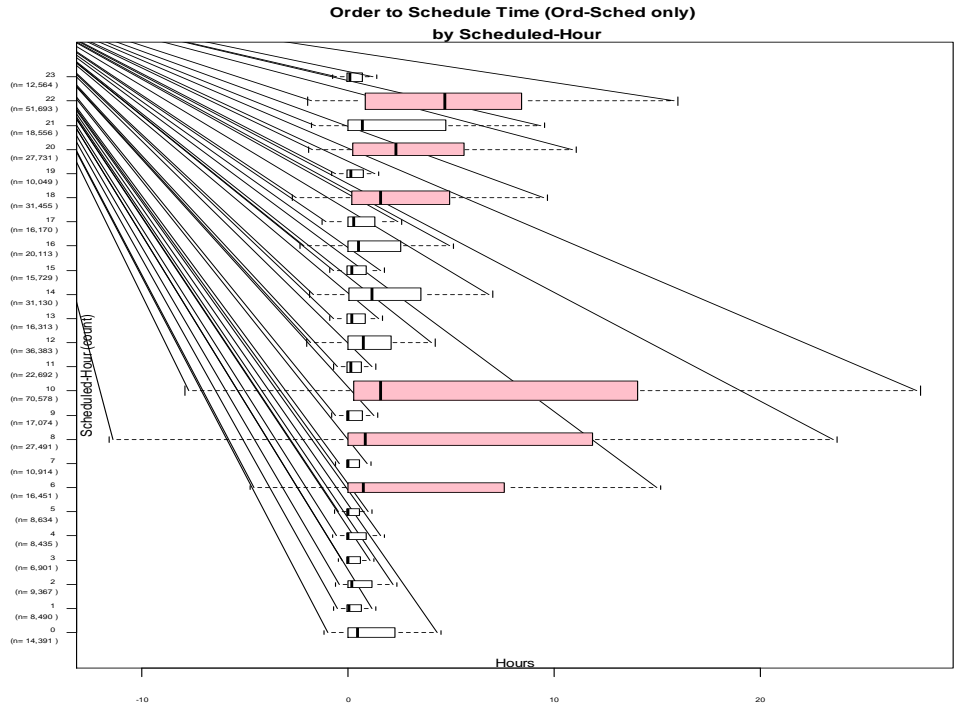


Figure 5-A: Ord-Sched intervals by scheduled hour. The box-thickness is proportional to, and thus reflects, the number of medication orders (shown in the parentheses) for the respective scheduled hours.

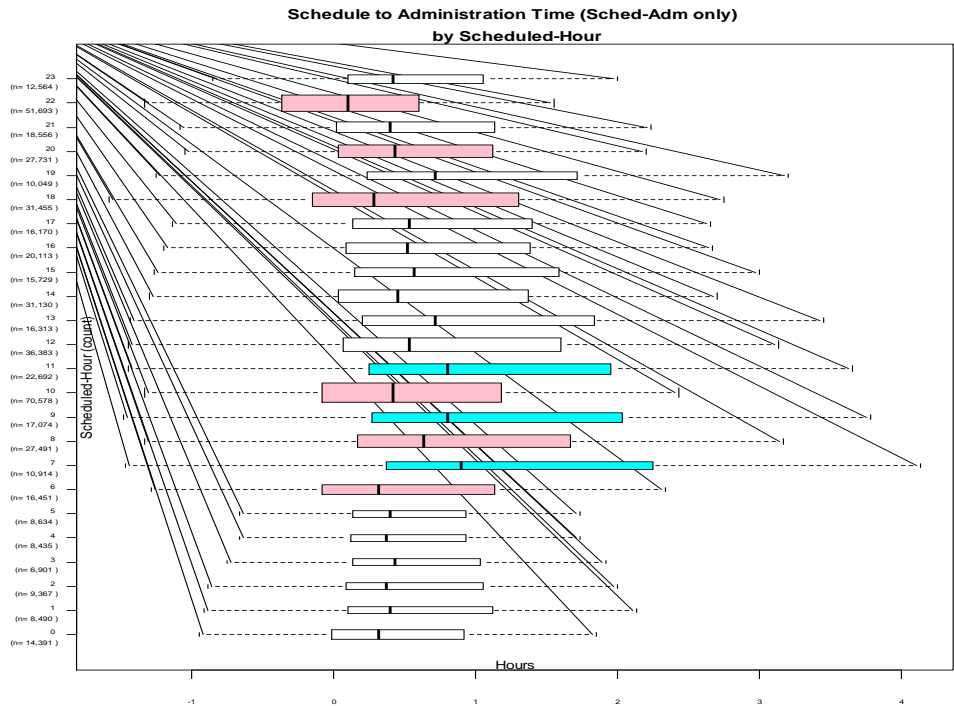


Figure 5-B: Sched-Adm intervals by scheduled hour. The box-thickness is proportional to, and thus reflects, the number of medication orders (shown in the parentheses) for the respective scheduled hours.

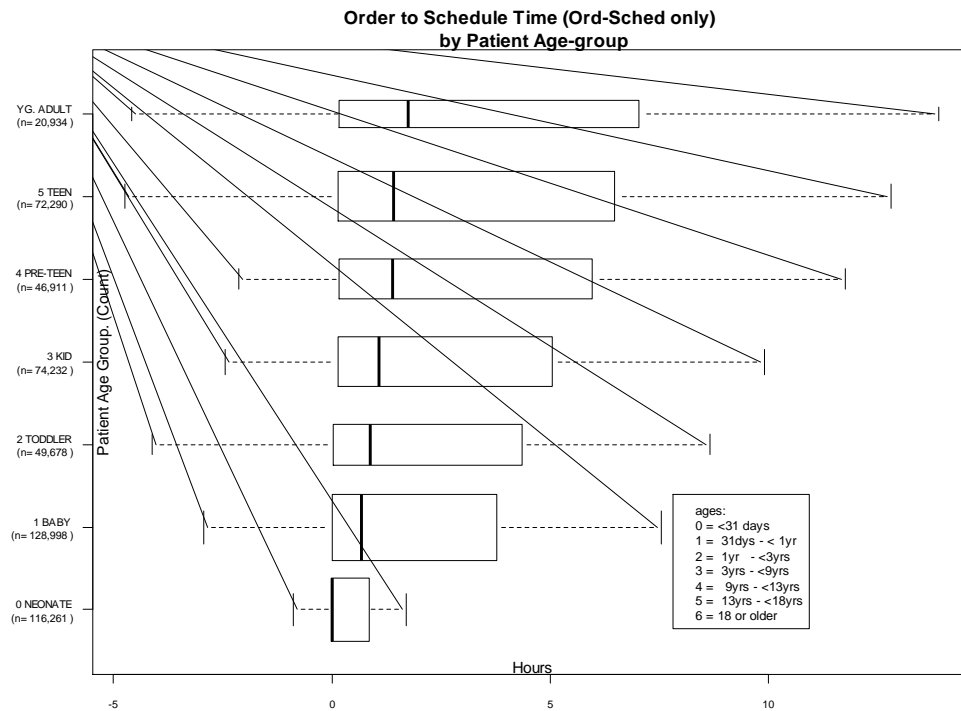


Figure 6-A: Ord-Sched intervals by age group. The box-thickness is proportional to, and thus reflects, the number of medication orders (shown in the parentheses) for the respective age groups.

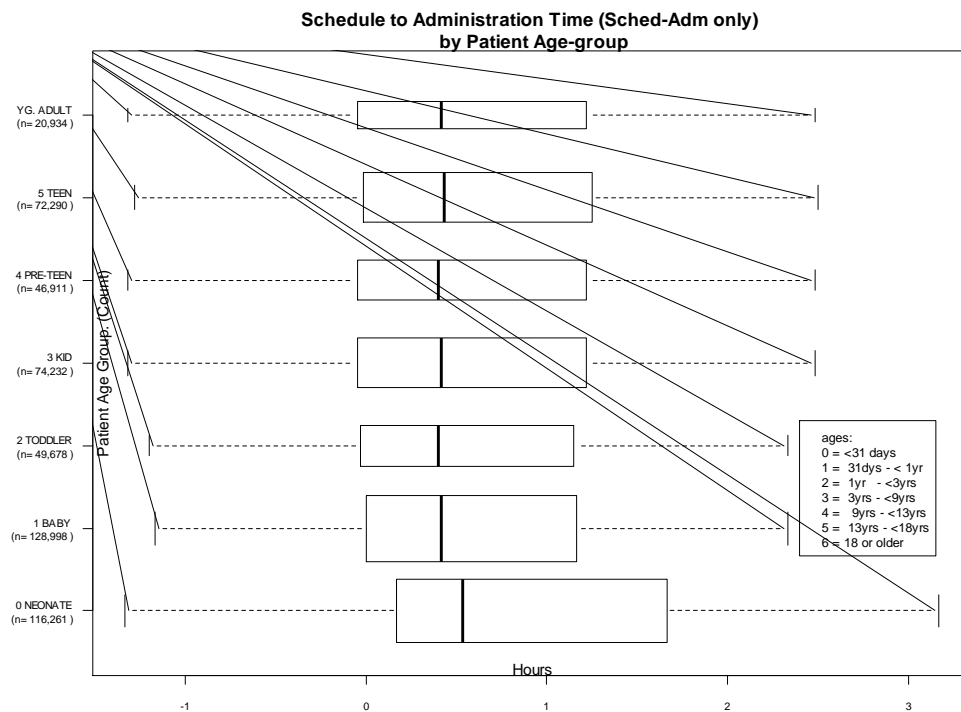


Figure 6-B: Sched-Adm intervals by age group. The box-thickness is proportional to, and thus reflects, the number of medication orders (shown in the parentheses) for the respective age groups.

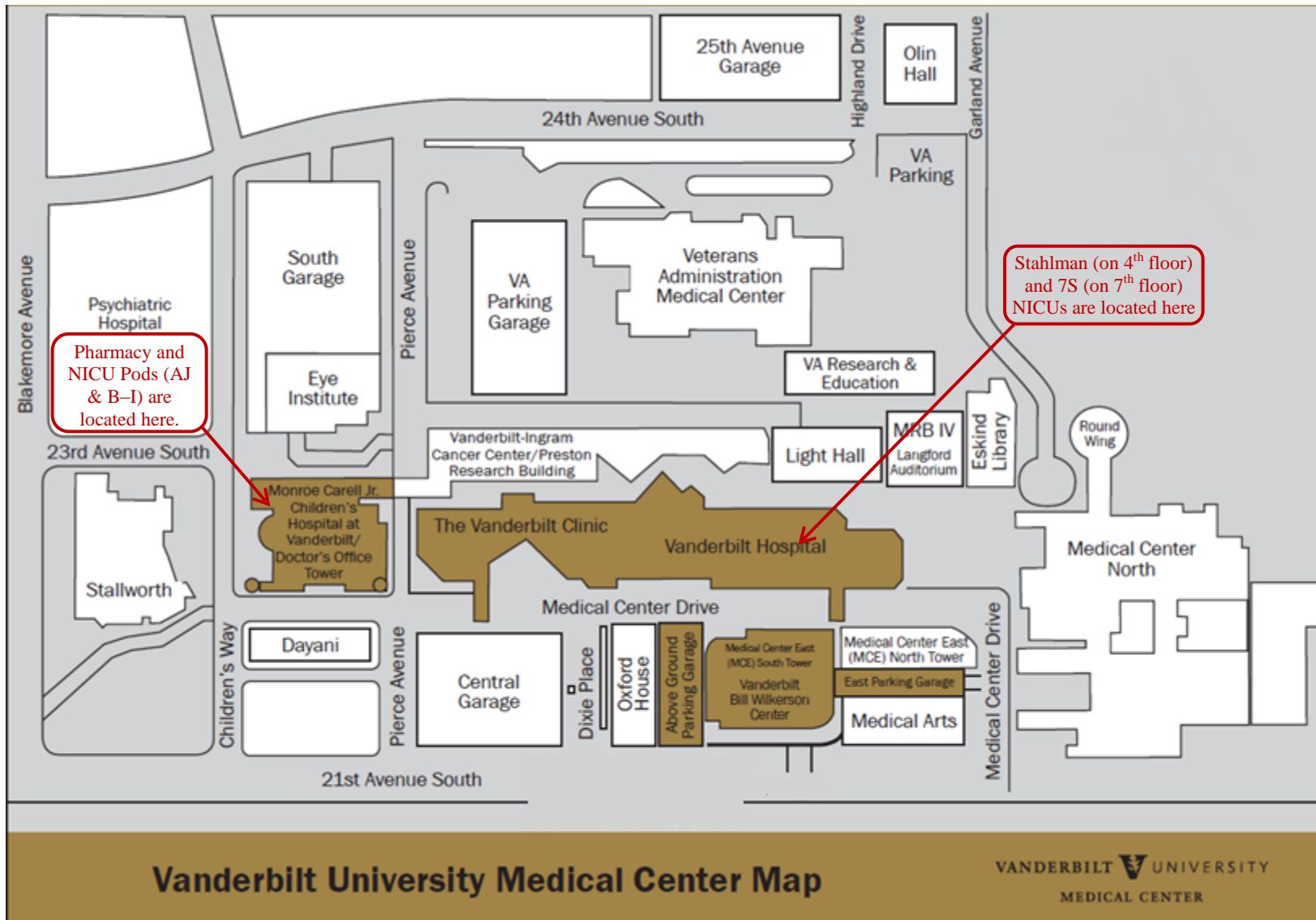


Figure 7-A: Vanderbilt University Medical Center Map showing the location of the NICU Pods AJ, B-I (at Monroe Carell Jr. Children's Hospital) and Stahlman NICUs (at Medical Center East North Tower).