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A Study of Critical Value Notification in the Outpatient Setting: The Relationship Between Physician Response and Patient Outcomes

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A Study of Critical Value Notification in the Outpatient Setting: The Relationship

Between Physician Response and Patient Outcomes

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor

of Philosophy at Virginia Commonwealth University

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Glossary of Abbreviations

AHRQ   Agency for Healthcare Research and Quality

CAP   College of American Pathologists

CLIA   Clinical Laboratory Improvement Amendments

DKA   Diabetic Ketoacidosis

HCUP   Healthcare Cost and Utilization Project

HHS   Hyperosmolar Hyperglycemic Stat

ISO   International Organization for Standardization

JC   Joint Commission

PT/INR   Prothrombin Time/International Normalized Ratio

RHS   Riverside Health System

Abstract

A STUDY OF CRITICAL VALUE NOTIFICATION IN THE OUTPATIENT SETTING: THE RELATIONSHIP BETWEEN PHYSICIAN RESPONSE AND PATIENT OUTCOMES

By: Kristie R. Finney, Ph.D.

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University

Virginia Commonwealth University, 2017

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Critical values are laboratory values that represent a life-threatening condition for which there is a treatment available. Laboratories make immediate notifications to ordering providers when critical values are identified so that they may quickly act to initiate a treatment for their patient. The majority of laboratories apply the inpatient critical value list to the outpatient setting, although there are many differences between an acutely ill inpatient population and an ambulatory outpatient population. The goal of this study was to determine if providers responded to the critical values in the outpatient setting and to determine if there was a difference in outcome indicators when providers responded to notifications and when they did not respond to notifications.

Data for 673 critical value notifications for PT/INR, Digoxin, and Glucose results were collected from Riverside Health System's five laboratories. Analysis suggested that the inpatient critical value lists and thresholds may not be appropriate to apply to the outpatient setting. In this study of 637 critical value notifications, providers chose not to respond to 25.7% of critical value notifications. Providers were more likely to respond to PT/INR and Digoxin critical value notifications that glucose critical value notifications. None of the cases for either of the three tests that went without a provider response resulted in death or serious harm to a patient, indicating that the critical value thresholds do not meet the definition of a critical value in the outpatient setting. In the future, laboratories should explore the utilization of a different critical value list and thresholds for the outpatient setting based upon patient outcomes.

Chapter 1: Introduction

Laboratory critical values are lab values that represent a life-threatening condition for which there is a treatment available (Lundberg, 1972). Every accredited laboratory is federally mandated to make immediate notification of all identified critical values to the responsible patient provider (Clinical Laboratory Amendments of 1988 [CLIA'88]). By definition, prompt identification and health provider notification of critical values should immediately result in a provider-initiated treatment or intervention to avoid severe illness or death of a patient. Critical value notifications are known to be costly in terms of laboratory staff and healthcare providers' time. Therefore, it is desirable to only make critical value notifications that result in physician interventions for the patients and have a positive impact on patient outcomes. This study investigated if providers respond to critical value notifications in the outpatient setting and if there is a difference in patient outcomes when providers respond versus when they do not respond to critical value notifications.

Background

It has been estimated that over 7 billion lab tests are performed annually in the United States (Silverstein 2003). Critical values have been determined to occur at a frequency between 0.25 to 2% of all laboratory values (Dighe, Rao, Coakley, & Lewandrowski, 2006; Hashim & Cuthbert, 2014; College of American Pathologists

[CAP], 2007). Studies have estimated the mean time for each completed critical value notification to be between 4 and 22 minutes. (Dighe et al., 2006; Howanitz, Steindel & Heard, 2002; Valenstein, Wager, Stankovic, Walsh, & Schneider, 2008). Using a conservative estimate of 4 minutes to make a critical value notification and 0.25% of 7 billion laboratory tests as the number of critical tests, laboratory staff in the United States spend 1,166,666 hours annually communicating critical values to healthcare providers. These hours do not include the time that it takes for the provider to receive, document, and act on the notifications. These hours do not include the time required to assess laboratory and hospital compliance with critical value notification procedures. Critical value notifications do result in physician interventions and treatments for patients (J. H. Howanitz & P.J Howanitz 2006, 2007), but are very costly in terms of laboratory, nursing, and physician resources. Each notification requires at least one of the laboratory staff members to give notification and one or more providers to receive and relay or document the result. There is a current shortage in laboratory technologists that is expected to increase (Garcia, Ali, and Choudhry, 2013; Bureau of Labor Statistics, 2014). Physicians and surgeon employment is also expected to increase by 18% and nurse employment by 25% from 2012 to 2022. In a recent survey, 81% of physicians described themselves as either overextended or at full capacity (The Physicians Foundation, 2014). Each critical value called by laboratorians and received by providers adds to this already full workload. In order to efficiently use resources, gain provider satisfaction, and increase patient safety while complying with accreditation standards, it is desirable to call only results that providers will truly utilize for immediate patient treatment.

Critical value lists and notification procedures are not standardized across laboratories. National surveys of critical value lists show a wide variation in tests that are selected for the lists and result thresholds that are identified as critical (Campbell & Horvath, 2014). Lundberg proposed the first list of critical values in 1972. In 2002, Heard et. al. found 28 analytes to be common among laboratory's critical value lists at 623 institutions. They reported that an additional 65 analytes were also included on critical value lists of various laboratories (2002). After 40 years, it is difficult to understand such variation of tests and thresholds that physicians and laboratory leaders have selected to represent life-threatening conditions. It has been suggested that the expansion of the critical values lists have been the result of laboratories testing for different populations, addition of new tests to laboratory menus, adoption of critical values that do not meet the definition of representing a life-threatening condition (Heard et al., 2002; Dighe et al., 2006), and lack of critical values list maintenance for removal of testing no longer performed (Hashim & Cuthbert, 2014).

It may be that critical value lists that were first compiled 30 years ago with little review and revision are also not reflective of the speed of current laboratory testing technology and enhanced and integrated communication methods. During the last 30 years, the time between the submission of specimens for testing and the receipt of results has changed from days to hours or even minutes. Current technology in laboratory instrumentation has reduced testing times. Increased instrument automation allows for analysis of multiple tests and multiple patients simultaneously. The majority of testing is no longer batched and run at specified intervals that may be days apart, but analyzed as received. These advances have impacted turn-around-times for both

outpatients and inpatients. Current communication technology has impacted outpatient

reporting times more significantly than inpatient testing reporting times. When critical

values were first described, the primary method for physicians to receive outpatient

results was by mail. This could take 3 to 5 business days, depending upon the distance

of the provider to the laboratory. Faxes, becoming widely available in the late 1980s,

changed the reporting time frame from days to a single day or possibly hours. Currently,

many laboratories are providing interfaces to the patients' electronic medical records.

These interfaces can potentially deliver real-time results to the ordering providers. It is

reasonable to assume that the number of tests for which results indicate a life--

threatening condition unless treated in 3 to 5 business days is much different than the

number of tests results that indicate a life-threatening condition unless treated in 24

hours or less.   General recommendations to decrease critical value notifications while

maintaining patient safety are to increase harmonization of critical value lists by

educating physicians on the concept of critical values, having different critical value lists

for different patient populations, removing tests and thresholds that result in "courtesy"

type calls, and encouraging more tests and result selection based on patient outcome

studies (Kost & Hale, 2010; Genzen et al. 2011; Don-Wauchope & Chetty, 2009,

Salinas et al., 2013). Heard et al., recommends that physician response to critical value

notifications be used as an outcome measure (2002). Many authors of the studies

listed have indicated that a move toward critical value analytes and thresholds based on

patient outcomes would lead to the most effective and efficient use of laboratory

resources while addressing patient safety (Piva, Pelloso, Penello, and Plebani, 2014;

Kost and Hale, 2010; Doering et al., 2014).

It is widely recognized that little data on provider response to critical values and effect on patient outcomes is available (J. H. Howanitz & P.J Howanitz, 2006). The studies, based on review of medical records, described above have common limitations when applied to patients in the outpatient setting. With the exception of Brigden et al., the majority of the critical values reviewed were from inpatients and/or inferences were made from review of physician responses to inpatient critical values only. Brigden et al., did evaluate outcomes of major bleeding, minor bleeding, and whether the patients had vitamin K or warfarin withheld for INR results ≥ 6.0. The study did not investigate whether physicians did or did not follow-up on critical values or why they did not have follow-up data for 24% (20) of the patients with INR values ≥ 6.0 (1998). Additional data have been made available based on physician self-reporting of critical value notification responses. These studies suggest that physicians respond to over 90% of critical value notifications and consider 4 hours or less to be an appropriate timeframe for physicians' response to a critical value (Piva et al, 2014; Montes, Fracis, & Cuilla, 2014). In contrast, a blind review of the electronic medical record reported that 10.2% of abnormal lab test results in an electronic record remained unacknowledged after 2 weeks, and timely follow-up was lacking in another 6.8% of acknowledged abnormal results (Singh et al., 2009). As indicated from these studies, self-reported responses to critical values do not agree with medical record abstractions. Critical value notifications in the outpatient setting are very different from notifications in the inpatient setting. The differences include pre-analytical errors associated with handling and storage of outpatient specimens, the operating hours of providers' offices versus around the clock staffing in a hospital, and the ability to locate an ambulatory outpatient versus a bed-

ridden inpatient. Although these differences are widely recognized, only 16% of labs reported a unique critical value list based on location (Wager et al., 2007).

Problem Statement

Critical value notifications are costly in terms of provider and laboratory staff resources. There is a gap in knowledge of whether providers receiving outpatient critical value notifications respond to them and whether their responses have an impact on patient outcomes. Although laboratories are required to make immediate notification of critical values, there are no studies suggesting faster notifications result in better patient outcomes. It is unknown if there are patient history, provider, and notification factors that are correlated with a provider's likelihood of responding to a critical value in the outpatient setting.

Purpose

The pattern of provider responses to laboratory critical value notifications of digoxin, PT/INR, and glucose in the outpatient setting were examined to determine if there was a difference in patient outcome indicators when critical value notification resulted in intervention or treatment for the patient and when it did not. The effect of quicker response times and different responses to critical value notifications on patient outcomes was explored. The relationships between a patient's clinical history, provider specific factors, or notification factors and a provider's likelihood of responding to a critical value notification in the outpatient setting were explored through statistical analyses. Additionally, the appropriateness of the critical value threshold for each test was examined.

Specific Aims

There were five specific aims for this study:

    Specific aim 1: To determine the provider utilization rate and response times for PT/INR, digoxin, and glucose critical value notifications for outpatients.

    This aim was determined by examining provider responses to all Riverside Health System critical value notifications for PT/INR, digoxin, and glucose test results on outpatient specimens as documented in the electronic medical record during the defined study period. The unit of analysis was each critical value notification. A critical value notification is a verbal delivery of a critical test result from the laboratory technologist to the provider responsible for the patient's care. The provider receiving the call may choose to respond or not respond to the notification. Responses include contacting the patient, ordering follow-up testing, stopping or changing the dosage of a medication, prescribing a new medication, scheduling follow-up appointments, and/or directing the patient to an emergency room. For this aim, any attempt to respond to a critical value notification was considered a response. For example, if the provider attempted to call the patient, but was never able to reach the patient, it was considered a response.   Any response should be documented in the patient's electronic medical record. More than one of these response types may result from any single notification. If one or more response types or an attempt to respond was documented, the notification was defined as utilized. The utilization rate for critical value notification is the total number of glucose, PT/INR, and digoxin critical values that resulted in a provider response for each test measured against total critical value notifications for each test.   Response times were categorized into 1) less than 4 hours and 2) between 4 hours and 24 hours.

Responses greater than 24 hours were not considered to be initiated by critical value notification. All laboratory results are available for viewing in the electronic medical record. New results prompt provider review and acknowledgement upon posting. Therefore, any response after 24 hours is considered as no response to the critical value notification.

Specific aim 2: To determine if there is a difference in patient outcome indicators when providers respond to critical value notifications, compared to when they do not respond to notifications.

For each critical value notification, the patient's record was reviewed for outcome indicators including unplanned emergency department admissions, death, and results of the next test. In addition, the medical records from patients with critical PT/INR values were reviewed for documented evidence of bleeding, the medical records from patients with critical digoxin values were reviewed for the documented symptoms of hyperkalemia and atrial fibrillation, and the medical record from patients with critical glucose values were reviewed for the documented symptoms of nausea, vomiting, or confusion. A comparison of patient outcome indicators was completed between those who had a response to critical value notifications and those who did not have a response. In this specific aim, unsuccessful notifications were treated as if there was no response because an unsuccessful response would have resulted in no intervention or treatment. The next test, depending on whether the result was a critical value, may or may not have triggered a notification. If a notification was triggered, then a retest indicator was collected as a part of the records review. This information was used in Specific Aim 4 and 5 as a potential predictor of provider response.

Specific aim 3: To determine if quicker response times result in better outcomes.

The Clinical Laboratory Improvement Act requires all accredited labs to have procedures in place for immediate notification of the ordering provider when a critical result is identified by the laboratory. There are no guidelines mandating physician response to critical values or a timeframe for response. However, based on a literature review, the acceptable timeframe for response to a critical value appears to be 4 hours or less (Montes, Francis, & Cuilla, 2014; Piva et al., 2014). Therefore, each response type was identified as occurring within less than 4 hours, greater than 4 hours and less than 24 hours, or greater than 24 hours.

Specific aim 4: To determine if there are provider or notification factors that influence a physician's likelihood to responding to a critical value.

Callen, Westbrook, Gerogiou, & Li found that between 6.8 and 62% of critical laboratory values were not followed-up in the outpatient setting (2011). This specific aim explored the reasons why a provider may choose to respond or not to respond to critical value notification. These factors include specimen age in minutes, whether the physician ordering the test was the patient's provider or the on-call provider, whether or not the notification was made during business hours, whether or not the notification was the result of a repeat test, years of provider experience, evidence of diabetes metillus for glucose critical values in the patient's historical record, and evidence of a notification for the same test for the same patient in the past year.

Specific aim 5: To determine if the magnitude of the test result predicts whether or not a provider will respond to a outpatient critical value notification.

Providers may chose not to respond to a critical value if they do not feel that the result represents a life-threatening condition for their patient. Provider's may not agree that the threshold at which the test result is determined to be critical is accurate for their patient. This specific aim explored whether there is any evidence that the current critical test thresholds need to be modified for the outpatient population based upon provider's response. An analysis of the standardized magnitude of the test result over or under the critical value range supported recommendations for any changes to critical value ranges.

Significance of the Study

Using conservative estimates, laboratorians spend 1,166,666 hours communicating critical values to healthcare providers annually. It is estimated that 16.9 to 20.5% of all critical values occur in the outpatient setting (Salinas et al., 2012; Piva et al., 2009; Dighe et al., 2006). It has been determined that making critical value notifications in the outpatient setting can take twice as long as those in the inpatient setting (Heard et al, 2002). This suggests that laboratories use twice has many hours to make notifications for outpatients compared with notifications for inpatients. No studies to date have evaluated the utility of critical values in the outpatient setting based on physician response and patient outcomes. However, all laboratories are required to develop critical value lists and most laboratories apply the same list to both the inpatient and the outpatient populations. This study will be the first investigation using an electronic medical record review of providers' responses to critical values and patient outcomes in the outpatient population. It will consider additional factors that are unique to the outpatient setting. This study will determine if the current practice of applying critical

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values lists and thresholds to outpatients is an appropriate use of limited laboratory staff and other healthcare provider resources. This study will address the response to critical values in the outpatient setting. It will address the current gap in knowledge if outpatient outcomes are different when physicians respond to critical values compared to when they do not.

Chapter 2: Literature Review

The following chapter will consist of background information on critical value notification. First, a description of laboratory testing and a definition of critical value will be provided. The next sections will provide the following chronological information:

- Federal guidelines and accreditation standards addressing critical value notification

- Information describing the selection of tests for critical value lists and test examples

- A discussion of critical value notification procedures

- A review of the financial impact and resource utilization of critical value notification procedures.

- Information specific the utilization of critical values in the outpatient setting.

A final summary will include the current gaps in knowledge in physician utilization of critical values in the outpatient setting.

Laboratory Testing

Over 7 billion laboratory tests are performed each year in the United States (Silverstein, 2003). Tests may be ordered for an inpatient, or person that has been formally admitted to a hospital under a physician's order. Tests also may be ordered for an outpatient, or patient whose visit occurs in an emergency room, physician office or

clinic and whose treatment does not require an overnight admission.   Providers may

order tests to screen for conditions, to diagnose an acute condition, manage chronic

conditions, or to monitor a patient's response to treatment or medication. These tests

may be ordered as routine testing with an expected result time of hours to days, or as

STAT testing with an expected result time of minutes to a few hours.   It is estimated

that laboratory data influence from 43 to 70% of medical decisions (Gardner, 1986;

Silverstein, 2003). Whether testing is ordered on hospitalized patients, emergency

room patients, or outpatients, providers need the laboratory data to be accurate and

available in a clinically relevant timeframe in order to make medical decisions for their

patients.   For laboratory test results that indicate that the patient is in need of

immediate medical intervention, the provider must be notified of the abnormal results as

quickly as possible so that treatment may be initiated. Test results that represent a life-

threatening condition for which a medical intervention is possible are called critical

values (Lundberg, 1972). The clinically relevant timeframe for notification of these

critical results is much different than for tests with results that do not represent a life-

threatening condition. All laboratories accredited to perform in-vitro diagnostic testing

must have procedures and policies in place to ensure that critical results are

communicated to a health care provider in an expedited manner (Clinical Laboratory

Improvement Amendments [CLIA], 1988).

Labo**ratory Accreditation**

    Laboratories operating in the United States are accredited and inspected by

professional organizations such as COLA, the College of American Pathologists (CAP),

and the Joint Commission (JC) (Warner, 2011). These organizations are deemed by

the Centers for Medicare and Medicaid Services (CMS) to have equivalent or more

stringent requirements than those specified in the federal guidelines These federal

guidelines are known as the Clinical Laboratory Improvement Amendments of 1988

(CLIA'88).   Laboratory inspections are routinely conducted to assess compliance with

federal regulations and standards of the professional organizations. Federal guidelines

and the professional organizations with deemed status require quality assurance

programs to be developed, implemented, and assessed. In response to these

regulations, laboratories have established standardized procedures in patient

identification, test implementation, testing personnel competency, quality control,

analysis, and reporting mechanisms designed to address overall quality of laboratory

results.   Since the implementation of CLIA regulations, many clinical laboratories have

demonstrated a reduction in errors (Carraro and Plebani, 2007; Wager and Yuan,

2007). These errors are typically attributed to one of three phases of testing. The first

phase, pre-analytical, encompasses all steps that take place before a sample can be

analyzed. This phase includes patient identification and specimen collection, handling,

transport, processing, aliquoting, and storage (Wager and Yuan, 2007). The analytical

phase of testing comprises the actual performance of the test. The post-analytical

phase includes retrieving and delivering test results to the ordering provider in a

clinically relevant timeframe.   Part of the post analytical phase that is often target for

error reduction and a focus of patient safety is the timely reporting of critical values

(Wager and Yuan, 2007). Critical value reporting is addressed directly in the federal

code known as CLIA '88.

Critical Value Regulations

Congress passed CLIA'88 in response to concerns over laboratory errors. The law expanded federal oversight to all laboratories performing clinical testing on human specimens, set forth minimum standards for operation and quality, and required sanctions for failure to comply. The goal was to standardize all laboratory testing and to ensure accuracy and quality of results in every clinical laboratory. In 1992, the final regulations were published. They included the following language that requires all laboratories to report critical values:

> "The laboratory must immediately alert the individual or entity requesting the test, and if applicable, the individual responsible for using the test results when any test result indicates an imminent life-threatening condition, or panic or alert value."

In 1995, the College of American Pathologists (CAP), an organization initially designed as a voluntary program for laboratory education and improvement, obtained deemed status for laboratory accreditation. In 1997, CAP introduced Accreditation Program Standard 01:4132, "Does the laboratory have procedures for immediate notification of a physician (or other clinical personnel responsible for patient care) when results of certain tests are within established 'alert' or 'critical ranges'?" This standard exceeded CLIA requirements for notification of critical values. In addition to the CLIA required immediate notification of critical values, it required laboratories with CAP accreditation to also have documented procedures. Since the introduction of these new standards, the CAP has conducted several quality studies that investigated various parameters of critical values and notification.

The Joint Commission, previously known as the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), also acquired deemed status from the federal government to accredit laboratories in 1995. Critical values and their notification were also addressed in a similar fashion and timeline as the CAP standards.   JC Standard LD 3.2.1 required the establishment of criteria for the immediate notification of the responsible practitioner when critical results were identified.

As laboratories' critical value lists and notification procedures became standard practice, the accreditation agencies began to expand their focus from simple notification of critical values to timeliness of notification. In 1997, the CAP conducted a study to evaluate the timeliness of critical value reporting. The goal of this study was to benchmark timeliness of critical value reporting and to introduce it to laboratories as an indicator of quality. Six hundred seventy-one institutions participated in this study. At that time, there were 4,241 CAP accredited labs in the CLIA database (Centers for Medicaid and Medicare Services, 2010).   In 2002, the CAP conducted a study that ultimately compared the lists of tests and threshold values considered life-threatening between laboratories. These lists of tests are referred to as Critical Value Lists. The study also investigated the procedures for development of the Critical Value Lists and procedures used for notification (Heard, Steindel, & Howanitz, 2002). The authors reported significant variation between laboratories in Critical Value Lists for chemistry and hematology. They also reported that 5% of notifications were never completed, and that more than 45% of critical values were unexpected.

Interest in critical values continued, and gained even more attention as the JC announced its first official set of patient safety goals in 2005. Goal 2 targeted improving

the effectiveness of communication among caregivers. Specifically, a test result "read-back" was required. The individual receiving the result must read the result back to the person who is reporting the result when communicating critical test results. The purpose of this practice was to identify any miscommunication regarding the test result.   In addition, organizations were required to measure, assess, and improve timeliness of reporting. The guideline set forth the requirement that the recipient of the notification to be a responsible, licensed caregiver (JC 2005). Although critical values and their notification had up to this time been largely a lab-focused quality measure, the JC Safety Goals broadened the standards of critical values to address the nursing department component of notification. Many laboratories allow critical values to be called to an intermediate non-licensed caregiver or to a nurse instead of directly to the ordering provider. These caregivers or nurses then notify the physician. Valenstein et al., estimate that the median additional time from a non-licensed caregiver to a licensed caregiver was 3 minutes (2008). The timeliness and accuracy of the second piece of notification from nurse to physician became included in the total notification time.

During the 2005 to 2007 time period, focus on critical value notification not only spread nationwide to hospital departments outside the laboratory, but also gained attention internationally. The Joint Commission has required JC accredited hospitals to establish Critical Result Lists for other testing such as imaging tests and electrocardiograms. The International Organization for Standardization published ISO EN 15189:2007, which required immediate notification of critical values. The Clinical Pathology Accreditation (CPA) organization in Great Britain and Northern Ireland also began to require procedures for notification (CPA 2007).

In 2012, the CAP followed the lead of the JC and included two standards that addressed critical values. Standard COM.30000 required procedures for immediate notification of established critical values that are important for patient management decisions.   Labs are required to maintain records showing prompt notification. Specific requirements include date, time, responsible laboratory personnel, first and last name of the person notified, and test results. It requires the investigation of any problems encountered during the notification process. Standard COM.30100 required the "read-back" of critical results. These standards are unchanged as of 2014 (CAP 2017). The 2014 JC National Patient Safety Goal 2 indicates all elements of performance of reporting critical results as risk areas, and requires documentation for managing the critical results of tests and diagnostic procedures.

Despite the inclusion of Critical Value Lists, reporting procedures, assessments of timeliness, and documentation in federal law and laboratory accreditation standards, there has been little standardization across laboratories. This lack of harmonization remains although it has been 40 years since Lundberg first defined a critical value. It has been suggested that there needs to be a more systematic approach to critical value notification. Critical Value Lists and thresholds should be based on patient outcome data (Howanitz, J.H and Howanitz,P.J. 2006; J. H. Howanitz & P.J Howanitz, 2007). However little data has been collected on how critical values impact clinician's decisions to treat patients (Piva, Pelloso, Penello, and Plebani, 2014) and there has been few studies addressing critical value harmonization using patient outcome data (Dighe et al., 2006; Genzen et al., 2011; Doering et al., 2014).

Critical Value Lists

Critical Value Lists are the specific lists of tests performed in the laboratory with accompanying threshold values that are considered to be potentially lethal unless appropriate treatment is initiated (Lundberg 1972). A more recent definition of a critical result is a result that "may signify a pathophysiologic state that is potentially life threatening or that could result in significant patient morbidity, or irreversible harm or mortality, and therefore requires urgent medical attention and action" (Campbell & Horvath, 2014, p.136). Currently, after more than 20 years of federally required critical value notification, there are no universal or standard test list or result thresholds for critical laboratory values. The lack of standardization is driven by a variety of reasons including the variances between the populations that each laboratory serves, variances in instrumentation and testing methods, clinical differences of opinions among physicians that have influence over the list, and the relative shortage of studies investigating patient outcomes in association with test specific critical thresholds (Dighe et al., 2006, Genzen et al., 2011).

The CAP accreditation standards allow each laboratory to define critical tests and values that pertain to its patient population. Standard COM.30000 (2014) requires the critical result list "be defined by the laboratory director, in consultation with the clinicians served." Depending upon the laboratory, the ordering clinicians may be oncologists in a cancer center, nephrologists in a dialysis center, or medical staff at an acute care hospital. The three specialties would likely have very different ideas about which tests should be on the list and what level defines a critical value. To accommodate this difference, the JC indicated in a National Patient Safety Goal (NSPG) FAQ 2008

update that "provisions" could be made for certain patients or patient diagnoses for which the different thresholds of critical values could apply. CAP also included this provision as of 2012. However, only 16% of labs have a unique critical value list based on location (Wager et al., 2007).

Several studies have assessed how these lists are actually derived. It has been reported that labs are establishing lists using reviews of current literature, laboratory meetings, recommendations of hospital committees, in-house studies, medical staff consultations, or a combination of these sources (Heard et al, 2002). A study of 730 laboratories in 2008 indicated that 22.6% of the respondents had not compared their critical values with the national norms (Dighe et al, 2008).   In another study of 90 Italian institutions, 21.1% indicated that their Critical Value List was derived solely on the opinions of clinicians at their institutions (Piva et al. 2010). Salinas et al., described their critical value list as "a short list of six fundamental critical values" (2014). Heard et al. (2002) did report that the same four chemistry tests and five hematology tests were present on greater than 80% of critical values lists from the 623 institutions surveyed. However, there were 84 other tests reported on some but not all critical values lists, indicating an extremely wide variety of critical tests among laboratories. This variation in tests selected for critical value notification is further complicated by the various thresholds at which each laboratory considers each test's results to be critical. For example, in the Heard et al. study, the low threshold for a critical sodium result was as low as110 mmol/L in some labs and as high as 125 mmol/L in other labs (2002).

The heterogeneity of testing and thresholds that have been reported indicate that all tests and thresholds selected for critical value notification may not truly represent life-

threatening. The definition of critical value requires two conditions to be met, 1) the

result is so abnormal as to be life-threatening or result in permanent harm or injury and

2) there is a clinical intervention available to resolve the condition. If either of these

conditions is not met, the result should not be considered for inclusion on the Critical

Value List. Heard et al., summarized that "it was clear that most [critical value lists]

included critical limits for analytes that were not life-threatening or for which some

corrective action could not be undertaken" (2002). Expansion of the list with tests that

do not represent life-threatening state or conditions for which there is no treatment,

increases the number of calls that the laboratory staff are required to make and thus the

number of calls that the providers must receive. These providers receiving the

numerous notifications often are the same providers that have medical influence over

the selection of tests for the lists. One study designed to assess the physician's

understanding of critical values, determined that 79% of the physicians did not fully

understand the concept of a critical value by indicating on a survey that it would be

acceptable to call certain critical values only during business hours (Don-Wauchope and

Chetty, 2009). However, a value that could be called on the next business day without

a negative patient outcome does not meet the definition of a critical value.

Several authors recommend a careful review of current critical value lists to select

values that truly represent life-threatening conditions and remove tests and thresholds

that are not urgent. (Piva et al., 2010; Genzen et al 2011; Heard et al,2002; Dighe et al.,

2006). This would increase laboratory efficiency and reduce unnecessary interruptions

for providers. One large medical center reduced calls by 2,136 per year by changing the

lower limit critical glucose value from less than 60 mg/dL to less than 45 mg/dL (Dighe

et al., 2006). This was done by examining the frequency of calls for each value below the critical cut-off. The clinicians decided that the marginal resource cost to call values between 45 and 59 mg/dL outweighed the marginal clinical usefulness. Salinas et al. reported that a pathologist's review of critical values in their STAT lab, effectively reduced their reported critical values to 25% of the number that would have been reported if the critical value list designed for their routine lab without pathologist intervention was used (2014). Another study evaluated critical limits for sodium by studying clinician responses and patient outcomes (J. H. Howanitz & P.J Howanitz, 2007). Although an earlier study conducted by Heard et al., 2002 found that the majority of labs use 160 mEq/L or more as a critical limit, J. H. Howanitz & P.J Howanitz discovered that 56% of inpatients who had sodium results between 155 to 159 mEq/L died. Their recommendation is to use 160 mmol/L as a starting point for evaluation of patient outcomes to determine whether lowering the critical value to 155 mEq/L as their lab has done is beneficial (2007). In 2006 J. H. Howanitz & P.J Howanitz reported that the physicians acted more rapidly with interventions or additional testing with lower critical calcium values. An additional study found that physicians responded to critical potassium tests quicker than critical sodium tests (Che-Kim, 2011). This data suggested that not all critical values are considered equal by physicians. It could indicate that the threshold levels for critical values for certain tests such as sodium in the Che-Kim study above may not be appropriate.

Although, it has been widely recognized that more standardization of the critical value lists would be beneficial, it has been slow to develop. General recommendations are to educate physicians on the concept of critical values, remove tests and thresholds

that result in "courtesy" type calls, and encourage more tests and result selection based on patient outcome studies (Kost et al., 2010; Genzen et al. 2011; Don-Wauchope et al., 2009).

Critical Value Test – Digoxin. Digoxin testing is performed in the majority of laboratories in the United States. The frequency of digoxin testing is due to its common use as a cardiac glycoside. It is usually administered orally or by IV injection. Digoxin raises the intracellular calcium concentrations and increases the force and velocity of myocardial systolic contraction. This drug is recommended by the American Heart Association for patients with heart failure and reduced ejection fraction, to decrease hospitalizations (2013).

Digoxin has a very narrow therapeutic range. From reanalysis of the DIG trial, a recommended target concentration goal is between 0.5 and 1.0 ng/mL. (Conner et al., 2003). Currently, the commonly used reference range for serum concentration is between 0.8 and 2.0 ng/mL (Terra et al., 1999). The American Heart Association's Guidelines advise physicians to use caution with administering digoxin, as many factors may alter its metabolism. Among those factors are hypokalemia, hypomagnesemia, hypothyroidism, or concomitant use of such drugs as clarithromycin, dronedarone, erythromycin, amiodarone, itraconazole, cyclosporine, propafenone, verapamil, or quinidine (AHA Guidelines 2013). The elimination half-life of digoxin is 36 hours. This is increased in patients with impaired renal function (Lexicomp, 2015).

Digoxin toxicity can be fatal. Potassium concentrations > 6.0 mmol/L are predictive of major toxicity (Dawson & Buckley 2016). Symptoms can range from palpitations, atrial fibrillation, dizziness, paraesthesias to visual disturbances. Complications can

include cardiac dysrhythimias (Eade et al., 2013) and electrocardiogram changes including extrasystoles and minor degrees of AV nodal block (Dawson and Buckley 2012). Treatments for toxicity include one or more doses of activated charcoal and the administration of Digoxin-Fab. These are Fab fragments of antibodies that bind specifically and rapidly to digoxin, and enhance renal excretion of the drug (Dawson and Buckley 2012). Considering the narrow therapeutic range and potential for toxicity, patient compliance with medication dosage is important. A systematic review of 10 studies investigating noncompliance with prescribed digoxin indicated that nearly 50% of outpatients treated with digoxin and 25% of patients after hospital discharge were non-compliant with therapy (Kongkaew et al., 2012). Between 2005 and 2010, it was estimated that 5156 patients presented to United States' emergency departments with digoxin toxicity. More than three quarters of these patients were hospitalized (See et al., 2014). The HCUP National Inpatient Sample (NIS) in 2012, estimates that 685 people were admitted to hospitals in the United States with the primary diagnosis of poisoning by cardiac glycosides. The mean cost for each patient admission was $8515.00. This translates to an annual cost of $5,832,775.00 to United States hospitals (Healthcare Cost and Utilization Project, 2014). More careful prescribing to high risk groups and improved monitoring of serum levels have been recommended (See et al., 2014).

Digoxin levels are on many laboratory critical value lists at many different thresholds. Published critical value lists have the threshold for critical digoxin results ranging from >2.5 ng/mL to >3.6 ng/mL (Hashim et al., 2014, Piva and Plebani, 2009, and Piva et al., 2009). Digoxin tests have been reported to be a frequently called critical value. One

lab has reported that digoxin represents 6% of all critical values from routine testing. Critical values for this test were the highest in relation to the test volume. (Piva et al, 2009).

In summary, digoxin is a frequently administered drug, has a very narrow therapeutic range, and lack of compliance with medication regimen or altered renal function often result in toxicity.   Since physicians can initiate treatment in response to digoxin therapy, the majority of labs include it in their critical value list.

Prothrombin/INR. PT/INR testing is used to monitor warfarin therapy in patients. Warfarin is one of a class of drugs known as anticoagulants. This class of drugs is used as a medication to prevent or treat thrombotic disorders. Venous thromboembolism (VTE) includes both deep vein thrombosis (DVT) and pulmonary embolism (PE).   Clinical practice guidelines from the American College of Cardiology Foundation and American Heart Association include warfarin in the management of patients with such conditions as atrial fibrillation, heart failure, stroke, and valvular heart disease (2013 ACCF/AHA Guidelines for the Management of ST-Elevation). Although newer oral therapies are arriving on the market, the oral anticoagulant most commonly used in 2012 was still warfarin (O'Donnell, 2012).

Warfarin acts by depleting functional vitamin K reserves and thereby reducing the synthesis of active clotting factors. Its onset of action, when taken orally, is 36 to 72 hours with the full therapeutic effect in 5 to 7 days. Its duration is 2 to 5 days with a half-life elimination of 20 to 60 hours (Lexicomp, 2015). Warfarin has several drug interactions, a narrow therapeutic index, and genetic and clinical factors that can increase sensitivity to warfarin. Increased levels of warfarin can result in serious

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complications including embryopathy, warfarin-induced skin necrosis, and bleeding. The most common acute complication is bleeding which is related to the degree of anticoagulation. Additional risks for bleeding include age, anemia, prior cerebrovascular disease, gastrointestinal lesions, and renal disease (Strecker-Mcgraw 2011). Acute toxicity may result in bleeding in almost any organ. Spontaneous bruising, hematuria, bilateral flank pain, and epistaxis can occur. Severe blood loss can result in hypovolemic shock, coma, and death (Vale and Bradberry, 2007).

Routine and emergency management of warfarin therapy is dependent upon the measurement of PT/INR/international normalized ratio. The prothrombin time is the number of seconds required for a fibrin clot to form in a plasma sample after tissue thromboplastin and an optimal amount of calcium chloride have been added to the sample. The INR is the patient's prothrombin test result expressed as a ratio to a normal population which has been standardized for the potency of the thromboplastin used in the assay (CLSI). The Agency for Healthcare Research and Quality (AHRQ) has published guidelines for warfarin therapy management using the INR values. Two therapeutic ranges are recommended. The INR target of 2.5 with a range of 2.0 – 3.0 for most indications and a target of 3.0 with a range of 2.5 – 3.5 for patients with a mechanical heart valve in the mitral position, and/or a non-bileaflet valve in the aortic position. (National Guideline Clearinghouse [NGC])

INR results within the target range are often difficult to maintain in patients due to many factors. Comorbid conditions may change, patient noncompliance may occur, and changes in diet could affect the pharmacokinetics of warfarin (Su, 2011). The AHRQ has published guidelines for interventions outside of the target range.

Dependent upon risk factors, medical treatment other than decreasing the dosage or omitting doses, may occur at INRs > 5.0 (NGC). Treatments include administration of vitamin K, addition of clotting factors using Fresh Frozen Plasma (FFP), and administration of prothrombin complex concentrates (PCCs). PCCs are now recommended over FFP due to the quicker correction of the INR (Strecker-McGraw & Mark Andrew, 2011). In 2011, data collected by the AHRQ, estimated 4,686 visits to the ED with the primary diagnosis of poisoning by anticoagulants. Two thousand one hundred seventy-three of these patients were admitted to the hospital (HCUP net).

Clinical laboratories have recognized the need for quick communication of PT/INR values above therapeutic range. PT/INR tests are on 90.7% of laboratory's critical value lists (Wagar, Friedberg, Souers, & Stankovic, 2007). Critical thresholds for INR values on the published lists range from >5.0 to >7.0 (Genzen & Tormey, 2011; Hashim & Cuthbert, 2014; Pai, Moffat, Plumhoff, & Hayward, 2011; Parl et al., 2009). One large academic center estimated that PT/INR critical values represented 4.8% of their critical values (Lewandrowski, Coakley, Rao, & Dighe, 2006). North American Specialized Coagulation Laboratory Association Labs estimated that between 1 and 15% of their critical values were INRs (Pai et al., 2011). In 2009, PT/INR was the most frequent critical value in outpatients in the Padua Hospital in Italy (Piva et al.) In a survey administered by the Department of Pathology in Padua, Italy, general practitioners reported the main response to a critical INR value was to change or stop the dosage of warfarin. In their study, additional actions included repeating the INR or medical examination. No patients had bleeding and none were referred for hospitalization (Piva et al. 2014). In contrast, Brigden et al., reported 2 of 7 patients with INRs >6.0

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experienced major bleeding and were hospitalized. The other 5 patients presented with minor bleeding (1998).

In summary, warfarin is a widely-used drug with a small therapeutic range. Metabolism of warfarin can be affected by many factors, resulting in toxicity. There is a readily available treatment for toxicity. Considering the factors above, the PT/INR test fits the definition of critical value and is on the majority of laboratory critical value lists (Piva and Plabani, 2009; Dighe et al, 2006; Jenkins et al., 2007).

Glucose. Glucose is also a test that is found on the majority of critical value lists (Dighe et al, 2006; Piva et al 2009; Heard et al. 2002). Glucose tests are ordered to screen for diabetes mellitus, and for the management of both critically ill hospital inpatients and outpatients with diabetes. The American Diabetes Association recommendations include screening patients without risk factors such as obesity for diabetes at 45 years of age. Patients with a normal fasting glucose should be screened every 3 years after that the initial screening (2013).   A glucose test is included in the CMS Comprehensive Metabolic Panel and Basic Metabolic Panel, two of the most commonly ordered lab panels.

Elevated glucose levels representing hyperglycemia could be the result of acute illness such as an infection, cerebrovascular or cardiovascular event, gastroenteritis, or dehydration. Hyperglycemia could indicate an uncontrolled condition in a diabetic (Katsilambros, Kanaka-Gantenbein, Liatis, Makrilaki & Tentolouris, 2011, p.178). There are three types of diabetes. In Type 1 diabetes, the body does not produce insulin that is needed to metabolize glucose. Type 2 diabetes is a progressive disease, beginning with insulin resistance, or the body's impaired response to endogenous and exogenous

insulin. Insulin production is increased to maintain normal glucose levels. Eventually,

the body cannot produce sufficient insulin and intervention is required to maintain

glucose levels. The third type of diabetes, is gestational diabetes that develops during

pregnancy. This type usually does not remain after pregnancy (Dunning, 20113). In

any of the three types, uncontrolled diabetes could lead to hyperglycemic crises and

death.

Severe hyperglycemia can lead to dehydration and electrolyte imbalance. Elevated

glucose levels in combination with insulin deficiency may lead to diabetic ketoacidosis

(DKA), (Katsilambros, Kanaka-Gantenbein, Liatis, Makrilaki & Tentolouris, 2011, p.149).

DKA is defined by hyperglycemia, metabolic acidosis, and ketonemia. Another

metabolic complication of diabetes is a Hyperosmolar Hyperglycemic state (HHS). HHS

is defined by severe hyperglycemia, hyperosmolality, and dehydration without

ketoacidosis. Symptoms of DKA and hyperosmolar hyperglycemic state include

polydipsia and polyuria, generalized weakness, altered mental status, weight loss, and

vomiting (Kitbachi, Umpierrez, Miles, & Fisher, 2009). Treatments for these conditions

include rehydration with intravenous fluids, insulin therapy, and electrolyte replacement

(Katsilanbros, p.15).

The American Diabetes Association (ADA) defines the alert value for hypoglycemia

as ≤ 70 mg/dl in plasma (2013). Hypoglycemia symptoms include anxiety, irritability,

fine tremor, tachycardia, hunger, cold sweats, headache, cognitive impairment, fatigue

and weakness, lightheadedness and dizziness, visual changes, slurred speech,

seizures, and coma. Hypoglycemia can be caused by a variety of factors including

drugs, liver or kidney disease, missed meals, gastrointestinal disease, hormone

deficiency, and as a result of tumors such as secreting fibrosarcomas and insulinomas (Alsahli and Gerich, 2013). Hypoglycemia can also be the result of diabetes treatment with insulin or oral medications (Downing, 2013).

Hypoglycemia can be fatal due to its effects on the central nervous system. Decreases below 40 mg/dl have resulted in sleepiness and behavioral changes. Decreases below 30 mg/dL can cause seizures, cardiovascular events, permanent neurologic deficits, and death (Alsahli and Gerich, 2013; Frier, Schernthaner, & Heller, 2011; Gold, MacLeod, Deary, & Frier, 1995;). Treatments for hypoglycemia include giving high glycemic index carbohydrates such as a soft drink or glucose tablets. For severe hypoglycemia, IM glucagons followed by close monitoring and complex carbohydrate low glycemic index food to maintain glucose levels (Downing, 2013).

From 1985 to 2002, 49,063 adults died from hyperglycemic crisis (Wang, Williams, Narayan & Geiss, 2006). In 2011, weighted national estimates from the Nationwide Emergency Department sample indicate 798,895 Emergency Room visits had a clinical classification software code of 50, or diabetes with complication. From those visits, there were 425,064 admissions and 325 deaths in the Emergency Room. Based on the weighted estimates, 2,291 of those patients admitted died during the hospital stay. An additional 318,048 visits were classified as diabetes without complication. Sixteen thousand, one hundred twenty-five of these patients were admitted to the hospital. It has been reported that overall death rates due to hyperglycemic crises among adults with diabetes has decreased in the United States. This same study did report that approximately one-third of deaths in adults 18 to 65 occurred at home (Wang et al., 2006). The authors identified preventing deaths that occur at home was an opportunity

for healthcare as DKA and HHS are generally avoidable with early diagnosis and treatment.

Abnormal glucose results can represent a condition that is life-threatening and treatable. In 2012, 29.1 million Americans, or 9.3% of the population had diabetes (ADA, 2014). Both hyperglycemia and hypoglycemia can result as a complication of diabetes. Hyperglycemia is additionally caused by stress, infection, and some acute illnesses (Falcigila 2007).   Thresholds for critical notification for glucose are < 40 mg/dL to <50 mg/dL in the low range, and >300 to >700 in the high range (Hashim et al. 2014; Heard et al., 2002). One institution reported 7.7 % of all of their critical values was glucose. This represented 0.6% of all glucose tests ordered for that institution (Dighe 2006). In summary, abnormal glucose results are widely encountered by laboratories and represent a life-threatening condition that is treatable. Therefore, most laboratories include this analyte on their critical value list (Heard et al, 2002).

Critical Value Notification Procedures

Once a critical value such as digoxin, PT/INR, or glucose is identified by the person performing and resulting a test, it must be quickly conveyed to the licensed provider. The patient's provider and phone number must be located to initiate the notification. Prior to the wide use of Laboratory Information Systems, this was a very manual process. In the last two decades, as laboratories introduced software systems designed to increase productivity while offering automated ways to meet regulations, the notification process has become increasingly less cumbersome. A survey in 2007 reported that 3,646 US hospitals operated some level of Laboratory Information System and an additional 375 sites either expected installation of an LIS or had awarded a

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contract (Harrison and McDowell, 2008).   In a 2010 CAP survey of LIS vendors, 31

vendors reporting having over 10,000 sites utilizing an LIS (College of American

Pathologists, 2010). These information systems are used throughout the notification

process, beginning with automated flagging of critical values. Staff no longer has to

compare values to a paper critical value list to determine what notifications are

necessary. Many systems can quickly provide the user with the name and phone

number of the ordering provider or patient unit. Most systems include software that

streamlines documentation of specific names, dates, times, and includes verification

documentation that the results were read-back.   Quality reports can be generated from

this documentation and evaluated for potential issues and improvements. Although the

majority of LIS's offer these solutions, there are still many variances between the

method of notification and documentation in laboratories (Wager et al., 2007; Dighe et

al., 2008; Valenstein et al., 2008).

In the United States, a variety of personnel make the notification phone calls. These

include the technologists performing the tests, section supervisors, laboratory managers

and directors, and clerical staff. Studies have shown that the majority of the individuals

in the laboratory making the notification are the persons performing the tests (Dighe et

al., 2008; Wager et al., 2007). However, it has been noted in the 2008 survey, that an

increasing number of laboratories are implementing call centers. Critical value

notification was centralized in 17% of labs surveyed for the purpose of increasing

productivity (Dighe et al.). These call centers are staffed with both technical and non

technical individuals.   It has been noted that nontechnical personnel are still permitted

to make the notification calls in many laboratories (Wager et al., 2007), although it has

been recommended that all critical values be reported by the personnel performing the tests (Heard et al, 2002). Providers may wish to ask questions concerning the suitability of the specimen for testing or inquire about the results of other lab tests to further help them decide on treatment options. These questions may best be answered by the person performing the test or someone with clinical knowledge of laboratory testing. For example, some institutions have the Lab Directors or physicians report critical results because additional consultation regarding the patient's status could be necessary (Piva et al. 2010). A United States survey by Dighe reported that 7.5% of institutions had Laboratory Directors and Managers making critical value notifications (2008).

There are also reported differences between institutions in the individuals that are authorized to receive critical value notifications. Laboratories have reported authorizing a combination of physicians, mid-level providers, licensed nurses, and unit secretaries/clerical staff to receive critical value notification. (Howanitz et al, 2002; Dighe et al, 2008). Dighe reported that most labs notify the ordering location/unit, the patient's physicians, a nurse, or a nurse manager (2008). The JC requires that the results be ultimately reported to a responsible, licensed caregiver. Therefore, calling an intermediate individual in a physician's office or a ward clerk requires an additional notification from that intermediate individual to the licensed caregiver. As many as 47.5% of labs surveyed have reported that office personnel are permitted to receive critical value notifications (Wager et al., 2007). Massachusetts General Hospital has reported the use of an intermediate Operations Associate (Dighe et al., 2006). These intermediate notifications add additional time to the period from when the critical result

is first identified to when it reaches the appropriate provider. This time has been estimated from 1.8 to 3 minutes (Dighe et al., 2006; Valenstein et al, 2008). The practice of authorizing a ward clerk to receive critical value calls has also been associated with increased rates of undocumented critical value notifications (Wager et al, 2007). A survey of 115 physicians suggested that physicians felt that the staff physician or resident on-call should receive critical values for inpatients (Don-Wauchope 2009).

The method for notification is also not standardized among laboratories. In a 2002 survey of 623 laboratories, 99.2% reported that they used telephone calls, 29.5% used fax machines or similar transmission devices, 10.0% used a computer report as a primary means, 42.2% used a computer report as a secondary means, and 6.9% used an answering machine or voice mail system (Heard et al.). In recent years, there has been an increased interest in implementation of automated notification systems and newer technologies (Piva, et al., 2009; Parl et al., 2010; Tate et al., 1994). In 2008, 8.6% of laboratories reported the use of wireless technologies to assist with critical value notifications (Dighe et al.). Automated systems have been slow to develop because of the requirement for the receiving provider to acknowledge receipt of the critical values. Laboratories are currently meeting this requirement in automated systems by either requiring providers to acknowledge receipt by dialing a number and typing in a code or by acknowledgement on a computer terminal (Parl et al., 2010; Tate et al., 1994). In a 2007 survey of 114 labs, only 1 reported using an automated system in which the identity of the provider is automatically captured when the provider calls back to receive the result. Since then, several large labs have been able to implement

an automated reporting system capable of recording the provider acknowledgment (Parl et al., 2010).

With increasing focus on the timeliness of notification, labs are defining the appropriate time from identification of the critical results to receipt by the caregiver. One large institution reported a criterion of 30 minutes for acceptable reporting (Dighe et al., 2006). A study by Valenstein recommended a laboratory goal of 15 to 30 minutes (2008). Another study reported a goal of no more than 40 minutes (Piva et al., 2014). Studies have reported an actual median of 4 to 19 minutes, with some notifications being abandoned due to being unable to reach a physician (Howanitz et al., 2002; Dighe et al., 2006). Parl et al., reported a mean time of 2.9 minutes for clinician acknowledgement of a critical value page, after implementation of an automated paging system (2010).

Documentation that the critical notification was successful generally includes the name of the individual communicating the result, the name of the person receiving the result, the date and time of the call, and verification that the results were repeated back. In a 2007 survey, 99.1% of labs reported documentation via LIS (College of American Pathologists, 2007). The JC has encouraged evaluation of this documentation to "measure, assess, and improve the timeliness" of reporting (JC 2005). Piva et al. demonstrated a reduction from a mean of 30 minutes to 11 minutes for critical value notification using an electronic notification system (2009). Several studies have suggested that the actual rate of undocumented critical values, including calls that were abandoned, is between 0.2 and 5.4% (Wager et al., 2007; CAP 2007; Heard et al, 2002). Electronic systems have been reported to reduce the rate of undocumented

calls.   Parl et al., reported that 89% of physicians directly acknowledged the critical value electronically with another 6.5% acknowledging via the operator. The 5% that remained unacknowledged by the provider were called to the nursing staff (2010). This study did not include patients from the outpatient setting which has been associated with delayed critical value notifications (Dighe et al., 2006). Abandoned calls are a significant patient safety issue as the definition of critical value suggests death or severe harm in the absence of clinical intervention.

Resource Utilization and Financial Impact

Critical value notification requires a significant amount of human resources.   It has been estimated that it takes between 4 and 13.7 minutes to for a laboratory employee to complete a critical value call (Heard et al., 2002; Valenstein et al, 2008). This includes the time it takes to locate the appropriate phone number, call the appropriate office or unit, wait while the appropriate person designated to receive results gets to the phone, relay the result, have the person repeat back the result, and complete the documentation. J. H. Howanitz & P.J Howanitz estimated that they may have spent as much at 80 hours in 3 months calling only critical calcium values (2006). Data collected at another hospital by Piva et al, estimated an average of 30 minutes of technologist time for each critical value notification by telephone. They reported 7320 critical values in 2007 (2009). This represents 1.8 FTEs dedicated to critical value notification. Hashim and Cuthbert reported the use of seven full time equivalents in a three-hospital system in 2012, based on a critical value frequency of 0.8% (2014). There is a current shortage in laboratory technologists (Garcia, Ali, and Choudhry, 2013) and the need for clinical laboratory technologists and technicians is projected to grow 22% from 2012 to

2022 (Bureau of Labor Statistics, 2014), potentially increasing the percentage of

position vacancies. Each notification requires at least one of the laboratory staff and

one or more providers to receive and relay or document the result. Physicians and

surgeon employment is also expected to increase by 18% and nurses by 25% from

2012 to 2022. The Association of American Medical Colleges predicts a shortfall of

physicians between 46,100 and 90,400 by 2025 (2015). In a recent survey, 81% of

physicians described themselves as either overextended or at full capacity (The

Physicians Foundation, 2014). Each critical value called by laboratorians and received

by providers adds to this already full workload. In order to efficiently use resources, gain

physician satisfaction, and increase patient safety while complying with accreditation

standards, it is necessary to call only results that providers will truly utilize for immediate

patient treatment.

Impact of Critical Value Notification on Patient Outcomes

Critical Values are important to physicians and patients. In a survey of 514

physicians, 94.9% found critical values lists valuable (Heard et al., 2002). Physicians

and other health care providers that order laboratory tests use critical values to change

treatment, prescribe new medications, stop current medications, or send the patient for

additional testing. One study reported that critical value notification led to a change of

treatment in 98.0% of patients admitted to a surgical unit and 90.6% of patients

admitted to a medical ward (Piva et al., 2014). Another study reported critical values

resulted in 66.3% of the tests being reordered (Heard et al., 2002).

Many authors have suggested that a move toward a critical value list and thresholds

based on patient outcomes would lead to the most effective and efficient use of

laboratory resources while addressing patient safety (Piva et al., 2014; Kost and Hale, 2010; Doering et al., 2014)   However, it is widely recognized that little data has been collected on physician response to critical values or on their effect on patient outcomes (J. H. Howanitz & P.J Howanitz, 2006). One such study did explore the outcomes of patients with elevated sodium results. Although an earlier study conducted by Heard et al., 2002 found that the majority of labs use 160 mEq/L or more as a critical limit, J. H. Howanitz & P.J Howanitz discovered that 56% of inpatients who had sodium results between 155 to 159 mEq/L died. Their recommendation is for laboratories using 160 mmol/L or more as a starting point and then evaluate patient outcomes at lower levels to determine whether lowering the critical value to 155 mEq/L is beneficial (2007). Another study resulted in the change of the critical threshold for glucose from 40 to 50 mg/dL based on provider responses to 8 critical values. Six of the 8 critical values resulted in treatments (Hashim and Cuthbert, 2014). The same institution also concluded that adding bicarbonate to the critical value list at a threshold of <12 mmol/L was not supported. In a one week audit, 28 critical value notifications resulted in specific treatment for only 5 notifications. Eight notifications resulted in no treatment at all and 15 resulted in normal saline for dehydration only. Raising the platelet threshold from 11 to 19 $x10^9$ L was also not supported due to lack of physician intervention in a one week audit of 36 notifications for 14 individual patients. Physicians did not initiate any treatment for 69% of the notifications.   A study by Brigden et al., determined that 7 patients out of 65 with INR values >6.0 had bleeding on presentation. Two of the patients were considered to have major bleeding and required hospitalization. Five were considered to have minor bleeding. The focus of the study was the difference in

outcomes between groups treated with vitamin K versus those not treated with vitamin K. Thirteen of the patients were treated with vitamin K, but the authors determined that the clinical outcomes between the treated group and the group that was not treated with vitamin K were similar. The study did not explore or suggest a threshold for an INR critical value (1998). Doering et al., reported that elevated glucose and aPTT results had no relationship with in hospital mortality (2014). They suggested that these tests lack utility as critical values.   The same study indicated that 30% of inpatients with a serum lactate value of ≥ 4.0 mmol/L did not survive the hospital admission. The authors suggest that elevated lactate, INR, and sodium, as well as low glucose, hemoglobin, hematocrit, and potassium indicate increased risk of death. These studies reviewed above have two common themes. The majority of the critical values reviewed were from inpatients and a small number of cases were reviewed in total.

There still remains a concern for the lack of follow-up for abnormal results. Howanitz and Cembrowski found that 3.5% of abnormal results were not documented in the patient's record (2000). In another study, over 23% of the patient records did not contain documentation of the abnormal result. It is unknown whether physicians chose to act upon these critical values or not.   It has been postulated that not all critical results are optimally chosen to predict mortality (Doering et al., 2014). Other possible reasons for the lack of intervention have been suggested. The abnormal result may offer no new additional information other than that already documented, the patient was already receiving appropriate care for the condition, or the patient had died (Singh et al., 2010).

Critical Values – Outpatient Settings

Laboratory testing and critical value notification in the outpatient population is different from the inpatient population or an emergency room population. Outpatients are seeking routine care or requiring a lower level of care than is delivered in the inpatient setting or an emergency room. Although the two populations are different, the majority of laboratories apply the same critical value list to all patient types. Wager et al. reported only 16% of labs had unique critical values by patient population and/or by location (2007).

The number of critical values reported for outpatient is usually less than the number for inpatients (Dighe et al. 2006; Zeng et al., 2013; Piva et al., 2009). Laboratories have reported the frequency of critical values in the outpatient setting to be from 0.4% to 0.84% of lab results (Piva et al., 2009; Zeng et al., 2013)   Dighe et al, reported that inpatient tests were 3.5 times more likely to result in a critical result that outpatient tests (2006). However, critical value notification is very important in the outpatient setting. Clinicians have reported that critical values were unexpected findings for as many as 65% of patients in the outpatient setting. (Piva et al., 2014). Hospitals report that 16.9 to 20.5% of all critical values are from patients in the outpatient locations (Dighe et al., 2006; Piva et al, 2009).

Critical values in the outpatient setting have unique issues. It has been noted that reporting critical values on outpatients could double the time that a laboratory technologist dedicates to a single critical value notification, making the selection of the tests and thresholds in the outpatient setting very important. One of the strongest predictors of critical value notification delays is the specimen being collected in the

outpatient setting (Dighe et al., 2006; Dighe et al., 2008). One study reported that it took 13.7 minutes on average to report a critical value on an outpatient in comparison with 6.1 minutes for an inpatient (Heard et al., 2002). Sciacovelli, L., et al. reported a mean of 11.03 minutes to report a critical value in an outpatient setting versus 4.66 minutes in the inpatient setting, citing the necessity of repeat calls to reach a provider as a barrier to timely notifications (2015). Dighe et al., reported an average time from a result entering the callback queue to being given to the unit or ordering physician was 22 minutes, with a 9-minute median time (2006).

Failure of providers to follow-up on abnormal laboratory test results for ambulatory patients has been reported to be 6.8 to 62% for ordered laboratory tests (Callen, Westbrook, Georgiou, and Li, 2011). These studies included results that were abnormal and not necessarily meeting the testing laboratory's critical result criteria. There are several reasons that follow-up in the outpatient setting may be more difficult than the inpatient setting. First the patient may not be a patient of the provider receiving the critical value. Specimens are often drawn several hours prior to being received in the testing lab. When the testing has been completed, the ordering physician may no longer be at the office. The critical value notification is often made to an on-call physician who is unfamiliar with the patient and the patient's condition.

Secondly, the provider may have trouble locating the patient. The provider may not have access to the patient demographics at the time the critical result is being received, the patient information may not be current, or the patient may be unavailable. Unlike inpatients, the patients are not in a defined location such as a hospital bed.

In addition, providers may question the accuracy of the result based on their assessment of the patient and the pre-analytical errors associated with specimen storage and transportation delays. Specimens are often stored for several hours in a physician's office before being transported to the testing lab. If serum remains unseparated from the cells during storage at room temperature, glucose concentrations decrease (Boyanton and Blick 2002). If serum is left in contact with the cells, glucose can decrease by 10% in 2 hours at room temperature compared to 4% after 2 hours at 4ºC. In contrast, potassium was more stable at room temperature, but increased by 9% at 4ºC after 2 hours (Oddoze, Lombard, & Portugal, 2012). The experience level of a provider identifying potential pre-analytical errors in laboratory testing may impact the provider's decision to respond to a critical value.

Finally, the provider in the outpatient setting may question the relevance of the result. If a test was drawn several hours before notification, it may be assumed that the patient has already taking another dose of medication, or the condition would have resolved itself, or forced the patient to seek emergency services. The provider may choose not to act on the result. The clinically relevant timeframe for an outpatient result is very different from an inpatient result.

There are a limited number of studies on provider response to outpatient critical values. The reasons that outpatient providers choose not to act on critical values is unexplored. It may be that the critical value list is not clinically appropriate for outpatients. Upon survey, 9.7% of more than 700 laboratories indicated that some or all of outpatient critical values are reported the following day (Dighe et al., 2008), suggesting that the values do not represent a life-threatening condition at all. Possibly

due to the difficulty in accessing outpatient records to track provider follow-up and treatment, the majority of the studies rely on physicians self-reporting their responses to critical value notifications. In a study by Piva et al., doctors were asked to provide information on any medical intervention in response to receiving a critical value. Physicians reported 100% follow-up for all critical values for patients admitted to wards and two groups of outpatients (2014). Piva et al. did include an audit of practitioner responses to 117 critical values from the two groups of outpatients representing 1) patients with critical potassium levels and 2) patients with critical INR values. One hundred percent of patients with critical potassium levels were reported to be treated within 4 hours of notification. A change in warfarin dosage or stopping the drug was the main clinical responses to all critical INR results. This study relied on the self-reporting of general practitioners (2014). Another survey based upon physician self-reporting in 70 primary care provider offices found that they communicated 52.9% of critical laboratory results to the patient in less than one hour from receipt and 37.1% in 1 to 4 hours from receipt (Montes, Francis, & Cuilla, 2014). In contrast, a blind review of the electronic medical record reported that 10.2% of abnormal lab test results in an electronic record remained unacknowledged after 2 weeks, and timely follow-up was lacking in another 6.8% of acknowledged abnormal results (Singh et al., 2010).

A few studies investigating appropriate tests and thresholds for critical values that do include outpatients, but do not include physician responses to critical values or did not include patient outcome data have been published. The Howanitz and Howanitz study evaluation of critical calcium results did not include physician responses or response time for the 37 outpatients included in their 2006 study, or the 13 outpatients

with critical sodium values in their 2007 study. In Hashim and Cuthbert's analysis of

three tests for threshold changes, only one outpatient was reviewed for a critical platelet

result. It was unclear if any of the nine patients with low bicarbonate values were

outpatients and it was not stated how many of the eight glucose values reviewed were

from outpatients (2014). The Brigden et al., study did focus on the outpatient population

for clinical responses to excessive oral anticoagulation. The goal of the study was to

follow patients with ≥ 6.0 INR values and identify factors associated with poor

anticoagulation control and report on management and outcomes of patient with poor

control. The study reported that 7 patients with INRs ≥ 6.0 did experience bleeding

complications. Two were considered to have major bleeding and 5 were considered to

have minor bleeding. No recommendation for PT/INR critical value threshold was made

(1998). The Doering et al. study analyzed 5 years of data to determine if critical value

thresholds indicated an increased risk of mortality, but only for in-hospital mortality

(2014).

   In summary, critical value notification for outpatients presents a very different set of

problems than critical value notification for inpatients. Outpatients require a different

level of care than inpatients. The time between specimen collection and notification of

results is hours instead of minutes, and the patient is not in a defined location for

treatment. However, laboratories generally use the same critical value list for both

populations. In order to limit the utilization of laboratory staff and providers' time to

activities necessary for patient safety, it has been suggested that critical value lists be

reviewed and only analytes that truly suggest a life-threatening condition be selected.

This is extremely important for outpatient critical values as It is also noted that critical

value notification in the outpatient population can take twice as long as inpatient

notification. There have been no studies to determine if an on-call physician is less

likely to respond to a critical value than the ordering provider. There have been no

studies to determine if provider experience affects the likelihood that a physician will

respond to an outpatient critical value. There have been no studies to determine if the

time from draw to delivery of result effects the providers' choice to respond to a critical

value.

Chapter 3: Methods

Introduction

In Chapter 1, the research problem, the significance of the problem, and the five specific aims that guided this research were presented. Variables were defined and operationalized for each aim. In Chapter 2, a literature review including the evolution of critical value lists, current accreditation standards for notification procedures, and an overview of the tests selected for the study was set forth. Published studies estimating the time involved in relaying critical values and associated labor costs were presented, leading to the significance of the problem and the importance of the variables selected for analyses. In Chapter 3, research methods and statistical analyses are discussed. The research design, the represented population, sampling and statistical power, data collection methods and records review protocols, statistical analyses tied to specific aims, and any changes to the original research protocol are specific topics in Chapter 3.

Problem Statement

Critical value notifications are costly in terms of physician and laboratory staff resources. There is a gap in knowledge of whether physicians receiving outpatient critical value notifications respond to them and whether their responses have an impact on patient outcomes. Although laboratories are required to make immediate notification of critical values, there are no studies suggesting faster notifications in the outpatient

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population result in better patient outcomes. It is unknown if there are physician, and notification factors that are correlated with a physician's likelihood of responding to a critical value in the outpatient setting.

Specific Aims

- Specific Aim 1: To determine the provider utilization rate and response times for PT/INR, digoxin, and glucose critical value notifications for outpatients.

- Specific Aim 2: To determine if there is a difference in patient outcome indicators when providers respond to critical values, compared to when they do not.

- Specific Aim 3: To determine if quicker response times result in better outcomes.

- Specific Aim 4: To determine if there are specimen, provider or notification factors that influence a provider's likelihood to responding to a critical value.

- Specific Aim 5: To determine if the magnitude of the test result predicts whether or not a provider will respond to a outpatient critical value notification.

Research Design

This study was a retrospective non-experimental study (Polit & Beck, 2008) with four specific aims. A true experimental study was not practical due to ethical considerations. Creating a control group of patients that would not receive treatment in response to a critical value notification would potentially cause significant harm or death to the patients. However, the provider choice whether to respond or not to respond to critical value notifications provided two patient groups to use for comparison in this study. The first three aims of this study were designed to determine if critical values are utilized by providers and if there is a difference in patient outcome measures when they do and when they do not respond. The fourth aim of the study was designed to explore factors

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that would potentially influence physician choice to respond or not respond to a critical value notification. The final aim of the study explored the appropriateness of the thresholds chosen as critical for each test.

Population

The reference population is all digoxin, PT/INR, and glucose critical value notifications for ambulatory outpatients and the associated provider responses. The sample for the study was all critical value notifications for outpatients with critical PT/INR and glucose results analyzed in Riverside Health System (RHS) Laboratories from October 1, 2014 to December 31st, 2015 and critical digoxin results from January 1, 2014 to December 31st, 2015. Thus the record of analysis was a critical value notification. Multiple critical value notifications per patient and physican were possible during the dates for which data was collected. Nursing home patients were excluded from the outpatient population as they are more similar to inpatients than outpatients. Nursing home patients have continuous supervised care in a specific location.

RHS is a integrated health network of providers and facilities that serve Eastern Virginia. The system has over 500 providers in various types of healthcare facilities including 5 acute care hospitals, 3 specialty hospitals, 3 retirement communities, and over 100 other diagnostic and outpatient care clinics. The Riverside Medical Group, the largest group of providers ordering outpatient laboratory testing for the system, delivers care to over 485,000 patients from Virginia's Eastern Shore to the Northern Neck. The medical group schedules over 1.3 million patient visits annually for routine well exams, sick visits, and monitoring of chronic illnesses. All laboratory testing for self-pay patients and insured patients not requiring a contracted laboratory are sent to Riverside

laboratories for analysis. Results are returned electronically to these providers. The

demographics of the patient populations served by the laboratories are extremely

diverse. The Health System is a medical provider for patients in the extremely rural

areas to the north and south to very urban areas on Virginia's eastern coastline. The

geographic market areas for Riverside Health Systems is shown in Figure 1. The data

for this study was collected from all five laboratories in the acute care hospitals

described below.
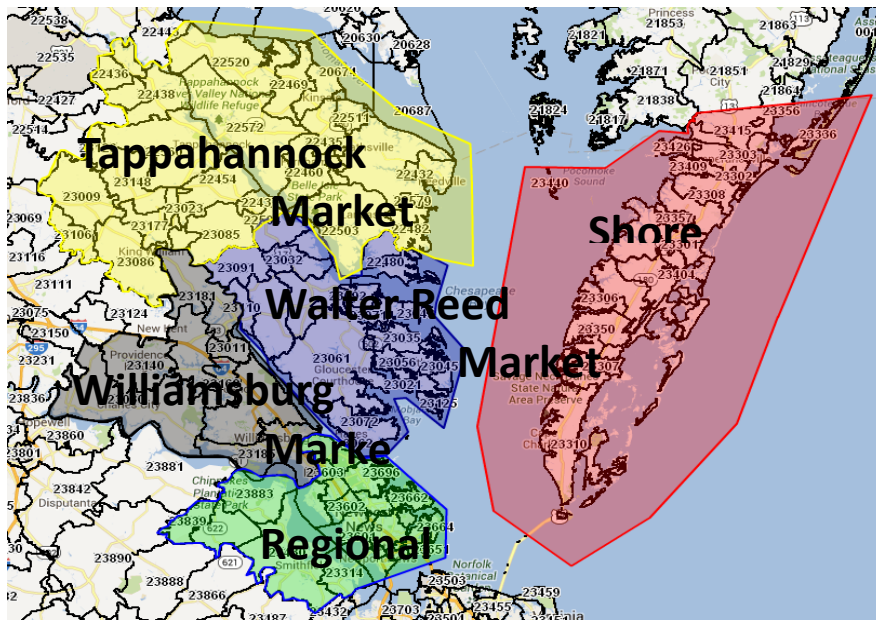
Figure 1. Riverside Health System Market Area

Riverside Tappahannock Hospital (RTH) Laboratory serves a 67 bed acute care

hospital that cares for citizens of the Tappahannock area, including Essex, Richmond,

and Westmoreland Counties. This area is referred to as Virginia's Northern Neck. RTH

Laboratory is located in Tappahanock, the largest city of Essex County, Virginia. The

county population is estimated to be 11,103. Over 7% of the population under 65 years

of age did not have health health insurance in 2013. The median household income is

$44,885.00 with 15.5% of persons living in poverty (United Census Bureau, 2014). Riverside Family Medicine has six medical centers in the Northern Neck. The Laboratory performs approximately 125,000 tests annually to support the hospital and the medical centers.   The Laboratory is staffed with 9.5 full time equivalents (FTEs) to cover this testing volume and perform duties including critical value notification.

Riverside Walter Reed Hospital Laboratory provides services for a 67 bed acute care hospital in Gloucester, Virginia in addition to several convalescent centers and Sanders Retirement Village. Gloucester County has an estimated population of 37,141. In 2013, 14.1% of residents were estimated to be without insurance. The median household income is $60,519.00 with 10.6% of the patients living in poverty (United Census Bureau, 2014). The Laboratory performs approximately 183,000 tests annually. The Laboratory is staffed with approximately 20 FTEs to cover this testing volume and perform duties including critical value notification.

Riverside Doctors' Hospital Laboratory provides services for the 40 bed acute care hospital in Williamsburg, Virginia. Williamsburg has an estimated population of 14,691. In 2013, 16.5% of the residents were uninsured. The median income is $48,616 with 21.1% of persons living in poverty (United Census Bureau, 2014).   The Laboratory performs approximately 90,000 tests annually. The Laboratory is staffed with approximately 10 FTEs to cover this testing volume and perform duties including critical value notification.

Riverside Shore Memorial Hospital Laboratory provides services for the 143 bed acute care center, 3 primary care facilities, several home health agencies, and 3 long term care facilities on the Eastern Shore of Virginia. This area includes both

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Northampton and Accomack Counties with populations of 12,121 and 33,021 respectively. In 2013, 20.9% of persons in Northampton County did not have health insurance. Accomack County had a similar rate of 20.5% of persons uninsured. The median household income was $33,635 in Northampton County and $39,328 in Accomack County in 2013. Over 22% of Northampton County and 19.3% of Accomack County residents live in poverty (United Census Bureau, 2014). The Laboratory performs approximately 197,000 tests annually and is staffed with 19 FTEs to cover this testing volume and perform duties including critical value notification.

Riverside Medical Group Shared Laboratory located in Riverside Regional Medical Center serves as the primary reference laboratory for the outpatient clinics, diagnostic centers, and the other four hospital laboratories. It also serves the laboratory needs of a 450 bed facility and Level II Trauma Center in Newport News, Virginia. The city of Newport News has a population of 182,965. Median household income is $51,027 with 15.2% of residents living below the poverty level in 2013 (United Census Bureau, 2014). Excluding pathology and transfusion service, the main laboratory performs approximately 1.8 million tests per year. It is staffed with approximately 80 FTEs.

Combined, the RHS laboratories perform approximately 2.4 million tests per year. Approximately 25,000 critical value notifications are made per year, representing 1.05% of the total tests performed. These notifications include both outpatient and inpatients. Approximately 3,600 critical value notifications are made to physicians in the outpatient setting, not including patients who are residents of long term nursing facilities. An estimated annual average of 300 PT/INR critical value notifications, 450 glucose critical value notifications, and 30 digoxin critical value notifications are made to providers for

patients the outpatient setting. Due to these volumes, data was collected for a 16

month period for PT/INR and glucose and for a 24 month period for digoxin. Historically,

critical values from PT/INR, glucose, and digoxin tests represent approximately 20% of

the total outpatient critical values.

The RHS sample was designed to be generalizable to all critical value notifications

for ambulatory outpatients in the United States. As described above, the population

served by the health system is very diverse, ranging from very urban areas to very rural

areas. Over 500 providers are responsible for more than 485,000 patients' care in over

130 locations. The laboratories are accredited by the College of American Pathologists

and thus are subject to all federal regulations and organizational standards concerning

the selection of critical tests and thresholds, the notification of critical values, and the

documentation of critical values. CAP accredits the majority, or 16,198 of the 16,431

labs holding Certificates of Accreditation in the United States (CMS, 2015).

Variables

All variables for the study were operationalized, defined, and listed by specific aim in

Table 1.   The first column of the table lists the variable names for the study, the second

column describes the level of measurement for each variable, the third column defines

the value or category for each variable, and the final column defines the variable as a

dependent or independent variable by aim. This table is described in the following

paragraphs and referenced throughout this chapter.

The first two rows of the table describe two important confounding variables. Patient

ID is an assigned study number. A single patient could have many critical value

Table 1. *Variable Table*

Variable	Level of Measurement	Definition of Observation Variable	By Aim, IV or DV
Patient ID	Nominal	Assigned study number	Confounding variable
Physician ID	Nominal	Assigned study number	Confounding variable
Provider Response/No Response	Nominal	1 if provider attempted to respond (successful or unsuccessful) 0 if provider did not attempt to respond	Aim 1 - DV Aim 4 - DV Aim 5 - DV
Successful Response/Unsuccessful or No Response	Nominal	1 if successful response 0 if no response 0 if unsuccessful response	Aim 2 - IV
Response Time	Nominal	1 = < 4 hours 2= ≤24 hours 3=> 24 hours	Aim 3 - IV
Contacting the patient	Categorical	1 = < 4 hours 2= ≤24 hours 3=> 24 hours	Aim 1 - IV
Order follow-up testing	Categorical	1 = < 4 hours 2= ≤24 hours 3=> 24 hours	Aim 1 - IV
Stopping or Changing medication	Categorical	1 = < 4 hours 2= ≤24 hours 3=> 24 hours	Aim 1 - IV
Prescribing new medication	Categorical	1 = < 4 hours 2= ≤24 hours 3=> 24 hours	Aim 1 - IV
Directing patient to the emergency department	Categorical	1 = < 4 hours 2= ≤24 hours 3=> 24 hours	Aim 1 - IV
Test Type	Categorical	1 = PT 2= Digoxin 3= Glucose	Aim 1 - IV Aim 2 - IV Aim 3 - IV Aim 4 - IV
Outcome/No Outcome	Nominal	1 if outcome, 0 otherwise	Aim 2 - DV
Unplanned emergency department visit	Dichotomous	1 if unplanned ED vast, 0 if no visit	Aim 2 - DV Aim 3 - DV

Patient Death	Dichotomous	1 if death, 0 if no death	Aim 2 - DV Aim 3 - DV
Result of the next	Categorical	1 = within reference range 2 = Above reference range 3 = critical value 4 = below reference range	Aim 2 -DV Aim 3 - DV
Evidence of bleeding (PT test only)	Dichotomous	1 if evidence of bleeding, 0 if no evidence	Aim 2 -DV Aim 3 - DV
Evidence of Hyperkalemia or atrial fibrillation for digoxin test only	Dichotomous	1 if evidence of symptoms, 0 if no evidence	Aim 2 -DV Aim 3 - DV
Evidence of nausea, vomiting, or confusion for glucose only	Dichotomous	1 if evidence of symptoms, 0 if no evidence	Aim 2 -DV Aim 3 - DV
Specimen age	Interval	Time in minutes from specimen draw to critical value notification	Aim 4 - IV
Physician Type	Dichotomous	Physician was ordering physician = 0, on-call physician = 1, office nurse =3	Aim 4 - IV
Notification Time	Dichotomous	Time of notification was during business hours = 0, was not during business hours = 1	Aim 4 - IV
Repeat Test for this test type	Dichotomous	If notification was from repeat test=0, if not = 1	Aim 4 - IV
Physician Experience	Interval	Number of years the provider has been licensed to practice	Aim 4 - IV
Previous diabetes diagnosis	Dichotomous	1 if patient had previously been diagnosed with diabetes, 0 if not	Aim 4 - IV
Historical test results for this test type	Dichotomous	If documentation of result higher than reference range in the past year = 1, if not =0	Aim 4 - IV
Delta above Critical value for this test type	Ratio	Difference between critical threshold and patient vale	Aim 5 - IV

notifications during the study period and was assigned the same identification number for each notification. Multiple critical value notifications for a patient presented an opportunity for physicians to respond differently to a single patient based upon knowledge the patient's medical history including previous outcomes after having elevated or critical laboratory values. This variable allowed exploration of patient specific bias in responses. Simarily the second confounding variable, physician ID, allowed physician specific biases in response to critical values to be explored. A certain physician may choose to never respond to a critical value for a particular test based upon their own experience with patient outcomes. This impact of these two variables were considered prior to logistic regression.

The next rows describe responses and response times. The Notification Response/No Response variable records the provider response to a critical value notification and was used as the dependent variable in Aims 1,4, and 5.   If the provider contacted the patient, ordered follow-up testing, scheduled a follow-up appointment, stopped or changed medication, prescribed new medication, or directed the patient to the emergency department, it was considered a response to a critical value notification and coded as a 1, and otherwise the variable was coded as a 0. In addition, an unsuccessful attempt to contact the patient was also coded as 1 and included in the response category for Specific Aims 1,4, and 5. The purpose of Specific Aim 1 was to describe providers' actions and make inferences about relationships between response, speeds, and tests. Specific Aim 4 explored factors that influenced a provider's liklihood of response in order to create models for prediction of provider response. Specific Aim 5 explored the impact of result magnitude on a provider's likelihood of response. In all

three aims, the providers' intent to act on the notification even if the attempt was

unsuccessful was the desired definition of the response variable; therefore unsuccessful

attempts to contact the patient were treated the same as a successful response.

However, in Specific Aim 2, the purpose of the aim was to explore the relationship

between response types, speeds, and outcomes. If the provider was unsuccessful in

contacting the patient, there would have been no intervention or treatment for the

condition indicated by the critical value. Therefore, line 4 operationalizes the response

variable to be used as the independent variable in Specific Aim 2 differently by coding

only the successful responses as a 1 and unsuccessful and no responses as a 0. The

next rows of the table describe the individual response type variables including

contacting the patient, ordering follow-up testing, scheduling a follow-up appointment,

stopping or changing a medication, prescribing a new medication, or directing the

patient to the emergency department. These are categorical variables that were

assigned a value depending on the response time that the action was taken. A fast

response time, defined as less than 4 hours was assigned a value of 1. A slow

response time, defined as within the 4 hour to 24 hour time period after the notification

was assigned a value of 2. A response of greater than 24 hours was assigned a value

of 3.   Any responses greater than 24 hours, were not considered a response to the

critical value notification, but still recorded so that a comparison of critical values never

addressed by a provider could be made with current literature. The individual response

type and time variables were used as the independent variable in Aim 1.   As explained

in the Results chapter, during analysis, the decision was made to recode both fast and

slow responses into a single dichotomous variable of 1 for a response and 0 for no

response. For example, a slow response to a critical glucose value notification, originally coded as a 2, was recoded as a 1. A fast response to a critical value notification remained a 1. A response greater than 24 hours, originally coded as a 3, became a 0. No response remained coded as a 0. This was done to eliminate the violation of assumptions for the chi square due to smaller than expected cell sizes in further analyses. The lack of a relationship between test and response speed further validated this decision.

The next row, named test type, is a categorical variable that is coded to a number for each test type, one for PT/INR, two for digoxin, or three for glucose.   It was used as an independent variable in Aim1, Aim 2, Aim 4, and Aim 5. This variable was used to determine if there were differences in liklihood of response, time of response, or type of response for each different test.

The next group of variables are the outcome variables. The overall outcome variable includes all types of outcomes. If any one of the outcomes defined in the table were coded as a 1, then the overall outcome variable became a 1. The following six variables describe the specific outcomes. Patient death, unplanned emergency department visits, and the result of the next test were outcome variables applicable to critical value notifications for all three tests. Evidence of bleeding applied only to PT/INR critical values, evidence of hyperkalemia or atrial fibrillation applied to digoxin critical values only, and nausea, vomiting or confusion was specific for glucose critical values. These outcome indicators were used as dependent variables in Aims 2 and 3. During analysis, it was determined that the removal of the result of the next test as an outcome indicator was necessary. The outcome indicator was inflated in the cases in

which the providers chose to respond to a critical value due to the ordering of repeat testing for verification. For example, a provider would respond to a critical value notification of a PT/INR by ordering a repeat test. The results of the repeat test would also be critical. This did not occur in the cases that did not have a provider response. Therefore the results of the next test was removed as a dependent variable in Aim 2 and Aim 3. During analysis, death was also removed as an outcome variable as there were no cases that resulted in death. This left an unplanned ED admission as the only outcome indicator common to all three tests.

The next group of variables in Table 1 are independent variables for Aim 4. They represent factors that could have affected a provider's choice to respond to the critical value. They include the age of the specimen at the time of the critical value notification, whether the provider receiving the notificaton was the ordering provider, an on-call provider or nursing staff, if the notification was during office hours, whether the critical value notification was from a repeated test, how long the physician had been practicing medicine, historical results for the patient, or a previous diagnosis of diabetes for the patient.

The final variable on the table is the delta above the critical value threshold for the test type. The numerical results were transformed to standard scores for the independent variable in Aim 5. The transformed scores allowed for a single variable representing magnitude of result to be used in analyses for all three tests whose raw scores are reported in different units.

Sample Size and Statistical Power

The necessary sample size for the study was prospectively determined to be between 300 and 400 critical value notifications. The largest number of predictors used in any multiple regression in this study was nine. Using Soper's calculation for multiple regression with nine predictors, and a 0.05 effect size, the estimated sample size is 321. This calculation uses an apriori sampling size (Soper, 2015; Cohen, 1988; Cohen, J., Cohen, P., & Aiken, 2003). This sample size allows detection of R^2 as low as 0.25 in any multiple regression involving nine operational variables with 80% confidence that there will not be a Type II error and 95% confidence that there will not be a type I error. The sample size was reviewed retrospectively after collection of data. Although approximately 650 critical values for glucose, 425 critical values for PT/INR and 40 critical values for digoxin were expected during the collection period, data were collected for 452 critical glucose values, 157 PT/INR values, and 28 digoxin values. The number of cases included in the study was lower than estimated due to a higher than expected frequency of critical values in the long term healthcare patient population which had been excluded from the study. A total of 637 critical results were included in the study, a sample size that was above that required by Soper's calculation. Sample size was also compared to guidelines specific for multiple logistic regression analysis. Peduzzi et al.'s suggests a minimum of 10 events per parameter are needed to have acceptable coverage of Wald-based confidence intervals and Wald tests of coefficients (1996). In order to apply this guideline to logistic regression analysis that have multiple terms for a number of covariates, it has been suggested that the guideline should be based upon the frequency of the least frequent outcome, or in the case of this study,

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critical value notifications for which there was no response (Hosmer, David & Lemeshow, Stanley, 2000). In the data set, there were 166 critical value notifications without a response. Based upon this estimation, logistic regression data analysis for a sample of this size should have no more than 16 predictors. In this study, no more than nine predictors were used for any logistic regression. Thus the sample size, 637 cases, was determined to be sufficient for all analyses with the exception of any follow-up analyis using the digoxin test only.

The sample size was designed to minimize the risk of failing to reject the null hypothesis that there is no difference in patient outcome indicators when physicians respond to critical values and when they do not when a difference actually exists with 95% confidence. This Type I error would result in an interpretation that critical value notifications fail to positively impact patient care when in reality they do impact patient care in the reference population. This type of error may influence a change in critical value list tests or threshold that would lead to truly critical conditions going untreated. It was also designed to minimize type 2 error, the possibility that the null hypothesis was either falsely accepted or rejected with 80% confidence. Implications of a small sample size, especially in the case of critical notifications for the digoxin test are addressed in the results chapter.

Critical Value Thresholds

All five laboratories make critical value notifications for the same tests at the same thresholds. Established thresholds for digoxin, PT/INR, and glucose results are shown in Table 2. Riverside Health System has no established critical levels for

subtherapeutic digoxin and PT/INR results. The glucose test has thresholds in both the low an high result ranges.

Table 2. *Riverside Health System Critical Values*

Test	Low threshold	High threshold
Digoxin	no low threshold	≥ 2.5 ng/mL
PT/INR	no low threshold	≥ 4.5
Glucose	≤ 40 mg/dL	≥ 400 mg/dL

RHS Laboratories are required to call outpatient results to the a licensed provider within 15 minutes of obtaining the specimen result. If it is after business hours, the provider on-call for the practice is paged. If the provider does not respond to the page within 30 minutes, the technologist will page again. If the provider has not returned the page within an hour, the result is given to the hospitalist or on-call pathologist. The technologists enters the licensed provider's name, date and time of the notification, and their technologist identification in the Laboratory System. This information is visible on all electronic and paper copies of the test results.

Data Collection

The data were extracted from multiple sources using different software. For the initial extraction of critical values and associated test resulting variables, Cerner Corporation's Millennium PathNet General Laboratory Module was used. The laboratories at the five hospitals use this software for result entry, result verification, documentation of critical value notifications, and results reporting. Cerner Corporation allows the use of Cerner Command Language (Cerner CCL) in the Cerrner DiscernVisualDeverloper.exe (DVDev), an operating system command-line editor, to select and report information from the Cerner Millennium database. Code was written in

the DVDev to return all critical values for all hospital laboratories for digoxin, PT/INR, and glucose tests. The code was written to limit the time period from October 1, 2014 to December 31st, 2015 for PT/INR and glucose results and January 1, 2014 to December 31, 2015 for digoxin results. In addition, the code limited the patient type to the outpatient type only. Twelve reports were extracted, one for each month. This method of extraction was chosen to limit the query to a manageable size and allow for uninterrupted flow of laboratory operations. The information in Table 3 was returned by the query. The patient data were compiled into an Excel Spreadsheet.

Table 3. *Critical Value Data Elements Extracted from Cerner Laboratory System*

Data Element	Format	LIS Entry Method
Name	Last Name, First Name	Auto-entry, software
Alias	5 to 7-digit facility medical record number	Auto-entry, software
Location	Facility Code followed by location code	Auto-entry, software
Date of Birth	MM/DD/YYYY	Auto-entry, software
Date and Time of Collection	MM/DD/YY HH:MM	Manual entry, phlebotomy
Date and Time of Result	MM/DD/YY HH:MM	Auto-entry, software
Test	Test Name	Auto-entry, software
Accession Number	0000YYYYDDDXXXX	Auto-entry, software
Ordering Provider	Last Name, First Name	Auto-entry, software
Result	NN.NN	Auto-entry, software
Documentation Time	MM/DD/YY HH:MM	Auto-entry, software at the time of result verification
Notification Information	"Critical (Laboratory test), called to and read back by (receiving provider) on MM/DD/YYYY HH:MM by (technologist ID)	Laboratory test, provider, date and time, and tech ID is manual entry

Note. MM = month; DD = day of month; DDD = day of year; HH:MM hours and minutes; XXXX= daily numerical order

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Two data elements listed above need further description. The documentation time is recorded by the software when the result is verified. Under normal circumstances, the technologist will document the critical value and then verify the result immediately afterwards. In this scenario, the documentation time will be the same as the notification time, However, if the laboratory system is down or the technologist was not at their computer when the critical result was given to the provider, the documentation time may be after the critical value notification. In this instance, the technologist documents the actual critical value notification time in the text field. When the two fields were in discord, the technologist documentation in the text field was recorded as the actual time of notification.

The charts from each patient with a critical value notification were accessed in Centricity, a GE software product. This system was the electronic medical record for Riverside Health System provider practices and many ancillary departments. Centricity provides access to over 785,000 patient charts in 132 Riverside locations. All Cerner laboratory results for testing ordered by the Riverside Medical Group were interfaced to this medical record. At the time of the critical value notification, the critical results are not available for provider review in Centricity. The technologist must first complete the electronic critical value notification documentation form at the time the results are released. Once the documentation is completed, the results are verified in the system. At this point, the results and all accompanying information such as low, high, or critical indicators, are queud for interfacing. Depending on provider preference, the results are interfaced to Centricity as a batch as little as once per day or individually in a real-time fashion. Any documentation related to provider response to the critical

value would not be placed within the Centricity lab test report, but within the document section of this software. This section of the software was reviewed for provider response to critical values. During the data collection period, it became apparent that providers did not use the same electronic formats to capture their responses. A more thorough review of procedure notes, nursing notes, phone notes, and office visit notes was required to collect all response elements. The following information was recorded for each patient:

1) Was the patient documented as having diabetes prior to the critical value notification? This would include International classes of diseases (ICD)-9 codes in the range from 250.00 to 250.93 or ICD-10 E08, E09, E10, and E11 code categories.

2) Was the critical value notification the result of a repeated test for a previous critical value notification? If the patient had previous results for glucose, PT/INR, or Digoxin levels above the reference range? The reference range for glucose is 70 – 120 mg/dL. The reference range for PT/INR 10 – 12.6 seconds. The reference range for digoxin is 0.8 to 1.5 ng/mL.

3) Was there documentation of any symptoms of digoxin toxicity, unplanned ED admission, or death within 72 hours after a digoxin critical value notification?

4) Was there documentation of any symptoms of anti-coagulant toxicity, unplanned ED admission, or death within 72 hours after a PT/INR critical value notification?

5) Was there documentation of symptoms of hypoglycemia or hyperglycemia within 72 hours after a glucose critical value notification?

6) Was the provider that received the critical value notification was the ordering provider, nursing staff, or on-call provider?

7) Did a provider respond to the critical value notification?

8) What was the length of time from specimen collection to critical value notification?

If a record of response to the notification was documented, the additional information in Table 4 was recorded. The type of provider, either ordering provider, nursing staff, or on-call provider receiving the notficaiton was included as medical offices often have physicians on-call after hours and this may influence their liklihood of responding to a critical value notification.

Table 4. *Physician Responses*

Response	Provider Type	Time Recorded
Provider documented receipt of critical	Nurse, Ordering, On-Call	Time of Response
Provider contacted the patient	Nurse, Ordering, On-Call	Time of Response
Provider ordered follow-up testing	Nurse, Ordering, On-Call	Time of Response
Provider stopped or changed dosage of medication	Nurse, Ordering, On-Call	Time of Response
Provider prescribed new medication	Nurse, Ordering, On-Call	Time of Response
Provider scheduled follow up appointment	Nurse, Ordering, On-Call	Time of Response
Provider directed them to the ED	Nurse, Ordering, On-Call	Time of Response

The chart from each patient with a critical result was also accessed in ED PulseCheck, the acute care hospitals' Emergency Department Information System (EDIS), a Picis Clinical Solutions product. For either unplanned or provider-directed

visits to the Emergency Department, provider-documented symptoms of toxicity for patients with digoxin or PT/INR critical values were recorded. Provider documented symptoms of hypoglycemia or hyperglycemia were recorded for patients with critical glucose results. Provider referrals, if available, were recorded. Any provider comment regarding their decision to either respond or not to respond to the critical value was recorded.

Once all of the critical value data has been collected and entered into an Excel Spreadsheet, the number of years each physician has been licensed to practice was recorded. This information was provided by the Riverside Health System Credentialing Office.

De-identification of Protected Health Information

During the collection of data, all Excel spreadsheets were stored on a Riverside Hospital Server Drive. The Safe Harbor Method of de-identification was used to protect individually identifiable health information (U.S. Department of Health & Human Services, Section 164.514 (a) of the HIPAA Privacy Rule). The patient name, date of birth, and medical record number were removed and replaced with a study number. Additional columns were added to the spreadsheet and the following information was calculated from the dates and times that were collected as described in Table 3 and Table 4:

1) Time from specimen draw to critical value notification (minutes)

2) Time from critical value notification to time of any of the physician responses described in Table 4

3) Time from critical value notification to ED Admission (minutes)

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All dates that were directly related to an individual including critical value notification dates and admission dates were removed from the spreadsheet. The remaining information did not fall within the definition of Protected Health Information (PHI) and therefore met the requirement for exemption of IRB review as defined by 45 CFR 46.101(b4). On 1/15/2016, the Riverside Health System Privacy Board approved the study. On 3/30/2016, the VCU Office of Research Subjects Protection qualified this study, HM20006735 for exemption.

Interrater Reliability

The primary researcher was responsible for interpreting provider documentation. If the provider was not explicit in his or her reasons for an intervention or treatment, it was left to the researcher to interpret whether these were responses to critical value notification. If the providers did not document in the EMR that patient symptoms were related to a condition represented by a critical value, the interpretation was made by the researcher. The primary researcher was a medical laboratory scientist with 19 years of clinical experience including chart review and abstraction. In order to increase the accuracy of the data another medical laboratory scientist with more than 30 years of clinical experience reviewed 30 randomly selected charts for the response variables and the patient outcome indicator variables. The primary researcher was considered reliable, if the agreement was greater than 80% and Cohen's Kappa is > 0.6. As suggested by McHugh, it may be better to use both the percent agreement and kappa as there are strengths and limitations to both (2012). High levels of interrater reliabiltiy are necessary in healthcare research that may change clinical practice.

This study was subject to threats in internal validity. The most significant threat to the study was that a patient outcome was assumed to be related to a critical value and coded as such for analysis, when it may not have been related to the critical value. For example, a provider may have documented in a patient's medical record that the patient had signs of confusion on the same day that the patient had a glucose critical value. This critical value may be due to another clinical condition such as a drug interaction or urinary tract infection, but misinterpreted during data collection as a symptom of hypoglycemia. This type of error may be detected by interrater reliability testing, but the number of cases reviewed a second time is low (30) compared to the number of cases in total.

The second threat to internal validity was caused by an atypical physician response to critical values. If a certain physician never chose to respond to critical values or chose the same response type to all critical values and that physician received a large number of critical value notifications during the study periond, the results of the analysis could be skewed. The variable of physician ID has been included in the data collection to explore the physician as a confounding variable.

A third threat to internal validity could be due to a patient specific response. If a physician received a large number of critical value notifications during the study time period for a particular patient, the physician may be more likely to respond differently based upon their experience with that patient's particular condition. The variable of patient ID was collected to explore the patient as a confounding variable.

A fourth threat to internal validity is the possibility that the provider responded to the critical value and did not document it in the patient's chart. The provider may not have

had access to the chart at the time of the notification and may have asked the lab for the patient's phone number. The call could have gone undocumented in this case if the provider never made note of this when they returned to the office. In order to limit the impact on the study, the ED record was reviewed for a provider referral. If the physician had notified the ED of a patient's impending arrival or if the patient reports that a provider asked them to come to the ED, it was recorded in the ED assessment. This prevented a planned ED admission caused by a provider response to the notification from being coded as an unplanned ED admission.

The final threat to historical validity would be an event that occurred within the health system during the study period that caused physicians to respond differently to critical values. This could be a negative patient outcome that resulted from a provider not responding to a critical value. At the opposite end of the spectrum, a provider may have been counseled about sending patients to the ED when they clearly did not have a condition that needed to be assessed by the ED. Riverside Health System maintains a "Team Up For Safety" Program that requires provider education on safety behaviors as well as documented reports for variances in patient care. This education includes a review of previous negative patient outcomes that occurred within the system. This program or even word of mouth at the physician offices could lead to a change in liklihood of responding or response type during the study period. A review of patient variances reported under the laboratory section during the study period was performed to determine if there may have been an historical bias in physician response due to a negative patient outcome associated with a critical value.

Data Cleaning Procedures

The date file was entered into SPSS Statistics, version 23.0 for windows. The data file was screened for errors and cleaned prior to analysis. Potential errors included the coding of variables, data entry errors, and missing data.   Since the data file was large, descriptive statistics were used to detect errors. The minimum and maximum values for each variable were checked. Two cases had minimum values that were not consistent with results expected from the test for which they were coded. These errors were corrected prior to analysis. Most of the variable coding requires a single digit, 0 to 3. Numbers outside of this range were identified and corrected. The exceptions are physician ID, patient ID, specimen age, and delta above critical values. Scatterplots were used to detect outliers and values that do not make sense. In addition, frequency tables were used to detect errors in specimen age and delta above critical values.   Any errors identified were corrected.

Missing data were identified. SPSS Univariate Statistics tables were used to determine the number of missing data points for each variable. SPSS MVA was used to highlight patterns of missing values. It was determined if data were missing completely at random, missing at random, or missing not at random. Univariate statistics table determined the number of values missing for each variable. The Missing Patterns Table was used to look at the patterns of missing data among the variables. The number of missing data points in this study was low as many of the variables on the table have a default coding. For example, for each of the response variables, there are three and only three possible responses. The provider responded within 4 hours, responded between 4 hours and 24 hours, or greater than 24 hours. For other variables, specimen

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age, physician ID,and patient ID are computer required for the critical value process to begin. Since the percentage of missing variables was less that 5 percent of total cases, and these variables were determined to be missing at random, they were dropped from the data set. No missing data was found not to be at random.

Hypothesis and Data Analysis by Specific Aim

All data analysis used to describe utilization and explore correlations in the specific aims described below were performed with SPSS Statistics 23 (IBM Corp, 2014). This study determined physician utilization of critical values in the outpatient setting and explored the impact of physician response on patient outcome indicators. There were five specific aims for this study. The hypotheses, variables, and statistical methods used are described in this section.

Specific aim 1 hypotheses

Specific aim 1: To determine the physician utilization rate, response times, and response types for PT/INR, digoxin, and glucose critical value notifications for outpatients

> $H1_0$: There is no relationship between test and provider utilization of critical value notifications.

> $H2_0$: There is no relationship between test and provider response time.

> $H3_0$: There is no relationship between test and provider response type.

Accredited laboratories are required to make critical value notification for results that indicate a life-threatening condition unless immediate medical intervention is initiated (CLIA '88). Over 94% of physicians indicate that critical results are valuable for patient

care (Wager et al., 2007). In outpatients, physicians have self-reported a 100%

response rate to critical PT/INR value notifications (Piva et al., 2014).

Specific aim 1 data analysis. In this study, a utilization rate for critical value

notification for each test was determined by using the electronic medical record

documentation. The unit of analysis was each critical value notification.   In addition,

the time of response was categorized into responses in less than 4 hours and

responses in 4 hours to 24 hours after notification. Any responses that were greater

than 24 hours were not considered responses to the verbal critical value notification as

all results would have been available in the patient chart for the physician to review and

acknowledge. The response variables and their categorization are described in Table

1. Provider utilization of critical value notifications and patterns of response were

described with descriptive, simple percentages. Contingency tables were provided for

each of the three hypothesis in the results chapter to explore relationships between test

and likelihood of response, test and response type, and test and response time. The

contingency coefficient was chosen as the measure of the magnitude of the relationship

for this aim, Specific Aim 2 and Specific Aim 3. It is considered as an appropriate

measure of association statistic for any size contingency table (Lee Abbott and

McKinney, 2012). Cohen (1988) has suggested small, medium, and large effect sizes

based on this statistic. Typically, 0.100 is considered a small effect, 0.300 is considered

a medium effect, and 0.500 is considered a large effect. Chi Square test for

independence was used to determine the statistical significance of the magnitude as

evidence of generalizability to the reference population (Lee Abbott and McKinney,

2012).

Specific aim 2 hypothesis.

Specific aim 2: To determine if there is a difference in patient outcome indicators when physicians respond to critical values compared to when they do not.

It has been suggested that critical value lists and thresholds should be based on patient outcomes (Piva et al., 2014; Kost and Hale, 2010; Doering et al., 2014). If patient outcome indicators are not impacted by critical value notification, the time and resources of the health care providers that are used for critical value notification may be better utilized by other methods that do impact patient health and safety.

H_0: There is no difference in patient outcome indicators when providers respond to critical values compared to when they do not.

By determining if there was a difference in the outcome indicators between the groups of patients whose providers responded and groups of patients whose provider did not respond, this study began to explore if the current practice of applying inpatient critical value lists to the outpatient population is appropriate. The independent variable was the dichotomous variable of physician response or no physician response. The dependent variables were unplanned emergency department admissions, death, and symptoms of hyperglycemia and hypoglycemia for critical glucose results, evidence of bleeding for critical PT/INR results, and hyperkalemia and atrial fibrillation for critical digoxin results.

Specific aim 2 data analysis. Summary information was provided for outcome indicators for all tests by outcome. The frequency of each outcome for each test and the total frequency of all outcomes were given. Comparison of the frequencies of the different outcomes for each test and frequencies of total outcomes by each test were

provided.   Significant relationships and magnitude were explored by the contingency coefficient and chi square statistics.

Specific aim 3 hypothesis.

Specific aim 3: To determine if quicker response times result in better outcomes. Kuperman et., al found that the median time between physician notification of a critical value and the ordering of appropriate treatment was 1.8 hours for inpatients (1998). There has been little information published regarding response times in the outpatient setting and no studies that correlate response times and patient outcomes.

H_0: Response times do not affect patient outcome indicators.

Specific aim 3 data analysis.   In this study, the time from notification to provider response for each notification that resulted in a response was collected. A contingency table of outcomes by response time and test was developed to explore the differences in patient outcome indicators when physicians responded within 4 hours and when physicians respond within 4 to 24 hours. As described in Table 4, the response variable was the independent variable with the outcome variables as the dependent variables for this aim. Significant relationships and magnitude were explored by the contingency coefficient and chi square statistics.

Specific aim 4 hypothesis.

Specific aim 4: To determine if there are factors that influence a provider's likelihood to responding to a critical value.

The dependent variable for this specific aim was dichotomous, the provider responded or did not respond. The independent variables are factors that may influence a provider's decision to respond to critical values are listed below:

1) The time period from draw to critical value notification

2) Was the physician receiving the critical value notification the physician who ordered the test, the on-call physician, or another provider?

3) Was the time of notification during business hours?

4) Was the critical value notification a repeat critical value notifcation?

5) How many years that the provider has been licensed to practice?

6) For patients with critical glucose values, has the patient already been diagnosed with diabetes mellitus?

7) For patients with critical PT/INR and Digoxin values, does the patient have a documented history of results outside of the reference range?

H_0: Patient, specimen, and provider factors do not correlate with physician likelihood to respond to critical value

Specific aim 4 data analysis. The null hypothesis was tested using logistic regression to produce a relationship model. The analysis performed on the outcome variable using nine predictors, the seven listed above with two additional dummy variables required for the analysis. A table showing the regression coefficients, Wald statistics, odds ratio, and 95% confidence intervals for the odds ratio for each predictor was presented. The Wald statistic was used to evaluate the statistical significance of each of the predictors. The data in this table determined the predictors that influence the provider's liklihood of responding to a critical value and the relative strength of those

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predictors. As described in the results chapter, additional follow-up analysis was performed for the PT/INR and the glucose notifications separately. Tables showing regression coefficients, Wald statistics, odds ratio, and 95% confidence intervals for the odds ratio for each predictor for the additional analyses were presented. Nagelkerke's R^2, the multiple correlation coefficient redefined for discrete models, was used to explain the proportion of variance explained by the model (Nagelkerke, 1991). This is a pseudo R^2 that approximates the proportion of the total variance accounted for by the model which can be used in logistic regression.

Specific aim 5 hypothesis.

Specific aim 5: To determine if the magnitude of the test result predicts whether or not a provider will respond to a outpatient critical value notification.

> H_0 : The magnitude of the test result does not predict whether or not a provider
>
> will respond to a critical value notification.

Are providers more likely to respond to critical values as the result gets further away from the threshold, suggesting a more serious condition? This could indicate that physicians do not feel that the current threshold for the critical result indicates a life-threating condition for the patient and are more likely to respond as the result becomes more abnormal. Riverside Health System's critical value lists has been approved by all medical specialties. The intent of the list is to be appropriate for both inpatients and outpatients. With the decreasing turnaround times and reporting times due to advancements in technology, the critical value list thresholds may no longer be appropriate. Don-Wauchope et al., reported physicians perceived 7 out of 11 critical values to not be at the appropriate threshold when surveyed based on their criteria of

>60% agreement and >20% rejection of the thresholds (2009). This part of the study was designed to see if there was evidence for modifying the current critical value thresholds for the outpatient populations.

   Specific aim 5 data analysis. The dependent variable was dichotomous. Was there a provider response or not? The difference from the critical threshold to the actual patient results was determined. For each of the different tests, these results were standardized to allow comparison. This allowed the data to have a mean of zero and a standard deviation of 1.This eliminated differences in scales between the three tests. The independent variable was the standardized difference of the value from the critical threshold. All previous predictor variables from Aim 4 were used to control for their effects. Correlation between magnitude of value and liklihood to respond was done by logistic regression. The analysis included a logisitic regression for all tests together and then for the PT/INR and glucose tests separately Tables showing regression coefficients, Wald statistics, odds ratio, and 95% confidence intervals for the odds ratio for each predictor for the additional analyses were presented. Nagelkerke's R^2, the multiple correlation coefficient redefined for discrete models, was used to explain the proportion of variance explained by the model (Nagelkerke, 1991). The z scores were converted back to the raw scores to evaluate the confidence intervals for overlap. Recommendations for changes to critical value thresholds were made based upon the table.

Summary

 The study explored physician responses to critical value notifications and their impact upon patient outcomes through five specific aims. This chapter has presented the

research design, population, sample size and statistical power, data collection and

cleaning, and statistical methods for analyses. A variable table that describes all

variables and their relationship to each aim has been presented. Chapter 4 provides

the results and findings of this study. Chapter 5 interprets the results and discusses the

findings in comparison with current literature.

Chapter 4: Results

Introduction

The purpose of the study was to characterize providers' responses to receiving

outpatient critical value notifications and the impact of these responses on patient

outcomes. In addition, this study explored the providers' perception of the threshold at

which test results were determined to be critical by the health system's established

critical value list. It is hoped that the results of this study can be used to recommend

changes to critical value lists based on patient outcomes and provider's perception of

the critical value thresholds. The data analysis is described, and results are reported in

this chapter based on each specific aim. For every hypothesis, data analysis as

contingency tables or logistic regression produced odds ratios or measures of shared

variance to document the magnitude of relationships in the sample. Chi Square

statistics were used as evidence of generalizability to the reference population. Specific

Aim 1 explored and compared the provider responses and timeliness of those

responses for each test in the study. Specific Aim 2 compared patient outcome

indicators when providers chose to respond to critical values to when they did not.

Specific Aim 3 explored the effect of timeliness of response on patient outcomes.

Specific Aim 4 determined if there were provider or specimen characteristics that made

providers more likely to respond to a critical value. Lastly, Specific Aim 5 explored the

appropriateness of the threshold for the critical values in terms of provider response. This information would aid in recommendations to raise or lower the current established thresholds.

Final Data Set

For the study period, 637 critical value notification cases in the outpatient setting were collected. Variables were examined by descriptive statistics and the variable table was completed. It was determined that less than 5% of the cases had missing values. Since the missing elements were determined to be missing at random, they were deleted from the study. As shown in Table 5 the study included 540 different patients and 167 providers. Confounding variables were examined. It was determined that of the 167 providers identified as receiving critical values in the study, no one provider accounted for more than 2.2% of the responses. Of the 540 patients that had critical test results, no one patient represented more than 1.1% of the total cases.   Due to the minimal contribution of one patient or one provider to the analyses, no attempt was made to control for patient ID or provider ID. The final data set and variables summarized in the tables below set was used for all analyses in this chapter.   Table 5 contains the potentially confounding variables and the test type variable. Table 6 contains the provider response type variables to a critical value notification. Table 7 contains the patient outcome type variables. Table 8 contains the variables that were used to explore a model to predictor a provider response to a critical value notification.

Interrater Reliability

For each of the 30 cases, up to 23 elements could have been collected for a maximum of 690 elements.   The review resulted in correction of four data elements for

Table 5. *Completed Variable Table 1*

Variable	Number/Percentage	Definition of Observation Variable
Patient ID	540	Assigned study number
Physician ID	167	Assigned study number
Test Type	24.6% 4.4% 71.0%	1 = PT 2= Digoxin 3= Glucose

Table 6. *Completed Variable Table 2: Response Type Variables*

Variable	Number/Percentage	Definition of Observation Variable
Notification Response/ No Response	74.3% response	1 if response
Response	69.7% 4.6% 14.6% 11.1%	1 = < 4 hours 2= ≤24 hours 3=> 24 hours 0 = No Response
Contacting the patient	% 1 % 2	1 = < 4 hours 2= ≤24 hours
Order follow-up testing	15.9% 1.1% 3.3%	1 = < 4 hours 2= ≤24 hours 3=> 24 hours
Schedule follow-up appointment	5.7% 0.8% 6.3%	1 = < 4 hours 2= ≤24 hours 3=> 24 hours
Stopping or Changing medication	31.4% 1.7% 3.8%	1 = < 4 hours 2= ≤24 hours 3=> 24 hours
Prescribing new medication	3.6% 0.2% 1.1%	1 = < 4 hours 2= ≤24 hours 3=> 24 hours
Directing patient to the emergency department	6.9% 0.0% 0.3%	1 = < 4 hours 2= ≤24 hours 3=> 24 hours

Table 7. *Completed Variable Table 3: Outcome Type Variables*

Variable	Number/Percentage	Definition of Observation Variable
Adverse Outcome/No Adverse Outcome	3.3% 96.7%	1 if outcome, 0 otherwise
Unplanned ED visit	1.6%	1 if unplanned ED visit, 0 if no visit
Patient Death	0%	1 if death, 0 if no death
Result of the next	19.9% 43.2% 17.4% 19.6%	1 = within reference range 2 = Above reference range 3 = critical value 4 = below reference range
Evidence of bleeding (PT test only)	4.4% (of PT/INR)	1 if evidence of bleeding, 0 if no evidence
Evidence of Hyperkalemia or atrial fibrillation for digoxin test only	3.6% of Digoxin	1 if evidence of symptoms, 0 if no evidence
Evidence of nausea, vomiting, or confusion for glucose only	1.8% of glucose	1 if evidence of symptoms, 0 if no evidence

Table 8. *Completed Variable Table 4: Predictor Variables*

Variable	Number/Percentage	Definition of Observation Variable
Specimen age	Mean = 403.54 SD = 245.2	Time in minutes from specimen draw to critical value notification
Physician Type	22.8% 42.4% 34.9%	0 = ordering physician 1 = on-call physician 3 = office nurse
Notification Time	34.2% 65.8%	Time of notification was during business hours = 0 was not during business hours = 1
Repeat Test for this test type	1%	0= notification was from repeat test 1= notification not from repeat test
Physician Experience	Mean = 18.5 SD = 12.1	Years of physician experience
Previous diabetes diagnosis	90.0%	1 if patient had previously been diagnosed with diabetes, 0 if not
Historical test results for this test type	69.7%	If documentation of result higher than reference range in the past year = 1, if not =0
Delta above Critical value for this test type	Mean and SD	Difference between critical threshold and patient value

our different cases. In two cases, a provider's response time was changed from the 4 to 24 hour time period to less than 4 hours. In one case, an additional response of change of medication was added, and an additional response of scheduling a follow-up appointment was made to another patient. Based on cases and not individual elements, there was agreement in 26 of 30 cases, or 86%. There was 100% agreement on the primary dependent variables of response/no response and outcome/no outcome. Therefore Cohen's Kappa for agreement of the primary variables was 1. During the process, the reviewer and primary researcher resolved one discrepancy regarding an outcome for a patient who was admitted to the hospital after having been directed to the ED by a responding provider. The patient died five days post admission. The death summary was reviewed for additional information. The cause of death was listed as lung cancer and septic shock. Both the primary researcher and the reviewer agreed the death was not an outcome of a critical glucose result. Based on Cohen's Kappa and the percentage of agreement, the primary researcher was considered reliable.

Specific Aim 1 Results

Response times and response types were collected for 637 critical value notifications during the study period.   The actual notifications were lower than expected during the study period, but was greater than the number required by Soper's calculation for a multiple regression involving all operational variables with 80% confidence that there would not be a Type II error and 95% confidence that there would not be a type I error. The notifications included 452, or 71.0% for glucose results, 157, or 24.6% for PT/INR results, and 28 notifications, or 4.4% for digoxin results. A

summary of the variables collected are shown in Table 4.5. The first column indicates the provider responses. The other columns show both frequency and percentage of responses to critical value notifications by test and response speed. Response speeds are categorized into "fast," responses or responses less than 4 hours, and "slow" responses, or responses that were done within a 4 to 24-hour timeframe. The percentages shown are within each "fast" or "slow" category for each response type responses, or responses that were done within a 4 to 24-hour timeframe. The percentages shown are within each "fast" or "slow" category for each response type Providers attempted to respond to 473 critical value notifications. Twenty-four of the attempted responses were unsuccessful, meaning they were unable to make contact with the patient within 24 hours. All 24 of these unsuccessful responses were for critical glucose result notifications. Of the responses, 145 were responses to PT/INR result notifications, 24 were response to digoxin result notifications, and 304 were responses to glucose result notifications, representing 30.66%, 5.07%, and 64.27% respectively of total successful responses. Since providers could choose to respond to each case, or each critical value notification, with more than one type of response, there were a total of 895 responses to the 427 notifications.   The responses are categorized into 843, or a4.2% fast responses and 52, or 5.8% slow responses.   Table 9 shows a summary of all responses.

   Provider response by test.   Providers receiving notifications could choose to respond or not to respond to the critical value notification.   Table 10 shows the response rate for the three different types of tests. The overall response rate for all tests and all notifications was 74.3%. Providers had a similar response rate to PT/INR

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Table 9. *Critical Value Responses by Test, Response Type, and Response Time*

Test	Protime		Digoxin		Glucose		All Tests	
Total Notifications (%)	157 (24.6%)		28 (4.4%)		452 (71.%)		637 (100%)	
Total Provider Response (%)	145 (30.7%)		24 (5.1%		304 (64.3%)		473 (100%)	
	Fast	Slow	Fast	Slow	Fast	Slow	Fast	Slow
Contact Patient	140	5	22	2	277	21	439	28
	(31.9%)	(17.9%)	(5.0%)	(7.1%)	(63.1%)	(75.0%)	(100%)	(100%)
Schedule Follow-up Appt	1	0	0	0	35	5	36	5
	(2.4%)	(0.0%)	(0.0%)	(0.0%)	(97.2%)	(100%)	(100%)	(100%)
Schedule Follow-up Test	79	4	5	0	17	3	101	7
	(78.2%)	(57.1%)	(5.0%)	(0.0%)	(16.8%)	(42.9%)	(100%)	(100%)
Change Timing or dose of med	127	3	19	2	54	6	200	11
	(63.5%)	(27.3%)	(9.5%)	(18.2%)	(27.0%)	(54.5%)	(100%)	(100%)
Prescribe new med	7	1	0	0	16	0	23	1
	(30.4%)	(100%)	(0.0%)	(0.0%)	(69.6%)	(0.0%)	(100%)	(100%)
Direct Patien To the ED	8	0	2	0	34	0	44	0
	(18.2%)	(0.0%)	(4.9%)	(0.0%)	(77.3%)	(0.0%)	(100%)	(100%)
Total	362	13	48	4	433	35	843	52
	(42.9%)	(23.1%)	(5.7%)	(7.7%)	(52.4%)	(69.2%)	(100%)	(100%)

and digoxin, 92.4% and 85.7%, respectively. Provider response rate to glucose notifications were lower, 67.3% of notifications elicited a response. A Pearson chi-squared test was used to investigate a relationship between provider response and test type.   The difference in response between tests was significant, (chi-sq=40.413, df=2, N=637, p <.001).   The relationship between provider response and test was small as demonstrated by a contingency coefficient of 0.244. The magnitude of the relationship was approximately 5.8% of the shared variance. It can be stated with 99.9% confidence that a relationship does exist between type of test and response. Providers were more likely to respond to critical value notifications for PT/INR and digoxin testing than for glucose testing. The null hypothesis that there was no relationship between test and provider response was rejected.

Table 10. *Response by Test Type*

Test	No Response n (% within test)	Response n (% within test)	Total n (% within test)
Protime	12 (7.6%)	145 (92.4%)	157 (100%)
Digoxin	4 (14.3%)	24 (85.7%)	28 (100%)
Glucose	148 (32.7%)	304 (67.3%)	452 (100%)
Total n (% within no response or response)	164 (25.7%)	473 (74.3%)	637 (100%)

(chi-sq=40.413, df=2, N=637, p<.001, C=0.244, p<.001)

Response time by test. In Table 11, the responses to each type of test was further categorized into fast responses, responses <4 hours of receiving notification, and slow responses, or responses that occurred between 4 and 24 hours after receiving notification. A survey of the current literature indicated that providers perceive a timeframe of 4 hours or less, an appropriate response time to a critical value notification (Piva et al., 2014; Montes, Francis, & Cuilla, 2014). In this table, the patterns of response speed to the three tests were similar. It should be noted that this table is based upon cases and not each response as shown in Table 4.5. Provider responses to critical PT/INR, digoxin, and glucose notifications were categorized as "fast" 96.6%, 91.7%, and 92.8% respectively. The relationship between type of test and response time was not significant with a contingency coefficient of 0.075, p=.264. It should be noted that the contingency table (chi sq=2.661, df=2, p=.264), violated assumptions for the chi square. The expected frequency of the slow responses to digoxin critical value notification created cell sizes of less than 5. Due to the violation of assumptions for statistical analysis and the lack of a relationship between test and response speed, the

Table 11. *Response Time by Test*

Test	<4 Hour Response (Fast Response)	<24 Hour (Slow Response)	Total
Protime	140 (96.6%)	5 (3.4%)	145 (100%)
Digoxin	22 (91.7%)	2 (8.3%)	24 (100%)
Glucose	282 (92.8%)	22 (7.2%)	304 (100%)
Total	444 (93.9%)	29 (6.1%)	473 (100%)

(chi-sq=2.661, df=2, p=.264, C=.075, p=.264)

decision was made to recode both fast and slow responses into the dichotomous

variable of response or no response for all further statistical analyses. The null

hypothesis that there is no relationship between test and response time was accepted.

Response type by test. Using the recoded dichotomous response variable of

response/no response, a summary table was created to look at response by test and

type. This table provides the clearest analysis to Specific Aim 1.   The percentages

shown in Table 12 are within test for easier comparison.

Providers responded to 92.4% of the PT/INR notifications, 85.7% of the digoxin

notifications, and 66.8% of the glucose notifications as shown in Table 12. Due to the

fact that that more than one response was possible for each notification, the Providers

responded to 92.4% of the PT/INR notifications, 85.7% of the digoxin notifications, and

66.8% of the glucose notifications as shown in Table 12. Due to the

fact that that more than one response was possible for each notification, the

assumptions for pure binary statistical testing could not be met. Instead, each possible

binary table was used to determine relationships between test and a response type if a

Table 12. *Critical Value Notification Response by Test*

		ResponseType					
		Contact Patient	Follow-up Appoint	Follow-up Test	Change med	New med	Direct to ED
Protime	Frequency	145	1	83	130	8	8
145 responses	% within test	92.4%	0.6%	52.9%	82.8%	5.1%	5.1%
Digoxin	Frequency	24	0	5	21	0	2
28 responses	% within test	85.7%	0%	17.9%	75.0%	28.4%	33.1%
Glucose	Frequency	252	40	20	60	16	33
452 responses	% within test	97.7%	15.5%	7.8%	23.3%	6.2%	12.8%
Total response		467	41	108	211	24	44
		73.3%	6.4%	17%	33.1%	75.5%	6.9%

notification resulted in response. Table 12 shows the distribution of response types for

each test. The most common type of response was contacting the patient. This

occurred in 467 of 473 responses. Again, the chi square assumptions for this table

were violated due to small cell size.   There was a small relationship between test and

likelihood of contacting the patient (chi sq=43.898, df=2, p<.001). The contingency

coefficient of .254 indicates this is responsible for 6.5% of the shared variance. There

was a small, but significant relationship between test and scheduling a follow-up

appointment (chi sq=26.172, df=2, p<.001). The magnitude of the relationship was

2.3% of the shared variance, as indicated by a contingency coefficient of 0.152.

Providers were more likely to schedule a follow up appointment for critical glucose

values. There was a moderate to large relationship between test and ordering a follow-

up test (chi sq=194.219, df=2, p<0.001). The magnitude of this relationship was 23% of

the shared variance as indicated by the contingency coefficient of .483.   Providers were

more likely to order a follow-up test in response to a critical value for PT/INR testing

than for digoxin and glucose notifications. There was also a significant relationship of

large magnitude between test and changing the dose or stopping a medication (chi

sq=277.475, df=2, p<0.001). The magnitude of this relationship was 30% of the shared

variance as indicated by the contingency coefficient of .551. Providers changed the

dose or stopped a medication for PT/INR test result than for either glucose or digoxin.

There was no significant relationship between test and the response of prescribing a

new medicine or directing the patient to the Emergency Department.

   Additionally, the category of no response was also examined. As defined in the

study, responses greater than 24 hours or no response at all were combined into the

category of no response since the definition of a critical value requires immediate

treatment. Although 74.2% of notifications were followed up in less than 24 hours,

another 93, 14.6% of notifications were eventually responded to, leaving 11.2% never

resulting in a provider response.

   In summary, providers responded to 74.2% of critical value notifications. When

providers responded to a critical value, approximately 93.9% of these responses were

made within 4 hours of receiving the notification. Providers were found to be less likely

to respond to glucose critical value notifications than PT/INR or digoxin critical value

notifications. A moderate to large relationship existed between type of test and two of

the response types, 1) a change in dose or timing of medication and 2) scheduling a

follow-up test. A change in timing or dose of medication was a more likely response for

both PT/INRs and digoxin critical value notifications than glucose. There was a small but significant relationship between two other response types, 1) contacting the patient and 2) scheduling a follow-up appointment. Of the six response types, two did not have any relationship with the type of test. These were 1) prescribing a new medication and 2) directing the patient to the Emergency Department. The null hypothesis that there was no relationship between test and response type was rejected.

Specific Aim 2

Providers responded to 473, or 74.2% of the 637 critical value notifications. For specific aim 2, unsuccessful notifications were included in the no response category because no treatment or intervention was initiated since the provider had been unable to contact the patient. Originally, the proposal had included critical results of the next test as an outcome. During analysis, the outcome was removed as it included serial testing ordered by providers to track the resolution of the condition. In many cases, the repeat testing results were still in the critical range, causing additional critical value notifications for the cases in which providers chose to respond to critical values.   In contrast, those notifications that did not achieve a response did not have repeat testing that resulted in critical values. This elevated the number of next test critical values for the response category. Therefore, this variable of critical results of the next test was removed as an outcome.

Outcome by test. In total, there were 21 patients who experienced a negative outcome with a total of 26 outcomes, as there could be more than one outcome per case. For example, a patient could have both nausea and an unplanned Emergency Department admission. Table 13 shows a summary of the outcomes by test. The

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Table 13. *Outcome Type by Test*

	Unplanned ED Admission	Death	Bleed	Hyperkalemia	Nausea
			Response Types		
PT/INR	2 (7.7%)	0 (0.0%)	7 (26.9%)	N/A	N/A
Digoxin	0 (0.0%)	0 (0.0%)	N/A	1 (3.8%)	N/A
Glucose	8 (30.8%)	0 (0.0%)	N/A	N/A	8 (30.8%)
Total	10 (38.5%)	0 (0.0%)	7 (26.9%)	1 (3.8%)	8 (30.8%)

(chi sq=.961, df=1, N=616, p=.327)

percentages are based on total negative outcomes. No patients with critical test results had an outcome of death. Death was removed as an outcome indicator for all further statistical analyses. Unplanned ED admissions occurred in only 10 patients, 2 with critical PT/INR results and 8 with critical glucose results. Seven patients with critical PT/INR results had a bleed, 1 patient with critical digoxin results experienced hyperkalemia or atrial fibrillation, and 8 patients with critical glucose results experienced nausea. In summary the 26 outcomes included 10 unplanned ED admissions, 7 patients with bleeds, 1 patient with hyperkalemia, and 8 patients with nausea.

Outcome by response/no response. Table 14 was created to examine the relationship between response and outcome. It shows that in 2.8% of all cases, patients who had critical value notification with provider response had one or more outcomes. Similarly, 4.3% of patients with critical value notifications with no provider response or an unsuccessful response had one or more outcomes. The contingency coefficient was not significant for a relationship between response and outcome (chi sq=.961, df=1, N=616, p=.327).

Table 14. *Outcome by Response/No Response*

	No Outcome	Outcome
Response to Notification	415 (97.2%)	12 (2.8%)
No Response to Notification	201 (95.7%)	9 (4.3%)
Total	616 (96.7%)	21 (3.3%)

(chi sq=.961, df=1, N=616, p=.327)

The data within the Contingency Table 14 included all three tests and all types of outcomes, with three of them test specific. A follow-up analysis was performed to include the remaining outcome indicator that was common to all three tests, unplanned ED admission. Table 15 violated the chi square assumptions because of one cell size with a frequency <5. The contingency coefficient was .10, p=.04, indicating a significant relationship of very small magnitude may exist between response and unplanned ED admissions.

Table 15. *Unplanned ED Admission by Response*

	No ED Admission	ED Admission	Total
No Response	203 (96.7%)	7 (3.3%)	210 (100%)
Response	424 (99.3%)	3 (0.7%)	427 (100%)
Total	627 (98.4%)	10 (1.6%)	637 (100%)

In summary for Specific Aim 2, no significant relationship existed between response and outcome existed when all outcomes for all tests were included. The chi square and contingency coefficient for test and unplanned ED admission indicated the possibility of

a relationship. However, due to low cell volumes, the assumptions of the chi square

were violated. Lastly, due to the low number of outcomes resulting in small cell

frequencies, no relationship could be explored between test, response, and outcome.

The hypothesis of no difference in patient outcome indicators when physicians respond

to critical values compared to when they do not respond could not be rejected.

Specific Aim 3

As already presented in Table 12, 21 cases, or 3.3%, of the 637 notifications

resulted in an outcome.   As shown in Table 16, there were a total of 10 outcomes when

providers responded to the notification in less than 4 hours and 2 outcomes when

providers responded in the 4 to 24-hour timeframe. These numbers are too small to

satisfy the required conditions for any statistical analyses.

Considering that death had been removed as an outcome, the only outcome

comparable across the three tests was unplanned ED admission. There were only two

unplanned ED admissions with a fast response and no unplanned ED admissions with a

slow response. Again, these numbers are too small for statistical analyses. The

hypothesis that response times do not affect patient outcome indicators could not be

rejected.

Specimen Aim 4

The data analysis for Specific Aim 4 was a direct logistic regression with

response/no response to a critical value notification as the dependent variable with nine

critical result predictors. The predictor variables were physician type, specimen age,

whether the critical value notification was made during business hours, whether the

was from a repeat test, the provider's years of experience, historical diagnosis of

Table 16. *Outcome by Response Time By Test*

Test		No Outcome	Outcome	Total
PT/INR	No Response	12 (92.3%)	1 (7.7%)	13 (100%)
	Fast Response	130 (94.9%)	7 (5.1%)	137 (100%)
	Slow Response	8 (100%)	0 (0.0%)	8 (100%)
Digoxin	No Response	3 (100%)	0 (0.0%)	3 (100%)
	Fast Response	21 (95.5%)	1 (4.5%)	22 (100%)
	Slow Response	2 (100%)	0 (100%)	2 (100%)
Glucose	No Response	186 (95.9%)	8 (4.1%)	194 (100%)
	Fast Response	225 (99.1%)	2 (0.9%)	227 (100.0%)
	Slow Response	29 (93.5%)	2 (6.5%)	31 (100.0%)
Total		616 (96.7%	21 (3.3%)	637 (100%)

diabetes (for critical value notifications of glucose), if the patient had historical results above the reference range, and type of test. Prior to analysis, these predictors were examined by descriptive statistics.   In order to avoid multicollinearity in the model, the provider type and test type were transformed into dummy variables as required by the analysis, including one less dummy variable than the number of categories.

1) Specimen age

    This was an interval ratio predictor defined as the time from the specimen was drawn to when the notification was made. The descriptive statistics are presented in Table 17. The minimum time was 21 minutes, and the maximum

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time was 1351 minutes. The mean specimen age was 369 minutes with a standard deviation of 242 minutes.   The specimen age for 90% of the specimens was 657 minutes, or approximately 11 hours or less.

As shown in the Table 17, specimen age was both high in kurtosis and skewness. This is naturally occurring in the population. There was almost a bimodal distribution to the histogram of specimen age as shown in Figure 2. The first peak occurred in the 50 to 100-minute range. This peak represents the values from specimens that were drawn at the hospital instead of the provider office. Often patients are given test requisitions for either STAT testing or testing to be performed at another time prior to a future appointment. These specimens are typically drawn at the hospital lab and transported directly to the lab for analysis. These results should be available in approximately an hour of draw, as shown by the first peak of the histogram. If the first peak was removed, a more normal distribution for the second peak would be apparent. These are the specimens that were drawn in the providers' offices and then transported to the lab at the end of the day. This peak starts at a specimen age of approximately 300 minutes and ranges to 500 minutes, or 5 hours to 8 hours old at the time of analysis. Since specimens from provider offices are usually transported to the testing laboratory in early evening hours, this peak represents the specimens collected at the provider's office during office hours. The kurtosis for specimen age is also naturally occurring in the population. Typically, a small number of critical value notifications that are not completed until late into night or the next morning, at which time the specimen could be drawn almost 24 hours prior.

Table 17. *Specimen Age Descriptive Statistics*

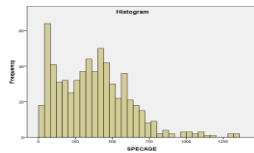| Valid N	Mean	Std. Error	Std.	Skewness	Std. Error	Kurtosis	Std. Error	Minimum
637	368.57	9.577	241.72	0.85	0.097	1.195	0.193	21

Figure 2*. Specimen Age Histogram*

These late notifications represent the specimens in which it was difficult to track

down a provider to receive the notification. In many cases, delayed notification is

the result of several pages before the provider returned the call or lack of a

provider phone number. In that case, the result notification may have been held

to the following morning when the provider office opened. Since both skewness

and kurtosis of specimen age violated assumptions of normality, the variable was

accepted for analysis because this is naturally occurring in the population.

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to be performed at another time prior to a future appointment. These specimens

are typically drawn at the hospital lab and transported directly to the lab for

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to the following morning when the provider office opened. Since both skewness

and kurtosis of specimen age violated assumptions of normality, the variable was

accepted for analysis because this is naturally occurring in the population.

2) Type of Provider

 If the provider receiving the notification was the same provider that ordered the

test, the provider type was "ordering provider." If the provider receiving the

notification was an on-call provider for the practice and had not ordered the test,

the provider type was "on-call provider." The third type, "nursing staff,"

comprised the notifications given to the nursing staff of the provider's office.

These would have to be relayed to the provider. During the study period, 145 notifications were made to the ordering provider, 270 notifications were made to the on-call provider, and 222 notifications were given to the office nursing staff. The majority of notifications, or 42.4% were made to the on-call physician as shown in Table 18. Two dummy variables were created from the three categories for use in the logistic regression.

Table 18. *Notifications by Provider Type*

Type	Number	Percent
Ordering Provider	145	22.8
On-Call Provider	270	42.4
Nursing Staff	222	34.9
Total	637	100

3) The third predictor, or notification time, was divided into two categories, notifications made during business hours and notifications made after business hours. During the study period, 218 notifications were made during business hours and 419 notifications were made after business hours. Roughly, one-third of notifications were made during business hours and two-thirds were made after business hours.

4) The fourth predictor was if the notification was made from a repeat test. During the study period, approximately 10 percent of the notifications were from repeat testing ordered by physicians.

5) The fifth predictor collected during the study period was the experience of the physician. As shown in Table 19, the years of experience for the providers ranged from months to 47 years. The mean physician experience was 18.5 years with a standard deviation of 12.1. Physician experience also demonstrated a high kurtosis as shown in the table. This violation of normality was also accepted since it does occur naturally in the population. The newly graduated providers often have more share of on-call duty than the older providers, and, thus were responsible for more critical value notifications.

Table 19. *Physician Experience Descriptive Statistics*

Valid N	Mean	Std. Error	Std.	Skewness	Std. Error	Kurtosis	Std. Error	Minimum
635	18.51	0.48	12.102	0.281	0.097	-1.15	0.194	0

6) The sixth predictor, previous diagnosis of diabetes, was collected. Of the 452 glucose notifications, 407 of the cases had been previously diagnosed with diabetes.

7) The seventh predictor, historical test results, was collected for all tests. Seventy percent of cases had previous results that were outside of the reference range.

8) The eighth predictor was test. Descriptive statistics for the test variable have been described in the data analysis section for Specific Aim 1. Two dummy variables were created to represent the three test types in the logistic regression.

A missing values analysis was not performed as the missing values in all variables was less than 5%. The test for multivariate outliers was also run. All cases with the exception of one fit into a multivariate normal population with 99.9% confidence. This case was eliminated from the analysis.

The logistic direct regression including nine predictors as a set was statistically significant against a constant only model in prediction of response versus no response (chi square=67.729, p<.001 with df=8). A Nagelkerke's R^2 of .155 indicated a small relationship. The model reduced classification, or the ability to predict whether the notification would result in a response or no response from 73.9 to 73.6%. The majority of predictors were not significant as demonstrated by p >.10. The Wald criterion indicated that two of the predictors, notification for PT/INR results and notification for results of a repeated test were significant. A stepwise regression was done to develop a more parsimonious model. Table 20 shows regression coefficients, Wald statistics, Exp (B) or odds ratios, and 95% confidence intervals for odds ratios for each of the three predictors.

Table 20. *Stepwise Logistic Regression Analysis of Response/No Response as a Function of Specimen, Provider, and Notifications Characteristics*

Variable	β	Wald Chi-Square	Sig	Exp(β)	95% C.I for Exp(β)	
					Lower	Upper
On-Call Provider	-.523	5.731	.017	.593	.386	.910
Repeat Test	1.270	15.731	.000	3.560	1.886	6.721
PT/INR Test	1.990	33.904	.000	7.310	3.743	14.289

The best model is a three-predictor model, in which the notification was for PT/INR results, the notification was for a repeated test, and the provider receiving the notification was not the on-call physician. This model explained 15.1% of the variance. In comparison with the direct regression which included nine predictors and explained 15.5% of the variance, this model is the most parsimonious. The prediction equation for the regression is in log-odds units:

Log(p/1-p) = -.295 -.523*On-Call Provider+1.270*Repeat Test+1.990*PT/INR Test

This estimates the amount of increase or decrease in the log odds of a response that would be predicted by a one unit increase or decrease in the predictor, holding all other predictors constant. Since these β coefficients are in log odds units and difficult to interpret, they can be converted into Exp(B), or odds ratios, for easier interpretation. This is done by the exponentiation of the β coefficient. In Table 4.16, the Exp(B) indicates that if the notification was not delivered to the on-call provider, it was .593 times more likely to result in a provider response. If the notification was for a repeat test, it was 3.56 times more likely to result in a provider response. If the notification was for a PT/INR critical value, it was 7.3 times more likely to result in a response than a notification for the other two tests. It is possible that the test type was potentially masking the contribution of the other predictors to explaining the variance. Therefore, the logistic regression was also run separately for the PT/INR test and the glucose test. No additional logistic regression was performed for digoxin, given the low frequency of critical result notification occurrence.

The logistic regression for the PT/INR test only resulted in a classification is 92.3% without predictors. Table 21 shows regression coefficients, Wald statistics, odds ratios, and 95% confidence intervals for odds ratios for each of the two predictors. There were two steps for the model, Step 1 (chi sq = 24.385, df= 1, p<.001) and Step 2 (chi sq=33.983, df=2, p<.001). The predictor of being a notification for a repeated test

Table 21. *Stepwise Logistic Regression Analysis of Response as a Function of Specimen and Provider Characteristics for PT/INR Notifications*

Variable	B	Wald Chi-Square	Sig	Exp(B)	95% C.I for Exp(B)	
					Lower	Upper
Specimen Age	0.012	4.737	.000	1.012	1.001	1.023
Repeat Test	2.862	11.739	.001	17.498	3.404	89.959

explained 34.6% of the variance and adding specimen age to the model explained an additional 12.2% of the variance, for a total 46.8%. The Odds Ratio indicates that a critical value notification for a repeated test is 17.5 times more likely to result in a provider response than for a test that was not repeated, holding specimen age constant. The model indicates a one unit change in specimen age is only .012 times more likely to result in a response. However, specimen age for PT/INR had a wide range of 21 to 743 minutes, indicating a potential large impact on likelihood of response in practice.   The classification was improved slightly from 92.3% to 93.6% with 33% no responses predicted and 98.6% of responses predicted. P >.10 in the remaining predictors indicated that they were not important in generalizing the sample to a population of notification for PT/INR.

Stepwise logistic regression analysis was performed for the same relationship for responses to glucose notifications only. The classification decreased and only one predictor variable, the notification having not been made to the on-call provider, was included. The model (chi sq=7.517, df=1, p=.006) was significant against a constant only model, but the classification did not improve and Nagelkerke R^2 of .023 was very

low. None of the variables in the regression contributed to further prediction of the model for response to glucose critical value notifications.

Overall, for Specific Aim 4, the initial logistic direct regression including nine predictors as a set was statistically significant against a constant only model in prediction of response versus no response (chi square=67.729, p<.001 with df=8). Therefore, the hypothesis that patient, specimen, and physician factors do not correlate with physician likelihood to respond to a critical value can be rejected. However, the majority of the shared variance explained by the direct regression is small and mostly attributed to the PT/INR notification as shown in the follow-up stepwise regressions for PT/INR and glucose tests separately. The PT/INR stepwise model indicated that a repeated test and specimen age were significant predictors of response. According to Wald criterion for the glucose test, the only significant predictor was that notification was not made to the on-call provider. Thus, in answering Specific Aim 4, a limited number of provider and specimen characteristics that demonstrate significance, but the variance is mostly attributable to the result being from a repeated PT/INR test. Greater than 97% of variance in the glucose test only model remained unexplained.

Specific Aim 5 Results

The data analysis for specific Aim 5 was also a logistic regression. The dependent variable was the same as in Aim 4, response/no response. The predictor variables were identical to those in Specific Aim 4 with the addition of the magnitude of the test result. In order to use this as a variable across the three tests, the critical values had to be standardized. PTs are reported in seconds, digoxin is reported in ng/mL, and glucose is reported in mg/dL. The actual critical value for each test type was

transformed into Z scores with a mean of 0 and standard deviation of 1. Once in the

same scale, they were entered as one variable.   The Table 22 shows the results of this

transformation. Once all three test results were in the same scale, the test results were

combined to form the single predictor as shown in Table 23. As expected, a positive

skew was observed in a population of critical value notifications. Several critical results

were around the mean and some extreme critical values in the positive direction.

Although violating assumptions of normality, the skew was accepted and the combined

test zscore used for analysis.

Table 22 *Descriptive Statistics of Zscores by Test*

	Minimum	Maximum	Skewness		Kurtosis	
	Statistic	Statistic	Statistic	Std. Error	Statistic	Std. Error
PT/INR	-.88594	7.50122	3.161	.193	18.995	.384
Digoxin	-1.39101	2.73168	.899	.448	.687	.872
Glucose	-.90019	5.45150	2.158	.115	5.771	.229

Table 23. *Descriptive Statistics for Combined Test ZScore*

	Minimum	Maximum	Skewness		Kurtosis	
	Statistic	Statistic	Statistic	Std. Error	Statistic	Std. Error
Z Score	-1.39101	7.50122	2.346	.097	8.692	.193

The test for multivariate outliers was run for 10 predictors and six cases were

removed prior to analysis. The direct logistic analysis was significant against a constant

only model (chi sq=75.080, df=9, p<.001) and explained 17.1% of the variance. The

classification was improved slightly from 73.8% to 74.4%. There were several variables

in the equation that were not significant. Stepwise regression was run to develop a

more parsimonious model resulting in four steps. The final model (chi sq=72.698, df=4,

p<.001), included the notification having not been given to the provider on-call, the

notification having been for a PT/INR test, the notification having been for a repeat test,

and the standardized critical value, representing the magnitude of the value. As with

the direct regression in Aim 4, the notification being from a PT/INR test contributed most

heavily to explaining the variance, as demonstrated by a Nagelkerke R^2 =.104. The

repeat note, the provider type, and standardized result brought the total explained

variance from 10.4% to 16.6%. The overall classification in this most parsimonious

model did not improve. Table 24 shows regression coefficients, Wald statistics, odds

ratios, and 95% confidence intervals for odds ratios for each of the four predictors.

Table 24. *Stepwise Logistic Regression Analysis of Response as a Function of Critical Value Magnitude and Provider Characteristics.*

Variable	B	Wald Chi-Square	Sig	Exp(B)	95% C.I for Exp(B)	
					Lower	Upper
Provider Type 1	-.549	6.121	.013	.577	0.374	0.892
Repeat Test	1.439	17.884	.000	4.215	2.164	8.211
PT/INR Test	2.031	34.997	.000	7.625	3.890	14.947
CV Zscore	.272	5.136	.023	1.312	1.037	1.659

Relating this model back to Specific Aim 4, the magnitude of the result, as

represented by the standardized score was a significant predictor of response. Holding

all other variables constant, a provider was 1.3 times more likely to respond to a critical

value with a one unit change in standardized score. The notifications for the PT/INR

resulted in a provider being 7.6 times as likely to respond. As in Aim 4, these results

indicated that the predictor of PT/INR test might be masking relationships between the

predictors and the other tests. The logistic regression was performed for the same

relationship for the PT/INR and glucose tests separately. The best model for the

PT/INR test (chi sq=29.564, df=2, p<.001) included the repeat test and the specimen

age as in Specific Aim 4, but the magnitude of the critical value was not included as a

significant predictor of response for this test. Nagelkerke R^2 was 0.468, indicating the

model explained 46.8% of the shared variance. The stepwise regression for glucose

critical test results resulted in a significant model of two steps (chi sq= 17.277, df=2,

P<.001) as shown in Table 25. The provider type of on-call provider entered the

regression in step 1 and the standardized delta was added in step 2. The classification

improved from 67.3% to 68.4%. Nagelkerke R^2, 0.053, was very low.

Table 25. *Stepwise Logistic Regression Analysis of Response as a Function of Critical Value Magnitude and Provider Characteristics for Glucose Test Notifications.*

Variable	B	Wald Chi-Square	Sig	Exp(B)	95% C.I for Exp(B)	
					Lower	Upper
Provider Type 1	-.667	8.113	.004	0.526	0.338	0.819
Zscore	.363	8.016	.005	1.438	1.118	1.850

The model indicates the provider is more likely to respond to the critical glucose

value result as the result increases in the cases that the provider notified is not the on-

call provider. As the standardized score changes by one unit, the provider is 1.4 times

more likely to respond. Converting standardized scores into raw scores for glucose, for

cases in which the notified physician was not the on-call provider, providers were 43.8%

more likely to respond to a glucose result for every 77 mg/dL increase in the result for

glucose notifications at the high critical value threshold. However, Table 26, including

only notifications that were not received for the glucose test by on-call providers shows

that there is a large amount of overlap in 95% confidence levels between those values

the providers chose to respond to and not to respond to.

Table 26. *Descriptive Statistics for Response/No Response for Glucose Test Notifications*

Test Type	Response Type	Mean critical value	SD	Lower 95% CI	Upper 95% CI
Glucose High Critical	Response	485.1	83.6	317.9	652.3
Glucose High Critical	No Response	469.3	62.2	344.9	593.7
Glucose Low Critical	Response	35.4	4.8	25.8	45.0
Glucose Low Critical	No Response	36.3	3.3	29.7	42.9

In summary, result magnitude is not a singificant predictor of response for PT/INR

testing. Result magnitude is a significant predictor for provider response for glucose

critical value notifications that are not called to on-call providers. The model only

explains 5% of the shared variance and only improves classification slightly. The

hypothesis that there is no relationship between magnitude of the result and liklihood of

provider response can be rejected for the glucose critical values. However, there is

overlap between the 95% confidence levels for the mean critical value, indicating no

change should be made in critical value notification thresholds. Ninety-five percent of

variance in the model remains unexplained.

Chapter 5: Discussion

Introduction

This chapter provides discussion and interpretation of the data presented in Chapter 4. First, a summary of the study will be presented. This will be followed by discussion and implications of the findings for each specific aim, including correspondence or discord with current literature. Finally, recommendations on inclusion of analytes for critical value lists will be offered based on the clinical evidence from this study.

Summary of the Study

Laboratory critical values are lab values that represent a life-threatening condition for which there is a treatment available (Lundberg, 1972). Laboratories are federally mandated to make immediate notification of all critical values to a responsible provider. This notification is costly in terms of laboratory staff and provider's time. There is currently a gap in knowledge of whether physicians receiving outpatient critical value notifications respond to them and whether their responses have an impact on patient outcomes. It is unknown if there are factors that correlated with a provider's likelihood of responding to a critical value in the outpatient setting. This study retrospectively examined the pattern of provider responses to laboratory critical value notifications of PT/INR, digoxin, and glucose results in the outpatient setting. The study attempted to determine if patients had better outcomes when a provider responded to a critical value

in comparison to when providers did not respond. In addition, the physician's

perception of the appropriateness of the critical value threshold for each test was

explored. The results of this study indicate that the current inpatient critical value list

and thresholds are not appropriate for application in the outpatient setting.

Specific Aim 1 Discussion

Specific aim 1: <u>To determine the provider utilization rate and response times for</u>

<u>PT/INR, digoxin, and glucose critical value notifications for outpatients</u>

Notification utilization rate. A total of 637 notifications for the three tests were

made during the study period. Approximately 72% of the notifications were for glucose

results, 25% for PT/INR results, and 4% for digoxin results. The overall provider

utilization rate to all three tests was 74.2%. There was a significant relationship

between the specific test and the likelihood of provider response (chi sq=69.858, df=2,

p<.001). Providers responded to PT/INR and digoxin results at a similar rate, 92.4%

and 85.7%, but were less likely to respond to critical glucose results, indicated by a

66.8% response rate.

The overall provider utilization rate of 74.2%, left 25.8% of critical values notifications

without a response. There are no benchmarks available from previous studies of the

response rate to critical value notification in the outpatient setting from a blind medical

record review available for comparison.   However, a benchmark of 100% response rate

to PT/INR critical value notification does exist from a study including self-reported

provider response rates in a study by Piva et al. (2014). Another potential benchmark

for comparison is Singh et al.'s study of abnormal, but not critical values that resulted in

6.2% of the results with no provider follow-up after 30 days (2010). In this study, 25.8%

of critical values were left without responses at 24 hours after the notification. Providers

eventually responded to another 14.6% of the notifications, leaving 11.2% never

resulting in a provider response. A comparison of Singh's 6.2% of abnormal results

without provider response to the 11.2% in this study is unexpected, since critical values

should represent a more immediate provider response than tests that are outside the

normal reference range.

The higher number of critical value notifications without a response in this study

compared to previous studies could be due to several reasons. First, the lack of

response may simply have been a documentation issue. The provider may have

responded to the notification, but did not document this in the patient's record in this

study. However, two of the response types, ordering another test or scheduling another

appointment, would have been electronically documented without additional

intervention, indicating that providers' lack of documentation could not have been

responsible for a large number of tests with no recorded response. Another possible

reason for the large number of notifications that went without response compared to

Singh et al.'s 2010 study is the difference in tests selected for the study. In this study,

72% of the study notifications were for glucose results. Singh et al.'s medical record

review included a different set of tests. A third possible explanation is that many of the

critical result notifications were for glucose results of patients previously diagnosed with

diabetes. Many of the patients that were included in the study were previously

diagnosed diabetic patients with established office visits every three months and a

historical pattern of elevated glucose values with no poor outcomes. For example, in

one instance the physician made a note in the chart that he chose not to respond to a

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glucose critical value of 421 mg/dL because "it was a chronic issue." However, in

Specific Aim 4, the patient having a previous diagnosis of diabetes was not a significant

predictor of provider response for glucose critical value notification. Other reasons were

also documented as justification for not calling. One on-call physician noted that she

did not respond to a glucose of 520 mg/dL because "it was late." The patient was noted

to have been previously diagnosed with diabetes and historically elevated results.

Another on-call physician made the decision to leave the response to a 592 mg/dL

glucose result to the ordering provider on the following day. It is possible that the

providers did not respond because they believe that the test result did not represent a

life-threatening condition for the patient.

Notification response times. The response times for the critical value

notifications did not significantly differ among the three tests (ch sq=4.563, df=2,

N=427). However, because of the small cell size due to the low frequency of digoxin

critical values, the assumptions of the chi square were violated. In total, 90.4% of the

responses that were made by the physicians, occurred within 4 hours of receiving the

critical value notification. Only 10% of the responses were undertaken between 4 hours

and 24 hours, indicating that if the provider was going to respond, they were more likely

to respond in the first 4 hours. This finding agreed with current literature that provider

offices notified the patients of their critical values within 4 hours of receipt for 90% of

their critical value notifications (Montes, Francis, & Cuilla, 2014). It appeared that when

providers did choose to respond to critical values, they typically responded within 4

hours for all tests.

Response types. As part of the specific aim, a relationship between test and type of response was explored. Inferential statistics were only available for the binary relationships between each test and each type of response due to the fact that more than one response was possible for each notification. Providers were more likely to schedule a follow-up appointment in response to glucose result notifications and more likely to schedule a follow-up test in response to PT/INR result notifications. Providers were also more likely to change the dose or stop the medication in response to a PT/INR or digoxin result than to a notification for a glucose result. This relationship explained 29% of the shared variance, indicating a moderate to large relationship.

The utilization pattern of provider responses, response types, and response times did confirm that providers responded to critical value notifications in the outpatient setting, although the response rate of 74.2% was less than would have been expected if providers perceived the results to indicate permanent death or harm to their patient without intervention. This indicates that the threshold for these three tests was not an appropriate threshold for a critical value in the eyes of the providers. Therefore, the results of this aim does not support applying the inpatient critical value list and threshold to the outpatient setting.

Specific Aim 2 Discussion

Specific aim 2: <u>To determine if there is a difference in patient outcome indicators when providers respond to critical value notifications, compared to when they do not respond to notifications.</u>

There were 21 patients in the study sample that experienced adverse outcomes. No patients died during the study period. It should be noted that many patients presented to the office with complaints prior to having their blood drawn. These included minor nose bleeding and bleeding from the gums. Since these complaints were made prior to the lab draw, they were not considered outcomes, as they sought medical treatment prior to a critical value having been noted. It also should be noted that responses to notifications elevated the number of negative outcome indicators. When contacting the patients in response to critical values, the providers would ask if they were symptomatic. This prompted a recall of symptoms that may have been unreported by patients who did not have a provider call them.

There was no significant relationship between outcome and response. There was a potentially small, but significant relationship between response and unplanned ED admissions. Approximately 3% of cases in which providers did not respond to critical values resulted in an unplanned ED admission, compared to <1% of cases that did have a provider response. The null hypothesis that there is no difference in outcomes when a provider responds to a critical value to when they do not respond could not be rejected.

The low number of negative outcomes for the 164 critical value notifications that resulted in no provider response suggests that the critical value tests and thresholds selected for this study may not actually meet the definition of a critical value. No single patient that went without a provider response either died or was permanently harmed by their condition during the study period. As Heard et al. (2002), has suggested, the critical limits that have been set in many labs do not meet the definition of a life-

threatening condition, as demonstrated in this study. This could be due to the technological advancements in result delivery to providers. When mail was the primary delivery method for outpatient lab results, the provider would not get results for 3 to 5 days. During this time, the patient's condition might worsen or an elevated level of a drug would continue to reach toxic levels as the patient continued to take additional doses during the period that the results were traveling through the mail. Stopping or changing the dosage of medication occurred in 82.8% of the cases in which providers chose to respond to PT/INR notifications and 75.0% of the digoxin cases. This indicates an intervention to avoid the condition escalating to a life-threatening condition, not an existing life-threatening condition for which the provider would recommend vitamin K administration for the critical PT/INR, or a dose of activated charcoal and Dig-Fab administration in the Emergency Room. The administration of vitamin K occurred a few times and the administration of activated charcoal and Dig-Fab never occurred in this study sample. The results of this aim do not support the application of the inpatient critical value list to the outpatient setting due to lack of outcomes when providers chose not to respond to a critical value notification.

Specific Aim 3 Discussion

Specific aim 3: To determine if quicker response times result in better outcomes. There were so few adverse outcomes in the study that a relationship between outcome and timeliness of response could not be explored. There were two unplanned ED admissions with a fast response and no unplanned ED admissions with a slow response. Although 25.7% of critical value notifications went without a response, there was no permanent harm or death of any patient in this study. This suggests the

application of inpatient critical value thresholds in the outpatient setting results in many

notifications to providers that do not represent life-threatening conditions for their

patients.

Specific Aim 4 Discussion

This study determined that there are provider, result, and specimen specific factors

that influence a provider's likelihood of response. The overall model, using nine

predictors, was significant (chi square =67.729, p<.001, df=8). Based upon the level of

significance in the model, it was determined that the test type may be potentially

masking the contributions of the other predictors so stepwise logistic regression was

performed separately for both the PT/INR critical test results and the glucose critical test

results. The model for PT/INR tests included the test being a repeat test and the age of

the specimen as statistically significant predictors of provider response to the

notification. This makes clinical sense as providers contacted the patient for 92.4% of

the critical PT/INR notifications and ordered repeat PT/INR testing for 52.9% of these

(Table 4.5). Their responses include instructions to change or stop their dose of

Coumadin, have a repeat test done, and wait to resume their medication until the office

contacts them with further instruction. Therefore, the model which predicts a higher

likelihood of response for repeat testing indicates that providers are awaiting the results

of the repeat testing, and respond to it by calling the patient and providing them further

dosage instructions.

Addressing Specific Aim 4 for glucose, the model that included glucose test

notifications only was significant (chi square= 7.517, df=1, p=.006) for the predictor of

the notification not being made to an on-call provider. However, the model decreased

classification and only explained 2.3% of the shared variance. Unlike the PT/INR

model, there were no strong predictors of likelihood to respond to a critical glucose

notification. Occasionally, a provider documented a reason that they chose not to

respond to a notification for this test. One provider noted that she did not call due to the

lateness of the hour. The result was 467 mg/dL and the time was 8:10pm. Two

providers left notes in the chart that they chose not to call due to the elevated glucose

being a chronic issue with the patient. Four providers left notes for the ordering provider

or office staff to follow-up the following day. Four providers documented that they

believed the result was due to lab error, therefore did not call the patient. Other reasons

for not calling were that the patient was already scheduled for a follow-up appointment,

the patient was under the care of an endocrinologist, the provider had spoken to the

patient the previous evening, and the patient had been non-compliant and left the clinic

earlier in the day. It appeared that many providers simply thought that the value did not

indicate a life-threatening condition for their patient.

As reported in previous studies by Dighe et al. (2008), the outpatient setting for

critical value notification imposes a difficulty in reaching the patients. Providers called

and left many voicemails and instructions to return calls. Many of these were returned

the same evening or early the next day, but resulted in an additional phone call and

additional provider time. Several of them were not returned and the provider offered no

additional follow-up. There were 33 instances documented by the provider that a

voicemail had been left for the patient, with no response. One provider documented

that the voicemail was full and another documented that the patient's number had been

disconnected. One provider that could not reach a patient with a glucose result of 713

mg/dL, called 911, and asked emergency services to pick the patient up and transport them to the ED.

In summary, the application of inpatient critical value lists and thresholds were not appropriate for the outpatient setting as illustrated by the exploration of the relationship between the provider, specimen, and notification characteristics and likelihood of response. No characteristics were able to reliably predict a response or no response to a critical value glucose notification, although 32.7% of the notifications went without a response. In several cases, documented comments were made by the providers indicated no intervention was necessary in order to avoid a harmful event. Since the results of this study confirm that there was no permanent injury or death, the inpatient critical value list and thresholds do not indicate a patient has a life-threatening condition in the outpatient setting.

Specific Aim 5 Discussion

The analysis for Specific Aim 5 indicated that the magnitude of the result did influence a provider's likelihood to respond to a critical value. When stepwise logistic regression was performed for PT/INR and the glucose notifications separately, it was discovered that the magnitude was significant only for the glucose notifications (chi sq=17.277, df=2, p<.001) and not the PT/INR notifications. For every 77 mg/dL increase in the glucose test result, the provider is 1.4 times more likely to respond if the provider notified was not the on-call provider. Although it is apparent that providers do not perceive all glucose critical value notifications to be life-threatening, as evidenced by the lack of response for 35.7% of these notifications, the results of the logistic regression indicate that there is a large overlap in the confidence intervals of values to

which the providers chose to respond, and to which they chose not to respond. This

makes it impossible to recommend revised threshold critical values for glucose, based

upon this study. It could be that many of the providers chose to respond, not because

they believed that the result represented a life-threatening condition, but because they

would be responsible if they did not respond and a patient had a negative outcome.

Future studies could include a survey of providers with a questionnaire to determine

their reasons for choosing to respond and choosing not to respond to critical value

notifications.

Limitations

The first limitation to this study was the low frequency of digoxin results, which

violated assumptions for statistical analysis for this test alone. Utilization of this drug is

decreasing, as it is being replaced by new drugs with less potential for toxicity. Due to

the low amount of resources required to make the notification on such a low volume

test, it should not be used for further critical value notification studies.   Stepwise logistic

regressions were performed for Specific Aim 4 and Specific Aim 5 for PT/INR

notifications only and glucose notifications only. These results would not have been

impacted by the low number of digoxin notifications.

Another limitation to this study was the small number of adverse outcomes. In total,

there were 21 patients who experienced a negative outcome. Nine of these patients

had no provider response and 12 had a provider response. There was no significant

relationship between response and negative outcome. With current technology, large

health systems are integrating the outpatient charts with the acute care charts, making it

possible to gather data from outpatient, inpatient, and ED visits simultaneously. It would

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be beneficial in a critical value study to select cases based on outcomes instead of notifications. Patients that had outpatient visits, critical outpatient values, and ED admissions could be selected by report. A study of sufficient size for statistical analysis could be obtained to explore a relationship between provider response to a critical value and negative outcome.

Recommendations

The results showed a very consistent pattern of provider response to critical PT/INR results. The provider called the patient 92.4% of the time and recommended that the patient stop their medication for a few days 82.8% of the time, and get the test repeated.   This intervention was not to provide treatment to a patient, but to avoid the patient taking an additional dose that would result in increased risk for bleeding. Therefore, health systems should explore utilizing alert values instead of critical values for outpatients, and potentially automate a process for alert values. Brigden et al., reported 2 of 7 patients with INR values greater than 6 experience major bleeding. In this study, one patient with an INR < 6.0 had minor bleeding as probably complications from an adominoplasty and liposuction a few months earlier. One patient with an INR of 7.82 was admitted to the ED for a GI bleed. Therefore, a value of between 4.0 and 5.2 could be used for an alert value and a value of >5.2 could become the critical value for outpatient critical value notification. Alert values could generate an automated call to the patient with instructions to discontinue medication and call the office the following day for further information. In this study, such an automated process for PT/INR values <5.2 would result in 28.7% fewer calls. Using a conservative estimate of 4 minutes for a technologist to complete a call and another 4 minutes for the provider to call the patient,

an automated message would save the health system a total of 6 hours of healthcare professionals' time for the cases in this study. Using an automated process for PT/INR values <6.0, the health system would save a total of 11.3 hours of healthcare professionals' time. Additional data could be collected for critical PT/INR values to select the optimal threshold for this automated process. This process could be used for some of the other 20+ tests on the health system's critical value list.

For glucose notifications, additional data should be gathered to determine the optimal threshold for notification. From the lack of response and provider comments, it is clear that not all providers believe that the current threshold represents a life-threatening condition. This is supported by the lack of negative outcomes for the 32.7% of glucose notifications that went without a provider response.

Summary

Critical result notification and provider response in the outpatient setting is a very resource intensive process to provide immediate intervention to patients with life-threatening conditions. In this study of 637 critical value notifications, providers chose not to respond to 25.7% of critical value notifications. None of the cases that went without a provider response resulted in death or serious harm to a patient, indicating that the critical value thresholds do not meet the definition of a critical value. This study began to explore whether certain provider, specimen, or test factors influenced a provider's likelihood of response. Although a few significant factors were found, the overall contribution of these to the shared variance of model was small. For the majority of the analyses, the models only improved the classification by a few percentage points or not at all, indicating that although a few predictor variables were significant, the

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overall model did little to improve prediction of whether a provider would respond or not

respond to a critical value notification. The large amount of variance left unattributed in

the models indicated that provider response to these tests cannot be reliably predicted

by any independent variable selected for this study. What could be predicted and

capitalized upon was the pattern of response to critical PT/INR tests and glucose

testing. Laboratories should explore the implementation of alert values, in addition to

critical values, for outpatients. The patterns of provider response, such as instructions

to discontinue medication, schedule a follow-up appointment, or seek additional testing

as determined in this study, could be delivered by automated messaging. More

appropriate critical value thresholds that require immediate provider intervention should

be established. The results of this study indicate that the current inpatient critical value

list and thresholds are not appropriate for the outpatient setting.

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