EVALUATION OF COMPUTERIZED NOTIFICATIONS FOR LABORATORY MONITORING OF POSTLIVER TRANSPLANT IMMUNOSUPPRESSIVE CARE

by

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ABSTRACT

Following liver transplantation, patients require lifelong immunosuppressive care and monitoring to prevent organ rejection, drug toxicity, and death. Traditionally, transplant centers use paper-based processes that are not scalable and can lead to inefficiencies and deficiencies in information management. Clinical decision support (CDS) tools may help to overcome information management challenges, and a system-agnostic approach may help to disseminate these tools nationwide. We sought to inform the development of new transplant information systems by analyzing existing information systems.

To meet this overall objective, we administered a survey and found that all liver transplant programs used manual, paper-based processes and nearly all used electronic health record (EHR) systems. Programs also had immunosuppression guidelines with similar logic patterns. Then we analyzed long-term use of a computerized notification system at one transplant center and found that a system designed specifically for the posttransplant workflow can meet long-term information management needs. Next, we assessed the clinical outcomes associated with computerized notifications for laboratory monitoring of immunosuppressive care and found that a system designed specifically for the posttransplant workflow was associated with improved clinical outcomes. Following this, we described workflow processes at two transplant centers and found that a transplant-specific notification system was associated with changes in workflow process

measures and the satisfaction of performing laboratory monitoring tasks compared to a general EHR notification system. Finally, we administered a questionnaire to coordinators using a transplant-specific notification system and identified the usage of specific data elements in computerized notifications for posttransplant laboratory monitoring.

Our findings show that near universal use of EHRs provides an infrastructure for implementing CDS tools, and logic patterns for posttransplant laboratory monitoring can be generalized to other U.S. transplant centers. Transplant-specific computerized notifications may be part of a system of processes that improve the scalability, quality, and satisfaction of patient management by postliver transplant coordinators. However, these systems must be flexible enough to accommodate new immunosuppressants and changing or additional parameters used in computerized logic as clinical practice or needs of the patient population evolve. Proactive notifications sent directly to patients regarding upcoming due dates via patient portals may also improve patient outcomes.

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GLOSSARY

CDS: clinical decision support

Cyclosporine (or Cyclosporin A): an immunosuppression medication

EHR: electronic health record

IH: Intermountain Healthcare

MELD: Model for End-stage Liver Disease

Rapamune (or Sirolimus): an immunosuppression medication

Tacrolimus: an immunosuppression medication

UNOS: United Network for Organ Sharing

UUHC: University of Utah Health Care

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CHAPTER 1

INTRODUCTION

More than 130,000 liver transplantations have been performed in the United States since 1988.[1] Liver transplant recipients require lifelong immunosuppressive care to prevent organ rejection, drug toxicity, and death. Transplant centers face challenges when implementing immunosuppressive care protocols, monitoring laboratory and other data, and managing the growing set of information for this high-risk patient population. As the number of liver transplant recipients increases each year and long-term survival rates improve,[1] transplant centers have a growing pool of patients generating information that must be prioritized and managed. Traditionally, transplant centers have used paper-based processes to receive or track immunosuppressive laboratory results. These manual, paper-based processes are not scalable and can lead to inefficiencies and deficiencies in information management.[2,3] Concerns about the availability or timeliness of information necessary for clinical decision making are not unique to immunosuppression care management.[4–8] However, these problems are exacerbated by growing patient populations and the complexity of immunosuppressive care protocols with narrow therapeutic indices and regimens that change based on time since transplantation, presence of comorbid conditions, and other factors.[9] Information management challenges may impact the safety, quality, and cost of lifelong immunosuppressive care.

Clinical decision support (CDS) tools have improved posttransplant care process measures and clinical outcomes. The biomedical literature includes descriptions of computerized transplant management systems,[3,10–14] but only two publications describe the use of more advanced clinical decision support (CDS) for postliver transplant immunosuppressive care.[3,10] One publication describes the use of integrated information displays to support physicians and coordinators performing comprehensive immunosuppressive care review.[10] Patients managed with the system experienced significantly fewer rejection episodes and tacrolimus toxicity events compared to patients managed with the prior paper charting system. The second publication describes work at Intermountain Healthcare (IH) regarding computerized notifications to support nurse transplant coordinators as they monitored immunosuppressive care.[3] Notifications were implemented using a CDS infrastructure to automate laboratory monitoring protocols and were delivered to an inbox integrated within the electronic health record (EHR). The system led to significant process improvements, such as improved completeness, timeliness, and reduced redundancy of laboratory result reporting compared to a manual, paper-based approach. However, both of these CDS tools are system-dependent and thus not sharable with other transplant centers.

System-agnostic CDS services are a promising approach to promote the widespread implementation of CDS across applications and care settings.[15] Thus, using this approach may be an effective method for sharing a CDS tool for posttransplant immunosuppressive care laboratory monitoring. Our motivation was to develop a system-agnostic CDS notification system for posttransplant laboratory monitoring. However, we identified research questions that should be investigated before this system

is developed, including:

- What are the information management needs and challenges of laboratory monitoring for posttransplant immunosuppressive care?
- What is the prevalence of prerequisites (eg, EHR infrastructure, availability of discrete data, or guidelines amenable to computable logic) necessary to implement transplant-specific CDS in U.S. transplant centers?
- How are computerized notifications for laboratory monitoring used by nurse transplant coordinators over time?
- Do computerized notifications for laboratory monitoring improve the clinical outcomes of posttransplant patients?
- How do computerized notifications impact the workflow of nurse transplant coordinators?
- How satisfied are transplant coordinators with the support of their information system with and without transplant-specific CDS?
- What data elements in a computerized notification message are used by transplant coordinators?

This dissertation seeks to answer these research questions in order to inform the development of a system-agnostic CDS tool for posttransplant laboratory monitoring. The goal of this dissertation was to investigate opportunities, barriers, and the impact related to implementing computerized notifications to support laboratory monitoring for postliver transplant immunosuppressive care. Chapter 2 includes a summary of the findings from a nationwide survey regarding readiness of transplant centers to implement CDS to aid laboratory monitoring for immunosuppressive care. This survey determines

the number of transplant centers who may benefit from a system-agnostic CDS tool for laboratory monitoring. Chapter 3 includes a description of the distribution of computerized notifications over time, with implications for how to improve notifications to meet the evolving needs of patients as time since transplantation increases. This study evaluates whether a system-agnostic CDS tool designed for a posttransplant workflow would be used long-term to meet information management needs. Chapter 4 includes an analysis of the clinical impact of computerized notifications on postliver transplant immunosuppressive care. A system-agnostic computerized notification system may have a similar impact on clinical outcomes. Chapter 5 includes a description of the processes performed by nurse transplant coordinators for outpatient immunosuppressive care and a comparison of the response time to new laboratory results and satisfaction with performing tasks among nurse transplant coordinators with or without access to transplant-specific computerized notifications. This analysis identifies the potential impact to workflow and process measures that may accompany a system-agnostic CDS notification system for posttransplant laboratory monitoring. Finally, this chapter also includes a description of usage of specific data elements presented with computerized notifications. This analysis identifies the data elements that should be included in other transplant-specific computerized notification systems.

The findings described in this dissertation address only part of the scope of postliver transplant immunosuppressive care, focusing on laboratory monitoring performed by nurse transplant coordinators. Understanding other processes of immunosuppressive care may also help to identify ways in which safety, quality, and cost of care may be improved for postliver transplant patients. It is likely that processes for

meeting the immunosuppressive care needs of other solid organ transplant recipients (such as kidney and heart) are similar. In addition, other areas in healthcare use similar processes to manage laboratory results and medications, including diabetes care and anticoagulation therapy. Such areas may also benefit from an in-depth understanding of the processes of care and the prudent application of CDS tools that support the management of pharmacologic therapies that require laboratory monitoring.

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CHAPTER 2

ASSESSMENT OF READINESS FOR CLINICAL DECISION SUPPORT TO AID LABORATORY MONITORING OF IMMUNOSUPPRESSIVE CARE AT U.S. LIVER TRANSPLANT CENTERS

Jacobs J, Weir C, Evans RS, et al. Assessment of readiness for clinical decision support to aid laboratory monitoring of immunosuppressive care at U.S. liver transplant centers. Appl Clin Inf 2014;5:988–1004. doi:10.4338/ACI-2014-08-RA-0060. Reprinted with permission from Schattauer GmbH.

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Assessment of Readiness for Clinical Decision Support to Aid Laboratory Monitoring of Immunosuppressive Care at U.S. Liver Transplant Centers

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Keywords

Organ transplantation, clinical decision support systems, clinical laboratory information systems, information management, clinical protocols

Summary

Background: Following liver transplantation, patients require lifelong immunosuppressive care and monitoring. Computerized clinical decision support (CDS) has been shown to improve post-transplant immunosuppressive care processes and outcomes. The readiness of transplant information systems to implement computerized CDS to support post-transplant care is unknown.

Objectives: a) Describe the current clinical information system functionality and manual and automated processes for laboratory monitoring of immunosuppressive care, b) describe the use of guidelines that may be used to produce computable logic and the use of computerized alerts to support guideline adherence, and c) explore barriers to implementation of CDS in U.S. liver transplant centers.

Methods: We developed a web-based survey using cognitive interviewing techniques. We surveyed 119 U.S. transplant programs that performed at least five liver transplantations per year during 2010–2012. Responses were summarized using descriptive analyses; barriers were identified using qualitative methods.

Results: Respondents from 80 programs (67% response rate) completed the survey. While 98% of programs reported having an electronic health record (EHR), all programs used paper-based manual processes to receive or track immunosuppressive laboratory results. Most programs (85%) reported that 30% or more of their patients used external laboratories for routine testing. Few programs (19%) received most external laboratory results as discrete data via electronic interfaces while most (80%) manually entered laboratory results into the EHR; less than half (42%) could integrate internal and external laboratory results. Nearly all programs had guidelines regarding prespecified target ranges (92%) or testing schedules (97%) for managing immunosuppressive care. Few programs used computerized alerting to notify transplant coordinators of out-of-range (27%) or overdue laboratory results (20%).

Conclusions: Use of EHRs is common, yet all liver transplant programs were largely dependent on manual paper-based processes to monitor immunosuppression for post-liver transplant patients. Similar immunosuppression guidelines provide opportunities for sharing CDS once integrated laboratory data are available.

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1. Background

Liver transplantation has been a life-saving procedure for over 125,000 persons in the United States since 1988 [1, 2]. Persons that undergo liver transplantation require lifelong immunosuppressive care and laboratory monitoring to detect and prevent organ rejection, toxicity, and death following this costly [3] and complex procedure. The demand for post-transplant immunosuppressive care is increasing because each year more patients are being transplanted and living longer [2]. This poses a growing challenge for care providers at U.S. transplant centers that must continue to monitor and report on previously transplanted patients, even after patients move or use laboratories external to the healthcare enterprise [4]. Effective post-transplant immunosuppressive care requires careful laboratory monitoring because immunosuppressive medication regimens can be complicated, cause side effects, and have narrow therapeutic indices [5]. For example, blood Tacrolimus levels above a therapeutic threshold put patients at risk for toxicity or infection; levels below a threshold put patients at risk for organ rejection [5]. Traditionally, this monitoring has been performed using paper-based flow sheets but two centers have published about their efforts to address this workflow [6, 7]. Laboratory results are often received on paper by fax or mail then transcribed chronologically onto a paper flow sheet along with medication dosages, vital signs, and other patient information. Later, transplant coordinators and physicians review the paper flow sheet to identify values and trends that may indicate complications. The paper flow sheet provides a summary of patient information needed by clinicians for monitoring and clinical decision making. Paper records, however, have inherent shortcomings and are not well suited for health record management. Paper records are prone to transcription errors, are time-consuming to maintain and difficult to reproduce if lost, and are not always accessible given that they can only be in one place at one time. Experts believe that electronic health records (EHR) will help to overcome shortcomings inherent in managing paper-based healthcare information [8, 9]. While EHRs are increasingly being adopted [10, 11], partly motivated by Meaningful Use regulations, EHRs may merely coexist with paper-based systems, adding inefficiencies and cost.

Adoption of EHR technology provides an infrastructure for computerized clinical decision support (CDS)[12,13] to improve drug management for patients with chronic conditions such as diabetes, coagulation care, and kidney disease [14–17]. Computerized CDS can improve drug monitoring for solid organ transplant patients as well, although a recent case report concerning the immediate post-transplant management of a heart transplant patient highlights the need for healthcare enterprises to review thresholds used to deliver alerts and potentially customize vendor-supplied CDS [18]. Concerning use of CDS for long-term outpatient post-transplant immunosuppressive care, we identified only two studies in the literature [6, 7]. Researchers at the University of Washington demonstrated that the availability of patient information summaries when reviewing laboratory data can improve outcomes and cost [7] while researchers with Intermountain Healthcare found that computerized alerts based on program-specific guidelines can improve workflow processes and the quality of laboratory data used for clinical decisions [6]. At Intermountain Healthcare, an analysis of transplant workflow and information management gaps [19] led to the development of a system to address two critical workflow challenges: a) standardized data entry of external laboratory results to integrate laboratory results into the EHR from a continually changing set of external laboratories [20]; and b) CDS alerts to identify patients with laboratory results (internal or external) that are new, out-of-range, or overdue based on time since transplantation [6]. This system led to significant improvements in the completeness, timeliness, and lack of redundancy of laboratory reporting. The liver transplant team at Intermountain Healthcare has continued (as of 2014) to use the data entry system and CDS alerts developed in 2004 to manage the growing population of liver transplant patients.

While other U.S. transplant programs could yield similar benefits for managing a high-risk population of solid organ recipients, little is known about the capabilities of clinical information systems used by transplant programs across the United States. We identified no literature describing information management needs and challenges for laboratory monitoring of immunosuppressive care, or the prevalence of prerequisites (such as an EHR infrastructure, availability of discrete patient data, and computable logic) for implementing the types of computerized CDS mentioned above.

2. Objectives

We sought: a) to describe the current clinical information system functionality and manual and automated processes for laboratory monitoring of immunosuppressive care, b) to describe the use of guidelines that may be used to produce computable logic and the use of computerized alerts to support guideline adherence, and c) to explore barriers to implementation of CDS in U.S. liver transplant centers. The results will inform development of computerized CDS tools to improve outpatient post-transplant laboratory monitoring for immunosuppressive care.

3. Methods

3.1 Study population

The study population included liver transplant programs registered with the Organ Procurement Transplantation Network (OPTN) as of August 2013 [1]. We used publicly available data from the OPTN website to determine the number of transplants performed, the number of consecutive years performing liver transplants, the population served (adult, pediatric, or both), and the geographic region served for each liver transplant program in the United States. We excluded 45 programs that performed fewer than five liver transplant procedures in 2010, 2011, or 2012.

3.2 Survey development

We developed survey questions to describe the transplant program, approaches to paper-based and electronic information management, EHR capabilities, laboratory results monitoring guidelines, and availability of CDS. These topics were derived from the protocols used and functionality required to implement alerts at Intermountain Healthcare to improve information management processes for outpatient post-liver transplant care [6]. To gather evidence of the availability of discrete laboratory data in the EHR for CDS, we queried about the ability to graph information. The ability to graph all internal and external laboratory results is an indication that discrete laboratory data are available for alerting.

The survey instrument was iteratively refined through multiple rounds of informal pilot testing with guidance from experts in survey development and transplant care. A formal pilot study of the survey was performed with three transplant programs. Cognitive interviewing techniques [21] were used to evaluate sources of response error and led to additional refinements. These iterative refinements improved construct validity: respondents understood the questions being asked and were able to match their response to the options provided. Study data were collected using REDCap [22], a browser-based electronic data capture tool for clinical and translational research. The survey, which included logic to skip irrelevant questions, was pilot tested to ensure the correct question flow. Each respondent encountered up to 50 questions that required 10–15 minutes to complete.

3.3 Survey administration

Each liver transplant program was contacted using information from the program website. A script was used to request the participation of the clinical or operations manager in charge of the nurse transplant coordinators. When a representative was unavailable, a message was left on voicemail or with a receptionist. Potential participants were informed that the survey was online, typically took 10–15 minutes, did not involve any protected health information, and that results would be anonymized for publication. At least three calls were made to contact the targeted representative.

Once a representative was identified, an email was sent that included the purpose of the study, a consent cover letter, and an organization-specific link to the survey. Participants were encouraged to complete the survey with assistance from colleagues with a working knowledge of the clinical and information management processes used by the program. Survey administration was performed September 13, 2013 through December 31, 2013.

If surveys were not completed within two weeks, we attempted to contact the non-respondents by email or phone at least three times. We also contacted participants who partially completed the survey or whose response required clarification.

3.4 Data analysis

We performed a descriptive analysis after combining survey data with publically available data from OPTN. To assess the representativeness of the sample, we compared non-respondents to respondents using the number of transplants performed, the number of consecutive years performing transplants, population served, and geographic regional representation [1]. According to OPTN, programs performed a median of 118 liver transplantations during the three years from 2010 to 2012. For convenience, large and small transplant programs were defined as those that performed 100 or more liver transplantations and less than 100 liver transplantations, respectively, during the three years from 2010 to 2012. For graphing capabilities, we defined 'usage' as the proportion of those who used the capability among those for whom it was available, and 'desire' as the proportion of those who wanted the capability among those who did not have it. We stratified responses by program size (large, small) and population served (adult, pediatric, both). When there was a significant difference ($p<0.05$) in responses after stratifying by these features, we reported the p-value. We used the Wilcoxon rank-sum test for continuous variables and used the Chi-squared test or Fisher's exact test (when more than 20% of the cells had an expected frequency less than 5) for categorical variables. Analyses were performed using R statistical software [23].

We performed a qualitative analysis of the narrative responses to a question about barriers to CDS implementation. A card sorting technique was used to organize the short narrative statements into higher-level generalizable categories [24, 25]. This technique is used to create categories based on implicit rules – a sort of folksonomy. The narrative responses were split into individual narrative phrases reflecting a single statement and printed onto individual cards. Researchers were asked to take the stack of "cards" and sort them into a set of categories that reflect their own implicit mental organization. No rules were provided as to the number of categories or the specific type of category to be generated. For this study, three of the authors completed the card sort independently followed by an iterative process of discussion and category identification through consensus. Common themes regarding barriers to CDS implementation were identified.

4. Results

4.1 Description of liver transplant programs responding to the survey

From the OPTN website, we identified 119 liver transplant programs in the United States that conducted at least five liver transplantations each year during 2010–2012. A total of 80 (67% response rate) surveys were completed by one or more transplant care team members. The remaining programs did not respond (n=35) or submitted incomplete surveys with less than 50% of available questions answered (n=4). Among the 80 completed surveys, the response rate for each question ranged from 90 to 100% (96% average).

Responding programs performed a median of 108 (range: 25–429) transplantation procedures during 2010–2012, had consecutively performed transplantations for a median of 24 years (range: 5–26), served adult (n=45; 58%), pediatric (n=12; 15%) or both adult and pediatric (n=21; 27%) populations, and were geographically distributed throughout the 11 regions of the U.S. (▶Table 1). There were no significant differences in the characteristics of responding and non-responding programs ($p>0.20$ for all comparisons; ▶Table 1).

Liver transplant patients require lifelong monitoring of immunosuppressive care. When the 62 programs that served an adult population were asked, "How long does your transplant team have primary responsibility for management of immunosuppression therapy?", the majority (89%) indicated that adult patients were managed by the transplant program until death. The remaining 7 (11%) programs reported that they eventually transferred care to a community physician (n=5) or

that care for some patients was managed by the transplant program while care for other patients was transferred (n=2).

4.2 Current information system functionality and processes

Among the 80 programs, 78 (98%) reported that they used an EHR to manage their liver transplant patients in the outpatient setting. To track immunosuppressant dosing and laboratory results, 33 (41%) programs used the EHR only. The remaining programs reported using paper flow sheets only (n=10, 13%), a non-EHR electronic system only (n=4, 5%), or multiple systems to manage immunosuppressive care (n=33, 41%), including a combination of a paper flow sheet with the EHR (n=24, 30%), a paper flow sheet with a non-EHR electronic system (n=1, 1%), the EHR with a non-EHR electronic system (n=1, 1%), or all three together (n=5; 6%). Two programs (3%) used both paper and electronic flow sheets but did not indicate which types of electronic flow sheet were used. Of note, seventeen different electronic systems were used and half (n=35, 44%) of the programs described using multiple electronic systems to manage information for their liver transplant patients.

Most programs had the capability of generating graphs for laboratory results, including creatinine levels (88%), liver function tests (88%), and immunosuppressive laboratory results (82%). However, less than half (42%) could integrate results from external laboratories with results from internal laboratories and view them together in a graph (▶Table 2). About half of the programs could graph prescribed dose of immunosuppressants (60%) or both immunosuppressive laboratory results and prescribed dose side-by-side (42%). The 'desire' for graphing features among those who did not have the functionality was always higher than the 'usage' among those who did have the functionality: creatinine levels (desire 78%, usage 66%); liver function tests (desire 78%, usage 67%); immunosuppressant drug levels (desire 77%, usage 59%); prescribed dose of immunosuppressants (desire 86%, usage 36%; $p<0.01$); and both immunosuppressant drug levels and prescribed dose in the same graph (desire 86%, usage 43%; $p<0.01$).

Nearly all (99%) of the 80 transplant programs reported that they received laboratory results performed by laboratories outside their network (i.e., external laboratories). In fact, most programs (85%) reported that 30% or more of their patients used external laboratories for routine testing (▶Figure 1). Only one program reported that none of their patients routinely used an external laboratory. There was no significant difference in the use of external laboratories between large and small programs ($p=0.64$).

External laboratory results were received in a variety of ways, but paper-based communication was prevalent. The majority of programs (81%) indicated that "most" or "nearly all" external laboratory results were received by fax (▶Figure 2). While half (47%) of the programs had electronic interfaces that could automatically input laboratory results into a database as discrete, computer-executable data, we found that only 19% of programs indicated that "most" or "nearly all" external laboratory results were received by this method. Most programs reported that "few" or "some" external laboratory results were received by mail (64%), electronic documents (e.g. PDF) (54%), or phone calls (59%). In addition, three programs (4%) commented that they used a website (presumably using a secure login) to receive some external laboratory results. Nearly all programs received external laboratory results by two (22%), three (34%), or four or more (42%) of the methods listed above.

Multiple processes are involved with recording immunosuppressive laboratory results onto paper or electronic records. Most (n=69, 86%) programs reported at least two different processes required to get the information into the flow sheets used for post-transplant immunosuppressant care. Most (80%) programs manually transcribed individual paper laboratory results from paper reports into an EHR system. Similarly, most (75%) programs scanned and linked paper laboratory reports to an EHR system. Twenty-two (28%) programs transcribed paper laboratory results (e.g. faxed reports) to a paper flow sheet and eleven (14%) transcribed paper laboratory results to a non-EHR electronic flow sheet. Nineteen (24%) programs transcribed electronic laboratory results to a paper flow sheet.

4.3 Guideline usage and computerized alerting to support guideline adherence

Most (92%) programs reported that they used guidelines that specified target ranges for immunosuppression drug levels (▶Table 2). Among these programs, target ranges varied based on time since transplant (93%), the presence of co-morbid conditions (87%), or other factors (67%) such as renal function, a history of infections, or the diagnosis necessitating liver transplantation. The proportion of programs considering 'other factors' varied by the population served: pediatric (100%), adult (54%), or both (72%) populations ($p<0.01$). Similarly, most (97%) programs used guidelines for routine laboratory testing schedules. The testing schedules varied based on time since transplant (97%), the presence of co-morbid conditions (80%), or other factors (58%) such as history of rejections, medications, or other laboratory test results.

While half (55%) of the programs reported to receive computerized alerts for recently available immunosuppressive laboratory results, computerized alerting to support guideline adherence was limited. For example, only 21 (27%) programs received alerts for results outside of a desired range, and only 15 (19%) received alerts for overdue results based on their testing schedule guideline (▶Table 2).

4.4 Barriers to implementing clinical decision support

When asked, "What do you believe are non-financial barriers to implementing clinical decision support?", 52 (65%) respondents provided a narrative response. In Table III, we list 10 themes identified regarding barriers to CDS implementation and present example responses for each theme. The themes span concerns about support from clinicians and administrators; changes in workflow; the need to backload and integrate data from multiple sources and have a functional EHR; and finally, despite asking about non-financial barriers, respondents mentioned financial barriers (▶Table 3).

5. Discussion

Our study is the first to describe the multiple paper-based and electronic systems concurrently used to manage the complex immunosuppressive care of over 60,000 post-transplant patients in the U.S. [2]. Despite widespread EHR adoption at medical facilities performing transplantations, less than half (41%) of the U.S. transplant programs exclusively used the EHR for outpatient post-transplant immunosuppressive care. More than half of the transplant programs used paper-based, non-EHR, or multiple systems, a situation that may expose programs to increased costs and information management problems. This situation is likely exacerbated by the finding that at least one-third of the patients in most (85%) programs had routine laboratory testing performed by 'external' laboratories, and only 19% of the programs received "most" or "nearly all" of the external laboratory results through an electronic interface. External laboratory results are usually received by fax, requiring manual transcription to integrate laboratory information into the flow sheet view of information used by the transplant team for decision making. The variety of methods for receiving and recording laboratory results may make it difficult for a transplant program to manage information efficiently and to integrate data into their EHR; however, once discrete data can be integrated, there are opportunities for providing the computerized CDS desired by the programs because the patterns of logic reported for identifying new, out-of-range, and overdue results were similar to those already successfully implemented at Intermountain Healthcare [6]. Even so, the respondents identified technical and sociological barriers that must be addressed before transplant programs can broadly implement CDS to support immunosuppressive care.

The difficulty with integrating external laboratory data into the EHR is a significant barrier to widespread use of CDS and the development of flow sheets and integrated views of drug levels and prescribed doses required for post-transplant care. Nearly all programs had patients receiving routine laboratory results from external laboratories, and less than half of the programs could integrate external and internal laboratory values to see trends in a graph. We found that integration required manually transcribing computerized results to paper or vice versa, or both. While it is technically

feasible and preferable to establish electronic interfaces [26,27], it is not always logistically or economically feasible. Only 47% of the programs reported the use of an electronic interface to receive external laboratory results, and these interfaces only handled a subset of the laboratories from which results were received. This situation may be present for several reasons. First, the cost of establishing and maintaining electronic interfaces may be prohibitive, particularly for smaller external laboratories or when the business need is only relevant for a single transplant department within a healthcare system. Electronic laboratory exchange is more likely available if a healthcare setting has a significant business need to establish an interface or is part of a health information exchange. Second, transplant patient populations use many different laboratories. A previous analysis of the external laboratories used by a 'small' (84 liver transplants during 2010–2012) transplant center found that over 80 different external laboratories were reporting results, and the three most frequently used laboratories comprised only 7% of all the external results received [20]. We did not query about the number of external laboratories used by transplant patients, but we suspect that this situation is common among U.S. transplant centers. Third, since lifelong monitoring is required, the set of external laboratories used changes over time when patients move or switch health insurance providers. Care for liver post-transplant patients is unique because lifelong monitoring is required even when patients reside great distances away [4]. For other chronic conditions, care is usually transferred to a physician within a reasonable proximity to the patient. Establishing an electronic interface may not be practical in a landscape of a changing set of external laboratories. Improved strategies for sharing laboratory results across enterprises will improve integration of external laboratory results.

We found that nearly all programs had immunosuppressive care guidelines that used similar patterns of logic, such as time since transplant or presence of a co-morbid condition, to individualize the response to a given laboratory value. We queried about these patterns because they are the basis of the CDS logic used internally at Intermountain Healthcare for the past ten years to alert nurse transplant coordinators about new, out-of-range, and overdue results [6]. It is not really important to know if one transplant program uses the same target range as another transplant program because variation is expected and can be managed through configuration. It is, however, important to know that most transplant programs would want the capability to define a target range, and they would want to modify the range based on time since transplant. These patterns of logic could be implemented in a CDS tool that allows an individual transplant program to trigger alerts as indicated in their own guidelines. In fact, the CDS tool could be system-agnostic and service-based, which is "an alternative and complementary strategy for knowledge-sharing" that can facilitate implementing CDS across applications and care settings [28]. Implementing system-agnostic CDS is fruitless, though, if discrete data are not available. Currently, only a quarter of the transplant programs are using computerized alerts to identify out-of-range or overdue immunosuppression laboratory results, probably partly due to limitations in the availability of discrete data needed to trigger an alert. Thus, despite the availability of guidelines that could become computable, most transplant patients are not having their immunosuppression managed by providers with access to CDS that supports guideline adherence.

While CDS in the form of patient summaries and alerts to support the immunosuppression management workflow may benefit patients and their care givers [29], improved outcomes may also impact the financial health of a transplant program. Reimbursements are sometimes fixed for the full spectrum of transplant care, thus avoiding preventable errors is a necessary cost containment strategy [3].

The qualitative analysis of open-ended questions uncovered additional organizational and sociotechnical barriers to implementing CDS. The barriers were common change management concerns about support (the need for physician buy-in or support from top administrators), impact on workflow, readiness, resistance to change, and trust in a new system [30]. Concerns about trusting the accuracy of electronic data or CDS recommendations may reflect either poor or no previous experience with CDS systems, or frequent complaints about the usability of EHRs [31]. Discordance between system expectations and use were evident from the finding that usage of graphs to view trends of laboratory and immunosuppressive doses information (among those with the capability) was always lower than the proportion of respondents that desired the functionality (among those who did not yet have the capability). Of note, to fully implement CDS, additional technical barriers such as those concerning user interfaces and clinical validation of logic would need to be addressed [30].

Surveys have limitations, particularly the potential for selection and recall bias. Study participants were self-selected based upon their willingness to complete the survey. While respondents to an online survey may be more technically savvy or have greater expectations and desire for automated systems to support patient care than non-respondents, we don't expect these characteristics to change a respondent's description of the systems and guidelines used by their program. We mitigated biases by preemptively informing participants that results would be reported without identifying individual programs, following up with non-respondents, encouraging respondents to seek input from others in the transplant care team, and using formal cognitive interviewing techniques to promote high construct validity in the development of our survey instrument. We succeeded in obtaining a high response rate (67%) with no significant difference in key characteristics between responding and non-responding programs. We believe findings can be generalized to other U.S. liver transplant programs. Finally, specific guidelines were not analyzed in detail as part of this study. Doing so would serve as future work by identifying additional important similarities or differences in guidelines across transplant programs.

6. Conclusions

Despite the ubiquity of EHRs, all transplant centers must use manual, paper-based methods for part or all of their process for managing post-transplant immunosuppressive care. Across the U.S. this impacts an estimated 60,000 liver transplant patients [2]. Most external laboratory results are not automatically integrated as discrete data into the EHRs used by transplant centers and thus are not usable by CDS without manual transcription. Moreover, only a quarter of the transplant programs in the U.S. currently use computerized systems to identify overdue or out-of-range immunosuppressant drug levels even though most transplant centers have guidelines for immunosuppressive care, and these guidelines use similar patterns of logic that can be implemented using rule-based computerized CDS. In addition to challenges with using both electronic and paper-based systems for laboratory information management, there are sociotechnical and organizational barriers that impede the implementation of CDS systems. Even so, many programs have key features required for success, namely guidelines, and systems capable of storing discrete laboratory results. Pressure to improve efficiency and clinical outcomes in the face of a growing population of patients and capitated reimbursement models will further the need for CDS to support outpatient post-transplant immunosuppressive care.

Clinical Relevance

Many transplant programs have features required for CDS, namely guidelines with similar patterns of logic and information systems that store discrete laboratory results. In the face of a growing population of patients and capitated reimbursement models, facilitating exchange of discrete data that replace manual paper-based processes may allow CDS implementations that improve efficiency and clinical outcomes for outpatient post-transplant immunosuppressive care.

Conflict of Interest

The authors declare that they have no conflicts of interest in the research.

Human Subjects Protections

The study was performed in compliance with the World Medical Association Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects, and was reviewed by the Institutional Review Board at the University of Utah.

Author Contributions

JJ, CS, and CW contributed to the design and conduct of the study, as well as the preparation of the manuscript. RSE assisted with data analysis and preparation of the manuscript. he authors would like to thank all who participated in taking the survey.

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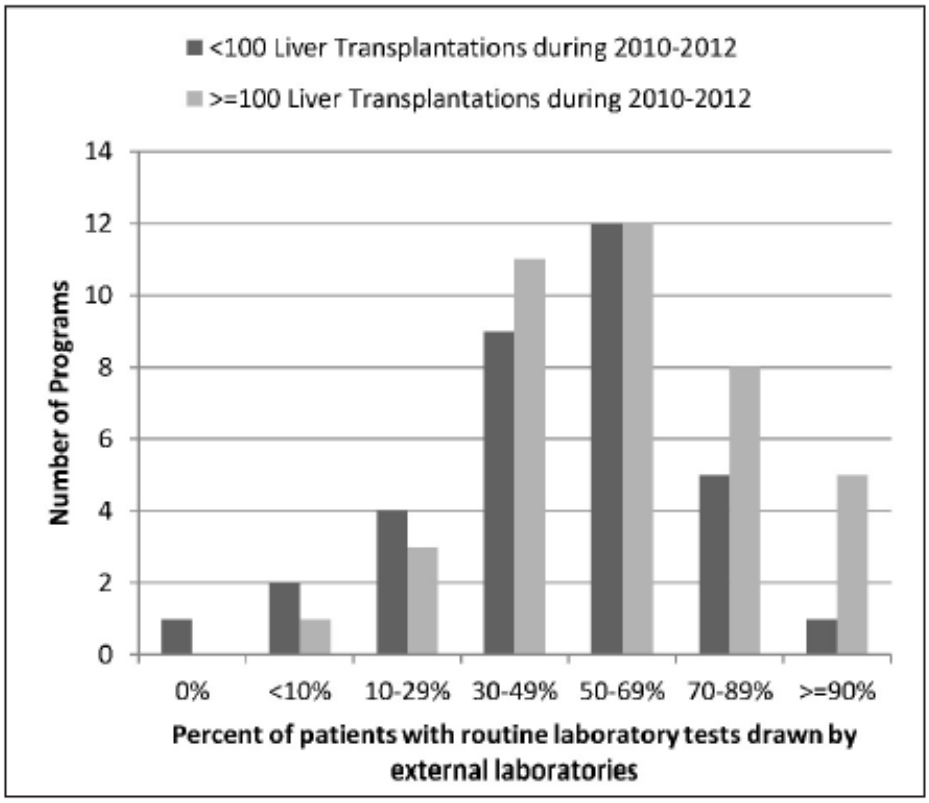

Fig. 1 Distribution of routine testing from external laboratories for outpatient post-liver transplant patients (n=78)

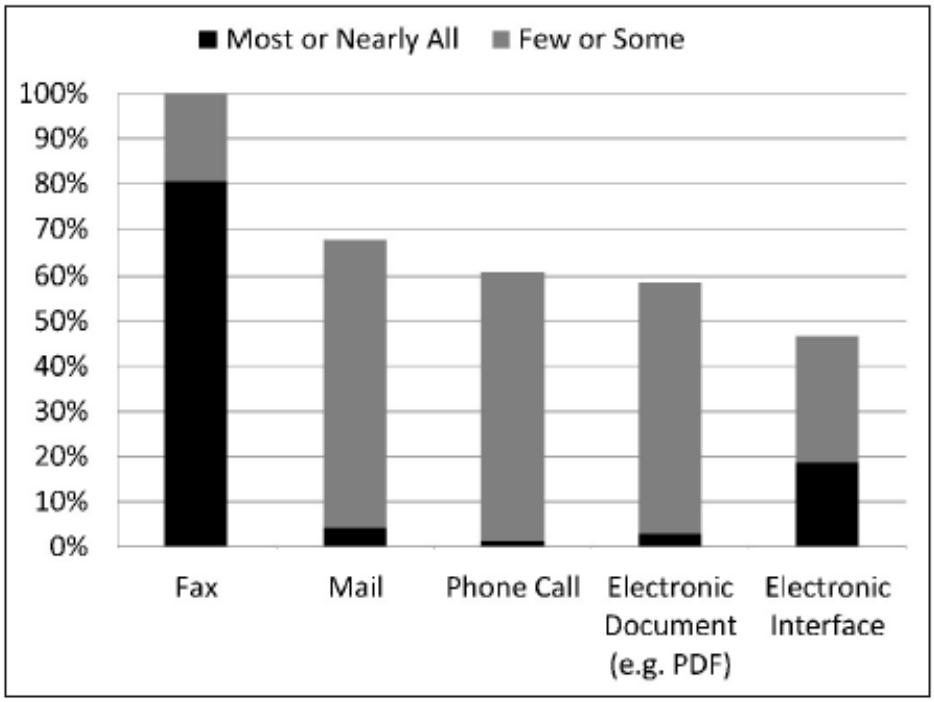

Fig. 2 Proportion of programs receiving external laboratory results by amount and method (n=80)

Table 1 Characteristics of the 119 liver transplant programs that met the selection criteria

	Respondents (n=80)	Non-respondents (n=39)	P Value
Total number of transplant procedures performed during the three years from 2010 to 2012			0.22[a]
Mean (SD)	150 (114)	170 (120)	
Median (IQR)	108 (181)	154 (113)	
Number of years consecutively performing transplants			0.32[a]
Mean (SD)	21 (6)	21 (6)	
Median (IQR)	24 (9)	23 (10)	
Age group transplanted			0.43[b]
Adult – # (%)	45 (58%)	28 (68%)	
Pediatric – # (%)	12 (15%)	3 (7%)	
Both – # (%)	21 (27%)	10 (24%)	
Geographic distribution			0.25[c]
1 – CT, ME, MA, NH, RI, eastern VT	5 (6%)	2 (5%)	
2 – DE, District of Columbia, MD, NJ, PA, WV, northern VA	15 (19%)	3 (8%)	
3 – AL, AR, FL, GA, LA, MS, Puerto Rico	10 (13%)	4 (10%)	
4 – OK, TX	9 (11%)	5 (13%)	
5 – AZ, CA, NV, NM, UT	9 (11%)	8 (21%)	
6 – AK, HI, ID, MT, OR, WA	3 (4%)	1 (3%)	
7 – IL, MN, ND, SD, WI	10 (13%)	2 (5%)	
8 – CO, IA, KS, MO, NE, WY	7 (9%)	2 (5%)	
9 – NY, western VT	2 (3%)	4 (10%)	
10 – IN, MI, OH	6 (8%)	2 (5%)	
11 – KY, NC, SC, TN, southern VA	4 (5%)	6 (15%)	

[a] Wilcoxon rank-sum test; [b] Chi-squared test; [c] Fisher's exact test

Table 2 Needs and capabilities of electronic health records being used in outpatient post-transplant care (n=80)

	Number of respondents	Number (%) responded 'Yes'
Does your liver program have a general guideline regarding pre-specified ranges for desired immunosuppressant drug levels for most patients?	79	73 (92%)
If "Yes":		
• Do pre-specified ranges change based on time since transplant?	70	65 (93%)
• Do pre-specified ranges change based on the presence of co-morbid conditions?	70	61 (87%)
• Are there other factors that determine the pre-specified ranges?	70	46 (67%)
Is a computer-generated alert received when an immunosuppressant lab result is outside the desired range?	77	21 (27%)
Does your liver program have a general guideline regarding pre-specified routine lab testing schedules for most patients?	79	77 (97%)
If "Yes":		
• Do pre-specified lab testing schedules change based on time since transplant?	75	73 (97%)
• Do pre-specified lab testing schedules change based on the presence of co-morbid conditions?	74	59 (80%)
• Are there other factors that determine the pre-specified lab testing schedules?	72	42 (58%)
Is a computer-generated alert received when an immunosuppressant lab result is overdue or missing?	75	15 (20%)
Is a computer-generated alert received when an immunosuppressant lab result is newly available?	77	42 (55%)
Does your electronic medical record system have the capability of graphing immunosuppressant drug levels from external labs?	78	33 (42%)
What is the status of graphing the following parameters in your electronic medical record system?		
• Lab results of creatinine	73	64 (88%)
• Lab results of liver function tests	73	64 (88%)
• Lab results of immunosuppressant drug levels	72	59 (82%)
• Prescribed dose of immunosuppressants	73	44 (60%)
• Both the prescribed dose and lab results of immunosuppressant drug levels in the same graph	72	30 (42%)

Table 3 Themes that emerged in comments when asked about non-financial barriers to implementing clinical decision support (n=52)

Theme/category identified	Example of narrative provided by the respondent
Physician buy-in/engagement is important for the success of any change.	"MDs sitting down setting individual pt thresholds (if need be) and then all MD sticking to these as they rotate on and off service."
Concerns about being able to trust the accuracy of only electronic data exchange.	"Team members reluctance to rely solely on electronic communication"
Support from top administrators is lacking.	"Lack of understanding on the part of organization administrators that may not understand the need for or value of technology."
Changes in workflow are a barrier.	"changes in workflow"
Readiness of the whole system is required in order to adopt any new electronic processes.	"Do not have a fully implemented EMR, still using a fairly manual system."
The challenges of integrating data from all sources are significant.	"Multiple computer systems within our own organization that have tremendous difficulty interfacing with each other."
Resistance to change or inertia is everywhere.	"systems already in place, comfort level with current workflow, computer giving a suggestion that physician may not agree with"
Backload existing data would require significant extra work.	"Anything that requires duplication of data entry"; "People to perform entry of the backload of patients who would need to be entered into a tracking database."
The system is too complex to lend itself to any CDS (patients and processes vary all of the time).	"insufficient complexity of CDS to account for patient-specific needs"
The cost or financial investment is substantial.	"it always seems as though there is a financial barrier!"

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CHAPTER 3

LONGITUDINAL ANALYSIS OF COMPUTERIZED ALERTS FOR LABORATORY MONITORING OF POSTLIVER TRANSPLANT IMMUNOSUPPRESSIVE CARE

A presentation based on this work was presented at the American Medical Informatics Association Annual Symposium Proceedings in November 2015.

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3.1 Introduction

More than 65,000 liver transplant patients are currently living in the United States.[1] These patients require lifelong immunosuppressive care and monitoring to prevent organ rejection, toxicity, and death following this costly[2] and complex procedure. A capitated model may be used to reimburse providers for the lifelong care of posttransplant patients, incentivizing transplant centers to minimize costs.[2] Achieving higher quality care at lower cost is the daunting challenge facing the United States in the era of the Patient Protection and Affordable Care Act and advancing Meaningful Use legislation.[3,4]

Computerized decision support aids have demonstrated potential to support higher quality health care. Their effectiveness has been shown in areas of relatively simple logic, such as checking for medication interactions or recognizing laboratory tests with out-of-range results.[5,6] When appropriately applied, such clinical decision support (CDS) has been shown to reduce errors, decrease costs, and encourage best practice.[7,8] The Office of the National Coordinator for Health Information Technology (ONC) has emphasized the importance of CDS to optimize health care outcomes and the need for its widespread adoption.[9] CDS has the potential to improve laboratory monitoring for posttransplant immunosuppressive care.[10]

In 2004, a computerized alerting system was implemented at Intermountain Healthcare (IH) to support the laboratory monitoring of postliver transplant patients.[11] While internal laboratory results were already available, a data entry program was created to input information regarding laboratory results from external laboratories as structured data in the EHR.[12] The availability of structured data for all laboratory results allowed

alerts to be generated for all posttransplant patients regardless of laboratory used for testing. Alerts were generated for new, out-of-range, or overdue immunosuppression-related laboratory testing using automated rules developed by experts in transplant management. The automated rules employed the same logic found in the protocols used by nurse transplant coordinators for routine laboratory monitoring. Alerts were delivered to an electronic inbox within the EHR and remained until accepted or rejected. Nurse transplant coordinators could view the alert message along with information useful for decision making (eg, date and value of the laboratory result that triggered the alert, date of and time since liver transplantation, and hospitalization status). Coordinators could accept or reject the alert, select the reason for the action taken, and leave a narrative comment. As of 2015, the liver transplant team at IH has continued to use the data entry system and the CDS alerts developed in 2004 to manage their growing population of over 500 active liver transplant patients. A previous study showed that this system led to significant improvements in the completeness, timeliness, and reduced redundancy of laboratory result reporting.[11] A more detailed description of the infrastructure, logic, and alerts delivered are available in previous publications.[11,13]

We found one other study that used CDS to support posttransplant laboratory monitoring.[14] Researchers found evidence that CDS improved clinical outcomes and decreased costs during the first year of posttransplant care. Other transplant centers have expressed an interest in implementing CDS to support the lifelong management of their posttransplant patient population.[15] Yet there are studies indicating that CDS may be disruptive or no longer used by target users after initial implementation.[16] While the initial study at IH analyzed alerts over the first five-month period after implementation,

there is a gap in the understanding of how alerts are used by nurse transplant coordinators for laboratory monitoring of postliver transplant patients over time, particularly as time since transplantation increases.

3.2 Objectives

In this study, we aimed to describe alerts delivered to nurse transplant coordinators from 2005 to 2012. Our objectives were to a) describe the alerts delivered to nurse transplant coordinators to manage patients after liver transplantation over an eight-year period, b) describe the distribution of the alerts and the time to respond to alerts as time since transplantation increased, and c) identify opportunities for improving alerts in order to improve the management of posttransplant immunosuppressive care.

3.3 Methods

The liver transplant program at IH performed 776 liver transplant surgeries from January 1, 1988, to December 31, 2012. The study population included patients who received a liver transplant at IH and who were monitored for posttransplant laboratory testing of immunosuppressive care by IH nurse transplant coordinators. We included alerts generated between January 1, 2005 and December 31, 2012 for this study. Since individual patient outcomes were not reported for this study, each transplantation was included for patients who received multiple liver transplants (n=15). We classified patients as lost to follow-up during a time period when there was a gap of 365 days or greater between an alert for overdue tacrolimus laboratory testing and an alert for a new tacrolimus laboratory result. We excluded overdue alerts for patients during the time

they were classified as lost to follow-up. Patients became active once an alert for a new laboratory result was received. All alerts were triggered by either new (including out-of-range) or overdue laboratory testing.

Data were extracted from the IH enterprise data warehouse (EDW) with the help of EDW experts and a transplant center data manager. Data included immunosuppression and related laboratory results, triggered alerts, and hospital admission and discharge dates and times.

We analyzed alerts based on the year an alert was triggered, time since transplantation, hospitalization status, alert type, action taken (accepted or rejected), reason given for the action taken, and narrative comments. Correlations among data elements were identified. We described the response time between alert generation and action taken, stratified by time since transplantation. We also described the time between an alert for an overdue laboratory test and an alert for a subsequent new laboratory result (including only the first in a series of alerts for overdue testing), stratified by time since transplantation. Time-based results were summarized using a box-and-whisker plot with the ends of the whiskers representing the lowest value within 1.5 times the interquartile range of the first quartile and the highest value within 1.5 times the interquartile range of the third quartile. Outliers (values outside the whiskers) were not shown.

Institutional Review Boards from Intermountain Healthcare and the University of Utah approved this study.

3.4 Results

Nurse transplant coordinators received alerts for 564 postliver transplant patients from January 1, 2005 to December 31, 2012. The number of active patients who received laboratory monitoring grew from 338 in 2005 to 418 in 2012 (Table 3.1).

From January 1, 2005 to December 31, 2012, there were 124,082 computerized alerts delivered to nurse transplant coordinators for laboratory monitoring of postliver transplant patients. Coordinators received an average of 42.5 alerts per day over this time period, and all alerts were either accepted or rejected. Nearly all (98.0%) alerts were accepted, and 22.8% of alerts were received while the patient was hospitalized. The most common alerts were triggered by new results for creatinine (41.5%) or tacrolimus (30.4%) or when patients were overdue for tacrolimus (12.1%) or creatinine (9.8%) laboratory testing (Table 3.2).

While the number of alerts per patient remained fairly stable, the number of alerts per day gradually increased over time (39.0 in 2005, 45.6 in 2012) (Table 3.1). This paralleled an increase in the number of active patients over the same period (338 in 2005, 418 in 2012), even though the number of transplantations declined. Alerts for overdue laboratory testing constituted a growing proportion of all alerts over time, increasing from 19.6% in 2005 to 29.3% in 2012. There was not a constant change over time in the proportion of alerts generated while patients were hospitalized. The proportion of alerts that were rejected decreased from 7.0% in 2005 to 0.6% in 2008 and remained below 0.6% per year through 2012 (Table 3.1).

Among alerts for overdue laboratory testing, few (<1%) alerts were generated while patients were hospitalized but up to half of these were rejected (Table 3.2). When

patients were not hospitalized, 8.3% of overdue creatinine alerts and 8.5% of overdue tacrolimus alerts were rejected. The most common reason for rejecting an alert was due to external laboratory results that were available but had not yet been entered into the EHR (Table 3.3). For accepted alerts, coordinators most frequently sent a notification letter or indicated that they had previously sought to notify the patient. No single patient constituted more than 1% of alerts for overdue laboratory testing.

Conversely, the proportions of alerts generated for hospitalized patients were greater among alerts for new laboratory results (range: 13.8-64.5%) than among alerts for overdue laboratory testing (Table 3.2). Whether for hospitalized patients or not, few (range: 0-2.2%) alerts for new laboratory results were rejected. Among actions taken for accepted alerts, 100% required no additional action and 48% indicated that the coordinator reviewed the results if the patient was hospitalized, but for nonhospitalized patients, coordinators responded to accepted alerts in a variety of ways, such as reviewing laboratory results, contacting the patient, consulting the physician, or indicating that no action was required (Table 3.3).

Among alerts received when patients were not hospitalized, the number of alerts per day and the proportion of overdue alerts increased over time (Table 3.4), similar to the pattern observed overall in Table 3.1. However, while the proportion of alerts for low tacrolimus laboratory results remained stable, the proportions for normal and high tacrolimus laboratory results declined over time (normal: 8.9% in 2005, 3.8% in 2012; high: 5.3% in 2005, 1.2% in 2012). Likewise, the proportions of alerts for high creatinine laboratory results remained stable while the proportion for normal creatinine laboratory results decreased (35.3% in 2005, 29.8% in 2012). The rejection rate for overdue

laboratory testing decreased from 25% or higher during 2005-2007 (range: 25.0-29.4%) to below 3% during 2008-2012 (range: 0.3-2.5%). The rejection rate for alerts of new laboratory results was 2.0% or lower throughout the study.

As time since transplantation increased, the number of alerts per patient declined from 95 to 21 (excluding 10+ years posttransplant) (Table 3.5). Likewise, the proportion of alerts received while patients were hospitalized decreased from 53.6% during the first period to 13.5% in the last period. Alerts for overdue laboratory testing constituted a growing proportion of alerts as time since transplantation increased from 2.0% for 0-3 months posttransplant to 44.1% for 10+ years posttransplant. In contrast, the proportion of patients with one or more overdue alerts appeared bimodal, with peaks at 3-4 years posttransplant and at 10+ years posttransplant. The proportion of alerts that were rejected ranged from 0.8% to 4.0% with no pattern as time since transplantation increased.

There was no trend in the response time between alert generation and the action taken for nonhospitalized patients by year. For new laboratory results, the nurse response time ranged from a median of 6 to 17 hours by year (Figure 3.1). For overdue laboratory testing, the nurse response time ranged from a median of 5 to 125 hours by year (Figure 3.2). However, for both new and overdue laboratory testing, there was a significant drop in the median response time to alerts from 2007 to 2008.

The response time between alert generation and the action taken for non-hospitalized patients increased with time since transplantation. For alerts of new laboratory results, the median response time increased from 6 to 17 hours (Figure 3.3). For alerts of overdue laboratory testing, the median response time increased from 6 to 23 hours (Figure 3.4) but peaked at 39 hours for patients 1-2 years posttransplant. The

median response time for alerts of both new and overdue laboratory testing remained fairly stable from 2-3 years posttransplant and beyond.

The time between an alert for overdue tacrolimus laboratory testing and the next alert for a new tacrolimus laboratory result for nonhospitalized patients increased with time since transplantation (Figure 3.5). The median interval increased from 5.8 to 41.2 days from 0-3 months to 10+ years posttransplant.

3.5 Discussion

While a few studies have explored how computerized alerts support laboratory monitoring of patients within the first year after transplantation,[11,14] no studies have analyzed how these alerts are used by nurse transplant coordinators as time since transplantation increases for patients beyond the first year. Our study shows that the distribution of alerts generated to support the laboratory monitoring of postliver transplant patients changes over time. As time since transplantation increases, there is a greater need to support the process of monitoring patients who are overdue for laboratory testing. In addition, even though the active patient population continued to grow, there was a decline in the number of new postliver transplant patients at IH. This shift in the population means that a greater proportion of time must be devoted to monitoring patients who are more prone to overdue laboratory testing. Liver transplantation graft failure rates have continued to improve and patients are surviving longer, further increasing the need to monitor immunosuppressive care, particularly for overdue laboratory testing. Transplant coordinators must juggle the contrasting needs of recently transplanted patients, who require frequent new laboratory testing, and the needs of

patients who are several years posttransplant and who receive less frequent laboratory testing but are more prone to being overdue for testing. Thus, computerized alerts should be implemented in a way that supports the evolving needs of managing this patient population.

There was a dramatic decrease in rejected alerts for overdue laboratory testing of nonhospitalized patients from 25% or greater during 2005-2007 to less than 3% during 2008-2012. During the study, 73% of these overdue alerts were rejected due to the availability of laboratory results from external laboratories that had not yet been entered into the EHR. The increasing number of overdue alerts generated over time and the substantial decrease in the proportion that were rejected after 2007 may indicate that additional time dedicated to data entry or implementation of electronic laboratory interfaces were used to improve the integration of laboratory results from external laboratories. A nurse transplant coordinator confirmed that an employee had been dedicated to data entry of external laboratory results in early 2008. The challenge of integrating external laboratory results as structured data into the EHR is a significant barrier to the widespread use of CDS.[15] Considerable effort, both in financial cost and in standards development, continues to be spent to overcome this barrier.

Analysis of computerized alerts over time illustrated the impact of increased resources on workflow process and nurse response time. After 2007, not only was the rejection rate of alerts significantly decreased, but the response time to alerts for new or overdue laboratory testing decreased. When an employee was dedicated to entering laboratory data into the EHR, alerts were received sooner and the response time decreased. In addition, the assistant quickened the response time to overdue alerts by

sending a reminder of laboratory testing to patients by letter. Transplant programs with computerized alerting systems may consider implementing a process for reviewing the data generated by alerts to hasten the identification of resource misallocations.

By the end of the study period, the proportion of overdue tacrolimus alerts increased while the proportion of new tacrolimus alerts decreased. In addition, the distribution of specific tacrolimus alerts differed: alerts for low tacrolimus results remained stable, but alerts for normal and high tacrolimus results decreased. Overall, the proportion of alerts for low (20.4%) or high (2.9%) tacrolimus laboratory results readily outnumbered the alerts for normal (6.9%) tacrolimus results. This is particularly unexpected when there was a decline in the number of new patients and an increase in the proportion of patients who have likely had sufficient time posttransplant for providers to maintain patients within the target range. Patient noncompliance is a possible but unlikely explanation. These unexpected differences may also be explained by a mismatch between the unaltered logic of automated rules that trigger the alerts and revised clinical practice. The protocol for immunosuppression had been revised since the automated rules had been implemented, with a downward shift in the target range. Under the revised protocol, nurse transplant coordinators were receiving alerts for low tacrolimus results that were no longer considered below the target range. The automated rules triggering computerized alerts should be updated when the laboratory monitoring protocol is revised. This process may be semiautomated by periodically reviewing generated alerts to identify mismatches of clinical practice and the logic of automated rules.

When the automated rules were implemented, time since transplantation was the

main determinant of the desired target range for immunosuppression. In practice, however, nurse transplant coordinators adjust this target range based on certain conditions (eg, Hepatitis C positive status). The target range for tacrolimus is manually decreased for postliver transplant patients with these conditions. Coordinators must determine whether a patient is positive for these conditions before knowing whether the alert is valid or should be adjusted. Alerts may be improved by further personalizing the logic based on these conditions.

Alert fatigue among physicians is a well-known unintended consequence of alerting systems.[17–19] While methods for reducing alert fatigue have been demonstrated,[20,21] the problem persists. One recommendation to minimize alert fatigue is to provide alerts that are noninterruptive.[22] The alerting system analyzed in this study used noninterruptive alerts, or "notifications," that nurse transplant coordinators viewed in an electronic inbox. This may have contributed to the 100% response rate and the 98% acceptance rate for the alerts received by nurse transplant coordinators. In addition, alerts were delivered in a team-based environment to support transplant patient management and were designed specifically to support this workflow.[10] After ten years of experience with the alerting system, nurse transplant coordinators continue to use the system for patient management.

This observational study has limitations. First, the study included only patients who were transplanted at one institution and who received monitoring of immunosuppressive care from the same institution. This population may not be representative of patients at other transplant centers. Second, our definition of patients who were lost to follow-up may have excluded patients who otherwise would have been

included in the study.

3.6 Conclusion

As patients progress after liver transplantation, overdue laboratory testing becomes more prevalent. Alerts should be capable of supporting providers as they monitor the evolving needs of posttransplant patients over time. Opportunities exist to further improve computerized alerts by maintaining the logic used by existing alerts and by including additional parameters as transplant clinical management practices advance. Implementation of automated laboratory reporting for a greater proportion of reported laboratory results may further reduce cost and the number of erroneous alerts for overdue laboratory testing.

Table 3.1. Distribution of patients and immunosuppression management alerts, by year

Year	Patients		Alerts					
	New Liver Transplantations (#)	Active Patients (#)	Total Generated (#)	Alerts per Patient (#)	Alerts per Day (#)	Overdue Alerts (%)	Received while Hospitalized (%)	Rejected (%)
2005	38	338	14220	42.1	39.0	19.6	18.1	7.0
2006	38	357	14344	40.2	39.3	16.5	23.0	4.3
2007	40	372	14733	39.5	40.4	16.9	28.3	4.5
2008	40	387	15749	40.7	43.1	19.7	25.9	0.6
2009	37	403	16518	41.0	45.3	21.3	24.6	0.5
2010	29	402	16146	40.2	44.2	25.1	19.4	0.1
2011	29	409	15740	38.5	43.1	25.6	21.6	0.2
2012	26	418	16632	39.8	45.6	29.3	21.9	0.2
Total	277		124082		42.5	21.9	22.8	2.0

Table 3.2. Description of immunosuppression management alerts generated from January 1, 2005-December 31, 2012

Alert Message	Alert Count (%)	% Generated While…		% Rejected While…	
		Hospitalized	Not Hospitalized	Hospitalized	Not Hospitalized
Overdue for tacrolimus testing	15010 (12.1%)	0.2%	99.8%	16.7%	8.5%
Overdue for creatinine testing	12217 (9.8%)	<0.1%	>99.9%	50.0%	8.3%
Creatinine (increased by 0.3 since last result)	3912 (3.2%)	42.5%	57.5%	0%	0.5%
Creatinine (increased by 0.3 between three results)	1409 (1.1%)	48.5%	51.5%	0%	0.1%
Creatinine (no significant increase)	46139 (37.2%)	30.2%	69.8%	<0.1%	0.4%
Tacrolimus (below target range)	25932 (20.9%)	24.6%	75.4%	<0.1%	0.2%
Tacrolimus (within target range)	8034 (6.5%)	18.0%	72.0%	0%	0.2%
Tacrolimus (above target range)	3791 (3.1%)	27.2%	72.8%	0%	0.9%
New cyclosporin A	2806 (2.3%)	28.4%	71.6%	0%	0.3%
New sirolimus	232 (0.2%)	13.8%	86.2%	0%	0%
Potassium (below target range)	2261 (1.8%)	64.5%	35.5%	0%	1.1%
Potassium (above target range)	521 (0.4%)	55.7%	44.3%	0%	2.2%
Magnesium (below target range within 30 days posttransplant)	1204 (1.0%)	21.3%	78.7%	0%	1.7%
Magnesium (below target range)	614 (0.5%)	39.5%	60.5%	0%	0.1%

Table 3.3. Summary of reasons given for rejecting or accepting immunosuppression management alerts, by hospitalization status when the alert was generated

Patient hospitalized when alert generated		Patient *not* hospitalized when alert generated	
Rejected	Accepted	Rejected	Accepted
Overdue laboratory testing alerts:			
57%: No reason given 43%: Non IHC labs available but not yet entered into EHR	83%: Patient previously notified 4%: Letter notification 4%: Patient in hospital 4%: Phone notification 4%: Unsuccessful phone call	73%: Non-IHC Labs available but not yet entered into EHR 13%: No reason given 13%: Lab testing interval extended by clinician	57%: Patient previously notified, waiting for labs 37%: Letter notification 3%: Unsuccessful phone call 2%: Phone notification 1%: No reason given <1%: Left message on messaging system <1%: Left message with household contact <1%: Spoke with patient <1%: In person notification <1%: Patient in hospital
New laboratory testing alerts:			
100%: No reason given	100%: No action required 48%: Reviewed labs 3%: No reason given <1%: Consulted physician <1%: Contacted patient <1%: Lab results already seen and acted upon	76%: No reason given 29%: Lab data charted incorrectly	47%: No action required 42%: Reviewed labs 39%: Contacted patient 14%: Consulted physician 5%: No reason given 5%: Lab results already seen and acted upon

Table 3.4. Distribution of immunosuppression management alerts generated while patients were not hospitalized, by year

Year	Alerts (#)	Alerts per Day (#)	Overdue Alerts[a] (%)	New Tacrolimus[b] (%) L | N | H	New Creatinine[c] (%) * | ** | O	Other Alerts[d] (%)	Rejected[e] (%) OD | New
2005	11650	31.9	23.9	18.7 | 8.9 | 5.3	2.6 | 0.7 | 35.3	4.6	29.4 | 2.0
2006	11052	30.3	21.4	21.9 | 8.9 | 3.9	2.4 | 0.8 | 36.1	4.7	25.0 | 0.3
2007	10569	29.0	23.5	22.1 | 8.2 | 3.4	2.8 | 1.0 | 35.0	4.1	26.5 | <0.1
2008	11666	32.0	26.6	21.6 | 6.7 | 2.9	2.0 | 0.7 | 34.3	5.3	2.5 | 0.2
2009	12450	34.1	28.2	19.3 | 7.6 | 3.1	1.9 | 0.7 | 34.6	4.5	2.2 | 0.1
2010	13017	35.7	31.1	21.1 | 6.5 | 2.1	2.3 | 0.7 | 32.8	3.4	0.3 | 0.1
2011	12345	33.8	32.6	21.3 | 5.2 | 1.6	2.3 | 0.7 | 32.1	4.1	0.6 | 0.1
2012	12987	35.6	37.5	18.0 | 3.8 | 1.2	2.5 | 0.7 | 29.8	6.6	0.5 | 0.1
Total	95736	32.8	28.4	20.4 | 6.9 | 2.9	2.4 | 0.8 | 33.7	4.7	8.4 | 0.4

a. The combined proportion of alerts indicating overdue laboratory testing for tacrolimus or creatinine.
b. The proportions of alerts that were (L) low, (N) normal, or (H) high compared to the target range for tacrolimus laboratory testing, respectively.
c. The proportions of alerts that were for (*) an increase of 0.3 units between two creatinine results, (**) an increase of 0.3 units between three creatinine results, and (O) all other results for creatinine laboratory testing, respectively.
d. The combined proportion of alerts indicating a new laboratory result for: magnesium, potassium, cyclosporin A, or sirolimus.
e. The proportions of alerts that were rejected for (OD) overdue or (New) new laboratory testing, respectively.

Table 3.5. Distribution of immunosuppression management alerts, by time since transplantation

Time since Transplantation	Active Patients (#)	Alerts (#)	Alerts per Patient (#)	Overdue Alerts (%)	Patients with ≥1 Overdue Alert (%)	Received while Hospitalized (%)	Rejected (%)
0-3 mo	272	25850	95	2.0	26.5	53.6	0.8
3-6 mo	271	10130	37	13.4	41.7	30.4	4.0
6-12 mo	273	10538	39	6.4	46.5	19.9	1.1
1-2 yr	288	11950	41	13.1	63.9	11.4	3.4
2-3 yr	280	10283	37	25.1	68.6	15.5	3.4
3-4 yr	264	8752	33	35.6	75.0	11.9	3.3
4-5 yr	249	6622	27	24.2	54.2	17.0	1.5
5-6 yr	231	5092	22	25.0	46.8	12.7	1.2
6-7 yr	221	4749	21	35.1	50.2	10.7	1.0
7-8 yr	200	4375	22	33.5	55.5	14.5	1.5
8-9 yr	193	3941	20	35.9	59.1	13.6	2.6
9-10 yr	174	3700	21	35.3	60.3	11.4	2.9
10+ yr	193	18100	94	44.1	82.4	13.5	1.6
Total	564	124802		21.9	84.9	22.8	2.0

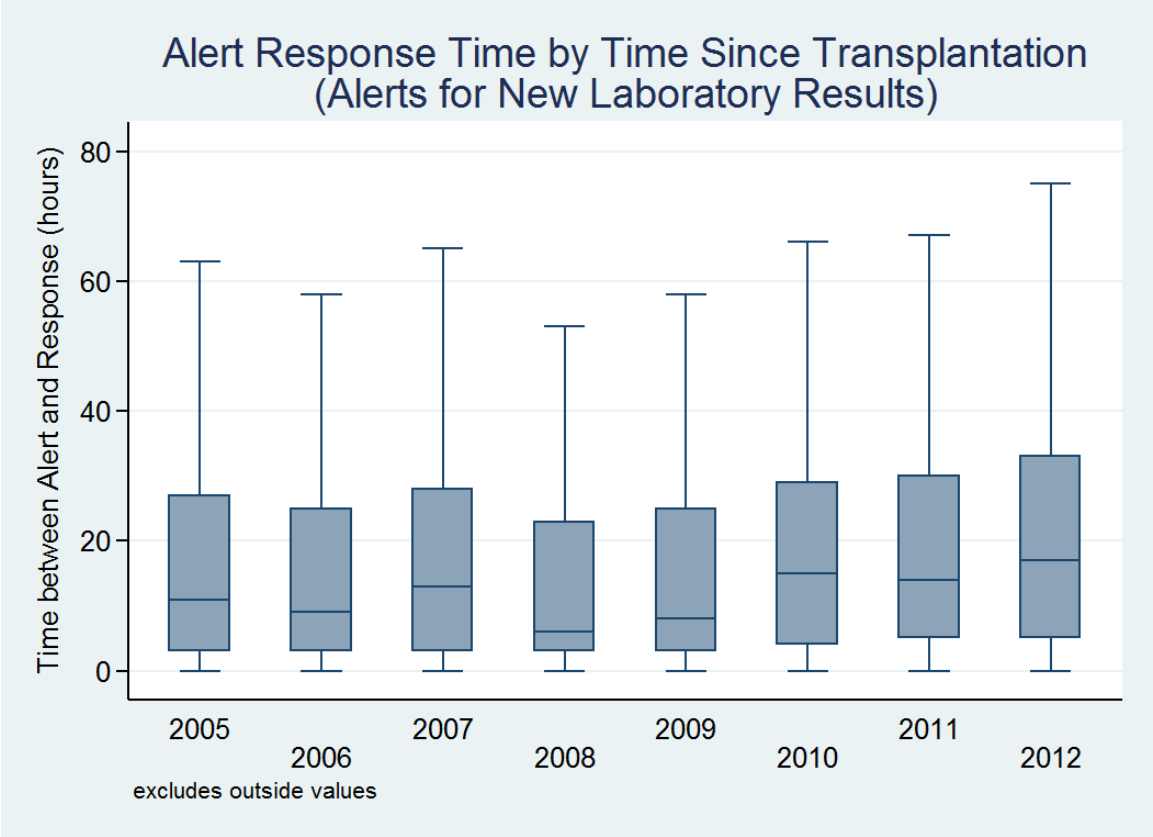

Figure 3.1. Time between a new laboratory testing alert for non-hospitalized patients and the action taken, by year

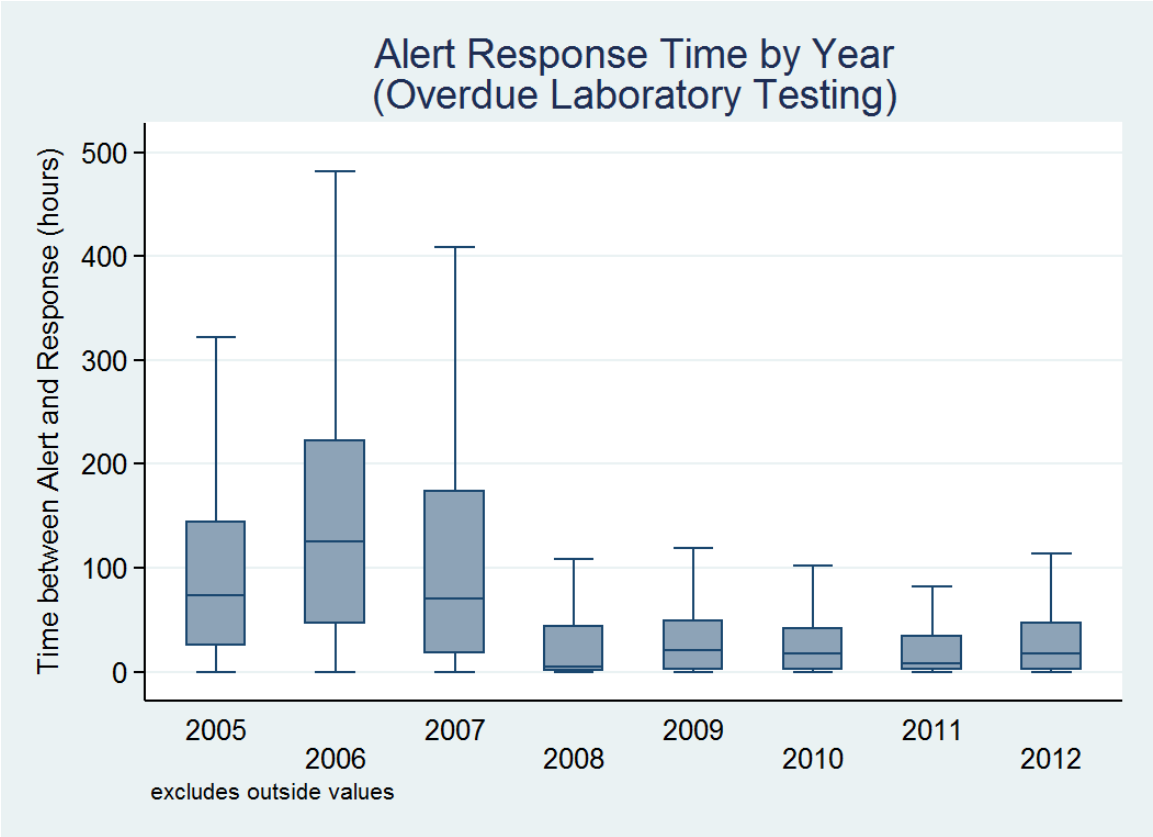

Figure 3.2. Time between an overdue laboratory testing alert for non-hospitalized patients and the action taken, by year

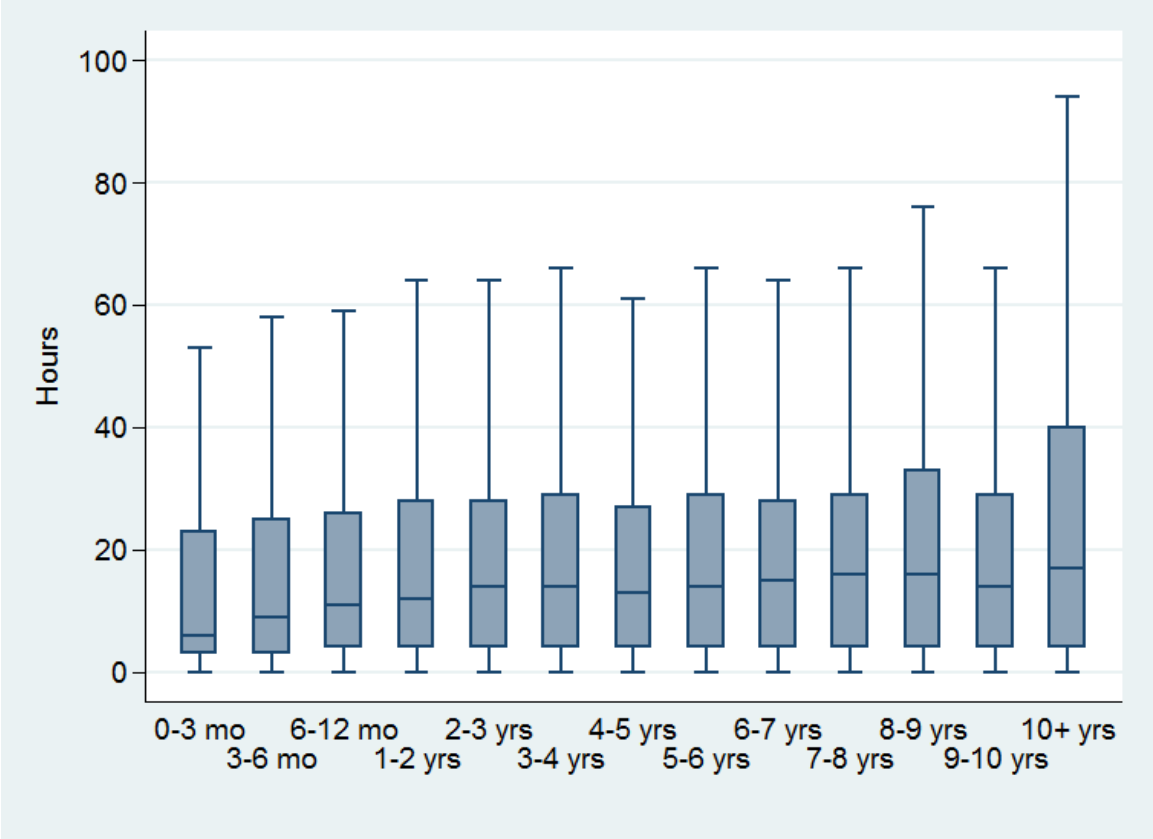

Figure 3.3. Time between a new laboratory testing alert for non-hospitalized patients and the action taken, by time since transplantation

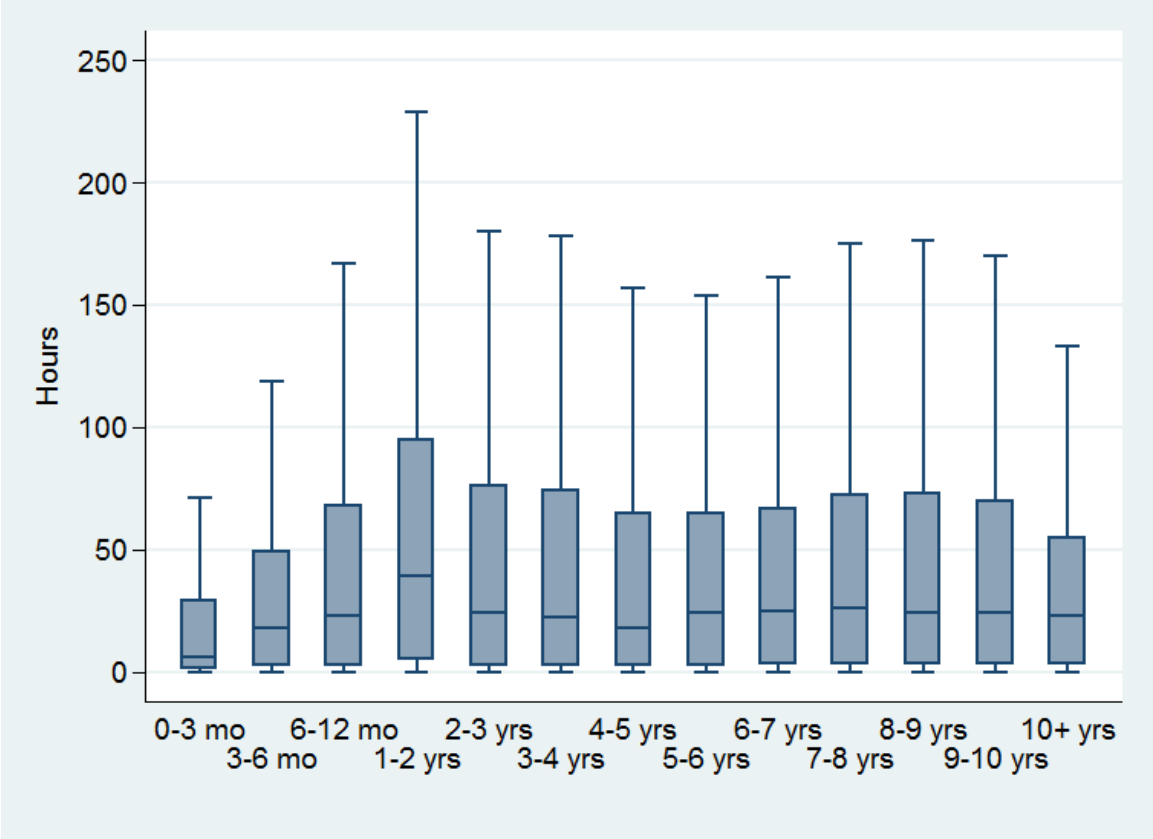

Figure 3.4. Time between an overdue laboratory testing alert for non-hospitalized patients and the action taken, by time since transplantation

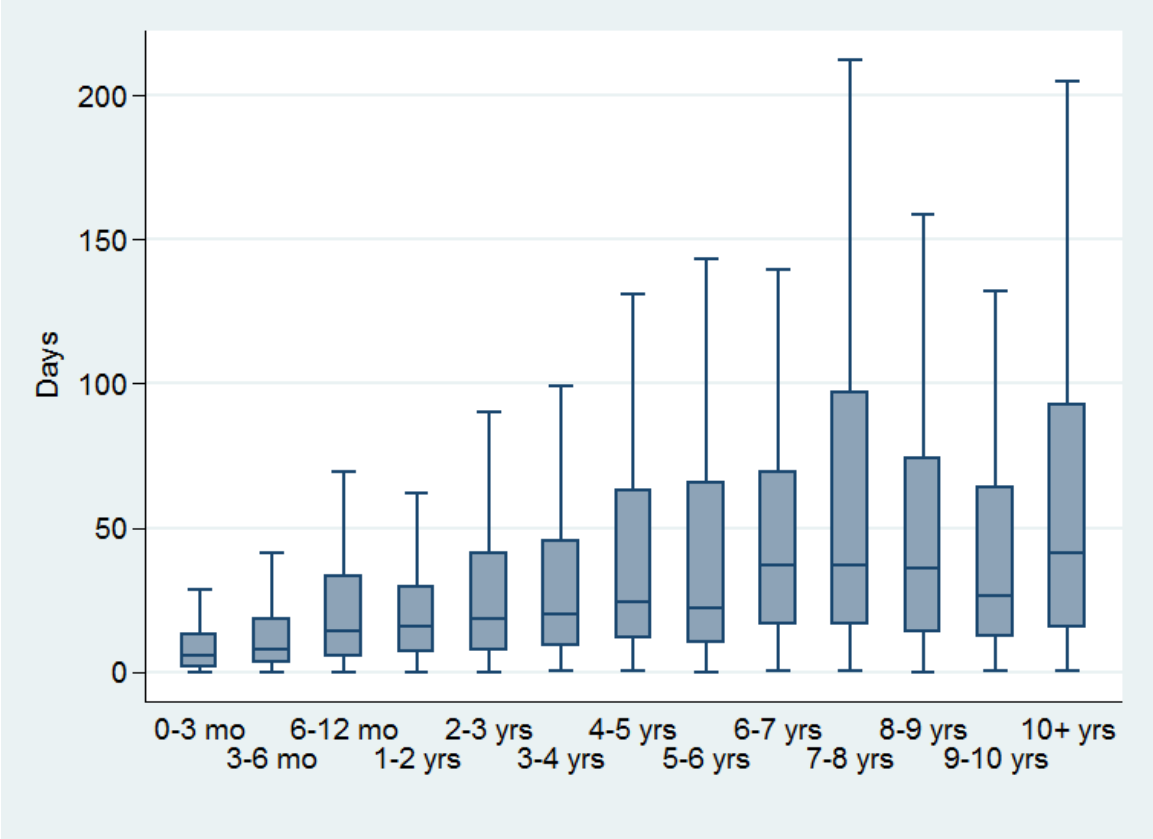

Figure 3.5. Time between the first in a series of overdue tacrolimus laboratory testing alerts for non-hospitalized patients and a new tacrolimus laboratory testing alert, by time since transplantation

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CHAPTER 4

IMPACT OF COMPUTERIZED LABORATORY MONITORING ON CLINICAL OUTCOMES FOR POSTLIVER TRANSPLANT IMMUNOSUPPRESSIVE CARE

4.1 Introduction

Liver transplant recipients require lifelong immunosuppressive care to prevent organ rejection, drug toxicity, and death. Transplant centers face challenges when implementing immunosuppressive care protocols, monitoring laboratory data, and performing other information management tasks for this high-risk population. Currently, transplant centers use manual paper-based processes to receive or track immunosuppressive laboratory results.[1] These manual processes are not scalable and can lead to inefficiencies and deficiencies in information management.[2,3] While concerns about information management for clinical decision making are not unique to immunosuppression management,[4–8] they are exacerbated in the context of transplant patient care. First, as the number of liver transplant recipients increases each year and long-term survival rates improve,[9] transplant centers manage a growing population of transplant recipients generating information that must be prioritized and managed. Second, immunosuppressive care protocols have narrow therapeutic indices and complex regimens that change based on time since transplantation, presence of comorbid

conditions, and other factors.[1,10] Information management challenges may impact the quality of lifelong immunosuppressive care, and may not be addressed by the "meaningful use" of electronic health record (EHR) systems incentivized by the HITECH Act.[11] EHRs often merely coexist with paper-based systems[1], adding complexity to the healthcare workflow.

The biomedical literature includes descriptions of computerized transplant management systems,[3,12–16] but only two publications describe the use of more advanced clinical decision support (CDS) for postliver transplant immunosuppressive care.[3,12] One publication describes the use of integrated information displays to support physicians and coordinators performing comprehensive immunosuppressive care review.[12] Patients managed with the system experienced significantly fewer rejection episodes and tacrolimus toxicity events compared to patients managed with the prior paper charting system. The second publication describes earlier work at Intermountain Healthcare (IH) by several authors of this paper regarding computerized notifications to support nurse transplant coordinators as they monitored immunosuppressive care.[3] Notifications were implemented using a CDS infrastructure to automate laboratory monitoring protocols and were delivered to an inbox integrated within the EHR. The system led to significant process improvements, such as improved completeness, timeliness, and reduced redundancy of laboratory result reporting compared to the previous manual, paper-based approach.[3]

As of 2016, the liver transplant team at IH has continued to use the computerized notification and data entry system developed in 2004 to manage their growing population of over 500 active liver transplant patients.[17] The transplant coordinators receive and

accept an average of 40-50 notifications each day. While the system was previously shown to improve care process measures, the relationship to clinical outcomes is unknown. In addition, we have a unique opportunity to evaluate functionality that is becoming more commonly available in vendor-based EHRs. Therefore, our objectives were to evaluate the association between implementation of computerized notifications and (a) compliance with the protocol-based laboratory testing schedule, (b) occurrence and response to toxicity episodes, and (c) occurrence of mortality and graft failure.

4.2 Methods

4.2.1 Study design, setting, and intervention

We conducted a retrospective cohort study with historical control to assess outcomes among liver transplant patients from Intermountain Healthcare (IH). The IH transplant center serves the Intermountain West (UT, ID, WY, MT, NV, and CO) and was located in LDS Hospital until October 2007 when it was transferred to Intermountain Medical Center. From January 1, 2001 to March 27, 2008, the number of postliver transplant patients actively managed by three IH nurse transplant coordinators increased from 250 to 420 patients.

Between routine outpatient visits, patients had a schedule for laboratory testing (Table 4.1) to be performed at a laboratory owned by IH or an external entity. All laboratory results were recorded on a paper flow chart. Beginning on March 12, 2004, new external laboratory results were also manually entered in the EHR using a structured data entry form, integrating IH and external laboratory results in the EHR.[18]

Using the IH decision support infrastructure, computerized notifications were

triggered in real time based on protocol logic (Table 4.1) and delivered to an electronic inbox in the EHR.[3] Notifications concerned new, out-of-range, and overdue laboratory testing, critical laboratory results, and other events important for immunosuppression management. Implementation began on March 28, 2004, and integration into the clinician workflow was completed by November 1, 2004. The computerized logic was unchanged during the study period.

4.2.2 Study population

Between January 1, 2001 and March 27, 2008, 261 patients received their first liver transplant at IH and had their tacrolimus levels and testing schedules continuously monitored by IH coordinators (Figure 4.1). We excluded 31 patients transplanted during the nine-month transition period for implementation and initial use of the notification system. We excluded patients who died during initial hospitalization for transplantation or within three days following hospital discharge (n=14) or who switched from tacrolimus to another immunosuppressant prior to hospital discharge following their transplantation (n=3).

The study population included preintervention *control* (n=110) and *intervention* (n=103) patients, transplanted before and after the transition period, respectively (Figure 4.1). We censored patients after death (n=11), graft failure/liver retransplantation (n=2), changing from tacrolimus to another immunosuppressant (n=2), transferring routine immunosuppressive care to another transplant program (n=8), or becoming lost to follow-up (n=7) (Table 4.2). Unless censored, patients in the control and intervention groups were followed through March 27, 2004 or March 27, 2008, respectively.

For analyses requiring laboratory data, we used a subset of the study population: patients for whom *all* tacrolimus testing was performed at an IH facility. Test results from external laboratories were not available electronically for the control group, and differences may exist in testing patterns between those using an IH or an external laboratory. In December 2004, one author (CS) compared all laboratory results documented on the transplant care paper flow charts with laboratory results available in the IH EHR.[18] From this analysis, we identified the subset of patients (n=54 (49%)) in the control group with no tacrolimus results from an external laboratory (Figure 4.1). We identified the subset of eligible patients (n=67 (65%)) in the intervention group using information about the testing facility documented in the EHR for each laboratory result.

4.2.3 Data collection

In 2014, we extracted data from the IH data warehouse: patient demographics, tacrolimus results, hospital admission and discharge dates, protocol status (ie, active or inactive), and risk factors determined to be important by a liver transplant physician (author GH) such as prior kidney transplantation or hepatitis C infection. For intervention patients, we extracted computerized notifications. If a patient had two or more tacrolimus results in a day, we selected the highest value or removed duplicate results (n=26; 0.3%). We excluded tacrolimus results obtained during the initial hospitalization for liver transplantation.

4.2.4 Primary outcomes and definitions

Primary outcomes included incidence of toxicity episodes or a missed due date for laboratory testing, time to respond to a toxic or an overdue tacrolimus test, and mortality and graft failure. A toxicity episode was defined as one or more consecutive tacrolimus laboratory results greater than 20 ng/ml. *Potential* days of follow-up are the time period between hospital discharge following liver transplantation and the end of the follow-up period, disregarding censoring. Graft failure was defined to occur on the date of re-transplantation. Model for End-stage Liver Disease (MELD) is used to assess the severity of chronic liver disease, with higher values corresponding to a greater likelihood of mortality.[19]

4.2.5 Data analysis

Unless otherwise indicated, we analyzed categorical variables using a Chi-square or Fisher's Exact test and continuous variables using a t-test. We used descriptive statistics to compare the study populations and describe computerized notifications. We classified tacrolimus results as "in-range" versus "out-of-range" and "on-time" versus "overdue" by emulating the protocol logic (Table 4.1) using Stata.[20] We validated our classification with notifications generated for the intervention group. Nearly all (98%) laboratory results triggered a notification. Using Cohen's kappa, we found significant agreement when classifying laboratory results as out-of-range (agreement: >99.9%; kappa>0.99, 95% CI: 0.96-1.02) or overdue (agreement: 99.3%; kappa=0.85, 95% CI: 0.82-0.88) between the emulated and the computerized logic.

When multivariable analyses were performed, the following variables were

included in the models: sex, age at transplantation, MELD score, hepatitis C status, days hospitalized following liver transplantation, days hospitalized during first year after liver transplantation, and categories of time since transplantation from the protocol.

The laboratory-based analyses included the subset of study patients who used an IH laboratory for all tacrolimus testing (Figure 4.1). To compare the incidence of toxicity episodes and of missing a due date for laboratory testing, we fitted mixed-effects, multivariable Poisson regression models, with laboratory results across time nested within patients. We controlled for the above variables and used backward-elimination for variable selection. To analyze the impact on maintaining tacrolimus levels within target ranges, we compared (a) the distribution of tacrolimus levels, and (b) the first tacrolimus levels obtained after a missed due date. To analyze the time to respond to a toxicity episode, we compared the distribution of time between the first tacrolimus result indicating a toxicity episode and the next tacrolimus result. Similarly, to analyze the time patients were overdue, we compared the average time between the laboratory testing due date and the next result. In a subgroup analysis, we stratified by time since transplantation.

To compare the relative risk of mortality and graft failure between control and intervention groups, we fit a Cox proportional hazards regression model and controlled for the above variables. We used backward-elimination for variable selection with $p=0.20$ as the cut-off.[21]

All analyses were performed using Stata 13.1.[20]

4.2.6 Ethical review

Institutional Review Boards from Intermountain Healthcare and the University of Utah approved this study. A waiver of informed consent was obtained.

4.3 Results

4.3.1 Description of study population and laboratory testing

Among 261 patients who received their first liver transplant between January 1, 2001 and March 27, 2008, 213 (82%) patients were included in the study (Figure 4.1). We found no difference in demographic characteristics or censoring events between study groups (Table 4.2). However, the severity of chronic liver disease prior to liver transplantation for both study populations ($p<0.01$) and the potential days of follow-up for the full study population ($p=0.03$) were significantly higher among the intervention group (Table 4.2). On average, intervention patients were sicker and were transplanted earlier in the follow-up period, allowing more time to elapse between transplantation and the end of the follow-up period. A subset of 121 (57%) patients was included in the laboratory-based analyses. This subset of patients generated 6,706 tacrolimus results and used an IH laboratory for all tacrolimus testing. The demographic and clinical characteristics of the patients included in this subset were not significantly different than the set of patients excluded from this analysis because they had one or more of their laboratory tests performed at a laboratory external to IH.

4.3.2 Description of the computerized notifications

During the 39-month intervention period, coordinators received 46,872 computerized notifications for their entire liver transplant population. Therefore, the three coordinators each received an average of 93 notifications per week. One third of the notifications (n=17,045; 36%) concerned patients in the intervention group selected for this study (Table 4.3).

Among all notifications for the intervention group, 7,507 (44%) concerned tacrolimus laboratory testing. Most (n=6,804; 91%) of these notifications were for new tacrolimus results, of which 61% were below the target range. The remaining 9% of tacrolimus-related notifications concerned overdue laboratory testing. Coordinators responded to all, and 'accepted' 95%, of the tacrolimus-related notifications. There was a significant difference between the full intervention group and the subset of the intervention group concerning the proportion of notifications for overdue tacrolimus or creatinine laboratory testing. Otherwise, similar patterns were observed for the subset included in the laboratory-based analyses (Table 4.3).

4.3.3 Compliance with the laboratory testing schedules

During the first six months posttransplant, the incidence rate of missing a due date for laboratory testing per 1000 patients-days was lower for the intervention group, but this difference was not statistically significant (Table 4.4). Conversely, after 180 days (ie, six months) posttransplant, the incidence rate of being overdue was higher in the intervention group ($p<0.01$) (Table 4.4). However, in a mixed-effects, multivariable Poisson regression model accounting for demographic and clinical variables and time

since transplantation, we found no significant risk of being overdue associated with computerized notifications (adjusted rate ratio=1.10; 95% CI: 0.90-1.34; p=0.37).

The average number of days from a missed due date to the next laboratory result was not significantly different across groups for any category of time since transplant (Table 4.4). However, after a missed due date, the average tacrolimus concentration of the next laboratory result was significantly lower for the intervention group than for the control group 30-90 days posttransplant (10.0 vs. 14.4 ng/mL; p=0.02) and more than 90 days posttransplant (7.4 vs. 9.7 ng/mL; p<0.01), and for both periods the control group was within the target range while the intervention group was below the target range (Table 4.4).

4.3.4 Impact on the occurrence and responsiveness to tacrolimus toxicity episodes

The average concentration (ng/mL) for tacrolimus levels was significantly lower among patients in the intervention group for each category of time since transplant (p<0.01) (Table 4.5). For both groups, the average tacrolimus concentrations were below the target range during the first 30 days posttransplant but within the target range after this period (Table 4.5). In addition, the incidence rate of toxicity episodes was significantly lower for the intervention group among laboratory testing performed more than 90 days posttransplant (p=0.02) (Table 4.5). In a mixed-effects, multivariable Poisson regression model accounting for demographic and clinical variables and time since transplantation, use of computerized notifications was associated with fewer toxicity episodes (adjusted rate ratio=0.68; 95% CI: 0.48-0.94; p=0.02), which

represented a 32% risk reduction.

The average time from a toxicity episode to the next laboratory result was always lower for the intervention group, but only significantly lower among laboratory results received 0-30 days and 30-90 days posttransplant (Table 4.5).

4.3.5 Impact on mortality and graft failure

Overall, 13 patients expired or experienced liver graft failure during follow-up (Table 4.2). The cumulative risk of the composite endpoint mortality or graft failure is displayed as a Kaplan-Meier graph (Figure 4.2). Use of computerized notifications was associated with a 75% reduction in risk of mortality and graft failure in a multivariable Cox regression model (adjusted hazard rate=0.25; 95% CI: 0.06-0.95; p=0.042).

4.4 Discussion

This is the first study to describe clinical outcomes associated with implementation of a computerized notification system for postliver transplant laboratory monitoring. After implementation of the system, we observed a significant decrease in the time to respond to toxicity episodes during the first 90 days posttransplant, a 32% decreased relative risk of the occurrence of toxicity episodes, and a 75% decreased relative risk of mortality and graft failure. These improvements are especially striking considering that the 1-year and 3-year relative risk of mortality and graft failure observed nationwide during about the same time period (2002-2006) decreased by less than 5%.[22] The 75% relative risk reduction we observed was approximately 15 times greater than the 5% reduction expected for a study using a historical control group during this time

period. During the study period, the composition of the transplant team and the written and computerized posttransplantation protocols did not change. While multiple unexplained factors may have improved postliver transplant mortality rates, the computerized notifications may have indirectly improved clinical outcomes by automating and facilitating earlier identification of patients at risk and supporting workflow even as the number of patients being managed increased by 68% (from 250 to 420 patients).

The computerized notification system was associated with a 32% reduction in the relative risk of toxicity episodes, which may lower the risk of subsequent renal failure or other side effects of drug toxicity such as mortality.[23] We also found, however, that tacrolimus levels across each category of time since transplantation were significantly lower for intervention patients, indicating that clinical practice may have changed during the study period by lowering the target range for intervention patients. While revised clinical practice likely impacted average tacrolimus concentration levels, computerized notifications may have also helped with early identification of rising tacrolimus concentration levels. Perhaps more important, however, is the significant reduction in time to respond to toxicity episodes during the first 90 days posttransplant. Both the average time to respond to a toxicity episode, as well as the variation in response time, decreased for patients in the intervention group. Typically, postliver transplant immunosuppression therapy begins at a high concentration level that is tapered over time;[23] therefore, the greatest risk of excessively high concentration levels occurs during the initial months following liver transplantation. This risk pattern was consistent with our observation of the decreasing incidence of toxicity episodes over time. Computerized

notifications may have decreased the time to respond to toxicity episodes, particularly during the initial weeks following liver transplantation when risk is highest, by automating and decreasing the time to notify transplant coordinators about new laboratory results with excessively high concentration levels.

The relationship between computerized notifications and overdue laboratory testing is unclear. Stratified analysis showed a nonsignificant decrease in the incidence of being overdue during the first six months, but a significant increase after six months posttransplant. The computerized notification system is unlikely to increase the incidence of missed due dates because overdue notifications were not generated until days or weeks after a missed due date (see Table 4.1). Other factors (eg, increased nursing workload while managing more patients) may have contributed to the increased incidence of missed due dates. Even so, after missing a due date, computerized notifications were associated with an improved response time to get tested. Computerized notifications likely enabled quicker identification and response to overdue laboratory testing.

This study has limitations. First, this study is assessing the impact of an intervention implemented 10 years ago. Nevertheless, the findings are relevant for understanding the impact of automated CDS and population management tools currently promoted in 'Meaningful Use' legislation.[11,24] In addition, the laboratory testing patterns observed in the study are similar to patterns observed through 2012 in another study published separately.[17] Second, the historical control design may create imbalances that impact results. In our study, patients in the intervention group had more severe liver disease prior to transplantation, thus we may in fact be underestimating the impact of the

notification system. Third, potential historical effects not controlled for in our study may confound our findings. We did not control for changes in surgical or clinical practice, donor factors, comorbidities not included in the analysis, or cause of death or graft loss. Therefore, while an association between the use of computerized notifications and changes in outcomes exists, we cannot assert that the notifications caused these changes. Fourth, we did not analyze the costs associated with entering external laboratory results as structured data into the EHR, and this is likely to vary widely among transplant centers. Fifth, we only analyzed patients who received tacrolimus immunosuppression therapy. However, over 90% of postliver transplant patients at IH were on tacrolimus immunosuppression therapy during the study period. Sixth, for the laboratory result based analysis, we were required to exclude patients who were tested outside IH during the control period because their results are not available in computable format. However, we believe the findings are generalizable because we found no significant differences in the demographic and clinical characteristics of the population among those included and excluded from the subset used for laboratory-based analyses. Finally, this study occurred at a midsized transplant center, and results may not be generalizable to all transplant centers. An experimental design may yield greater confidence in determining the relationship between computerized notifications and clinical outcomes, but implementing such a design is not practical.

Despite these limitations, the notification system and the study have strengths that should be considered. First, the computerized notifications were delivered to nurses, whereas most evaluations in the literature focus on CDS tools for physicians. Targeting nurses, rather than physicians, spawned from a thorough system analysis,[2,25,26] and likely

played a critical role in the impact, high usage, and acceptance of the notification system. Second, even though the number of active liver transplant patients during the study increased 68% from approximately 250 to 420, the same number of coordinators (three) spent the same amount of time monitoring laboratory results. The computerized notification system provides greater scalability for the processes of laboratory monitoring than the manual, paper-based approach used during the control period. Third, other healthcare domains use similar clinical processes to manage laboratory results and medications, such as diabetes care or anticoagulation therapy. We hypothesize that a similar CDS tool could improve clinical processes for other chronic care domains.

Transplant-specific computerized notifications delivered to nurse transplant coordinators are associated with improved care processes and clinical outcomes and provide greater scalability for laboratory monitoring workflow processes. The utility of computerized notifications may be further improved by incorporating additional factors (eg, comorbidities, history of rejection, other medications, etc.) important for optimizing postliver transplant care.

Table 4.1. Automated rules for generating notifications based on laboratory testing of immunosuppression, kidney function, and critical values

Rule	Time since liver transplantation (days)	Notify if…	Add additional message if…
New Tacrolimus	>0 and ≤30	New result received	Result is: • <15 (below target range), • ≥15 and ≤18 (within target range), or • >18 (above target range)
	>30 and ≤90		Result is: • <12 (below target range), • ≥12 and ≤15 (within target range), or • >15 (above target range)
	>90		Result is: • <12 (below target range), • ≥8 and ≤12 (within target range), or • >12 (above target range)
New Cyclosporine	n/a	New result received	
New Rapamune	n/a	New result received	
New Creatinine	n/a	New result received	Increase greater than 0.3 between two consecutive levels within the past two months
			Increase greater than 0.3 between three consecutive levels within the past two months
Overdue Immuno-suppressant/ Creatinine	>0 and <90	[a] 14 days since last result	
	≥90 and <180	[a] 21 days since last result	
	≥180 and <1460	[b] 45 days since last result	
	≥1460	[c] 120 days since last result	
Low Potassium	n/a	<3.5	
High Potassium	n/a	>5.9	
Low Magnesium	>0 and ≤30	<1.6	
	n/a	<1.2	

Table 4.1 Continued

[a] Notification of overdue testing is generated if no laboratory result is received 7 days after the due date. An overdue notification is repeated every 3 days after the initial notification until a new laboratory result is received.

[b] Notification of overdue testing is generated if no laboratory result is received 15 days after the due date. An overdue notification is repeated every 14 days after the initial notification until a new laboratory result is received

[c] Notification of overdue testing is generated if no laboratory result is received 30 days after the due date. An overdue notification is repeated every 14 days after the initial notification until a new laboratory result is received

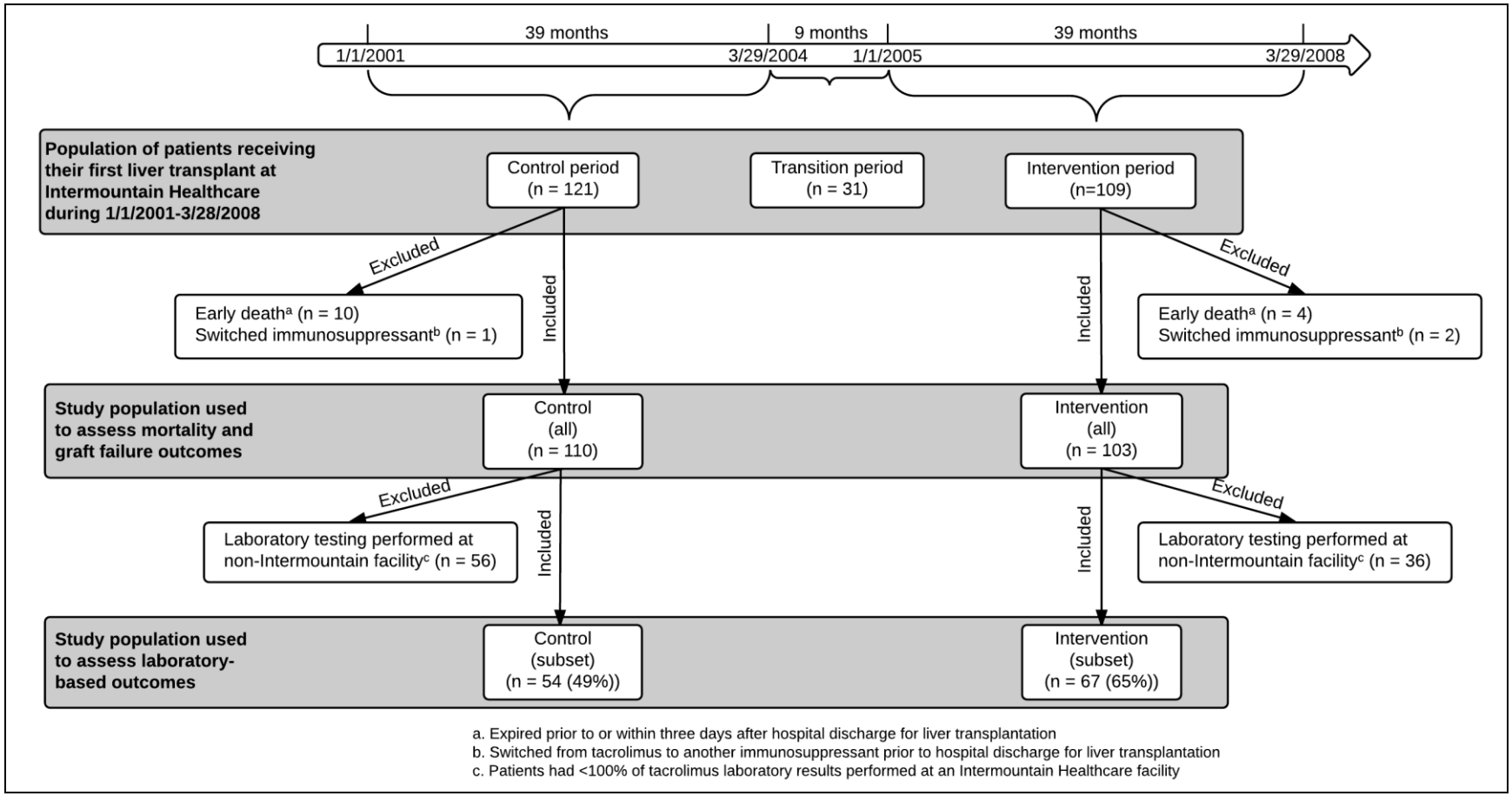

Figure 4.1. Patient eligibility flow diagram

Table 4.2. Description of the study population and the subset of patients selected for laboratory-based analyses for whom all tacrolimus testing was performed at an Intermountain facility

	All			**Subset for laboratory-based analyses**		
	Control (n=110)	Intervention (n=103)	p value	Control (n=54)	Intervention (n=67)	p value
Subpopulation that used an Intermountain laboratory for *all* tacrolimus testing	54 (49%)	67 (65%)	0.02	N/A	N/A	N/A
Male: %	61.8%	66.0%	0.53	66.7%	67.2%	0.95
Age in years at liver transplantation: mean (SD)	50.6 (9.8)	51.3 (12.6)	0.62	51.1 (9.2)	51.4 (12.8)	0.89
Model for End-stage Liver Disease [MELD] score immediately prior to transplantation: mean (SD) [b]	17.1 (7.5)	24.1 (8.8)	<0.01	17.5 (8.3)	23.4 (8.2)	<0.01
Patients with at least one positive Hepatitis C test result: %	30.0%	23.3%	0.27	27.8%	26.9%	0.91
Patients that underwent kidney transplant before or concurrently with liver transplantation: number (%)	0 (0%)	1 (1.0%)	0.49	0 (0%)	0 (0%)	>0.99
Days hospitalized for liver transplantation procedure: mean (SD)	21.0 (23.2)	19.1 (17.9)	0.50	18.3 (18.5)	17.7 (17.7)	0.87
Days hospitalized during first year after hospital discharge for liver transplantation: mean (SD)	7.0 (12.1)	8.7 (19.0)	0.43	5.9 (12.5)	8.1 (20.0)	0.46
Potential days of follow-up: mean (SD)	484 (332)	588 (345)	0.03	487 (312)	568 (328)	0.16
Patients who were censored during the follow-up period due to: number (%)						
• death	8 (7.3%)	3 (2.9%)	0.13	1 (1.9%)	2 (3.0%)	0.58

Table 4.2 Continued

	All			Subset for laboratory-based analyses		
	Control (n=110)	Intervention (n=103)	p value	Control (n=54)	Intervention (n=67)	p value
• liver re-transplantation	1 (0.9%)	1 (1.0%)	0.73	0 (0%)	1 (1.5%)	0.55
• other reason [c]	11 (10.0%)	6 (5.8%)	0.19	1 (1.9%)	2 (3.0%)	0.58
Laboratory tests per 100 days of follow-up: mean (SD)	N/A	N/A	N/A	15.5 (9.8)	14.4 (10.1)	0.53

[a] We imputed missing values of MELD scores for 25% of patients in the control group, as reporting was not required prior to February 2002. Imputation is reliable up to 50% missing.[27] Imputation was done using the truncated regression imputation method, restricting the range of imputed values for MELD to be in the range 1 to 40.[28]

[b] Other reasons include: change to another immunosuppressant, transfer to another transplant program, or lost to follow-up status.

N/A means Not applicable.

Table 4.3. Description of the computerized notifications delivered between January 1, 2005 and March 27, 2008 for patients in the intervention groups

	Intervention (all)		Intervention (subset)	
Number of patients	103		67	
Total number of notifications generated	17,045		10,297	
Number of notifications generated for:	# (%)		# (%)	
Overdue for immunosuppression testing	703 (4.1%)		179 (1.7%)	
Overdue for creatinine testing	609 (3.6%)		208 (2.0%)	
New creatinine results	7,888 (46%)		4,899 (48%)	
Increased by 0.3 since last result*		571 (7%)		325 (7%)
Increased by 0.3 between three results*		277 (4%)		170 (4%)
No significant increase*		7,040 (89%)		4,404 (90%)
New tacrolimus results	6,804 (40%)		4,329 (42%)	
Within target range*		1,613 (24%)		1,036 (24%)
Below target range*		4,161 (61%)		2,673 (62%)
Above target range*		1,030 (15%)		620 (14%)
New cyclosporin A	70 (0.4%)		48 (0.6%)	
New sirolimus	10 (<0.1%)		9 (<0.1%)	
Potassium (below target range)	281 (1.6%)		173 (1.7%)	
Potassium (above target range)	58 (0.3%)		24 (0.2%)	
Magnesium (below target range within 30 days posttransplant)	526 (3.1%)		355 (3.4%)	
Magnesium (below target range)	96 (0.6%)		63 (0.6%)	
Number of notifications “accepted” by a coordinator	16,432 (96%)		10,161 (99%)	

Table 4.3 Continued

	Intervention (all)		Intervention (subset)	
Number of notifications generated for:	# (%)		# (%)	
Number of notifications generated while patient was hospitalized (after discharge for the initial hospitalization for transplantation)	4,966 (29%)		2,888 (28%)	

* Message included concerning target range (based on time since transplantation)

Table 4.4. Description of metrics related to being overdue for tacrolimus testing, among the subset of patients that used an Intermountain laboratory for all tacrolimus testing

	Control	Intervention	p value
Number of patients	54	67	-
Incidence rate of being overdue for laboratory testing (per 1000 patient-days)			
Days posttransplant: >0 to <90 days	8.2	5.9	0.22
Days posttransplant: ≥90 to <180 days	7.9	7.4	0.79
Days posttransplant: ≥180 days to <4 years	7.0	9.4	<0.01
Average number of days between a missed due date and the next laboratory result – mean (SD)			
Days posttransplant: >0 to <90 days	4.1 (5.3)	4.3 (4.6)	0.94
Days posttransplant: ≥90 to <180 days	8.7 (9.1)	8.1 (6.8)	0.77
Days posttransplant: ≥180 days to <4 years	11.9 (10.6)	12.7 (15.0)	0.54
Average tacrolimus concentration (ng/mL) of next laboratory result after a missed due date – mean (SD)*			
Days posttransplant: >30 to ≤90 days (Target range: 12-15)	14.4 (3.8)	10.0 (6.1)	0.02
Days posttransplant: >90 days (Target range: 8-12)	9.7 (4.0)	7.4 (3.5)	<0.01

* Omitted results for time period ≤30 days posttransplant due to insufficient sample size

Table 4.5. Description of the occurrence and responsiveness to tacrolimus toxicity episodes, among the subset of patients that used an Intermountain laboratory for all tacrolimus testing

	Control	Intervention	p value
Number of patients	54	67	-
Number of tacrolimus results	2,816	3,890	-
Average tacrolimus concentration (ng/mL) for all laboratory results – mean (SD)			
Days posttransplant: >0 to ≤30 days (Target range: 15-18)	13.9 (5.1)	12.7 (5.3)	<0.01
Days posttransplant: >30 to ≤90 days (Target range: 12-15)	13.8 (5.3)	12.3 (5.3)	<0.01
Days posttransplant: >90 days (Target range: 8-12)	10.5 (4.4)	8.2 (3.9)	<0.01
Incidence rate of toxicity episodes (per 1000 patient-days)			
Days posttransplant: >0 to ≤30 days	37.9	24.2	0.11
Days posttransplant: >30 to ≤90 days	18.5	13.9	0.15
Days posttransplant: >90 days	1.7	1.0	0.02
Average number of hours between a tacrolimus laboratory result >20 ng/mL and the next laboratory result – mean (SD)			
Days posttransplant: >0 to ≤30 days	56.9 (25.5)	42.9 (13.9)	<0.01
Days posttransplant: >30 to ≤90 days	85.2 (62.6)	67.8 (36.8)	0.03
Days posttransplant: >90 days	200.5 (310.3)	136.8 (162.0)	0.21

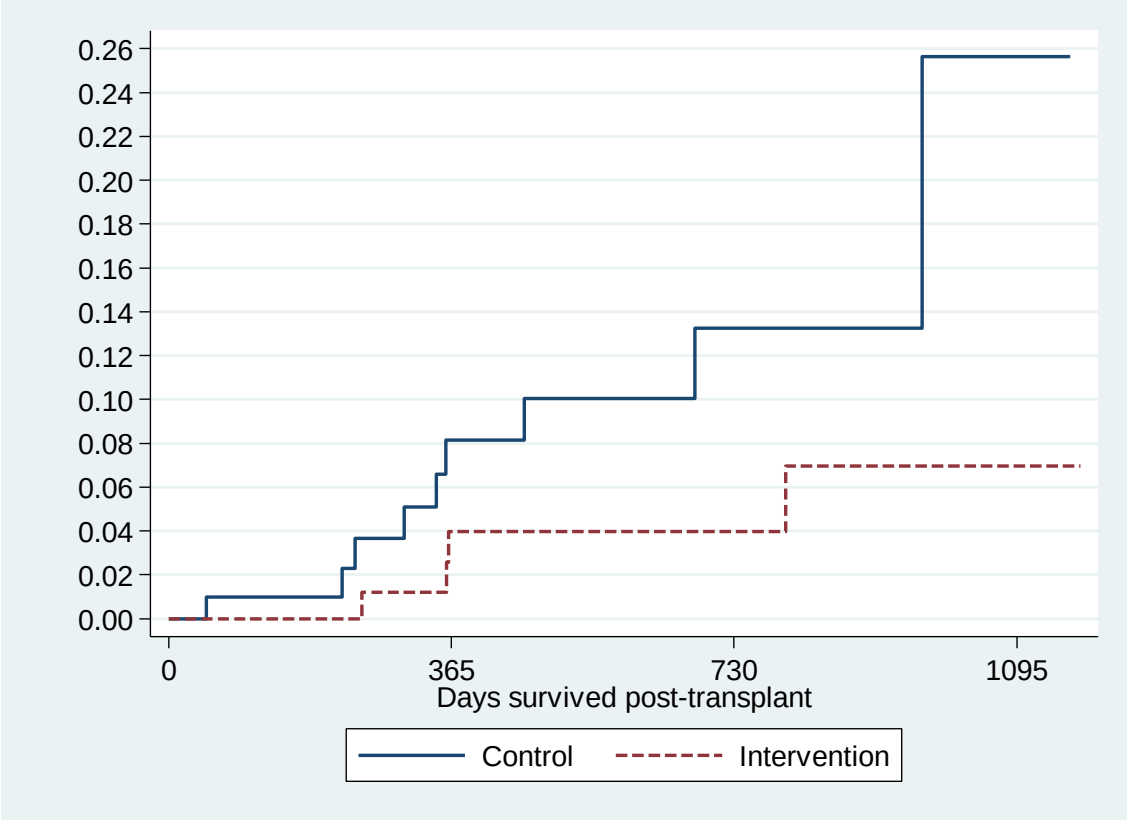

Figure 4.2. Cumulative risk of mortality or liver failure after liver transplantation using Kaplan-Meier failure estimates

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CHAPTER 5

THE EFFECT OF COMPUTERIZED NOTIFICATIONS ON WORKFLOW PROCESSES OF OUTPATIENT POSTTRANSPLANT LABORATORY MONITORING OF IMMUNOSUPPRESSIVE CARE

5.1 Background

While EHR use at liver transplant centers is nearly universal, paper-based processes continue to be used by all transplant centers to receive or track immunosuppression laboratory results.[1] These paper-based processes are not scalable and can lead to inefficiencies and deficiencies in information management.[2] In addition, paper records are prone to transcription errors, can only be located in one place at a time, and are not being amenable to computerized clinical decision support (CDS).[2] Regardless, nurse transplant coordinators are expected to carefully monitor a large and growing volume of laboratory testing results for their patient population.[3]

In 2001, Staes conducted a system analysis to assess the information system needs of the transplant center at Intermountain Healthcare (IH).[4] Information management issues were discovered, and researchers identified an opportunity to improve the laboratory monitoring processes for posttransplant immunosuppressive care. A computerized notification system was implemented in 2004 to address the identified

information management issues.[2] In particular, this system provided computerized notifications to automate the identification of immunosuppression or physiological function laboratory tests that were new, out-of-range, or overdue. Evaluation studies of computerized notifications for laboratory monitoring found an association with improvements in process measures as well as clinical outcomes of postliver transplant patients.[2,5] Also, there is evidence that a computerized notification system continues to be used long-term and that even a large volume of notifications is accepted by nurse transplant coordinators.[3] However, we found no studies describing the effect of computerized notifications on the workflow of transplant coordinators. In particular, it is unknown if the information management issues previously identified at IH are similar to those faced by coordinators at different transplant centers without a transplant-specific CDS system. Evaluating workflow processes may help to identify opportunities to better meet information management needs, potentially improving patient safety, quality, and cost of care.[6]

Transplant centers at University of Utah Health Care (UUHC) and IH are located in the same region of the United States and have performed a similar number of liver transplantations since 2010.[7] Nurse transplant coordinators at UUHC have used the Epic outpatient EHR to manage the ambulatory care of their patient population since 2012. Conversely, coordinators at IH used a proprietary EHR called HELP2 with an integrated computerized notification system designed specifically for the posttransplant laboratory monitoring workflow.[2] We sought to understand how workflow process measures of laboratory monitoring differed across similar transplant centers with different information system functionalities and whether similar opportunities for improvement exist at a

transplant center without transplant-specific CDS and population management tools.

5.2 Objectives

Our objectives were to: a) understand the workflow and data flow in transplant programs with and without transplant-specific laboratory monitoring CDS, b) measure the impact of transplant-specific CDS on laboratory monitoring process measures, particularly for those processes performed by the nurse transplant coordinators and those performed by their assistants, c) compare the satisfaction of transplant coordinators regarding their laboratory monitoring workflow, and d) evaluate usage of information provided in transplant-specific computerized notifications.

5.3 Methods

5.3.1 Study design, study population, and setting

We conducted prospective observational studies at two transplant centers: Intermountain Healthcare (IH) in Murray, UT, and University of Utah Health Care (UUHC) in Salt Lake City, UT. Both transplant centers serve the Intermountain West. From January 1, 2010 to December 31, 2014, the transplant centers at IH and UUHC performed 152 and 133 liver transplantations, respectively (Table 5.1). The study population included postliver transplant coordinators and assistants at both transplant centers. At IH, the immunosuppressive care for approximately 600 postliver transplant patients was monitored by three coordinators with the aid of one assistant; at UUHC, the immunosuppressive care for approximately 250 postliver transplant patients was monitored by two coordinators with the aid of four assistants (three of whom split time

between pre- and posttransplant patients) providing the equivalent of 2.5 full-time effort. The size of the patient populations varied because liver transplantation started earlier at IH (1986) than at UUHC (2006). At both transplant centers, assistants supported the work of coordinators by entering new laboratory results into the EHR or paper record, requesting reports from laboratory facilities, calling patients to request laboratory testing, and managing the schedule of patient visits to the outpatient clinic. The proportion of laboratory results received from an external laboratory facility was approximately twice as high at UUHC compared to IH (Table 5.1).

5.3.2 Computerized notifications

Prior to November 1, 2004, coordinators at IH identified new laboratory results by receiving a faxed laboratory report or by searching for them in the EHR or paper record of a patient. On November 1, 2004, IH researchers implemented a transplant-specific computerized notification system along with a data entry application to integrate external laboratory results into the EHR. Since then, computerized notifications for new, out-of-range, and overdue immunosuppression or physiological function laboratory tests have been delivered to an electronic inbox within the IH EHR (see example in Figure 5.1). Notifications were generated for patients who had been enrolled in an electronic registry. Coordinators were informed of all new laboratory results available in the EHR in one place without checking individual patient records. Conversely, coordinators at UUHC relied on a general EHR notification system to identify new laboratory results available from the UUHC laboratory. UUHC coordinators also identified new laboratory results by other methods, such as receiving a faxed laboratory report or searching for new results

in the EHR or paper record of a patient.

5.3.3 Development of workflow process diagrams

To understand the workflow processes of laboratory monitoring, coordinators from each transplant center were observed over a 1-week period during the Fall of 2015. The observations included short interviews during which coordinators were asked to explain what they were doing and their purpose for performing the task. A workflow process diagram was generated and iteratively refined by observation of and feedback from coordinators until no new processes related to laboratory monitoring were identified.

5.3.4 Data collection

To record process measures associated with receiving laboratory reports and entering laboratory data into the EHR or other information systems, we created a data collection form (Appendix A) that was used by transplant assistants. The form identified whether a laboratory report contained a laboratory result for immunosuppression or creatinine and whether each result had been previously seen. To ensure understanding of the data collection form and method, we modeled the steps and observed the assistants as they recorded data on the form using recently received laboratory reports. Finally, we asked each assistant to record a new entry on the data collection form each time a laboratory report was received from an external laboratory facility and entered into the EHR. Since patients at UUHC were more likely to get laboratory testing at an external laboratory, the UUHC assistant collected data for two weeks, and the IH assistant

collected data for a month.

Based on the workflow processes identified, we created another data collection form (Appendix A) to record the events that triggered coordinators to check for new laboratory results and whether new immunosuppression laboratory results were identified. We interviewed coordinators from each transplant center to determine days and times when tasks related to postliver transplant monitoring, evaluation, and reporting would be performed in the administrative office setting. We selected five consecutive workdays for observation at each transplant center (UUHC: October 7-13, 2015; IH: October 14-20, 2015), and coordinators confirmed that the workdays were expected to be representative of a normal week. We excluded observations when coordinators were attending hospital rounds, outpatient clinic visits, or other scheduled time during which laboratory monitoring was not the primary activity. Observations were performed in blocks, the size of each block in hours was equal to the number of coordinators (UUHC: two; IH: three), and we randomly assigned each coordinator to a single one-hour interval within each block. Before data collection, each coordinator was given a document indicating the data elements that would be collected during observations and was asked to communicate these data elements each time the coordinator was looking for new laboratory results. During observations, we explicitly asked coordinators for these data elements if not provided. After the five-day observation period, coordinators were asked to complete a questionnaire regarding their satisfaction with performing specific tasks associated with laboratory monitoring using their current information systems (Appendix B). For coordinators at IH, the questionnaire had an additional section about the frequency of usage of each data element in a notification message. This section included

a picture of a typical notification message, and each data element referenced in the questionnaire was uniquely identified with a number (Appendix B).

5.3.5 Outcomes

The outcomes concerning the workflow of transplant assistants were designed to measure inefficiencies related to receiving, reviewing, and entering external laboratory reports into the EHR or other information systems. The outcomes were:

1. the distribution of delivery methods of laboratory results,
2. the proportion of times that no new immunosuppression or creatinine laboratory results were identified in newly received external laboratory reports that contained immunosuppression or creatinine results, and
3. the time from specimen collection to data entry of external laboratory results into the EHR.

The outcomes concerning the workflow of transplant coordinators were designed to measure inefficiencies and satisfaction with monitoring laboratory results. The outcomes were:

1. the distribution of events triggering a search for new immunosuppression laboratory results,
2. the proportion of unsuccessful searches for new immunosuppression laboratory results,
3. the time from specimen collection to identification of new immunosuppression laboratory results,
4. the satisfaction with performing tasks supported by the information systems, and

5. the frequency of usage of each data element provided in computerized notifications.

5.3.6 Data analysis

We compared categorical variables using a Chi-square test (or Fisher's exact test when appropriate) and compared continuous variables using a Wilcoxon rank-sum test. Analyses were performed using Stata 14.1.[8] We defined the data entry response time as the time between specimen collection and the time the assistant manually entered the laboratory result into the EHR as recorded during observations. We defined the coordinator response time as the time between specimen collection and the time the coordinator acted on the laboratory result as recorded during observations. We compared coordinator response time using only new laboratory results from internal laboratory testing facilities to control for differences in the proportion of laboratory testing done at external laboratories and differences in laboratory processing and reporting time.

Using the questionnaire, we measured satisfaction of performing tasks using a 7-point Likert scale and reported the proportion of responses that were a 6 or 7 ("Mostly satisfied" or "Very satisfied," respectively) as well as the range of responses. The labels for the other options were: "Slightly satisfied," "Neither satisfied nor dissatisfied," "Slightly dissatisfied," "Mostly dissatisfied," and "Very dissatisfied." We summarized suggestions for improving tasks for laboratory monitoring. We also measured the frequency of usage of each data element in a notification message using a 5-point Likert scale with the labels "Rarely or never," "Infrequently," "Sometimes," "Often," or "Almost always or always." Table 5.2 provides a list of each data element and a short

description. We summarized these responses and identified data elements within the notification message that received the highest or lowest usage by all coordinators.

5.3.7 Ethical review

Institutional Review Boards from IH and the University of Utah approved this study.

5.4 Results

5.4.1 Description of laboratory monitoring workflow processes

The laboratory monitoring workflow process follows a similar pattern at both transplant centers (Figure 5.2). We identified seven general steps:

1. A patient has blood drawn.
2. The laboratory facility receives the blood sample, processes the laboratory test, and creates a laboratory report based on the test results.
3. The laboratory sends the report to the transplant center.
4. The laboratory report is received by the transplant center.
5. The laboratory report is integrated into the EHR and/or a paper flow sheet.
    a. Reports from an external laboratory are:
        i. Automatically integrated into the EHR (if an electronic interface has been established with the laboratory); otherwise, manually entered into the EHR.
        ii. Manually transcribed to a paper flow sheet, or an updated paper flow sheet is printed from an electronic flow sheet.

b. Reports from an internal laboratory are:
    i. Automatically integrated into the EHR.
    ii. Manually transcribed to a paper flow sheet or an updated paper flow sheet is printed from an electronic paper flow sheet.
6. A transplant coordinator reviews the flow sheet and identifies a new or overdue laboratory testing result.
7. A transplant coordinator takes appropriate action.

For a more detailed process diagram and a step-by-step narrative specific to each transplant center, see Figure 5.3 (UUHC) or Figure 5.4 (IH). We identified seven major differences in the laboratory monitoring workflow at the two transplant centers (Table 5.3).

5.4.2 Process measures about entry of external laboratory data by transplant assistants

Among newly received external laboratory reports that were being processed for data entry by a transplant assistant, the proportion of laboratory reports that resulted in identification of no new laboratory results was significantly lower at IH (Table 5.4). At IH, duplicate immunosuppression drug levels were only reported for 4.3% of the results compared with 23% of the results at UUHC ($p<0.01$) (Table 5.4). Conversely, for newly received external laboratory reports that were being processed for data entry by a transplant assistant, the response time from specimen collection to data entry in the EHR was significantly lower at UUHC than at IH ($p<0.01$) (Table 5.4). At IH, the median response time to new immunosuppression results was 123 hours compared with 48 hours

at UUHC ($p<0.01$). Similar patterns of duplicate reports and response times were found for laboratory reports with creatinine laboratory results (Table 5.4).

5.4.3 Process measures about checking for new laboratory results by transplant coordinators

From October 7, 2015 to October 20, 2015, we collected 301 searches by coordinators for new laboratory results (UUHC: 138; IH: 163) (Table 5.5). Of these, 168 (56%) were searches for new immunosuppression laboratory results (UUHC: 57; IH: 111). Each coordinator at UUHC checked for new laboratory results an average of 14 times per day while each coordinator at IH checked an average of 11 times per day.

For coordinators at UUHC, the most common triggers for checking for new laboratory results were receiving a computerized notification for any new laboratory result (59%), remembering to check laboratory testing for a specific patient (15%), and being reminded by seeing a paper chart that was previously set aside (9%) (Table 5.5). Conversely, for coordinators at IH, the most common triggers were receiving a computerized notification for an immunosuppression or a physiological function laboratory test (48%), receiving a paper chart delivered by a transplant assistant (33%), and being reminded by seeing a paper chart that was previously set aside (9%) (Table 5.5). Of note, when an assistant at IH delivered a paper chart to a coordinator, the assistant was usually notified by checking for computerized notifications for new laboratory results which were then transcribed to the paper flow sheet. The notifications were delivered to an electronic inbox that was accessible to the coordinators and the assistant. Thus, computerized notifications at IH directly or indirectly triggered checking

for new laboratory results 81% of the time.

5.4.4 Impact of computerized notifications on unsuccessful searches for new immunosuppression laboratory results

Overall, there was no significant difference between UUHC and IH in the proportion of unsuccessful searches by coordinators for new immunosuppression laboratory results (n (%): UUHC: 56 (16%); IH: 111 (14%); p=0.66) (Table 5.5). When stratified by trigger, there were also no significant differences in the proportions of unsuccessful searches (Table 5.5).

5.4.5 Impact of computerized notifications on response time to new immunosuppression laboratory results received

We found differences in response times of coordinators to new immunosuppression laboratory results performed at an internal laboratory facility. Most (n=121, 72%) of the immunosuppression results we evaluated were for tacrolimus blood concentration levels. Coordinators at IH had a significantly shorter response time to new tacrolimus results than was observed at UUHC (median (IQR) [n]: UUHC: 23 (22-25) hours [11]; IH: 9 (6-26) hours [63]; p=0.049) (Table 5.5). There was no significant difference in the response time to new cyclosporine results between the two sites.

Everolimus is an immunosuppressant that had not yet been included into the logic for the notification system at IH. We found that coordinators at UUHC had a significantly shorter response time to new everolimus results (median (IQR) [n]: UUHC: 25 (24-25) hours [2]; IH: 48 (31-249) hours [14]; p=0.04) (Table 5.5).

5.4.6 Satisfaction with laboratory monitoring using current information systems

Transplant coordinators at IH expressed greater satisfaction with the support they received performing posttransplant laboratory monitoring tasks with their current information systems (Table 5.6). Among eight key tasks performed using the current information systems, the two coordinators at UUHC were less than "Mostly satisfied" or "Very satisfied" with each of the tasks with the exception of one coordinator who reported being "Mostly satisfied" with identifying patterns of laboratory results over time (Table 5.6). In contrast, one or more of the three coordinators at IH were "Mostly satisfied" or "Very satisfied" with six of the eight key tasks (Table 5.6). When asked how they would improve the task of identifying patients with new laboratory testing results, coordinators at both sites indicated that there was a lag between when a new laboratory result is available and when a notification is received by the coordinator that could be minimized or eliminated. In addition, a coordinator at IH expressed a desire to receive notifications for other laboratory tests, a functionality that was already part of the information system at UUHC. Finally, when asked how they would improve the task of identifying patients who were overdue for laboratory testing, UUHC coordinators expressed an interest in receiving a notification as well as sending notifications that informed patients (eg, via a patient portal) regarding upcoming or missed laboratory testing due dates. Coordinators at IH asked for the ability to adjust the computerized logic regarding the expected testing frequency.

5.4.7 Usage of data elements in IH computerized notification messages

The coordinators at IH were queried about their usage of data elements included in the transplant-specific computerized notifications (see Appendix B). The laboratory test date/time, name, and value, and the hospitalization status were used most frequently (Table 5.7). The least frequently used data elements included the patient contact information, the value of the laboratory results relative to the target range (above/within/below), the target range, and the alert status. When we inquired about low usage of data elements concerning target ranges, the coordinators reported that the target ranges had changed over time and that the protocol they use no longer matched the target ranges encoded in the logic of the computerized notifications.

We found that among the information provided in the computerized notifications, each data element was used at least "Sometimes" by one or more of the three coordinators (Table 5.7). We expect that different coordinators used data elements provided in notifications to satisfy different workflows or information needs.

5.5 Discussion

Our study describes the laboratory data flow processes of two midsized transplant centers and compares the processes of posttransplant immunosuppressive care and their association with a transplant-specific computerized notification system. We also assessed satisfaction using performance of specific tasks identified in the workflow analysis as the metric. This allowed us to better ensure task-technology fit and to identify areas of improvement with greater validity.[10] While both transplant centers have

performed similar numbers of liver transplantation procedures in recent years, these procedures have been actively performed for twenty years longer at the IH transplant center and therefore the coordinators at IH collectively managed twice as many patients as the coordinators at UUHC. Transplant-specific computerized notifications were associated with a different response time by coordinators to new tacrolimus laboratory results – the main immunosuppressant used – and a higher satisfaction of performing tasks related to posttransplant laboratory monitoring.

Transplant team members at UUHC were significantly more likely to review duplicate laboratory results from an external laboratory facility. At IH, laboratory reports were reviewed first by an assistant and duplicates were discarded, so duplicate reports were never reviewed by transplant coordinators. Conversely, UUHC coordinators were given each external laboratory report to review for urgency before reports were given to an assistant. This may hasten response times to laboratory results indicating an urgent need, but it also means that the coordinators must review every result, including those that would be identified as a duplicate report by the assistant and discarded. Regarding the time from specimen collection to data entry for external laboratory results, both new immunosuppression results and creatinine results were ready to be viewed in the EHR sooner at UUHC. These times are likely impacted by multiple factors, such as the responsiveness of external laboratory facilities and how well the data entry capacity of the transplant center meets the demand of laboratory testing. Integration of external laboratory results into the EHR may be significantly improved by implementation of an electronic interface with external laboratory facilities, however this may be neither logistically or economically feasible.[1]

Of the triggers that coordinators used to search for new immunosuppression laboratory results, there was no significant difference between the transplant centers regarding the proportion of unsuccessful searches for new immunosuppression laboratory results. This finding may be related to the fact that when a patient has blood drawn for posttransplant laboratory monitoring, both immunosuppression and physiological function tests are usually included in the same order. However, immunosuppression laboratory results are often received a few hours or more after creatinine and other physiological function laboratory results arrive. Thus, the arrival of creatinine laboratory results informs transplant coordinators that new immunosuppression results are expected within a few hours. In addition, transplant coordinators usually know the times of day that immunosuppression laboratory results are processed and sent by a laboratory facility to the transplant center. Therefore, predicting the arrival of new immunosuppression laboratory results may be easier and less likely to benefit from a transplant-specific computerized notification system. In contrast, a transplant-specific computerized notification system may have a lower proportion of unsuccessful searches when physiological function test results are received, although this was not measured. Regardless, coordinators should be accessing information that adds value to their workflow. If the available information has already been seen, then effort is wasted by coordinators searching for new information.

While coordinators at IH responded more quickly to new tacrolimus laboratory results, coordinators at UUHC were quicker to respond to new everolimus laboratory results. There are two factors to consider regarding these differences. First, while tacrolimus is the primary immunosuppressant used for most patients, everolimus is

becoming more popular as a primary or a secondary immunosuppressant at transplant centers. Second, IH coordinators rely on the list of computerized notifications to identify new immunosuppression laboratory results; thus, other laboratory results not received as a computerized notification may be missed or have a lower priority and searching for these laboratory results may be less frequent. This was validated during observations: each time a patient had a pending everolimus laboratory result, coordinators at IH placed the patient's chart in a marked bin, and multiple days passed before coordinators reviewed some of these charts and looked for everolimus results in the EHR. The response time to new everolimus laboratory results would likely be improved by generating computerized notifications for this laboratory test similar to the notifications generated for tacrolimus. It is important to note that we did not analyze differences in lab turn-around times at internal laboratory facilities, and we assumed that differences were related to workflow after new laboratory results were received by the transplant center.

Differences in laboratory data flow processes may have impacted process measures of the study. At both transplant centers, new results from an internal laboratory facility were automatically integrated into the EHR and the transplant-specific information system. The UUHC coordinators often had to manually check a list of laboratory results to identify new results. On the other hand, IH coordinators received computerized notifications for all patients to inform them of newly available laboratory results. We discovered a potential drawback of the workflow at IH: if a coordinator acted on a notification for a new laboratory result but did not have access to the paper flow sheet, there was a risk that the transplant assistant would view the computerized notification at a later time, transcribe the new result to the paper flow sheet, and bring the

patient chart to the transplant coordinator. This resulted in the coordinator reviewing the patient chart even though the newly transcribed laboratory result had already been seen by the coordinator. Another significant finding was the difference in the distribution of triggers used to determine when to check for new or overdue laboratory results. While computerized notifications could be generated regarding any laboratory result for any patient for UUHC coordinators, in practice, this was uncommon. In addition, these coordinators relied on several different triggers to identify new laboratory results. Conversely, coordinators at IH relied on two triggers to identify most laboratory results, and these triggers relied directly or indirectly on computerized notifications. While the proportion of unsuccessful searches for new immunosuppression laboratory results was not significantly different, relying on several different triggers may decrease response time. In addition, some triggers require more effort to update, such as an Excel spreadsheet or a whiteboard, and are prone to transcription errors.

Coordinators who relied on transplant-specific notifications of new, out-of-range, or overdue laboratory testing were associated with greater satisfaction with the support of their information systems, and this may be logical based on the differences of the two information systems and workflow processes we identified in this study. However, we identified opportunities to improve the laboratory monitoring process at both transplant centers. First, notifications systems should be flexible enough to support the evolving needs of clinical practice, such as changing laboratory testing schedules, shifting target ranges, or inclusion of new immunosuppressants or laboratory tests without requiring significant involvement of information technology (IT) staff. Second, developers and implementers should seek to minimize the delay between when a new laboratory result is

available in the EHR and when a notification is generated. Third, notifications should be sent to patients regarding *upcoming* laboratory testing due dates, not just after the laboratory testing due date has been missed.

Our analysis also identified the usage of specific data elements provided in transplant-specific computerized notifications at IH. We found that coordinators exhibited different patterns with using specific data elements. Therefore, when gathering requirements to design a new system, we recommend that feedback be sought from all transplant team members, not just one coordinator or the manager of a transplant center. This strategy will ensure that data elements included in transplant-specific computerized notifications will meet the distinct information management needs of coordinators. Furthermore, we suggest that implementers periodically analyze the usage of data elements provided in notification messages. This assessment may facilitate the identification of mismatches between the information needs of transplant coordinators and the information provided in notification messages. In particular, we suggest that for data elements that are infrequently used, implementers seek feedback from coordinators regarding how the information may be improved, whether data elements may be added to or removed from the notification messages, and whether the logic of the notification system remains accurate.

This study has limitations. First and foremost, we did not assess the completeness of reporting about new laboratory results that *should have been* reported to the transplant coordinators. Our assessment focused on workflow concerning results that were reported or identified, but we do not know the impact of the transplant-specific notification system on laboratory results that should have been identified but were not. This assessment

would require further analysis of tests that were performed. Additional limitations were identified. For example, second, we analyzed the workflow processes and information systems at two midsized transplant centers, and these may not be similar to those used by other transplant centers. Third, we performed our observational study of the coordinators at each transplant center for only one week. Additional observations may have greater statistical power to identify differences in process measures and outcomes, especially for less common processes or laboratory tests. Fourth, we analyzed the usage of data elements by transplant coordinators provided in computerized notifications at one transplant center with three coordinators, and the patterns of usage may not be generalizable. However, this notification system has been in use for over ten years, has a high response rate by coordinators,[3] and other transplant centers are beginning to implement population management tools that provide similar data elements. Thus, this analysis can be used to inform the information management needs of coordinators at other transplant centers.

5.6 Conclusion

We have outlined critical differences in the laboratory monitoring workflow at transplant centers with and without access to transplant-specific computerized notifications. These computerized notifications are associated with a faster response time of identifying new tacrolimus laboratory results by transplant coordinators. Coordinators with access to a transplant-specific notification system were each managing nearly twice as many patients, yet we identified a high level of satisfaction with use of a transplant-specific notification system compared to those using general EHR functionality. We

identified opportunities to improve how computerized notification systems may facilitate the laboratory monitoring processes for nurse transplant coordinators.

Table 5.1. Description of transplant centers, as of November 2015

	University of Utah Health Care	Intermountain Healthcare
Year of first liver transplantation	2006	1986
Number of liver transplantations performed between January 1, 2010 and December 31, 2014	133	152
Number of actively managed postliver transplant patients	~250	~600
Number of nurse transplant coordinators (full time equivalents)	2	3
Number of transplant assistants (full time equivalents)	2.5	1
Proportion of laboratory results received from an external laboratory facility	~70%	~30%

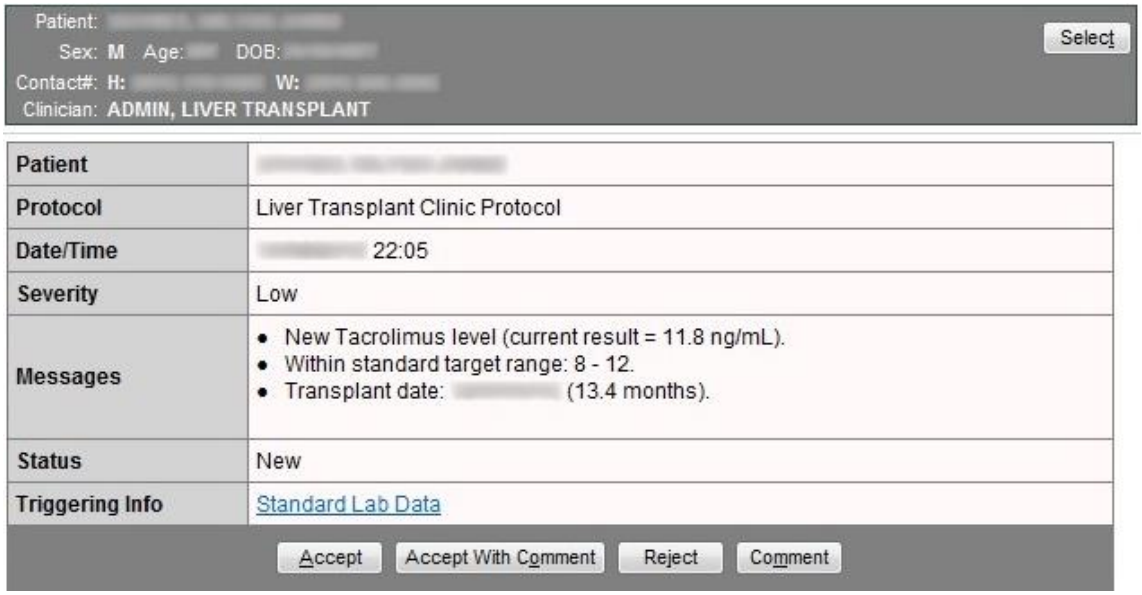

Figure 5.1. Example of a notification message triggered by a new laboratory result for nurse transplant coordinators at Intermountain Healthcare

Table 5.2. Data elements included in computerized notifications provided to nurse transplant coordinators at Intermountain Healthcare

Data Element	Description
Demographics	Sex, age, and date of birth
Contact information	Home and work phone numbers
Link to the patient record	Opens the patient record in the EHR
Date/time of laboratory test	Date and time of the specimen collection for the laboratory test
Severity	Indicator to help prioritize notifications. Levels of severity are assigned to notification messages using one of the phrases: • "requires action" • "low" • "medium" • "high"
Laboratory test	The name of the laboratory test performed
Laboratory value	The value of the laboratory result
Laboratory value relative to target range	Value of the laboratory result compared to the target range for the time since transplantation using one of the phrases: • "below target range" • "within target range" • "above target range"
Target range	The range of tacrolimus concentration levels defined in the clinical protocols used by the transplant team. The ranges change based on time since transplantation.
Transplant date	Date of most recent liver transplantation
Time since transplantation	Number of days, months, or years since the most recent date of liver transplantation
Hospitalization status	Indicator of whether the patient is currently hospitalized at an internal facility
Alert status	An indicator of whether the notification was new or revised
Triggering information	Provides a link to the EHR data that triggered the notification (eg, the laboratory data)
Accept or Reject button	Allows the coordinator to indicate that they accept the notification and document the actions taken or reject the notification and document the reason
Comment button	Allows the coordinator to comment on the information presented in the notification message

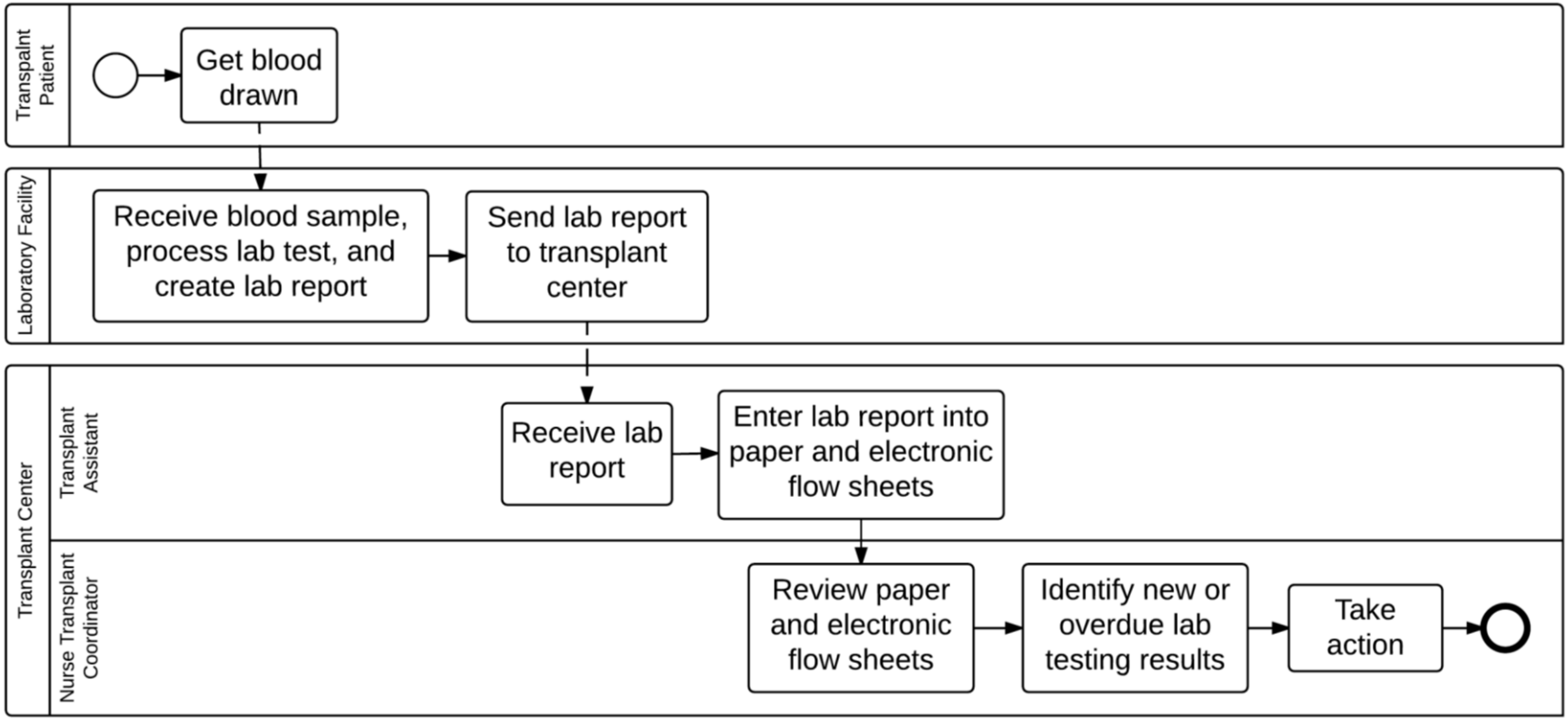

Figure 5.2. High-level workflow process for laboratory monitoring at a transplant center

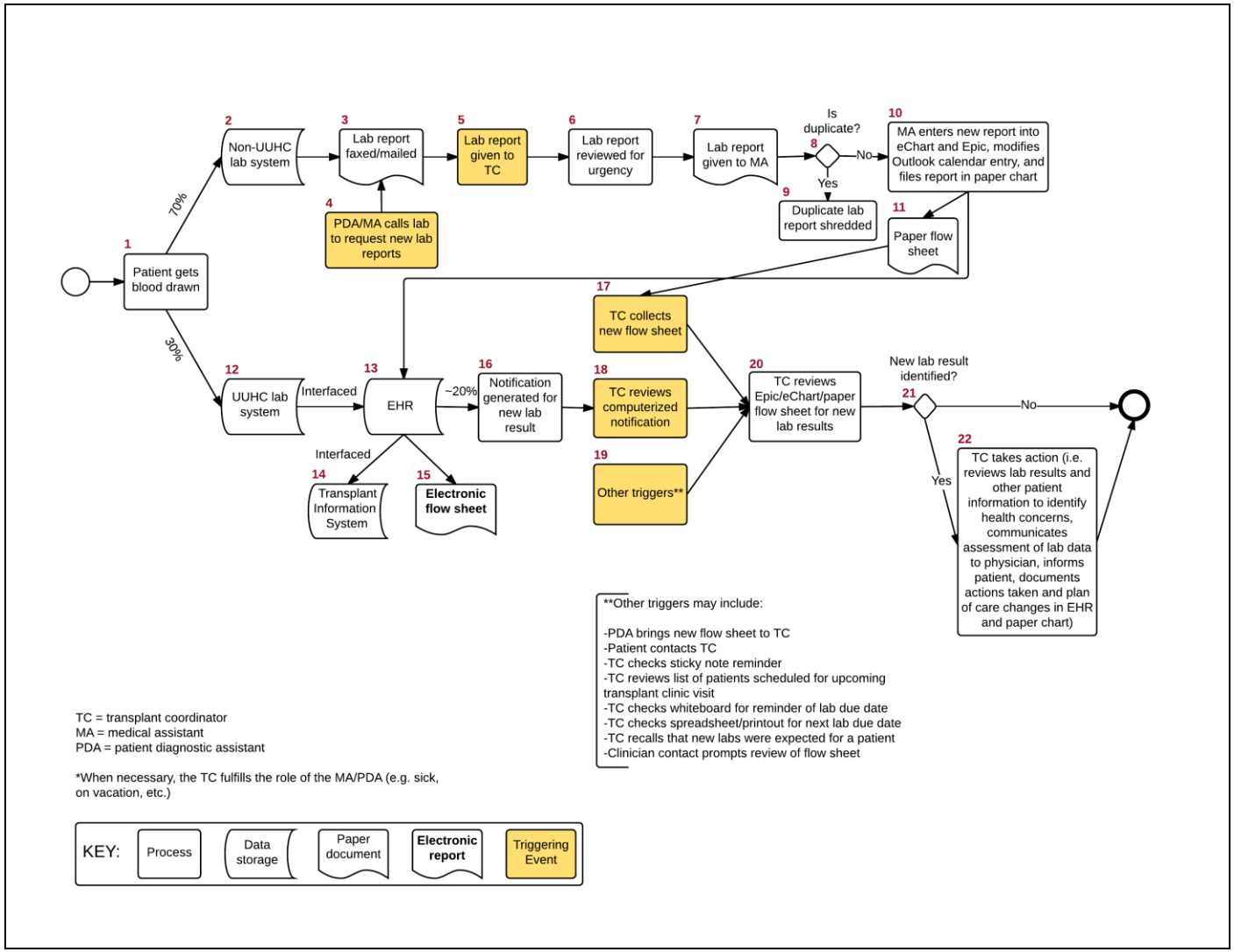

Figure 5.3. Process of laboratory monitoring at University of Utah Health Care Transplant Center

Step-by-step narrative

1.	Actor:	Patient	Action:	Draw blood sample

A posttransplant patient gets their blood drawn.

2.	Actor:	Non-UUHC laboratory facility	Action:	Receive blood sample, process laboratory test, and create laboratory report

The blood sample is received by an external (non-UUHC) laboratory facility, the laboratory test is processed, and a laboratory report is created and stored in the laboratory information system of the external laboratory facility.

3.	Actor:	Non-UUHC laboratory facility	Action:	Fax/mail laboratory report

The laboratory report is sent to the ordering clinician at the UUHC Transplant Center via fax, mail, or other method.

4.	Actor:	PDA/MA	Action:	Call non-UUHC laboratory facility to request laboratory report

If an expected laboratory report was not received by the transplant center, the patient diagnostic assistant (PDA) or medical assistant (MA) calls the external laboratory facility to request that the laboratory report be sent to the transplant center.

5.	Actor:	TC/PDA/MA	Action:	Give laboratory report to TC

Newly received laboratory reports are given to or collected by the transplant coordinator (TC).

6.	Actor:	TC	Action:	Review laboratory report for urgency

The TC reviews the laboratory report for any laboratory results that indicate an urgent healthcare situation and takes action, if necessary.

7.	Actor:	TC	Action:	Give laboratory report to MA

The TC gives the laboratory report to the MA for data entry.

Figure 5.3 Continued

8.	Actor:	MA	Action:	Determine if laboratory report was previously seen

The MA determines if the laboratory report is a duplicate laboratory report that has already been received.

9.	Actor:	MA	Action:	Shred duplicate laboratory report

If the laboratory report is a duplicate, it is shredded.

10.	Actor:	MA	Action:	Enter new report into Epic and file report in paper chart

If the laboratory report is a not a duplicate, the MA manually enters the laboratory results into the Epic EHR, scans the laboratory report and attaches the scanned file to the patient chart, then files the laboratory report in the paper chart.

11.	Actor:	MA	Action:	Print new paper flow sheet

The MA prints a new paper flow sheet and places it in a bin to be collected by the TC.

12.	Actor:	UUHC laboratory facility	Action:	Receive blood sample, process laboratory test, and create laboratory report

The blood sample is received by an internal (UUHC) laboratory facility, the laboratory test is processed, and a laboratory report is created and stored in the laboratory information system of the internal laboratory facility.

13.	Actor:	Laboratory information system	Action:	Integrate laboratory results into Epic EHR

The laboratory results are automatically entered into the Epic EHR.

14.	Actor:	Epic EHR	Action:	Integrate laboratory results into eChart

The laboratory results are automatically entered into the patient record in eChart.

15.	Actor:	Epic EHR	Action:	Make laboratory results available in electronic flow sheet

The laboratory results are available to the TC in the electronic flow sheet.

Figure 5.3 Continued

16. Actor: Epic EHR Action: Generate computerized notification

If the TC ordered the laboratory tests in the EHR, a notification is generated and available to the TC in a list; otherwise, this notification is only available if it is forwarded by the ordering clinician to the TC.

17. Actor: TC Action: Collect new paper flow sheet

The TC collects the new paper flow sheet from the bin.

18. Actor: TC Action: Review computerized notifications

The TC reviews the list of computerized notifications for new laboratory results.

19. Actor: TC Action: Trigger to look for new laboratory results

The TC is triggered by other events to look for new laboratory results.

20. Actor: TC Action: Review Epic/eChart/paper flow sheet for new lab results

A trigger causes the TC to review the Epic EHR/eChart/paper flow sheet to look for new laboratory results.

21. Actor: TC Action: Determine if new laboratory result is available

The TC determines if a new laboratory result is available.

22. Actor: TC Action: Take action to resolve any health concerns

If a new laboratory result is available, the TC takes action to resolve any health concerns (eg, reviews laboratory results and other patient information to identify health concerns, communicates assessment of laboratory data to physician, informs patient, documents actions taken and plan of care changes in EHR and paper chart).

Figure 5.3 Continued

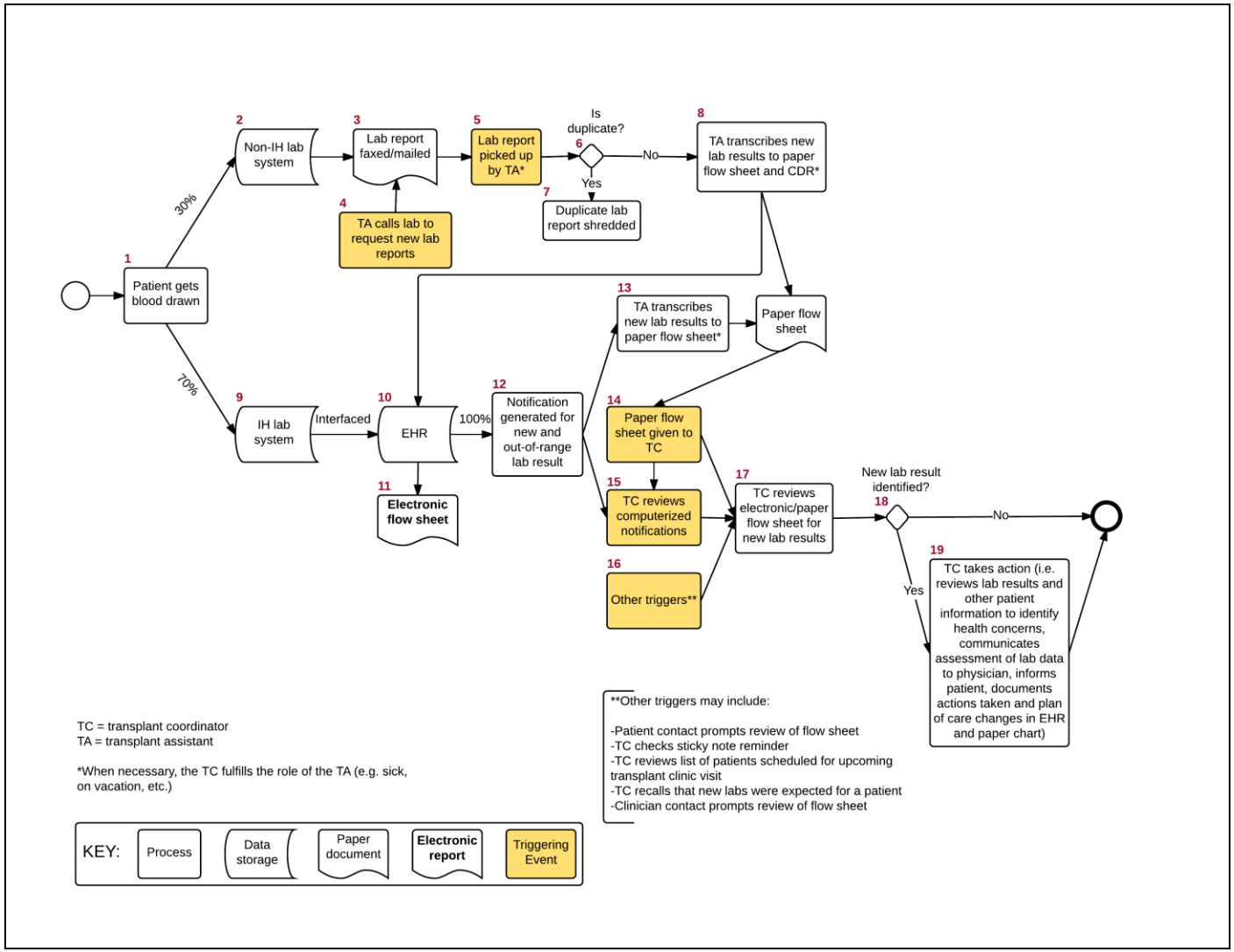

Figure 5.4. Process of laboratory monitoring at Intermountain Healthcare Transplant Center

Step-by-step narrative

1.	Actor:	Patient	Action	Draw blood sample

A posttransplant patient gets their blood drawn.

2.	Actor:	Non-IH laboratory facility	Action:	Receive blood sample, process laboratory test, and create laboratory report

The blood sample is received by an external (non-IH) laboratory facility, the laboratory test is processed, and a laboratory report is created and stored in the laboratory information system of the external laboratory facility.

3.	Actor:	Non-IH laboratory facility	Action:	Fax/mail laboratory report

The laboratory report is sent to the ordering clinician at the IH transplant center via fax, mail, or other method.

4.	Actor:	TA	Action:	Call non-IH laboratory facility to request laboratory reports

If an expected laboratory report was not received by the transplant center, the transplant assistant (TA) calls the external laboratory facility to request that the laboratory report be sent to the transplant center.

5.	Actor:	TA	Action:	Collect laboratory report

Newly received laboratory reports are given to or collected by the transplant coordinator (TC).

6.	Actor:	TA	Action:	Determine if laboratory report was previously seen

The TA determines if the laboratory report is a duplicate laboratory report that has already been received.

7.	Actor:	TA	Action:	Shred duplicate laboratory report

If the laboratory report is a duplicate, it is shredded.

Figure 5.4 Continued

8.	Actor:	TA	Action:	Enter new results onto paper flow sheet and into CDR, and file laboratory report into the patient chart

The TA transcribes the laboratory results onto the paper flow sheet, files the laboratory report in the paper chart, then manually enters the laboratory results into the CDR

9.	Actor:	IH laboratory facility	Action:	Receive blood sample, process laboratory test, and create laboratory report

The blood sample is received by an internal (IH) laboratory facility, the laboratory test is processed, and a laboratory report is created and stored in the laboratory information system of the internal laboratory facility.

10.	Actor:	Laboratory information system	Action:	Integrate laboratory results into EHR

The laboratory results are automatically entered into the EHR.

11.	Actor:	EHR	Action:	Make laboratory results available in electronic flow sheet

The laboratory results are available to the TC in the electronic flow sheet.

12.	Actor:	EHR	Action:	Generate computerized notification

If a new laboratory report includes a result for certain immunosuppression or physiological function laboratory tests, a notification is generated and is available to the TC in a single list.

13.	Actor:	TA	Action:	Transcribe laboratory results onto paper flow sheet

The TA reviews the list of notifications and transcribes the laboratory result to the paper flow sheet.

14.	Actor:	TA	Action:	Deliver new paper flow sheet to TC

The paper flow sheet is delivered to the TC at set times each day.

15.	Actor:	TC	Action:	Review computerized notifications

The TC reviews the list of computerized notifications for new laboratory results.

Figure 5.4 Continued

16.	Actor:	TC	Action:	Trigger to look for new laboratory results

The TC is triggered by other events to look for new laboratory results.

17.	Actor:	TC	Action:	Review electronic/paper flow sheet for new lab results

A trigger causes the TC to review the EHR/ paper flow sheet to look for new laboratory results.

18.	Actor:	TC	Action:	Determine if new laboratory result is available

The TC determines if a new laboratory result is available.

19.	Actor:	TC	Action:	Take action to resolve any health concerns

If a new laboratory result is available, the TC takes action to resolve any health concerns (eg, reviews laboratory results and other patient information to identify health concerns, communicates assessment of laboratory data to physician, informs patient, documents actions taken and plan of care changes in EHR and paper chart).

Figure 5.4 Continued

Table 5.3. Differences in laboratory monitoring workflow between transplant centers

Occurrence in Workflow Process	University of Utah Health Care	Intermountain Healthcare
1. Actions before data entry of external laboratory results	Coordinator checks results to assess urgency of needed actions	
2. Data entry of external laboratory results – additional steps after assistant manually enters external laboratory results into EHR	Assistant manually enters external laboratory results into transplant-specific information system	
	Assistant prints a new paper flow sheet and sets it in bin for coordinator	Assistant transcribes results to paper flow sheet and sets it in bin for coordinator
3. Actions after receiving new internal laboratory results	Coordinator prints new paper flow sheet printed	Coordinator or assistant transcribes new laboratory results to paper flow sheet
4. Laboratory results that generated computerized notifications	All laboratory results	All tacrolimus and sirolimus immunosuppression and creatinine results and selected physiological function results
5. Patients for whom computerized notifications were generated and sent directly to the coordinator	Patients for whom the coordinator ordered the laboratory test in the EHR	Any patient enrolled in the transplant management protocol (ie, the patient record number was added to the patient list)
6. Triggers for determining when to check for new or overdue laboratory results	Coordinator remembered to pick up new paper flow sheets printed by the assistant	Assistant delivered the patient chart to the coordinator
	Coordinator checked a manually updated Excel spreadsheet to track laboratory testing due dates for each patient	
	Coordinator maintained a whiteboard to track laboratory testing frequencies of certain patients	
7. Person who can view computerized notifications	The clinician who ordered the laboratory test	Any transplant coordinator or assistant

Table 5.4. Workflow and process measures associated with entry of external laboratory results by transplant assistants

	UUHC*	IH	p value
Number of assistants performing data entry	1	1	
Number of weeks observed	2	4	
Total number of laboratory reports reviewed	170	91	
• Number of laboratory reports reviewed with an immunosuppression result	92	46	
• Number of laboratory reports reviewed with a creatinine result	111	76	
Method of delivery of immunosuppression laboratory results – n (%)			
• Fax	92 (100%)	41 (89%)	<0.01
• Mail	-	5 (11%)	<0.01
Method of delivery of creatinine laboratory results – n (%)			
• Fax	111 (100%)	70 (92%)	<0.01
• Mail	-	6 (8%)	<0.01
Proportion of newly received external laboratory reports with immunosuppression and creatinine results that, in fact, contained no new immunosuppression or creatinine laboratory results: - n (%)			
• Immunosuppression	22 (24%)	2 (4%)	<0.01
• Creatinine	37 (33%)	9 (12%)	<0.01
Time from specimen collection to data entry of new laboratory results (hours) - median (IQR)			
• Immunosuppression	48 (27-89)	123 (72-170)	<0.01
• Creatinine	31 (23-77)	73 (30-135)	<0.01

* At UUHC, 176 laboratory reports were reviewed. However, due to missing data, we excluded 7 creatinine and 3 immunosuppression results from the analysis.

Table 5.5. Description of posttransplant laboratory data monitoring measures of nurse transplant coordinators

	UUHC	IH	p value
Number of nurse transplant coordinators	2	3	
Number of hours observed (per transplant center)	35	34.5	
Number of times searching for new laboratory results	136	163	
Proportion of checks for new immunosuppression laboratory results - % (n)	41% (56)	68% (111)	
Distribution of triggers for checking for new immunosuppression laboratory results - % (n)			
• Received notification for any new laboratory result (UUHC)	79% (44)	-	<0.01
• Received notification for a new immunosuppression or physiological function laboratory result (IH)	-	38% (42)	
• Received paper chart delivered by assistant	2% (1)	38% (42)	<0.01
• Reminded by a paper flow sheet that was previously set aside	11% (6)	14% (15)	0.61
• Remembered to check laboratory testing for a specific patient	7% (4)	7% (8)	0.99
• Other	2% (1)	4% (4)	0.52
Proportion of unsuccessful searches for new immunosuppression laboratory results - % (n)	16% (56)	14% (111)	0.66
• Received notification for any new laboratory result (UUHC)	14% (44)	-	0.27
• Received notification for a new immunosuppression or physiological function laboratory result (IH)	-	5% (42)	
• Received paper chart when delivered by assistant	0% (1)	17% (42)	>0.99
• Reminded by a paper flow sheet that was previously set aside	17% (6)	13% (15)	>0.99
• Remembered to check laboratory testing for a specific patient	50% (4)	37% (8)	>0.99
• Other	0% (1)	25% (4)	>0.99

Table 5.5 Continued

	UUHC	IH	p value
Internal Laboratory Results only			
Response time to a new immunosuppression laboratory result (hours) - median (IQR) [n]			
• Tacrolimus	23 (22-25) [11]	9 (6-26) [63]	0.049
• Everolimus	25 (24-25) [2]	48 (31-249) [14]	0.04
• Cyclosporine	28 (23-71) [3]	23 (8-24) [10]	0.13

Table 5.6. Satisfaction with using the current information systems for postliver transplant laboratory monitoring

	University of Utah Health Care (n=2)	Intermountain Healthcare (n=3)
How satisfied are you with the support of your current information systems to perform the following tasks:	% Mostly or Very satisfied (Range*)	
Identifying patients who are hospitalized	0% (5-5)	100% (7)
Identifying patterns of laboratory results over time	50% (2-6)	100% (7)
Identifying patients with a new laboratory result	0% (3-5)	100% (6-7)
Identifying patients with an out-of-range laboratory result	0% (2-3)	67% (5-7)
Identifying patients who are overdue for laboratory testing	0% (2-2)	67% (3-7)
Identifying a patient's time since transplantation	0% (3-4)	33% (4-6)
Identifying the target range of an immunosuppressant for a patient	0% (2-5)	0% (3-4)
Generating a list of all patients who are currently overdue for laboratory testing	0% (3-3)	0% (3-4)

*Based on a 7-point Likert scale: 1 – very dissatisfied; 2 – mostly dissatisfied; 3 – slightly dissatisfied; 4 – neither satisfied nor dissatisfied; 5 – slightly satisfied; 6 – mostly satisfied; 7 – very satisfied.

Table 5.7. Frequency of usage of data elements in notifications provided to nurse transplant coordinators at Intermountain Healthcare (n=3)

	Rarely or never (%)	Infrequently, sometimes, or often (%)	Always or almost always (%)
How often do you use the information in the notification message when it is presented to you*:			
[1] Demographics	33%	0%	67%
[2] Contact information	67%	33%	0%
[3] Link to the patient record	0%	33%	67%
[4] Date/time of laboratory test	0%	0%	100%
[5] Severity	0%	33%	67%
[6] Laboratory test	0%	0%	100%
[7] Lab value	0%	0%	100%
[8] Lab value relative to target range (above/within/below)	33%	67%	0%
[9] Target range	33%	67%	0%
[10] Transplant date	0%	67%	33%
[11] Time since transplantation	33%	33%	33%
[12] Hospitalization status	0%	0%	100%
[13] Alert status**	50%	0%	50%
[14] Triggering information	0%	33%	67%
[15] Accept or Rejection button	0%	0%	100%
[16] Comment button	0%	100%	0%

*Based on a 5-point Likert scale: 1 – rarely or never; 2 – infrequently; 3 – sometimes; 4 – often; 5 – always or almost always.

**Based on two responses only.

5.7 References

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CHAPTER 6

CONCLUSION

With an increasing population of liver transplant recipients and improving long-term survival rates, transplant centers must manage a growing pool of transplant recipients with an increasing volume of information. Traditional methods of information management rely on manual, paper-based processes which are ill-suited to meet the complex needs of posttransplant immunosuppressive care. Electronic health records (EHR) and clinical decision support (CDS) systems may better meet the information management needs of posttransplant laboratory monitoring while a system-agnostic CDS approach may be leveraged to disseminate these systems to transplant centers nationwide. Our motivation was to inform the development and implementation of transplant-specific CDS systems. However, we identified several prerequisite questions regarding transplant-specific CDS for which we found no answers in the literature. We conducted research studies with the goal of answering these questions.

The findings of these studies have indicated the feasibility of using a system-agnostic CDS approach as well as provided suggestions for the development or enhancement of information systems for posttransplant care. While a system-agnostic approach may be used to develop a transplant-specific CDS tool, EHR vendors are beginning to offer transplant-specific or population management modules within their

EHR systems that may provide some of the features desired. However, it is likely that these systems are still lacking features we have identified as desirable within the posttransplant workflow, and thus our recommendations presented below may be useful for enhancing the functionality of these current systems.

6.1 Significance

The objectives of the research described in this dissertation were met, and our findings inform the development of CDS systems intended to support the information management needs of the posttransplant laboratory monitoring workflow. The nationwide survey revealed the ubiquity of both paper-based processes and electronic health records (EHR) for managing posttransplant immunosuppressive care. The survey also showed that transplant programs used guidelines for laboratory monitoring with similar patterns of logic that can be implemented using rule-based computerized CDS. The longitudinal analysis was successful in showing how the distribution of alerts evolved over time and that CDS systems tailored to a workflow may be useful to target users for several years even without significant improvements or technical modifications. The cohort study demonstrated that a computerized notification system for laboratory monitoring was associated with improvements in the mortality and toxicity rates of posttransplant patients. While changes in clinical practice may have impacted this change, we observed these improvements despite a large volume of patients and an intervention group with more severe chronic liver disease overall. In addition, this study showed that computerized notifications may provide greater scalability to posttransplant laboratory monitoring workflow processes. The workflow analysis indicated that a

transplant-specific computerized notification system was associated with improved response time, and differences in the functionality of the systems that may explain this finding. The questionnaire showed that a transplant-specific notification system promoted greater satisfaction with performing tasks associated with laboratory monitoring, and that the usage of data elements in computerized notifications should be assessed to determine whether information needs of transplant coordinators are met. These studies produced recommendations to inform the development of transplant-specific CDS systems.

6.2 Recommendations

Given the prevalence of EHR use in transplant centers, the functions of transplant-specific information systems should be integrated into EHRs and not provided in a separate information system. These transplant-specific functions are generalizable beyond the posttransplant patient population, thus integration allows these functions to benefit other patient populations. In addition, posttransplant patients also have general clinical needs, so the workflow of transplant coordinators may be improved by integrating transplant-specific functions with general clinical functions of an EHR instead of forcing the coordinator workflow to switch between an EHR and a transplant-specific information system. Therefore, integration of the functions of transplant-specific information systems may improve patient safety, quality, and cost of care for posttransplant laboratory monitoring.

We recommend that the following requirements be considered when designing features for an EHR to support posttransplant laboratory monitoring information needs:

- Laboratory results data exchange: Ensure that laboratory results are recorded efficiently and accurately as discrete data and are available to EHRs; where feasible, automate laboratory data exchange by implementing electronic interfaces with laboratory facilities.
- Population management: Allow clinicians to define a patient population and computerized notifications to be sent to clinicians when triggered by new data about that patient population.
- CDS for laboratory results monitoring: Implement computerized notifications for new, out-of-range, and overdue laboratory testing to support laboratory results monitoring based on protocols used by the transplant team.
- Flexibility of CDS logic: Design the logic of computerized notification systems to be flexible enough to allow transplant clinicians to revise the target ranges, adjust the expected laboratory testing frequency, or include additional laboratory tests for monitoring without requiring the involvement of information technology (IT) staff. In addition, these systems should support advanced logic for triggering notifications based concurrently on multiple parameters (eg, time since transplantation and presence of specified comorbidities).
- Performance of CDS: Transplant team members typically should not receive computerized notifications after the triggering laboratory result has already been reviewed in the EHR. Minimize the time between when a new laboratory result is received in the EHR and when a computerized notification is generated.
- Unread notification status: Transplant team members should be able to quickly distinguish between notifications not yet seen and those already reviewed but not

yet acted upon and removed from the electronic notification inbox. Provide a visual cue that differentiates computerized notifications as read or unread (as is common with the use of a bold font for unread email messages).

- Governance of CDS logic: Ensure timely governance of CDS systems by linking changes of clinical practice (eg, decrease in target range of immunosuppression) to revision of computerized logic.
- Monitoring of CDS systems: Couple CDS systems with a periodic process for monitoring the data generated by the system. This monitoring may help to identify resource misallocations, mismatches in clinical practice and computerized logic, and other opportunities to improve processes of laboratory monitoring.

Following these recommendations may improve the process measures and clinical outcomes of posttransplant laboratory monitoring by transplant coordinators.

6.3 Future Work

While the research in this dissertation has answered our original research questions, it has also prompted new research questions warranting future work.

First, SMART on FHIR is a promising software platform for providing system-agnostic CDS tools.[1] For example, Cerner has committed to support the SMART platform and has unveiled an online sandbox to support development of SMART apps. Furthermore, several SMART apps have been released by developers from various healthcare provider organizations or software vendors. However, research is needed to determine whether this approach can support the requirements listed above. In addition,

it is necessary to understand how broadly this platform is supported by vendor-based EHR systems and thus implementable in transplant centers nationwide.

Second, we hypothesize that providing prospective notifications regarding upcoming laboratory testing due dates directly to patients may improve patient compliance with testing. However, patient use of EHR portals and the impact of prospective monitoring (rather than the current reactive monitoring when patients are overdue) are unknown. Delivery of notifications may be accomplished through increasingly prevalent patient portals. We propose a study regarding the impact on process measures and clinical outcomes of prospective notifications delivered to patients.

6.4 Conclusion

In summary, we have systematically investigated major questions relevant to developing a transplant information system, and we have evaluated transplant information systems currently in operation in order to inform the development of new or enhanced transplant information systems for posttransplant immunosuppressive care. Our recommendations may improve the processes measures and clinical outcomes associated with posttransplant laboratory monitoring. Furthermore, we have found that the information systems at transplant centers nationwide meet certain prerequisites necessary to use a system-agnostic CDS approach for disseminating features we identified as important to the posttransplant workflow.

6.5 References

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APPENDIX A

DATA COLLECTION INSTRUMENTS TO ASSESS WORKFLOW MEASURES OF POSTTRANSPLANT LABORATORY MONITORING

Date: ___________ Observer: _______ Start Obs. Time: _________ End Obs. Time: __________ Location: ___________ Role: ______________

Method of delivery:	F - fax	E - email
	M - mail (postal)	O - other (explain in comments)

Start Time	Spec. Collection Date/Time	Method of delivery	Is there an *Immuno* result?	Has the Immuno result **previously** been seen?	Is there a *Creatinine* result?	Has the Creatinine result **previously** been seen?	Comments
		F M E O	Y N	Y N	Y N	Y N	
		F M E O	Y N	Y N	Y N	Y N	
		F M E O	Y N	Y N	Y N	Y N	
		F M E O	Y N	Y N	Y N	Y N	
		F M E O	Y N	Y N	Y N	Y N	
		F M E O	Y N	Y N	Y N	Y N	
		F M E O	Y N	Y N	Y N	Y N	
		F M E O	Y N	Y N	Y N	Y N	
		F M E O	Y N	Y N	Y N	Y N	
		F M E O	Y N	Y N	Y N	Y N	
		F M E O	Y N	Y N	Y N	Y N	
		F M E O	Y N	Y N	Y N	Y N	
		F M E O	Y N	Y N	Y N	Y N	
		F M E O	Y N	Y N	Y N	Y N	
		F M E O	Y N	Y N	Y N	Y N	
		F M E O	Y N	Y N	Y N	Y N	
		F M E O	Y N	Y N	Y N	Y N	
		F M E O	Y N	Y N	Y N	Y N	
		F M E O	Y N	Y N	Y N	Y N	

Figure A.1. Data collection form for measuring workflow processes of transplant assistants

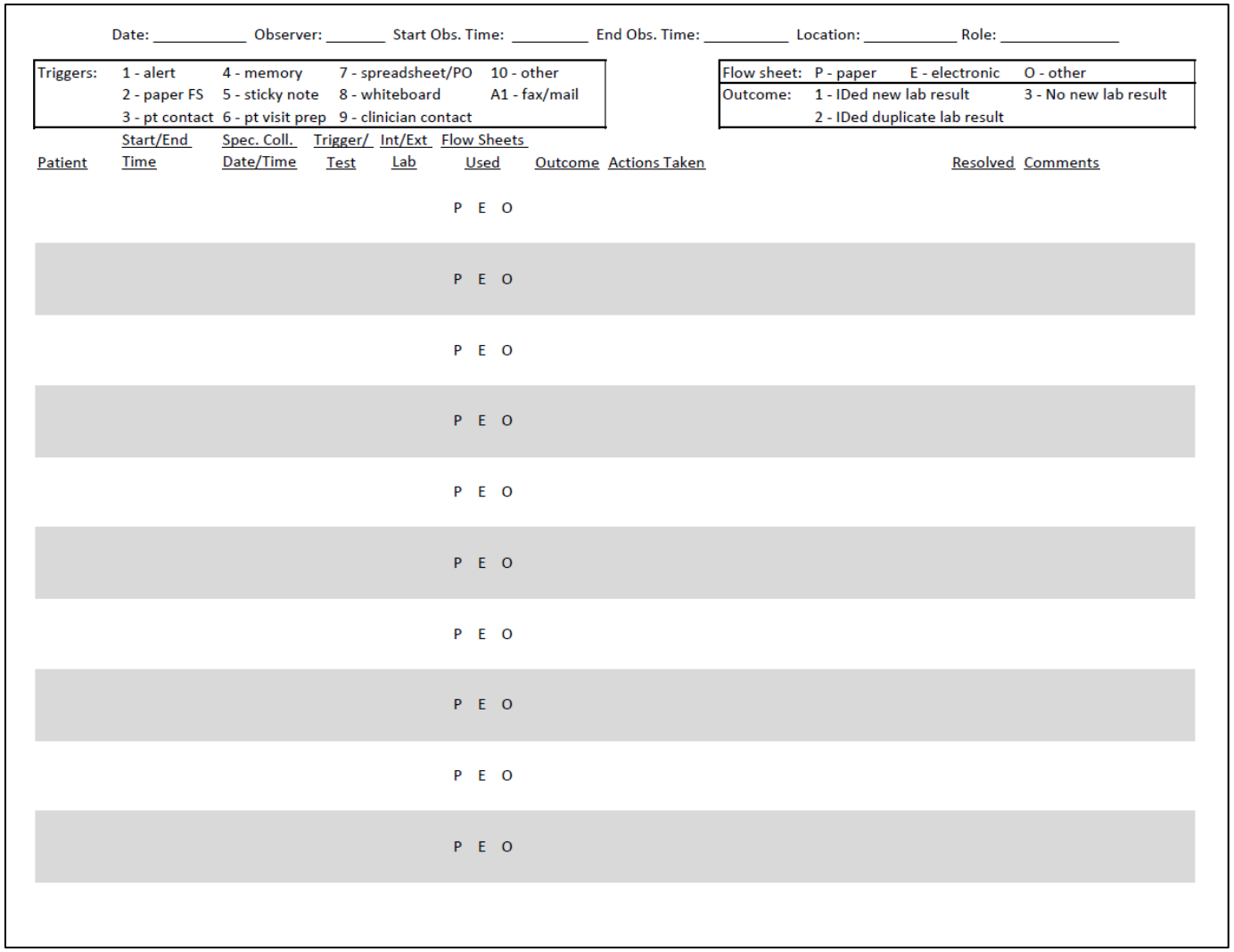


Figure A.2. Data collection form for measuring workflow processes of transplant coordinators

APPENDIX B

QUESTIONNAIRE TO ASSESS SATISFACTION OF USING CURRENT INFORMATION SYSTEMS TO SUPPORT POSTLIVER TRANSPLANT LABORATORY MONITORING

1. How satisfied are you with the support of your current information systems to perform the following tasks:

	Very dissatisfied	Mostly dissatisfied	Slightly dissatisfied	Neither satisfied nor dissatisfied	Slightly satisfied	Mostly satisfied	Very satisfied
Identifying patients with a new laboratory result	☐	☐	☐	☐	☐	☐	☐
Identifying patients with an out-of-range laboratory result	☐	☐	☐	☐	☐	☐	☐
Identifying patients who are overdue for laboratory testing	☐	☐	☐	☐	☐	☐	☐
Identifying the target range of an immunosuppressant for a patient	☐	☐	☐	☐	☐	☐	☐
Identifying a patient's time since transplantation	☐	☐	☐	☐	☐	☐	☐
Identifying patients who are hospitalized	☐	☐	☐	☐	☐	☐	☐
Identifying patterns of laboratory results over time	☐	☐	☐	☐	☐	☐	☐

2a. Can you use your EHR (e.g. Epic or HELP2) to generate a list of all patients who are currently overdue for laboratory testing?

Yes (go to 2c) No (go to 2b)

2b. Do you have a different system to generate a list of all patients who are currently overdue for laboratory testing?

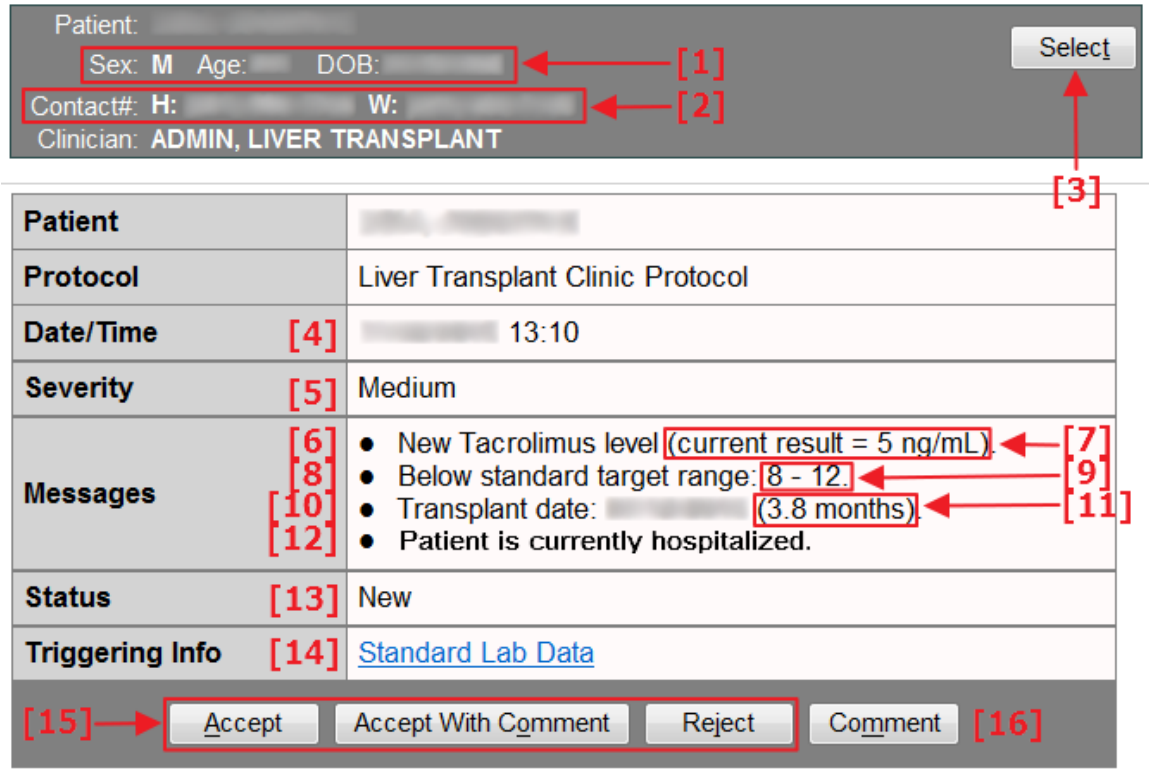
Yes (go to 2c) No (go to 3)

	Very dissatisfied	Mostly dissatisfied	Slightly dissatisfied	Neither satisfied nor dissatisfied	Slightly satisfied	Mostly satisfied	Very satisfied
2c. How satisfied are you with this system (mentioned in 2a or 2b)?	☐	☐	☐	☐	☐	☐	☐

3. What suggestions do you have to improve how identifying patients with new laboratory testing results is performed?

4. What suggestions do you have to improve how identifying patients who are overdue for laboratory testing is performed?

5. [Intermountain transplant coordinators only] Please refer to the following image as you answer the next question:



The table below shows information that is presented to you in a computerized alert for new or overdue immunosuppression laboratory testing. How often do you use the information in the alert message when it is presented to you (e.g. if the information appears infrequently, but you look for it or use it nearly every time it does appear, then mark “Almost always or always”):

	Rarely or never	Infrequently	Sometimes	Often	Almost always or always
[1] Demographics	☐	☐	☐	☐	☐
[2] Contact information	☐	☐	☐	☐	☐
[3] Link to the patient record	☐	☐	☐	☐	☐
[4] Date/time of laboratory test	☐	☐	☐	☐	☐
[5] Severity	☐	☐	☐	☐	☐
[6] Laboratory test	☐	☐	☐	☐	☐
[7] Lab value	☐	☐	☐	☐	☐
[8] Lab value relative to target range (above/within/below)	☐	☐	☐	☐	☐
[9] Target range	☐	☐	☐	☐	☐
[10] Transplant date	☐	☐	☐	☐	☐
[11] Time since transplantation	☐	☐	☐	☐	☐
[12] Hospitalization status	☐	☐	☐	☐	☐
[13] Alert status	☐	☐	☐	☐	☐
[14] Triggering information	☐	☐	☐	☐	☐
[15] Accept or Rejection button	☐	☐	☐	☐	☐
[16] Comment button	☐	☐	☐	☐	☐

6. [Intermountain only] What suggestions do you have to improve the information represented within the computerized alerts for immunosuppressive care laboratory monitoring?