UNDERSTANDING DELIVERY OF COMPUTER-BASED INTENSIVE INSULIN THERAPY

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LIST OF ABBREVIATIONS

APACHE..... Acute Physiology and Chronic Health Evaluation
BG..... blood glucose
CDR..... clinical data repository
CDSS..... clinical decision support system
CPOE..... computerized provider order entry
D50..... fifty percent dextrose solution in water
GTR..... greater than recommended
HED..... Horizon Expert Documentation
HEO..... Horizon Expert Orders
ICU..... intensive care unit
IIT..... intensive insulin therapy
ISS..... Injury Severity Score
IQR..... interquartile range
LIS..... laboratory information system
LTR..... less than recommended
MD..... medical doctor
NA..... nurse aide
R..... recommended
RN..... registered nurse
SICU..... surgical intensive care unit
SSI..... sliding scale insulin
TICU..... trauma intensive care unit
TRC..... Thomas Richmond Campion
VUH..... Vanderbilt University Hospital

CHAPTER I

PEERS, REGULATORS, AND PROFESSIONS: THE INFLUENCE OF ORGANIZATIONS IN INTENSIVE INSULIN THERAPY ADOPTION

Introduction

In 2001 the Leuven study demonstrated morbidity and mortality improvements in surgical intensive care patients as a result of tight glycemic control achieved through an intensive insulin therapy (IIT) protocol [1]. Professional organizations heralded the results of the single-site randomized trial as the new standard of care for diabetics and non-diabetics alike, and health care organizations adopted IIT protocols. To accommodate IIT, hospitals and health systems enacted considerable changes to organizational structure—the formal policies that dictate roles, responsibilities, and standard operating procedures—involving clinical workflow, nurse workload, blood glucose testing, evidence-based medicine, and, in some approaches, computerization [2]. However, a 2008 meta-analysis of randomized IIT trials showed no mortality benefit for patients treated with IIT as well as an increased risk of hypoglycemia [3]. The expenditure of labor and capital to provide IIT without corresponding outcome improvements suggests the adoption of IIT produces inefficiency in organizations.

Such widespread change in the absence of conclusive benefit can be explained through the lens of institutional theory, a sociological view that examines the way in which organizations in a field interact, define behavioral norms and expectations, and evaluate each other [4]. Institutionalists posit that organizations are evaluated by

legitimacy, the social view that an organization is "appropriate, rational, and modern," more so than efficiency [5]. To enhance their prospects of survival, organizations establish and maintain legitimacy by adopting the "prevailing rationalized concepts of organizational work" endorsed by successful peer organizations, regulatory agencies, and professional societies [5]. This results in organizations becoming more similar but not necessarily more efficient, a process called institutional isomorphism [6]. In this article, we use institutional isomorphism to examine the role of organizational influence in intensive insulin therapy's adoption and effect on organizations. By understanding the role of peers, regulators, and professions in organizational change, health care leaders can make informed decisions concerning the adoption of innovations.

Theoretical Background

Institutionalization is a process in which social behavior is established as a formal structure that serves as a means to an end for an organization and signals to other organizations that an organization is legitimate [5, 7]. Suchman defines legitimacy as "a generalized perception or assumption that the actions of an entity are desirable, proper, or appropriate within some socially constructed system of norms, values, beliefs, and definitions" [8]. When an organization adopts institutionalized forms, its personnel and other organizations are more likely to view it as legitimate, which enhances the organization's prospects of survival [5]. However, efficient organizational practice may require divergence from institutionalized forms, a move which threatens legitimacy. In response, organizations become loosely coupled, or "[build] gaps between their formal structures and actual work activities" [5]. The struggle between adherence to

institutionalized forms and real world practice results in ceremonial conformity to maintain legitimacy and reduced overall organizational efficiency [5].

Institutional isomorphism functions through mimetic, coercive, and normative mechanisms.[6] *Mimetic* isomorphism occurs when an organization copies the practices of another organization it perceives to be successful, particularly for problems "with ambiguous causes or unclear solutions" [6]. Hospitals' adoption of Continuous Quality Improvement as a comprehensive management program is an example of mimetic isomorphism [9]. An organization experiences *coercive* isomorphism when another organization on which it depends requires it to adopt a structure. An example of coercive isomorphism is in U.S. hospitals' adoption of practices required by the Joint Commission for Medicare reimbursement eligibility. *Normative* isomorphism involves the diffusion of organizational norms through training and socialization as well as the networks professionals develop through practice societies, educational activities, and common knowledge bases. Examples include physicians who complete fellowships in critical care approaching clinical issues and strategic decisions similarly, and hospitals voluntarily complying with Leapfrog Safe Practices in order to meet professionally defined levels of acceptable clinical care. Through each of the three isomorphic mechanisms, organizations conform to institutionalized structures and attain legitimacy.

Organizational Changes Required for Intensive Insulin Therapy

Before examining the role of organizational influence in intensive insulin therapy adoption, it is important to first understand the changes to organizational structure necessary for IIT. Whether transitioning to IIT from continuous insulin infusion or

sliding scale subcutaneous insulin therapy, a health care organization introduces a substantial practice change. Compared to its predecessors, IIT has a lower blood glucose threshold for therapy initiation, which results in patients receiving insulin therapy sooner, and requires different titration logic to maintain euglycemia. Clinicians and managers must develop an IIT protocol, gain staff buy-in through education and training, and modify workflow. Nurses experience an increase in workload in terms of increased frequency of blood draws, dosing calculations, insulin rate adjustments, and corresponding documentation. Laboratories increase their testing capacities in terms of devices, testing supplies, maintenance, and training. Pharmacies dispense more insulin and infusate. If computerized clinical decision support systems are used, informatics personnel must support software that is either developed internally or purchased from a vendor. All of these changes require labor and capital expenditures.

Organizational Influence in the Adoption of Intensive Insulin Therapy

Following the landmark Leuven study, health care organizations have become more similar but not necessarily more efficient in their efforts to implement intensive insulin therapy. Organizational influence has played a role in the adoption of IIT, and the mechanisms of institutional isomorphism provide a framework for understanding how "individual efforts to deal rationally with uncertainty and constraint often lead, in the aggregate, to homogeneity in structure" and inefficiency [6]. It is important to note that the mechanisms are analytical: they may overlap in practice but provide valuable perspective concerning the causes and consequences of organizational change. The following sections explain the mechanisms of institutional isomorphism and the

organizations involved in the adoption of intensive insulin therapy. Table 1 presents a summary.

Table 1. Mechanisms of institutional isomorphism and organizations involved in IIT adoption

Mimetic	Coercive
• Leuven study	• Joint Commission
Normative	
Professional societies	
• American Association of Critical-Care Nurses • American College of Chest Physicians • American College of Emergency Physicians • Canadian Critical Care Society • European Society of Clinical Microbiology and Infectious Diseases • European Society of Intensive Care Medicine • European Respiratory Society • International Sepsis Forum • Japanese Association for Acute Medicine • Japanese Society of Intensive Care Medicine • Society of Critical Care Medicine • Society of Hospital Medicine • Surgical Infection Society • World Federation of Societies of Intensive and Critical Care Medicine • German Sepsis Society • Latin American Sepsis Institute	
Practice councils	
• Institute for Healthcare Improvement • Volunteer Hospital Association • Michigan Health and Safety Coalition • American Association of Clinical Endocrinologists • American Diabetes Association	

Mimetic isomorphism

As indicated by its high citation count, the Leuven study captured the critical care community's attention and prompted practitioners and researchers to attempt to replicate the findings in myriad settings. Organizations tend to imitate other successful organizations' approaches when facing ambiguity and uncertainty in technologies, problems, and solutions [6]. Intensive insulin therapy provided a promising possible

solution to the problem of mortality in the critically ill [3], and the techniques described in the single-site randomized Leuven study served as the model for hospitals to copy en masse. On an individual hospital level, the results of local pilot site studies may have spurred other hospital units to copy the pilot site's IIT approach [10]. Because of its novelty, the Leuven approach and its effects may not have been fully understood by imitators. Although mortality reduction is a clear goal, the steps to achieve it are ambiguously defined in the Leuven protocol [11]. A large number of confounding variables in clinician behavior and patient demographics also can complicate IIT delivery. Furthermore, metrics for understanding protocol performance and comparing study sites are not widely accepted [12]. Although it lacked external validity, the single-site Leuven study "[served] as a convenient source of practices"[6] for organizations to adopt in order to respond to problems and attain legitimacy.

Coercive isomorphism

Regulatory requirements resulting from the Leuven study may explain adoption of intensive insulin therapy. U.S. hospitals depend on the Joint Commission for accreditation for Medicare reimbursement eligibility and certification for quality reporting purposes. According to the Joint Commission website, certification provides "the best signal" of effective care to a hospital's patients and peer organizations [13]. Among the requirements for Inpatient Diabetes Certification are the use of protocol-based approaches for blood glucose management and collection of blood glucose performance data [13]. Because of the Joint Commission's status as a legitimacy-conferring organization, hospitals adopt organizational changes to accommodate

intensive insulin therapy. Similar to hospitals' dependence on JCAHO, units in a hospital and hospitals in a health system rely on upper management for resources and must enact management's policies. One large commercial health system has implemented IIT in over 100 hospitals presumably because of health system policy, not because of hospitals volunteering [14].

Normative isomorphism

The participation of physicians, nurses, and administrators in continuing education, workforce socialization, and professional societies may explain the proliferation of Leuven-inspired intensive insulin therapy. Published in a high impact factor journal, the Leuven study reached a broad audience of health care professionals. Sixteen professional societies and five practice councils, including the American Diabetes Association, endorsed the use of intensive insulin therapy following publication of the Leuven study [3]. IIT has become the standard of critical care because of the influence of individuals and professional societies in shaping the definition of their work [6]. Healthcare organizations have responded to the prevailing critical care norms reflected by their clinicians through implementation of IIT. Within a health care organization, IIT diffusion among hospital units may be due to local patterns of socialization amongst clinicians as reported at one institution [11]. It is conceivable that a faculty member may present the results of a local IIT study at grand rounds, which prompts other faculty members to consider implementation in their care units.

Discussion

Examining the adoption of intensive insulin therapy using institutional theory can help researchers, practitioners, and managers reconsider the evidence thresholds and motivations for implementing clinical measures of this magnitude. Regulators and professional societies should consider the external validity of studies as well as the scope of their influence before endorsing particular practices, and hospital decision makers should recognize that practice changes require organizational changes beyond the boundaries of a pilot unit. Although organizations may indicate their conformity to an institutionalized form like intensive insulin therapy, actual work processes may differ substantially and explain the variation in intensive insulin therapy trial results following the Leuven study. Institutional theory provides a useful analytical framework for health care decision makers to understand past events and approach future scenarios.

Specific Aims

As established in this chapter, this research draws from social theory to frame a quantitative and qualitative investigation of factors affecting computer-based intensive insulin therapy. The following chapters address three specific aims, one of which has two parts:

1. A literature review and case study of intensive insulin therapy clinical decision support systems (IIT CDSS) to demonstrate underreporting of social, organizational, and contextual characteristics affecting IIT CDSS performance
2. A quantitative analysis of IIT CDSS performance with respect to workflow features including

    a. The effects of data mismatches
    b. The characteristics and effects of nurse overrides
3. A naturalistic study of IIT CDSS informed by the previous aims to identify sociotechnical interactions affecting IIT CDSS performance

The analysis concludes with a summary of findings along with recommendations for future work.

CHAPTER II

SOCIAL, ORGANIZATIONAL, AND CONTEXTUAL CHARACTERISTICS OF CLINICAL DECISION SUPPORT SYSTEMS FOR INTENSIVE INSULIN THERAPY: A LITERATURE REVIEW AND CASE STUDY

Introduction

The U.S. National Research Council recently endorsed the use of clinical decision support systems (CDSS) and "organizational systems-level research" of health information technology to help drive healthcare transformation [15]. Historically evaluations of CDSS have focused on practitioner performance [16] rather than social, organizational, and contextual factors [17, 18]. Kaplan noted that CDSS evaluation studies measure CDSS effects on clinical performance, use experimental study designs or randomized controlled trials, disregard naturalistic study methods, ignore contextual issues surrounding system usage, investigate the perspectives of physicians rather than other clinical roles, and consider only the CDSS intervention, not other clinical information systems in use [17]. The reporting of findings in the literature reflects a rationalist scientific orientation [17] and shows clinical and medical informatics investigators' preferences toward objectivist rather than subjectivist approaches to evaluation [19]. Although subsequent reviews have identified dimensions of workflow integration as critical to CDSS success [20], researchers have yet to fully embrace the National Research Council's directives or address the gaps identified by Kaplan.

Studies of clinical decision support systems for intensive insulin therapy (IIT), a treatment combining frequent blood glucose monitoring and insulin drip adjustments to maintain tight glucose control [1], follow the general CDSS evaluation trend. Investigations using experimental designs have demonstrated improved clinician protocol adherence and achievement of target glucose levels using computer-based IIT protocols instead of paper-based versions [2, 10, 14, 21-29]. However, these evaluations have paid little attention to the context of interventions, including the complex interaction between staff, testing devices, and computers that may result in inefficiency and error. Nurses use computer-based IIT advisors to document care and calculate insulin doses, but investigations mostly rely on anecdotal feedback to understand nurse perspectives of CDSS and rarely consider CDSS usage with respect to other care processes and clinical information systems. The literature describes paper-based IIT protocol implementation barriers [30] and effects on nurse work [31] but does not explore the complexity and organizational change related to computer-based IIT approaches.

Understanding the mechanisms of effective intensive insulin therapy CDSS is important because IIT is the standard of care for critically ill patients [32]. In 2001 the Leuven study demonstrated morbidity and mortality improvements through an intensive insulin therapy protocol [1], and subsequent studies at other institutions have produced similar results [33, 34]. However, a 2008 meta-analysis of randomized trials raised concerns about the therapy's mortality benefit and safety [3]. Differences in care protocols ranging from nutrition provisions [11] to target blood glucose ranges [11, 35], insulin administration [36], and intended patient populations [37] may explain variation

in IIT outcomes, but researchers have not determined comprehensive solutions, especially ones that address computer-based approaches.

Although care protocols define the decision-making behavior clinicians should exhibit under certain conditions [38] and represent the evidence-based, formal structure of healthcare organizations, actual work activities usually differ from official practice definitions [5]. In patients treated with computer-based intensive insulin therapy in the surgical intensive care unit at Vanderbilt University Hospital, researchers found fourteen percent of blood glucose measurements were not taken on time [39]. Significant relationships between late blood glucose measurements and episodes of hyper- and hypoglycemia [39] as well as blood glucose variability and mortality [40] suggest that workflow may be a factor in computer-based IIT performance and patient outcomes [39]. In sociology and organizational studies, institutional theory [4, 5, 7, 41-43] examines the way rules, policies, and procedures affect and are affected by "assumptions, norms, values, choices, and interactions" [43]. This approach has informed investigations of information technology in law [44], banking [45], and research workplaces [46], and informatics researchers have focused on similar issues to influence system design [47-49]. To improve intensive insulin therapy protocol performance and patient outcomes, researchers and practitioners can use institutional theory to address care process execution issues related to human behavior.

This paper takes a subjectivist approach [18] to the study of computer-based intensive insulin therapy and illustrates the need for additional research in two parts: 1) a literature review, which uses institutional theory to take inventory of formal structure and social organization [42] reported in computer-based IIT evaluations, and 2) a case study

that builds on the literature review and emphasizes social, organizational, and contextual aspects typically absent from computer-based IIT evaluations. The literature review can potentially serve as a source for other CDSS evaluators interested in social, organizational, and contextual elements, and the case study shares the experience of computer-based IIT at one institution so other institutions can make informed decisions. Overall the analysis shows a gap in the computer-based IIT literature concerning complexity of protocol execution, opportunity for error in staff-device-CDSS interaction, effects on other workflow and care processes, and the magnitude of organizational change necessary for implementation.

Literature Review of Computer-based Intensive Insulin Therapy Evaluations

In May 2008 we searched ISI Web of Science for articles citing the Leuven study (1,783 articles) and containing the keyword "protocol" (129 articles). Because the Leuven study played a significant role in IIT protocols becoming the standard of critical care, we used it to focus our search. From the "protocol" corpus we identified fifteen evaluations of computer-based IIT protocols. Fourteen evaluations used experimental designs or randomized trials, and one was a practice report. The studies examined eighteen intensive care units in twelve healthcare organizations excluding the hundreds of sites evaluated in a longitudinal study of a commercial product [14].

One of the authors (TRC) reviewed the studies through the lens of institutional theory [4, 5, 7, 41-43] to identify aspects of computer-based intensive insulin therapy's formal structure—the prescribed, written policies established to govern and evaluate behavior—and social organization of computing—the interaction of people, process, and

technology across different locations and over time [42]. Researchers have used these dimensions to understand the interdependence of technology and human behavior in shaping organizational activity in banking [45], legal [44] and university research settings [46]. For example, through the implementation of a locally hosted digital legal library, a metropolitan court system sought to improve attorneys' legal research and limit cost [44]. Formal structure, manifested in system policies, defined access according to professional role and discouraged use of expensive remote subscription services in favor of the local digital library [44]. The social organization of computing was critical to effective digital library usage: convenient terminal access, workflow integration, favorable attitudes toward computing, separate computer work areas for competitive attorney groups, individualized training, and the emergence of social norms regarding digital library usage in courts [44].

Kling describes three main components of the social organization of computing: equipment configurations, skills and roles, and support infrastructure [42]. Equipment configurations involve the locations of hardware, software, functionality modules within software, and peripherals; skills and roles encompass the various members of an organization who use, supply, or affect an information system's data; and support infrastructure concerns the ways that system stakeholders (e.g. users and managers) obtain assistance and direction [42]. Additionally, temporal aspects of system use, such as periodic (e.g. morning vs. evening) and long-term change over time (e.g. initial vs. established patterns of usage), are salient for analysis [42].

Formal structure of computer-based intensive insulin therapy

Formal structure, defined as the codified procedures intended to govern and evaluate behavior, is well-documented in the computer-based intensive insulin therapy literature. Researchers frequently reported protocol algorithm details as well as evaluation measures in terms of practitioner and patient outcomes, which have been previously defined [16].

Protocol algorithm details

Computer-based IIT approaches used two main algorithmic techniques to determine insulin dosing: linear equations [14, 21-23, 28, 50] based on the work of Bode [51] and White [52] and conditional logic [2, 27, 29, 53]. Other approaches included model predictive control [54] and engineering control math [25]. Most researchers disclosed the logic of computer-based insulin dosing algorithms [2, 14, 21, 22, 26-29, 50, 53], and some researchers disclosed previously [21, 22] or concurrently used [25] paper-based IIT protocols.

Practitioner outcomes

Measures of practitioner outcomes included blood glucose target achievement (e.g. time in target range [2, 10, 21, 25, 26, 50, 53], percentage in target range [10, 21-23, 25, 27], time before reaching target range [10, 14, 22, 23, 25-27, 50]), blood glucose mean and median (e.g. overall [2, 22, 23, 25, 28, 29], after 24 hours [10, 26], per day [2, 21, 50]), total blood glucose measures (e.g. overall [2, 22, 25, 27, 29, 50] and per day [2, 10, 21, 26]), hyperglycemia [2, 10, 21-23, 26, 27, 50], hypoglycemia [10, 14, 21-23, 25, 27, 29, 50], insulin administration totals [10, 14], and protocol compliance (e.g. time to initiation of protocol [10, 21, 26], measurement and dosing per protocol schedule [10, 27,

53], administration of recommended insulin dose [10, 53]). Evaluation measures and clinical performance varied between studies. Only one study noted a low percentage of blood glucose results in target range and high percentage of tests not performed on time [27]. Based on rare occurrences of hypoglycemia and reductions in hyperglycemia, most studies deemed IIT protocols "safe and effective" for glucose management.

Patient outcomes

Few studies evaluated patient outcomes in addition to practitioner outcomes [22, 28, 29]. Despite demonstrating improved practitioner outcomes, two studies showed no difference in patient outcomes [22, 29] while another showed reduced morbidity and length of stay but increased mortality [28]. Most studies were preliminary and lacked statistical power to detect patient outcome changes.

Social organization of computer-based intensive insulin therapy

Compared to formal structure, social organization—the interaction of people, process, and technology was less consistently reported in the computer-based intensive insulin therapy literature. Computer-based approaches to IIT involved various levels of computer systems integration and interaction with testing devices as well as impact on and influence of other care processes and hospital units. The following reviews the social organization of computer-based IIT implementations in terms of equipment configurations, skills and roles, and support infrastructure [42]. Table 2 provides a summary.

Table 2. Social organization of computer-based IIT reported in the literature

	Equipment Configurations			Skills and Roles		Support Infrastructure	
	CDSS location	**Blood glucose testing devices**	**CDSS-device interface**	**Nurse feedback**	**Other care process**	**Design & training**	**Diffusion**
Boord [21]	Embedded	Handheld	Manual	Easy to use		Workflow importance	
Davidson [14]			Manual				Other ICUs, units, hospitals; created organization
Dortch [22]	Embedded	Handheld	Manual		Steroids, nutrition	Multidisciplinary team; workflow importance; training	Other ICUs
Hermayer [50]	Calculator		Manual		Disease management service	Training	Other ICUs
Juneja [23]	Embedded		Manual	Increased workload			Other ICUs, units, hospitals
Meynaar [2]	Calculator	Handheld	Manual				
Plank [54]	Embedded/ Standalone	Non-handheld	Manual	Increased workload			Created organization
Rea [55]	Calculator	Handheld	Manual	Increased autonomy*		Multidisciplinary team	
Rood [53]	Embedded	Handheld	Automatic				
Saager [25]		Handheld					
Shulman [27]	Embedded	Handheld		Increased workload	Nutrition	Multidisciplinary team	
Thomas [29]	Calculator	Handheld and non-handheld	Manual	Easy to use	Steroids, nutrition, surgery, imaging	Multidisciplinary team	
Toschlog [28]		Handheld					
Vogelzang [10, 26]	Embedded/ Standalone	Non-handheld	Automatic	Easy to use**	Nutrition	Workflow importance; training	Other ICUs

Blank cells indicate the authors did not disclose this information
*Stated goal of protocol implementation
**Only study using a formal questionnaire

Equipment configurations

Equipment configurations include the placement of computers, software, software functionality, and peripherals within large information systems in particular settings [42]. For computer-based IIT, this includes decision support system location and integration, blood glucose testing device usage, and device-computer interface. Figure 1 depicts the interaction of these elements in computer-based IIT workflow reported in the literature.

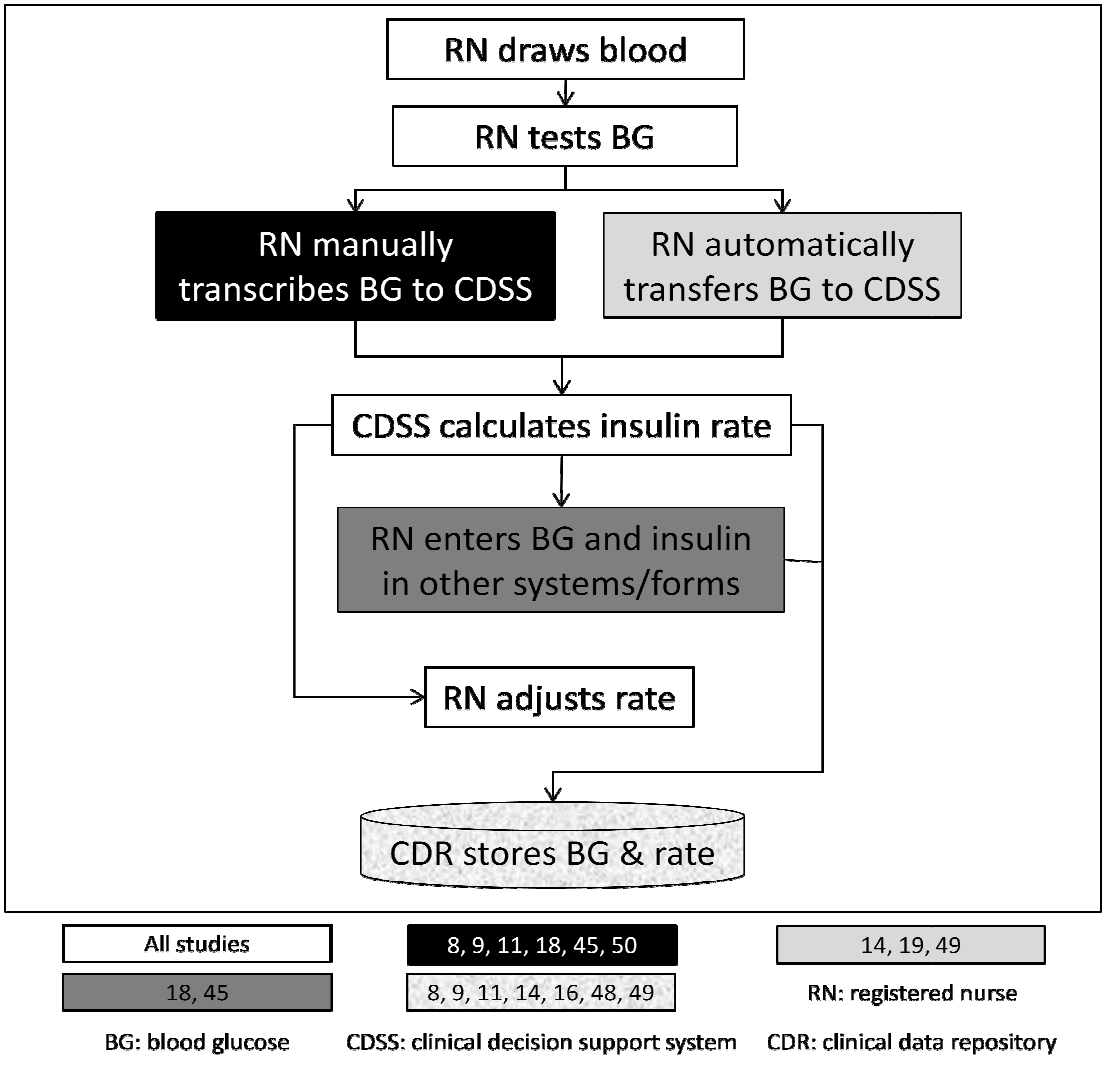


Figure 1. Computer-based intensive insulin therapy workflow reported in the literature

IIT CDSS location and integration with clinical data repositories

Clinicians used three IIT CDSS mechanisms: 1) modules embedded within existing primary clinical information systems, including care provider order entry (CPOE) systems, that are accessible from hospital workstations and store blood glucose and insulin dosing data in clinical data repositories (CDR) [21-23, 26, 27, 53, 54]; 2) "calculators" accessible on a hospital network that do not store data in a CDR [2, 55] and may require additional documentation in a clinical information system [29] and/or use of a preprinted order set [50]; and 3) applications installed on standalone computers[1] [26, 54]. Few studies reported location of hospital workstations [53], electronic data interchange with patient monitoring equipment [53], and use of other clinical information systems that are related to or may affect IIT CDSS, workflow, or care processes (e.g. nursing documentation) [29].

Blood glucose testing device usage

Clinicians used handheld glucometers [2, 21, 22, 25, 27, 28, 53, 55], non-handheld blood gas analyzers [26, 54], and a combination of both [29] to obtain blood glucose measurements. The importance of handheld glucometers was demonstrated by additional glucometer investment before implementation [29], shortages during implementation [55], and the mechanical failure of a single non-handheld blood gas analyzer temporarily halting protocol use [26].

Interface between CDSS and blood glucose testing devices

Clinicians manually transcribed blood glucose values from testing devices to CDSS [21-23, 29, 50, 55], automatically transferred test results through docking stations in real time [53], or automatically transferred test results from non-handheld blood gas

[1]In these studies the authors described use of the CDSS in embedded and standalone configurations.

analyzers in real time [10, 26]. Depending on clinical information systems integration, nurses recorded blood glucose results and insulin rates in both CDSS and nursing documentation tools [29]. Continuous monitoring technology was identified as a possible alternative in the future [14, 27, 54].

Skills and roles

Skills and roles include the various members of an organization who use, supply, or affect an information system's data [42]. For computer-based IIT, this involves nurses as well as care members engaged in other processes that influence system use.

Nurse feedback

Nurse feedback regarding IIT CDSS was mostly positive but evaluation methods lacked rigor. One study used a formal questionnaire to gauge nurse perceptions before and after implementation [26], whereas most studies reported anecdotal nurse feedback related to the interventions' ease of use [21, 29] and increased nursing workload [23, 27, 54]. In one study researchers identified increasing nurse autonomy as a goal of the implementation [55]. Although nurses are the primary users of IIT CDSS, nurse feedback is not a focus of investigations.

Other care processes

Other care processes that may affect IIT and use of IIT CDSS were frequently overlooked. One study reported the concurrent activity of a diabetes disease management service [50]. Demands from surgery and imaging occasionally interrupted IIT usage [29], and ICU nurses administered steroids [22, 29] and nutrition [22, 26, 27, 29] that may have affected patients' blood glucose levels. Description of IIT CDSS workflow

integration with respect to the disruptive nature of healthcare was not present in the literature.

Support infrastructure

Support infrastructure concerns the ways in which system stakeholders (e.g. users and managers) obtain assistance and direction [42]. For computer-based IIT, this focuses on the activities of information technology professionals, care team members, and hospital administrators.

Design and training

Multidisciplinary teams consisting of physicians, nurses, pharmacists, and informaticians were responsible for the creation of IIT care protocols and computer-based advisors [22, 27, 29, 55]. Some approaches to computer-based IIT stressed the importance of embedding decision support systems in clinical workflow [21, 22, 26]. Training procedures included pre-implementation multidisciplinary instruction [22, 26] and web-based nurse training [22] as well as "continued need for staff instruction and compliance regarding the protocol" [50].

Diffusion of IIT CDSS

All computer-based IIT protocols originated in an ICU setting, and many diffused to other ICUs within the same institution [10, 14, 22, 23, 50] as well as medical-surgical floors [14, 23, 50], recovery [50], labor and delivery [50], and progressive care units [23]. Two approaches diffused to multiple hospitals after initial usage [14, 23], and two research teams created organizations to advance research and adoption of their respective systems [14, 54].

Summary of literature review

Computer-based intensive insulin therapy studies reported formal structure consistently and social organization inconsistently, which reflects the objectivist approach predominating CDSS investigations [17] and the norms of the clinical literature. Most evaluations provided algorithm details and measurements of practitioner performance, but consideration of real world system usage and effects on healthcare organizations in terms of equipment configurations, skills and roles, and support infrastructure varied. Although most interventions relied on the use of handheld glucometers, none recognized the complexity and capacity for error of nurse-device-computer interaction. Studies irregularly described the effect of computer-based IIT on other care processes and clinical information systems usage and *vice versa*. Although nurses were the primary users of computer-based IIT interventions, most evaluations did not explicitly evaluate nurse feedback. Some studies described the importance of workflow integration and multidisciplinary cooperation, but the literature lacked a comprehensive description of unintended consequences and change management strategies. Evaluations did not address social, organizational, and contextual issues related to computer-based intensive insulin therapy.

Case Study: Intensive Insulin Therapy in the Vanderbilt University Hospital SICU

Intensive insulin therapy represents a set of organizational changes involving the recursive relationship between formal structure and actual work practices, a process which the following case study demonstrates. Based on review of the literature, most computer-based intensive insulin therapy studies ignore the social, organizational, and

contextual aspects that explain the effectiveness of interventions. By examining the transition from *ad hoc* sliding-scale insulin therapy to standardized intensive insulin therapy in the surgical intensive care unit at Vanderbilt University Hospital, this case study illustrates aspects usually omitted from evaluations of computer-based IIT: the importance of local leadership, the expenditure of labor and capital, the relationship between the ICU and other organizational entities, and the influence of technology on clinical process and *vice versa*. Additionally, the case draws attention to consequences of computer-based IIT—staff- device-computer interaction and the therapy's effect on other care processes—that represent opportunities for error and require additional research. Rather than treat the research setting as static, we aim to show how its dynamic properties change over time and affect and are affected by physicians, nurses, laboratory personnel, and informatics personnel.

We used naturalistic methods [56] to create a three stage chronological narrative of insulin therapy in the study site: glycemic regulation before IIT, paper-based IIT, and computer-based IIT. For stage one, we interviewed nurses, physician leadership, and laboratory personnel. For stage two, we reviewed colleagues' publications [21] and interviewed nurses and informatics support staff. For stage three, we interviewed nurses, physician leadership, informatics support staff, and laboratory personnel in addition to directly observing workflow and reviewing colleagues' publications [21]. Preceding the narrative stages, we also gathered site background information based on review of internal documents and interviews with unit leadership. The Vanderbilt University Institutional Review Board approved this study.

Site background

At Vanderbilt University Hospital (VUH), a large academic urban tertiary care center consisting of 501 beds, the surgical intensive care unit (SICU) admits 1,300 patients each year. The SICU occupies a single floor of the hospital and has a horseshoe layout with a nurse station and supply room in the middle and 21 beds lining the exterior. Each patient room contains at least one clinical workstation connected to the hospital network. Additional workstations are located on mobile carts, at the central nurse's station, adjacent to isolation rooms in antechambers, and throughout the corridors. At VUH the use of electronic patient care information systems has a fifteen year history and is engrained in clinician culture. Clinicians use locally developed electronic medical record and provider order entry systems in addition to vendor applications for ancillary functions and nursing documentation.

Since 2001 the SICU has been under the leadership of a medical director focused on strengthening unit operations as well as promoting collaboration with other hospital units. Efforts include increasing the number of SICU beds from 14 to 21, expanding the use of evidence-based guidelines, shifting cardiovascular surgery patients out of the SICU into a new intensive care unit, collaborating more closely with trauma ICU, creating a full-time SICU critical care service to replace an elective service comprised of critical care and anesthesiology faculty, and facilitating the creation of a separate emergency general surgery service. During this period of growth, SICU experienced increased patient volume and illness severity compared to pre-2001 levels.

Glycemic Regulation Before Intensive Insulin Therapy

Dependence on clinical judgment, inconsistent care processes, and documentation difficulties characterized sliding scale insulin (SSI) therapy, the standard of care for SICU glycemic regulation prior to paper-based intensive insulin therapy. All diabetic patients, as well as non-diabetics with blood glucose issues caused by sepsis or medications, received SSI treatment. Although nurses generally contacted physicians when a blood glucose measurement exceeded 150-200 mg/dL, no explicit criteria defined the threshold of hyperglycemia and when a SICU patient should begin insulin therapy. Physicians' SSI orders defined blood glucose measurement intervals and specific insulin doses for blood glucose ranges. Less experienced nurses adhered to SSI orders whereas more experienced nurses would use clinical judgment (e.g. accounting for a patient's glucose-affecting therapies) in determining subcutaneous insulin injection dosing and subsequent blood glucose monitoring intervals (e.g. Q1H to Q6H) using LifeScan Basic® handheld glucometers. In addition to subcutaneous sliding scale insulin, patients received insulin infusions along with electrolytes as part of total parenteral nutrition. This dosing was also non-standardized and relied on physician discretion. Physicians and nurses depended on experience to initiate therapy, adjust subcutaneous insulin doses, and monitor blood glucose levels.

SSI data management was problematic. Following each blood glucose measurement and insulin administration, nurses documented data on the paper ICU flowsheet, daily glucose log, and medication administration record. Once per day a carbon copy of each patient's daily glucose log was transported to the laboratory for entry into the laboratory information system (LIS). Recording blood glucose (BG) results in

the LIS enabled the institution to track resource utilization, assess point-of-care testing compliance, manage billing, and meet regulatory requirements. The LIS also interfaced with the clinical data repository, which clinicians accessed from hospital workstations to view lab results. However, blood glucose and insulin data appeared in the CDR only about 40% of the time: SICU staff were often too busy to transport logs, and the laboratory did not routinely send personnel to SICU to check compliance and collect log sheets. Physicians turned to paper charts instead to obtain blood glucose and insulin data.

A non-protocol-based approach to care, sliding scale insulin permitted variability in clinical decision making. Treatment using SSI was reactive rather than proactive in that it treated hyperglycemia instead of attempting to prevent it, which allowed fluctuation of blood glucose levels and risk of hyper- and hypoglycemia in patients [57]. Non-standardized care and workflow breakdowns typified sliding scale insulin in the SICU.

Paper-based Intensive Insulin Therapy

In August 2003 the VUH SICU implemented a paper-based intensive insulin therapy protocol [21] based on the Leuven study [1], but labor requirements, task complexity, and workflow integration hindered protocol performance. The protocol increased nurse workload by requiring blood glucose measurements, insulin rate adjustments, and subsequent documentation at two hour intervals for both diabetic and non-diabetic patients. Under the new protocol, nurses initiated intensive insulin therapy when a patient's BG level exceeded 110 mg/dL instead of waiting for BG levels to reach a discretionary level as under the previous SSI standard of care. This increased the

number of patients treated with insulin. After performing BG tests at the bedside using LifeScan Basic glucometers, nurses consulted the paper medication administration record for the protocol's instructions to manually calculate insulin titrations, a process which required nurse interpretation of the protocol (e.g. "increase infusion by 1-2 units/hr" or "decrease infusion by 25-50%"). Nurses then recorded BG and insulin data on the ICU flowsheet, daily glucose log, and medication administration record. Further complicating implementation was a local nursing shortage. Staff disagreed with the protocol, ignored recommendations, lacked time to perform calculations, and made mental mistakes. Although the purpose of the protocol was to improve care through standardization, variability persisted while demands on nurses increased and potential patient safety threats emerged.

The new protocol also created difficulty for the laboratory, which affected SICU staff. Because of the increase in blood glucose tests performed, laboratory personnel required more time to transcribe test values into the system, which resulted in a processing backlog. Illegible daily glucose logs caused laboratory personnel to occasionally transcribe BG results incorrectly, which caused values in the CDR to not match up with paper documentation. Nurses and physicians became frustrated because they were unable to access accurate BG values through the CDR in a timely fashion.

Overall physicians and nurses were not satisfied with IIT's impact on work processes, and auditing protocol performance was labor intensive due to manual chart review. The average patient blood glucose value, 140-150 mg/dL, exceeded the target of 80-110 mg/dL. Despite organizational changes to standardize patient care, nurse work processes varied and practitioner outcomes did not meet goals.

Computer-based Intensive Insulin Therapy

A multidisciplinary team implemented a computer-based advisor in the VUH SICU that improved intensive insulin therapy performance [21] and produced unintended consequences. In May 2004 an informatics faculty member approached the SICU medical director, a surgeon and critical care physician respected by staff, about developing a computerized IIT approach to improve protocol adherence and capture of process variables for subsequent analysis (e.g. blood glucose values, insulin doses). The SICU medical director commissioned a team of staff nurses, nursing leadership, pharmacists, physicians, and informaticians to assess the IIT process and develop the functionality and interface for a clinical decision support system. Because care provider order entry usage was a regular part of clinical workflow, the team decided to embed the decision support module in the institution's CPOE system. The team tested the intervention and worked with "super user" nurses to refine the tool's ease of use, validate its effectiveness, and assuage concerns about computer-based dosing recommendations. The team also created a training regimen for staff consisting of classroom training for nurses, physician training through orientation, pharmacist training through rounds, continuous informatics staff support, and *ad hoc* instruction from a SICU nurse practitioner educator.

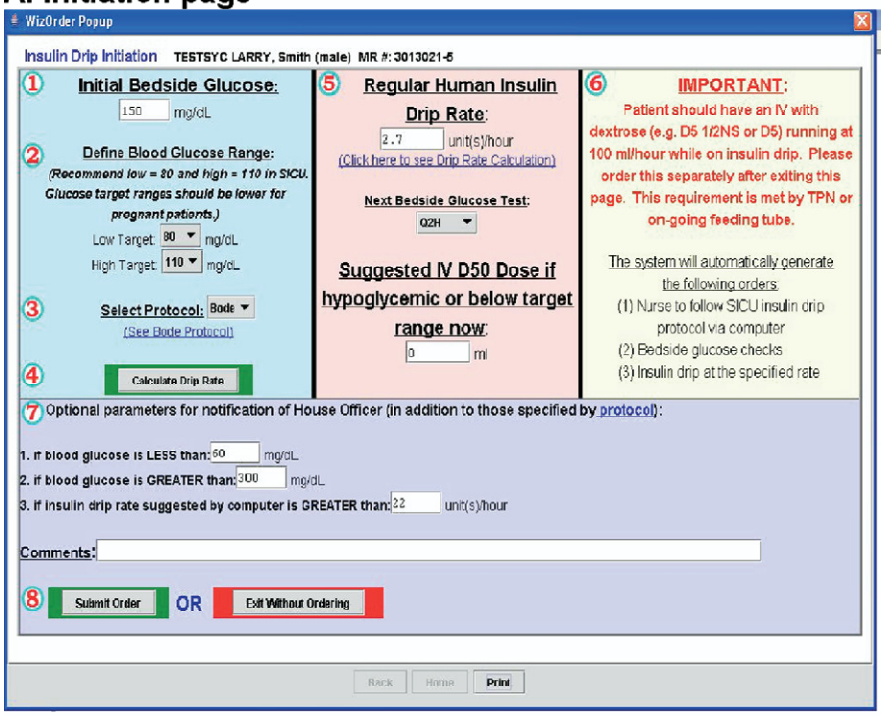
A separate laboratory investment decision influenced nurse IIT workflow, CDSS design, and project timing. Independent of the SICU in September 2004, the laboratory replaced all glucometers across the institution with Lifescan® SureStep® Pro™ devices ($550 each) and installed a data infrastructure consisting of docking stations ($300 each)

and a software interface ($90,000 5-year contract) to automatically transfer blood glucose results from testing devices to the LIS and CDR, thus alleviating the laboratory daily glucose log processing problem. However, test results took up to ten minutes to transfer from device to CDR. Furthermore, devices would not send results until errors were resolved, which occasionally lengthened the transfer process. Data transfer issues coupled with the time-sensitive nature of IIT affected CDSS design: nurses would manually transcribe the latest blood glucose value from the glucometer to the CDSS. To initiate a blood glucose measurement, a nurse used the SureStep® Pro's™ integrated barcode reader to scan barcodes attached to his name badge and the patient's bedside. If barcode scanning failed, a nurse manually entered identification numbers for himself and/or the patient. For legal and billing purposes, the laboratory required BG results entered directly into the LIS by laboratory personnel or automatic device transfer, not manual nurse transcription. Once per shift nursing assistants collected devices and placed them in one of two docking stations to transfer test results and accompanying identification information. After use of SureStep® glucometers became a regular part of workflow, the SICU team resumed its CDSS implementation effort in December 2004.

The computer-based IIT approach introduced a tool to assist nurses with glucose maintenance as well as a practice change to increase physician involvement in glycemic regulation. Instead of starting the protocol when a blood glucose reading exceeded 110 mg/dL, a nurse contacted a physician to initiate therapy using the CDSS module, which consisted of two parts [21]: an initiation screen for a physician to specify care and "notify house officer" parameters, and an insulin rate adjustment screen for a nurse to manually enter blood glucose values (Figure 2). Following a physician's one-time use of the

initiation screen, the nurse accessed the CDSS module according to the protocol schedule (usually Q2H) in order to document blood glucose results and calculate new insulin titrations. The CDSS module utilized a linear equation to determine an insulin titration [21], which eliminated the need for nurses to manually calculate insulin infusion rates. However, nurses could override the CDSS module's recommendations and enter an insulin titration using their clinical judgment when necessary (e.g. simultaneous administration of glucose-affecting medication). After using the CDSS, nurses manually adjusted rates of pharmacy-prepared regular insulin drips (150 units in 150mL normal saline solution with a 24 hour expiration) on Alaris® infusion pumps equipped with Guardrails® software, which was not configured to transfer infusion data to the CDR. Although several years later the institution implemented a barcode medication administration system integrated with other clinical software for administering intermittent medications, nurses did not use it for infusions.

A. Initiation page



B. Titration page

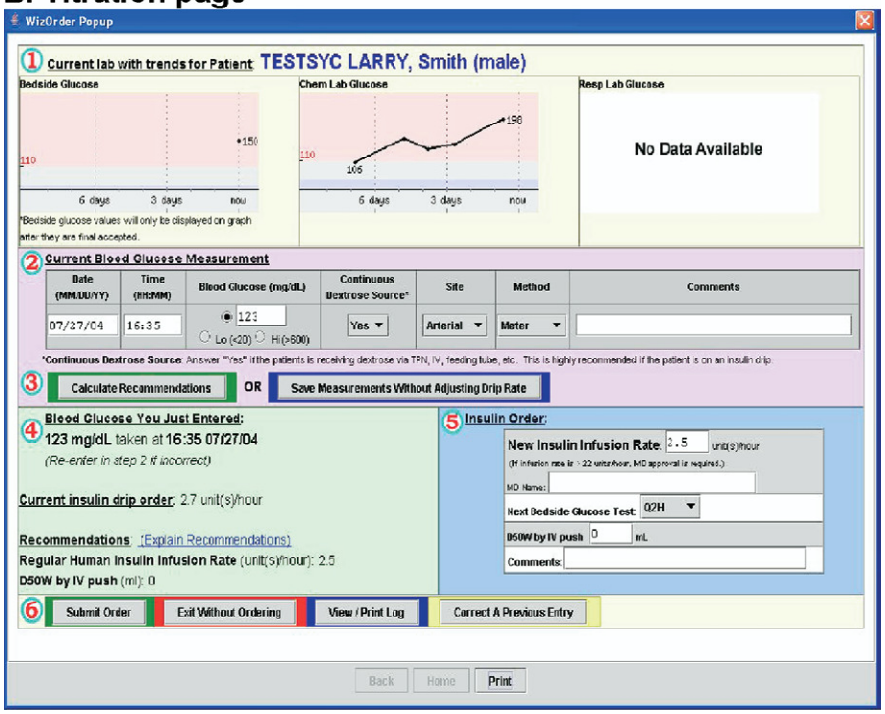


Figure 2. Screenshots of clinical decision support system. Reproduced from Journal of the American Medical Informatics Association, Boord JB et al., 14(3), 278-87, 2007 with permission from BMJ Publishing Group Ltd.

Compared to its paper predecessor, the SICU computer-based IIT protocol increased protocol adherence, reduced time to initiate treatment, expanded the percentage of blood glucose readings in the target range, and simplified record keeping [21]. The hospital's medical, neurological, cardiovascular, and trauma ICUs adopted the same computer-based approach to IIT, and the trauma ICU demonstrated glycemic regulation improvements using the intervention [22]. Neither the SICU or trauma ICU studies were sufficiently powered to detect patient outcome improvements, but in terms of glycemic regulation improvements, the computer-based approach to IIT was a success at the institution.

In addition to improving practitioner performance, the intervention produced unintended consequences related to workflow and technology. First, IIT and other redesigned clinical activities contributed to increased overall CPOE usage, which resulted in clinicians waiting to use terminals in SICU. In response, the institution purchased additional workstations. Second, the clinical data repository's blood glucose and insulin data appeared in duplicate—one set of values entered manually by nurses into the CDSS module, the other captured from the glucometer—with slightly different timestamps and occasionally different values. This resulted in visual clutter in CDR data displays, which may have contributed to clinician confusion or cognitive overload. Third, nurses "double documented" blood glucose and insulin values in the CDSS module and an electronic nursing documentation system, which was implemented two years after the introduction of computer-based IIT and the completion of protocol evaluations in the SICU [21] and trauma ICU [22]. This resulted in a third set of values appearing in the clinical data repository. Furthermore, the approach to computer-based IIT assumed nurses never

made errors when transcribing blood glucose values to calculate and adjust insulin doses. Despite these issues, computer-based IIT remains the standard of care for critically ill patients at VUH.

Summary of case study

In the transition from sliding scale insulin to paper-based IIT to computer-based IIT, Vanderbilt University Hospital enacted considerable organizational changes related to evidence-based protocol development, nurse workload, physician involvement, blood glucose testing and infrastructure, and informatics development and support. Forces beyond SICU control—a local nursing shortage, the laboratory's decision to upgrade glucometers, and the institution's decision to implement nursing documentation software—affected the trajectory of intensive insulin therapy efforts over time, but SICU leadership and multidisciplinary cooperation helped ensure the project's success. Other institutions may experience similar organizational changes as part of their computer-based IIT efforts. Changes to glycemic regulation, glucometer usage, and computerization occurred gradually over time at VUH, which conceivably enabled stakeholders to adapt to process modifications more easily. In contrast, other institutions may face greater change management challenges if abruptly shifting from sliding scale insulin to computer-based IIT. Computer-based intensive insulin therapy is a complex, multifaceted organizational undertaking that requires substantial commitment to change and presents opportunities for further inefficiency and error reduction.

Discussion

Kaplan's themes of clinical decision support system evaluation [17] are present in evaluations of computer-based intensive insulin therapy. In order to optimize computer-based intensive insulin therapy process execution, researchers and practitioners should address social, organizational, and contextual issues determining how and why implementations are successful. From our literature review and case study, three aspects of computer-based IIT appear particularly salient: (1) the relationship between clinical information systems, CDSS, testing devices, users, and error; (2) nurse perspectives; and (3) organizational change.

Technology, users, and error

The interaction of hardware, clinical information systems, clinical decision support modules, blood glucose devices, and clinicians is complex, time consuming, and susceptible to error, yet most evaluations of computer-based IIT take it for granted. For example, a study of computer-based IIT conducted at Vanderbilt University Hospital stated that "[blood glucose] values are downloaded directly from the glucometer to the computer order entry system" [39], which misrepresents the reality of manual data entry and possibility for error inherent in the process. Installation of additional docking stations at each bedside to facilitate data transfer may be cost prohibitive or hindered by slow data transfer times. The purchase of glucometers that transmit data wirelessly across a hospital network to clinical data repositories in a reliable fashion may also be cost prohibitive. Furthermore, controversy surrounds the use of handheld glucometers for intensive insulin therapy due to possible inaccurate results [58-61]. Some studies

suggest continuous glucose monitoring technologies can replace handheld glucometers today [62, 63] while others propose additional refinement [64-66] or recommend against their usage [67]. In contrast to computer-based IIT, computer-based anticoagulation therapy [68] relies on a central laboratory's activated partial thromboplastin time results, which are processed less frequently [69] and are arguably more accurate than handheld glucometer test results. For computer-based intensive insulin therapy, the optimal configuration of testing devices, computers, decision support interfaces, and personnel is not yet understood.

Nurse perspectives

Few studies have focused on nurse perspectives regarding intensive insulin therapy, particularly for computer-based approaches, and additional study can potentially improve protocols and workflow. A direct observation study of a paper-based IIT protocol showed that nurses required between three and nine minutes (mean 4.72, SD 1.13, median 4.67) to obtain a testing device, measure blood glucose, and adjust insulin [31]. A separate time-motion study found nurses required 20-30 minutes to complete IIT tasks and document care [70]. Times varied due to treatment differences for hypoglycemia, hyperglycemia, and euglycemia [70] as well as nurses locating devices, troubleshooting devices, caring for patients with isolation precautions, and occasionally ignoring hygiene and safety requirements [31]. Such issues may also influence provision of computer-based IIT, and CDSS and other computer system usage during IIT administration may have other unintended consequences that add to nurse work or detract

from patient safety. In a study of computer-based IIT[2], nurses indicated the following reasons for declining CDSS recommendations: patient blood glucose trends, concurrent administration of medications prepared in a glucose solution, nutrition changes, concurrent epinephrine administration, hypothermia, agitation, and previously entered incorrect data [71]. The results of this study show some of the effects of CDSS on IIT and demonstrate the value of nurse-focused evaluation of computer-based IIT in making workflow and care barriers explicitly understood. New dosing algorithms can potentially incorporate such factors so that IIT protocols reflect the realities of clinical practice and judgment.

Organizational change

The same computer-based intensive insulin therapy protocol used in two hospitals, or two units in the same hospital, might produce variability in social processes and clinical performance. Examining the social organization of computer-based IIT evaluations shows that the effects of computer-based IIT implementations on healthcare organizations are not explicitly reported. Our case study demonstrates how a surgical intensive care unit with strong leadership and institutional informatics support overcame technological and organizational barriers to implement computer-based IIT. Although other ICUs in the institution now use the same computer-based IIT approach, the intervention may or may not appropriately match workflow, organizational, and clinical needs because it was designed for the SICU. A recent multi-site IIT trial [72], which showed increased mortality for patients treated with IIT versus those treated with

[2]This study did not meet literature review criteria as it was published in June 2008 (and not yet indexed in ISI Web of Science) and did not cite the Leuven study.

conventional therapy, used the same computer-based IIT dosing calculator in all sites [73]. The researchers did not explore computer-based IIT process execution across sites although such issues may have affected clinical performance.

Future research

To understand computer-based IIT usage, future studies should combine quantitative and qualitative methods. First, by comparing manually entered blood glucose data and automatically captured values from glucometers, we can determine the frequency and effect of incorrect data on insulin dosing and blood glucose variability. Most computer-based IIT studies utilize handheld glucometers and assume the transcription of blood glucose values from testing devices to CDSS is error free. A study examining ventilator settings automatically captured from a device versus manually entered into a computerized CDSS showed 3.9% of computer-generated recommendations contained incorrectly entered data [74]. Blood glucose value errors may potentially contribute to blood glucose variability, which has been associated with mortality [40].

Second, investigating the impact of CDSS insulin dose overrides can assess the effectiveness of nurses' clinical judgment. Studies of medication-related CDSS embedded in CPOE systems show physician override rates of computer-based recommendations as high as 91% [75, 76], and researchers suggest using quantitative and qualitative methods to understand clinician-CDSS interaction [75]. Nurses deviate from CDSS suggestions when a clinical situation is more complex than a computer algorithm's parameters [71]. However, little is known about whether nurses' clinical judgment is

appropriate under these circumstances. Quantifying the frequency and effect of insulin dose overrides on blood glucose variability can potentially answer this question. Examining medication administration records and clinical documentation corresponding to nurse overrides of CDSS recommendations may provide indication of additional variables for IIT dosing algorithms to consider (e.g. corticosteroids).

Third, the use of ethnographic methods to study computer-based intensive insulin therapy can potentially lead to software and process enhancements. An approach from anthropology, ethnography has been used in clinical research to improve surgical resident handoffs [77] and in informatics research to identify and resolve incorrect software design assumptions [47, 78]. Extensive direct observation of clinicians using CDSS for IIT in the field can reveal benefits and drawbacks of the current approach with respect to computer system usage, care processes, and issues currently unknown. Additionally, ethnographic study of computer-based IIT in multiple ICUs can potentially show site-specific differences in social organization of the intervention that may affect clinical performance. By understanding the use of computer-based IIT in real world settings, researchers and practitioners can make care workflow and protocol modifications to potentially achieve the morbidity and mortality improvements demonstrated in the Leuven study.

Limitations

There are limitations to this study. First, we examined intensive insulin therapy in one intensive care unit at a single institution with sophisticated clinical informatics systems. Findings may not generalize to sites with less informatics development. Future

research will examine additional ICUs at Vanderbilt University Hospital and then proceed to additional institutions. Second, other theoretical approaches might be more illuminative than institutional theory's social organization of computing in examining computer-based intensive insulin theory. For example, social interactionism, "fit," and "the 4 C's" may be potentially useful methods [18].

Conclusion

Our analysis contributes to the understanding of computer-based intensive insulin therapy's social, organizational, and contextual aspects. More broadly, this paper addresses the underreported elements explaining how and why clinicians use CDSS interventions. We suggest future IIT CDSS research involve quantifying error, assessing clinical judgment in overriding CDSS recommendations, and directly observing nurse use of IIT CDSS with respect to other care processes and clinical information systems. Researchers and practitioners can use this study to approach computer-based intensive insulin therapy and clinical decision support system improvement projects.

CHAPTER III

EFFECTS OF BLOOD GLUCOSE TRANSCRIPTION MISMATCHES ON A COMPUTER-BASED INTENSIVE INSULIN THERAPY PROTOCOL

Introduction

Intensive insulin therapy (IIT) is the standard of critical care but concerns exist regarding its effectiveness and safety [79]. In surgical and trauma intensive care unit patients treated with a computerized intensive insulin therapy protocol [21, 22], blood glucose variability [80] and insulin resistance [81] were associated with mortality, and delayed blood glucose measurements were associated with severe hyper- and hypoglycemia [10, 39]. These findings suggest that workflow may influence computer-based IIT performance and patient outcomes [39]. Clinical decision support systems (CDSS) for IIT are commonplace [82, 83] and many implementations rely on manual transcription of blood glucose values to generate recommendations, a practice that could yield unintended consequences including error [82, 83]. CDSS IIT approaches that ignore transcription mismatches—when manually entered values do not equal corresponding automatically captured device values—implicitly assume differences between matched and mismatched data are non-significant and do not affect IIT protocol performance. The purpose of this study was to measure the frequency of blood glucose transcription mismatches and their effect on intensive insulin therapy protocol performance.

Methods

The cohort included all critically ill or injured mechanically ventilated patients treated with the computer-based intensive insulin therapy protocol in the surgical and trauma intensive care units at Vanderbilt University Hospital, an urban tertiary care facility. We examined only patients with five or more CDSS IIT values. Table 3 presents patient characteristics.

Table 3. Characteristics of study patients.

	SICU n = 1,883	**TICU** n = 2,152
Treatment period	November 2004-February 2009	October 2005-February 2009
Number of beds	21	31
Nurse to patient ratio	2:1	2:1
Age, years	58.9 ± 14.6	41.5 ± 18.8
Male sex, no. (%)	1,130 (60%)	1,576 (73%)
Body mass index, kg/m^2	29.6 ± 11.8	26.9 ± 6.9
Admission service		
Trauma	71 (3.8%)	2044 (95%)
Liver transplant	342 (18.2%)	
Emergency general surgery	338 (18.0%)	
Vascular surgery	194 (10.3%)	
General surgery	154 (8.2%)	62 (2.9%)
Cardiac/thoracic surgery	119 (6.3%)	1 (< 0.1%)
Oncology/endocrine surgery	97 (5.2%)	1 (< 0.1%)
Urology	83 (4.4%)	
Orthopaedics	76 (4.0%)	20 (0.9%)
Other	409 (21.7%)	24 (1.1%)
APACHE II (SICU)	18.9 ± 6.5	
ISS (TICU)		27.7 ± 11.9
History of diabetes	206 (10.9%)	71 (3.3%)
Hospital length of stay, days	17.8 ± 16.1	14.1 ± 13.9
ICU length of stay	9.1 ± 10.6	9.6 ± 10.6
Mortality	284 (15.1%)	323 (15.0%)

Data represent mean ± standard deviation unless noted. SICU, surgical intensive care unit. TICU, trauma intensive care unit. APACHE, Acute Physiology and Chronic Health Evaluation. ISS, Injury Severity Score. Nurse to patient ratio changes to 1:1 for complex patients.

Figure 3 and Table 4 describe CDSS IIT in detail. CDSS [21, 22, 81, 83] uses a linear equation [51] that adjusts a "multiplier" according to current and previous blood

glucose (BG) values. Slight (e.g. 138 vs. 139) and large differences (e.g. 138 vs. 238) in BG value transcription can have major, minor, or no effects on dosing recommendations depending on clinical scenario.

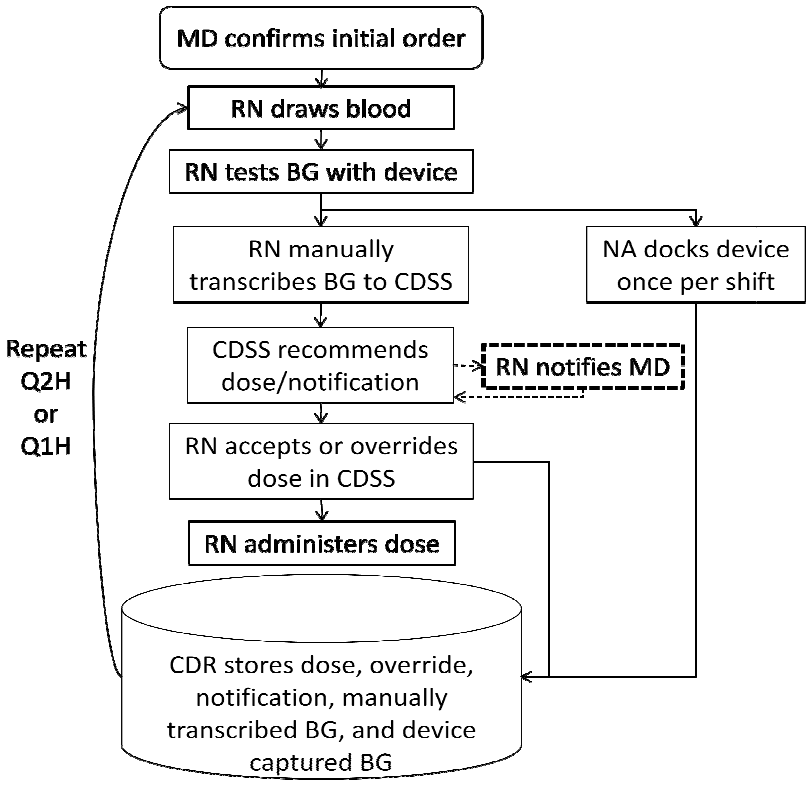


Figure 3. IIT CDSS workflow. SICU and TICU patients with a blood glucose (BG) value ≥ 110 mg/dL receive intensive insulin therapy according to a standardized protocol embedded in the institution's computerized order entry system. A physician (MD) confirms the therapy's blood glucose target range (usually 80-110 mg/dL) and critical parameters (blood glucose and insulin values) for generating an alert for a nurse (RN) to notify a MD (process designated by dashed lines). A nurse (RN) performs blood glucose measurements of arterial blood when possible using a Lifescan® SureStep® Pro™ handheld testing device. The system does NOT remind nurses to measure BG. The device stores each BG value along with a patient's medical record number, which the nurse scans from a barcode or enters manually. A nurse can accept a CDSS recommended dose or type in a different dose amount to be administered, which the system logs as an override. A nurse aide (NA) places handheld testing devices in a docking station so that blood glucose values, along with timestamps and patient identifiers, transfer to the clinical data repository (CDR) once per nursing shift.

Table 4. CDSS IIT algorithm

Variables

- BG = manually transcribed blood glucose value (mg/dL)
- Previous BG = manually transcribed BG value from previous protocol iteration
- Low = low BG target
- High = high BG target
- Multiplier = initially 0.03; never less than 0
- D50 = intravenous 50% dextrose rounded to nearest 5 (mL) to treat hypoglycemia

Measurement interval

- Nurse measures BG every 2 hours.
- If BG < 60, nurse measures every 1 hour until BG > 60 and then resumes 2 hour interval.

Initiation

- Physician specifies therapy parameters (default values shown)
    - Low = 80
    - High = 110
    - Critical threshold values for system to alert nurse to notify physician
        - Critical low BG = 60
        - Critical high BG = 200
        - Critical insulin rate = 22
- If BG < 60
    - D50 = 0.5 * (100 - BG)
    - Multiplier = 0
- If BG < Low AND BG > 59
    - D50 = 0.5 * (100 - BG)
    - Multiplier = 0
- If BG > Low
    - Multiplier = 0.03

Ongoing titration

- If BG < 60
    - D50 = 0.5 * (100 - BG)
    - Multiplier = Multiplier - 0.02
    - Measurement interval = 1 hour
- If BG < Low AND BG > 59
    - D50 = 0.5 * (100 - BG)
    - Multiplier = Multiplier - 0.01
- If BG <= High AND BG >= Low
    - Multiplier = Multiplier
- If BG > (1.5 * High) AND Multiplier = 0
    - Multiplier = 0.01
- If BG > 200 OR BG > High AND Previous BG > High
    - Multiplier = Multiplier + 0.01
- If BG > High AND BG < 200 AND Previous BG < high
    - Multiplier = Multiplier
- If Previous BG > (1.25 * High) AND BG >= Previous BG AND Multiplier = 0
    - Multiplier = 0.01

Formulation calculation

- Insulin rate (units/hour) = (BG - 60) * Multiplier

For each patient, we retrospectively linked each manually transcribed BG value with the device BG value closest to the manually transcribed value's timestamp within a

one hour window—one hour before or one hour after—to accommodate for time variations between computers and devices. Manually transcribed and device captured BG value pairs that were equal were designated matched and those unequal mismatched. For mismatched instances, we recalculated CDSS recommendations using corresponding device BG values. We assumed nurses transcribed BG values independently; thus, we considered previous input to be correct and examined the effect of each manual transcription on CDSS output.

Measurements

The study objective was to determine the frequency of blood glucose mismatches and their effect on IIT protocol performance. We hypothesized (1) manually transcribed blood glucose values do not always equal device values; (2) matched and mismatched data differ in terms of alerts generated by CDSS; (3) matched and mismatched data differ in terms of blood glucose variability; (4) matched and mismatched data differ in terms of dosing; and (5) recalculated doses differ from corresponding actual doses but are similar to recommended doses generated with matched data.

To assess alerts, we compared historical CDSS output versus output generated from corresponding automatically captured device values. To measure BG variability, we focused on blood glucose excursions in terms of successive device BG change [80], hypoglycemia (i.e. current manually transcribed BG $\geq$ 60 and next manually transcribed BG $<$ 60), and hyperglycemia (i.e. current manually transcribed BG $<$ 200 and next manually transcribed BG $\geq$ 200). Successive BG change reflects both steady and rapid

fluctuations in the distribution of BG values [80]. Hypoglycemia[3] and hyperglycemia measure safety and effectiveness, respectively.

To evaluate dosing, we examined insulin dose, equation multiplier, and intravenous 50% dextrose (D50) dose. Insulin dose and multiplier have been identified as markers for insulin resistance [81]. To control the effect of nurse overrides, we excluded override doses and examined recommended doses. We then compared matched doses, mismatched actual doses generated with manually transcribed values, and mismatched recalculated doses generated with corresponding device values. Matched recommended doses, free of override bias and mismatched data, served as the reference standard of IIT protocol adherence.

Statistical analysis

To summarize and compare normally distributed continuous variables, we determined mean and standard deviation and used two sample *t* tests for independent samples. To summarize and compare non-normally distributed continuous variables, we determined median and interquartile range (IQR) and used the Wilcoxon rank-sum test for unpaired data and Wilcoxon signed rank test for paired data. We used a χ^2 test to compare differences in proportions. A two-sided *p* value less than 0.05 indicated statistical significance. To perform calculations we used STATA 10.1 (STATA Corp., College Station, TX). All patient data was stored in a secure, password-protected database and de-identified prior to analysis and reporting. The Vanderbilt University Institutional Review Board approved this study.

[3] We defined hypoglycemia as BG < 60 in accordance with National Quality Forum "never event" specifications for reporting adverse events in United States hospitals [84].

Results

Mismatched pairs accounted for 5.3% of IIT data (Figure 4). Matched and mismatched pairs differed in most respects. Mismatched data caused CDSS to trigger 93 false alerts and fail to issue 170 alerts for nurses to notify physicians. Blood glucose variability differed between matched and mismatched data in four of six measures. Tables 5-7 presents detailed findings.

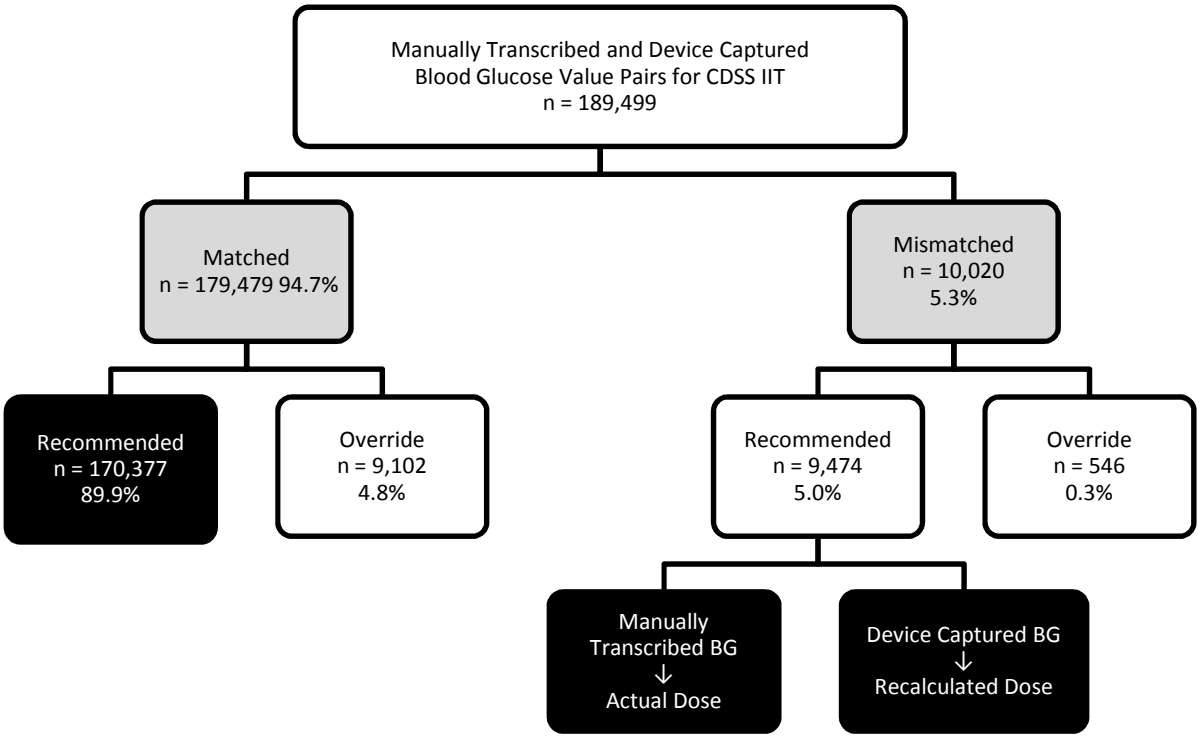


Figure 4. Categorization of IIT manually transcribed and device captured pairs and subsequent insulin doses generated using blood glucose (BG) values. Gray areas include recommended and override doses whereas black areas include only recommended doses to control for effect of overrides. 203,188 IIT instances were available for analysis. 11,901 manually transcribed blood glucose values had no corresponding device value identified and were excluded. An additional 1,788 IIT instances (< 1%) produced output unequal to historical CDSS recommendations and were excluded. 189,499 pairs of manually transcribed and device captured blood glucose values remained for analysis

Table 5. Characteristics of matched and mismatched IIT data.

	Matched n = 179,479	**Mismatched** n = 10,020		**Matched vs. Mismatched p < 0.05**		
Insulin override	9,102 (5.1%)	546 (5.4%)		0.094		
D50 administration	11,399 (6.4%)	635 (6.3%)		0.076		
BG mg/dL	**Matched**	**Manually Transcribed**	**Device Captured**	**Matched vs. Transcribed**	**Matched vs. Device Captured**	**Transcribed vs. Device Captured**
BG > 200, no. (%)	5,298 (3.0%)	571 (5.7%)	629 (6.3%)	**< 0.001**	**< 0.001**	**< 0.001**
BG 150-200	17,734 (9.9%)	1,357 (13.5%)	1,373 (13.7%)	**< 0.001**	**< 0.001**	**< 0.001**
BG 110-150	67,575 (37.7%)	3,451 (34.4%)	3,513 (35.1%)	**< 0.001**	**< 0.001**	**< 0.001**
BG 80-110	76,101 (42.4%)	3,926 (39.2%)	3,466 (34.6%)	**< 0.001**	**< 0.001**	**< 0.001**
BG 60-80	10,654 (5.9%)	579 (5.8%)	858 (8.6%)	0.594	**< 0.001**	**< 0.001**
BG < 60	2,117 (1.2%)	136 (1.4%)	181 (1.8%)	0.092	**< 0.001**	**< 0.001**
BG mean ± SD	117 ± 36	124 ± 48	125 ± 49	**< 0.001**	**< 0.001**	**< 0.001**

Percentages are based on column n. Proportions compared using χ^2 and mean ± SD compared using *t*-test. Overrides and D50 administrations occurred similarly between matched and mismatched. Matched mean BG was significantly less than manually transcribed and device captured values. Differences in proportions within mismatched pairs show a tendency toward manual transcription of values in the BG 80-110 band. Mismatched pairs had smaller proportions of BG 80-110 and 110-150 and greater proportions of BG 150-200 and >200 compared to matched pairs, which may explain mean BG differences.

Table 6. Alerts generated by CDSS using matched and mismatched data and mismatched data only.

	Matched and Mismatched				**Mismatched Only**		
	Recalculated				**Recalculated**		
Actual		**Alert**	**No alert**	**Actual**		**Alert**	**No alert**
	Alert	8,921	93		**Alert**	439	93
	No alert	170	180,315		**No alert**	165	9,323

CDSS alerts nurse to notify physician if BG input or insulin dose equals one of three physician-specified values (typically BG ≤ 60, BG ≥ 200, and insulin ≥ 22 U/h). Specificity, the proportion of alerts correctly not issued, was high (0.999). Sensitivity, the proportion of alerts correctly issued, was high (0.981) for matched and mismatched but considerably lower (0.727) when examining mismatched only.

Table 7. Blood glucose variability of matched and mismatched data.

	Matched	**Mismatched**	**p < 0.05**
Successive change BG_n - BG_{n+1} (mg/dL)	-1.85 ± 33.53	-2.02 ± 37.57	0.574
Successive change absolute	17 (4.5-29.5)	16 (2-30)	**< 0.001**
Successive change positive	17 (4.5-29.5)	19 (5-33)	**< 0.001**
Successive change negative	-17 (-29 to -5)	-20 (-34.5 to -5.5)	**< 0.001**
Hypoglycemia	1,948 (1.1%)	125 (1.2%)	0.129
Hyperglycemia	1,552 (0.9%)	228 (2.3%)	**0.016**

Mean ± SD compared using *t*-test and proportions compared using χ^2 test. Successive change reflects steady and rapid fluctuations in BG levels while hypoglycemia (current manually transcribed BG >= 60 and next manually transcribed BG < 60) and hyperglycemia (current manually transcribed BG < 200 and next manually transcribed BG >= 200) measure potential safety threats and effectiveness, respectively.

Compared to matched data, mismatched data generated lower dosing parameters overall with some exceptions (Table 8). Hypoglycemia occurred in 1.1% (n=2,073) of total CDSS IIT activity. 6% (n=125) of these instances contained mismatched data, and actual dose was 22.9% higher than recalculated ($p<0.001$). Additionally, matched recommended dose was 37.2% higher than recalculated ($p<0.001$). Hyperglycemia occurred in 0.9% (n=1,780) of total CDSS IIT activity. 12.8% (n=228) of these instances contained mismatched data, and actual dose was 42.4% lower than recalculated ($p < 0.001$). Additionally, matched recommended was 14.6% lower than recalculated ($p=0.006$).

Table 8. Dosing parameters for matched and mismatched data including recalculated doses.

	Total (Recommended & Override)			**Recommended Only**					
	Matched	Mismatched	Matched vs. Mismatched	Matched Recommended	Mismatched Actual	Mismatched Recalculated	Matched Recommended vs. Mismatched Actual	Matched Recommended vs. Mismatched Recalculated	Mismatched Actual vs. Mismatched Recalculated
Overall n (%)	179,479 (94.7%)	10,020 (5.3%)		170,377 (94.7%)	9,474 (5.3%)				
Insulin Units/hour (U/hr)	3.8 (2.1-6.5)	3.6 (2.0-6.1)	**< 0.001**	3.9 (2.1-6.5)	3.6 (2.0-6.1)	3.7 (2.0-6.2)	**< 0.001**	**< 0.001**	0.6991
Multiplier	0.076 (0.048-0.117)	0.066 (0.038-0.109)	**< 0.001**	0.760 (0.048- 0.117)	0.0650 (0.038-0.108)	0.0647 (0.037-0.107)	**< 0.001**	**< 0.001**	**< 0.001**
D50 mL	15 (5-10)	15 (5-10)	0.283	15 (5-10)	15 (5-10)	15 (5-10)	0.251	**< 0.001**	**< 0.001**
Hypoglycemia n (%)	1,948 (1.0%)	125 (0.1%)		1,872 (1.0%)	107 (0.1%)				
Insulin U/hr	4.2 (2.2-7.3)	3.4 (1.7-6.0)	**0.012**	4.3 (2.25-7.3)	3.5 (1.8-6.0)	2.7 (1.1-5.7)	**0.022**	**< 0.001**	**< 0.001**
Multiplier	0.079 (0.050-0.120)	0.060 (0.033-0.116)	**0.01**	0.080 (0.051-0.120)	0.060 (0.033-0.119)	0.060 (0.030-0.120)	**0.008**	**0.002**	**< 0.001**
Hyperglycemia n (%)	1,552 (0.8%)	228 (0.1%)		1,411 (0.8%)	214 (0.1%)				
Insulin U/hr	4.1 (2.2-7.0)	3.3 (2.15-4.2)	**< 0.001**	4.1 (2.4-7.1)	3.3 (2.3-4.2)	4.7 (3.8-6.7)	**< 0.001**	**0.006**	**< 0.001**
Multiplier	0.061 (0.032-0.100)	0.030 (0.030-0.059)	**< 0.001**	0.060 (0.031-0.099)	0.030 (0.030-0.056)	0.030 (0.030-0.056)	**< 0.001**	**< 0.001**	0.317

Recommended Only controls for effect of override doses. Matched and mismatched data generated significantly different insulin dosing parameters, especially for episodes of hypoglycemia and hyperglycemia. 27.5% of patients (n = 1,110) experienced at least one episode of hypoglycemia (current BG $\geq$ 60 and next BG < 60). Severe hypoglycemia (current BG $\geq$ 40 and next BG < 40) occurred in 172 instances (0.09% overall), and six contained mismatched data. 3.9% of patients (n = 157) experienced at least one episode of severe hypoglycemia. Recalculated D50 dose (mean SD: 14 ± 9) was significantly lower than mismatched actual (mean SD: 17 ± 8, $p < 0.001$) and matched recommended (mean SD: 16 ± 5, $p < 0.001$). D50 doses in table are skewed because of 5mL dose increments.

Discussion

Manual transcription of blood glucose values is a source of intensive insulin therapy process variability associated with patient care changes and affecting clinical data and provider workflow. Manual transcription may affect paper-based IIT, but computer-based approaches provide detection of mismatches more readily. In a review of CDSS IIT approaches, Eslami et al identified manual transcription of blood glucose values as a "critical safety issue" [82]. In our study, overall insulin doses generated with matched and mismatched data differed, but recalculated doses were similar to actual doses, suggesting that the effect of mismatched data is insignificant overall. However, in cases of hypoglycemia and hyperglycemia, dosing differences caused by mismatched data may be clinically significant: the administration of recalculated doses that were less than and greater than actual recommendations, respectively, might have prevented "never events" [84] from occurring. Other patient-level factors may contribute to blood glucose variability, but this study quantifies mismatched data as a parameter to consider for IIT improvement.

Matched and mismatched data exhibited significantly different characteristics and may represent distinct populations. Compared to matched data, mismatched data showed a significantly greater mean BG value, lower multiplier, greater magnitude of successive BG change, and greater occurrence of hyperglycemia. Additionally, mismatched data generated fewer "notify physician" alerts than would have occurred had transcribed values matched device values. Mismatches occurred about as frequently as three other system events—D50 administrations and nurse-initiated insulin overrides, which were expected, and manual transcriptions missing device values, which were unanticipated.

Table 9 lists potential reasons for mismatched and missing data [30, 85]. Manual BG transcription affects protocol performance, and our future work involves direct observation and nurse interviews to understand CDSS IIT usage.

Table 9. Potential reasons for missing data and mismatched data observed in study.

Missing Data	Mismatched Data

• Testing device malfunction
• Testing device clock set incorrectly
• Incorrect medical record number used on testing device
• BG value obtained from testing device not integrated with laboratory information system
• Failure/forgetfulness to check a BG value
• Deliberate falsification of BG value
• Device to laboratory information system transfer failure
• Laboratory information system to clinical data repository transfer failure
• Other clinical information system failure (e.g. data backup)
	• Chance
	• Nursing workload and human factors [13]
	  o Two hour vs. one hour monitoring interval
	• Units of measure (mg/dL vs. mmol/L)
	  o A device value of 138 mg/dL may be transcribed incorrectly as 238 mg/dL, but it is less likely that 7.6 mmol/L (138 mg/dL) would be entered as 13.2 mmol/L (238 mg/dL).
	• Deliberate action
	  o Entering lower BG value in order to administer less insulin due to "fear of hypoglycemia" [14]
	  o Entering different BG value to avoid triggering alert (e.g. 61 mg/dL vs. 60 mg/dL)
	  o Entering different BG value to avoid changing multiplier (e.g. 110 mg/dL vs. 111 mg/dL)
	  o Entering different BG value to avoid administering D50 (e.g. 80 mg/dL vs. 79 mg/dL)

Our time-based approach to linking manually transcribed and device captured BG values for data comparison—one hour before to one hour after— might have also produced missing and mismatched data. However, the approach is justified given the challenge of examining voluminous retrospective data that is only identified by medical record number and timestamp. Additionally, missing data suggests that additional mismatches could have occurred. See [83] for more detail regarding BG device data transmission issues

Results of this study will fuel the debate for replacing handheld glucometers with continuous monitoring technology [62, 63]. The rate of insulin doses generated with mismatched data exceeds the 3.4 per million events defect rate in industrial Six Sigma quality efforts [86] but compares favorably with studies of data entry error and CDSS [87, 88]. Although automatic capture of device data can improve CDSS recommendations [74], implementing new monitors that automatically measure and

record BG data poses challenges related to cost, systems integration, and unintended consequences. Researchers and practitioners can explore incremental variability reductions through CDSS interface design, nursing staff education, and electronic surveillance.

This study has strengths and weaknesses. The large dataset reflects standardized care for two intensive care units, and high compliance with computerized recommendations shows the protocol is well received by clinicians. Findings may not generalize to sites using different dosing equations or with less informatics development and/or organizational commitment. However, several institutions [82, 83] use the equation studied [51, 52]. Because we calculated the multiplier using mismatched current but not mismatched previous device BG values, this analysis does not show impact over time of improper multiplier adjustments. This study examined IIT protocol performance, not individual patient effects, and showed correlation, not causation, between data mismatches and BG changes.

Mismatched data occurred relatively infrequently, influenced IIT performance, appear to have varying clinical impact and etiology, may compromise patient safety, and may represent a different population than matched data. Researchers and practitioners should pay greater attention to frequency and effect of mismatched blood glucose data on IIT performance.

CHAPTER IV

CHARACTERISTICS AND EFFECTS OF NURSE DOSING OVERRIDES ON COMPUTER-BASED INTENSIVE INSULIN THERAPY PROTOCOL PERFORMANCE

Introduction

Intensive insulin therapy (IIT) is the standard of critical care but recent studies question the treatment's mortality benefit and safety [72, 79, 89, 90]. Intensive care units commonly employ IIT, a nurse-driven treatment combining frequent blood glucose measurements and insulin titrations, to achieve tight control of patients' blood glucose levels. Factors affecting intensive insulin therapy performance include patient populations, blood glucose monitoring techniques, blood glucose target ranges, nutrition provisions, nurse staffing ratios, and molecular and cellular features [91]. Institutions increasingly use computerized clinical decision support systems (CDSS) to deliver protocol-based intensive insulin therapy [82, 83], and computer-based workflow has been identified as another source of variability affecting IIT [10, 39, 83, 92]. Researchers have shown a relationship between timing of blood glucose measurements and hypo- and hyperglycemia [10, 39], and previously we demonstrated the effect of data entry error on IIT CDSS recommendations and blood glucose variability [92]. In the present study we examined nurse insulin dosing overrides, or deviations from IIT CDSS protocol recommendations, to determine if and how the behavior affects intensive insulin therapy performance.

Existing studies have quantified the frequency and rationale of nurse overrides, but little is known about the quantitative characteristics of IIT CDSS overrides and their effect on blood glucose variability and insulin resistance, two measures of IIT CDSS protocol performance associated with mortality [80, 81]. Compliance with IIT CDSS recommendations varies from 77% [53] to up to 98% [10, 71, 93], and nurse reasons for overrides include concerns about hypoglycemia due to data trends, administration of glucose-affecting medications, and co-morbidities [71]; disagreement with dose recommendations [71, 93]; and workflow issues [71, 93]. The objective of this study was to determine the conditions leading to and resulting from nurse override of IIT CDSS recommendations. We compared blood glucose variability and insulin resistance when nurses administered recommended and override doses. We hypothesized that rates of hypoglycemia and hyperglycemia would be higher for recommended than override doses.

Methods

Setting

This study focused on IIT CDSS usage in the 21-bed surgical and 31-bed trauma intensive care units (SICU and TICU) at Vanderbilt University Hospital, a 501-bed academic urban tertiary care facility in Nashville, Tennessee. Critical care attending physicians from the Division of Trauma and Surgical Critical Care oversee unit management and patient care decisions using evidence-based protocols intended to standardize care and reduce practice variability. Although clinicians in other intensive care units at the institution treat patients using IIT CDSS, we focused our investigation on

SICU and TICU due to the units' common management and care processes. The ratio of patients to nurses is 2:1 overall and 1:1 for complex patients. All patients admitted to the SICU and TICU receive standardized nutrition through D5, D10, enteral, or parenteral sources.

SICU piloted IIT CDSS in November 2004 and required nurses to treat all eligible patients using IIT CDSS starting in December 2005 [21]. In June 2005 IIT CDSS was modified to require nurses to identify a patient's nutrition source and automatically trigger an order for intravenous 10% dextrose if a patient had no nutritional support and a current BG less than 80 mg/dL. The intent of the change was to limit hypoglycemia. TICU implemented IIT CDSS as the standard of care in October 2005 [22]. The IIT CDSS recommendation algorithm has remained unchanged since project inception, and SICU and TICU researchers have demonstrated effective hyperglycemia control with limited hypoglycemia [21, 22]. We investigated all SICU and TICU IIT CDSS recommended and override doses over time.

IIT CDSS description

Critically ill or injured mechanically ventilated patients with a blood glucose value above 110 mg/dL receive intensive insulin therapy according to a protocol embedded in the institution's computerized order entry system. As described elsewhere [21, 22, 83, 92], a physician confirms the initial protocol order, which directs a nurse to measure a patient's blood glucose and administer insulin according to CDSS recommendations at two hour intervals by default or one hour intervals due to hypoglycemia risk. IIT CDSS instructs a nurse to administer an intravenous 50%

dextrose dose and recheck the patient's blood glucose in one hour if BG < 80 mg/dL. For BG < 60 mg/dL, the protocol additionally instructs a nurse to stop insulin administration for one hour. All other protocol iterations occur at two hour intervals. IIT CDSS does not remind nurses to measure BG, and timing of BG measurements can vary in practice [39].

Based on Bode [51] and White [52]'s dosing equation, IIT CDSS adjusts a coefficient "multiplier," an estimate of a patient's insulin resistance according to current and previous blood glucose measurements, for use in this formula: insulin dose (units/hour) = (blood glucose in mg/dL - 60) * multiplier [21]. Initially set to 0.03, the multiplier increases by 0.01 when BG levels indicate hyperglycemia, decreases by 0.01 or 0.02 depending on degree of hypoglycemia, and cannot fall below zero [21]. A greater multiplier value reflects increased insulin resistance. After the initial order sets the multiplier, IIT CDSS obtains the previous multiplier by solving the dosing formula using the previous BG and insulin rate stored by the order entry system as inputs.

IIT CDSS calculates recommendations after a nurse manually transcribes, or enters via keyboard, a blood glucose value obtained from a handheld testing device, selects a patient's nutrition source, and clicks the "calculate recommendations" button [21, 22, 83, 92]. Upon reviewing the CDSS dose recommendation, a nurse can either accept or override it by replacing the recommended dose value in the IIT CDSS interface via keyboard. After a nurse confirms IIT CDSS activity in the interface, the order entry system updates the existing order and logs the insulin rate, multiplier, override status, blood glucose value, nutrition source, and timestamp along with patient and nurse identifiers. The nurse then adjusts the intravenous insulin pump to use the IIT CDSS

insulin rate. There is no electronic interface between intravenous insulin pumps and clinical information systems. Handheld testing devices store each BG value with a timestamp as well as a nurse identifier and patient medical record number; nurses input these identifiers by scanning barcodes or entering them manually. At the beginning of each twelve hour nursing shift, a nursing assistant collects handheld BG testing devices and places them in docking stations so data transfer to the clinical data repository [83].

Data collection

We retrospectively collected order entry and handheld blood glucose testing device data from the institution's clinical data repository for all SICU and TICU patients with more than five IIT CDSS values between November 2004 and February 2009. We stored study data in a secure, password-protected database and de-identified it prior to analysis and reporting. The Vanderbilt University Institutional Review Board approved this study.

Because IIT CDSS logs both recommended and override doses that nurses administered but not calculated doses nurses elected to override, we recreated the conditions for each insulin administration in order to determine calculated doses. For each patient, we processed blood glucose values and insulin rates to determine multiplier and recommendations per the IIT CDSS dosing algorithm. If the care team discontinued and later reinitiated the protocol for a patient, we treated these as separate runs of IIT CDSS to assure correct calculation of recommendations and comparison of blood glucose values. We identified instances that did not recreate multipliers and/or recommended insulin doses in the log data. To control for the effect of keystroke error of BG values

contributing to override decisions, we linked each IIT CDSS blood glucose value with a corresponding device BG value and identified pairs of mismatched values as well as IIT CDSS values lacking a device value [92].

Data analysis

We determined the frequency, blood glucose variability, and insulin resistance associated with recommended and override doses. We divided overrides into greater than recommended (GTR) and less than recommended (LTR) doses. Additionally, for each override dose, we computed the degree of deviation of an actual dose from a calculated dose by determining the absolute value of the difference of the actual dose and the calculated dose divided by the actual dose [94]. We identified three types of deviations: "small" as ≤ 25%, "medium" as 26% to 49%, and "large" as ≥ 50% [94].

Previous studies have associated blood glucose variability and insulin resistance with mortality in SICU and TICU patients treated with IIT CDSS [40, 81]. To assess blood glucose variability, we examined blood glucose values before (BG_{n-1}), during (BG_n), and after (BG_{n+1}) each insulin administration (n) for both recommended and override doses. We assessed successive blood glucose change, which reflects both regular and abrupt fluctuations in the distribution of BG values [40], as well as hypoglycemia and hyperglycemia, which measure IIT safety and effectiveness, respectively. We defined hypoglycemia[4] [84] as $BG_n \geq 60$ mg/dL at time of dose followed by subsequent $BG_{n+1} < 60$ mg/dL and hyperglycemia[5] as $BG_n < 200$ mg/dL at time of dose followed by subsequent $BG_{n+1} \geq 200$ mg/dL. We assumed nurses performed

[4] We used the National Quality Forum "never event" definition of hypoglycemia as BG < 60 mg/dL [84]
[5] We defined hyperglycemia as BG ≥ 200 mg/dL as specified in our protocol

IIT CDSS iterations independently; thus, we considered blood glucose input to be correct and examined each dose instance BG value along with immediately preceding and succeeding dose BG values. Although timing of IIT CDSS iterations varied [39], we assumed nurses made a good faith effort to adhere to the protocol, and we evaluated records chronologically for each patient. To assess insulin resistance [81], we compared insulin dose and multiplier between recommended, greater than recommended, and less than recommended doses. For override instances, we compared actual versus calculated insulin doses. To assure quality, we examined only recommended and override instances with successfully recreated output and matching BG values so that we could reliably determine calculated doses in the event of override.

Statistical analysis

We summarized and compared normally distributed continuous variables using mean ± standard deviation and two sample *t* tests for independent samples. For non-normally distributed continuous variables, we summarized and compared data using median and interquartile ranges (IQR) and used the Wilcoxon rank-sum test for unpaired data and Wilcoxon signed rank test for paired data. To compare differences in proportions, we used a χ^2 test. Data represent grand summaries of IIT data and do not address repeated measures within patients. A two-sided *p* value less than 0.05 indicated statistical significance. We used STATA version 10.1 (STATA Corp., College Station, TX) to perform calculations.

Results

203,188 IIT CDSS and 423,463 blood glucose testing device values were available. Figure 5 shows the IIT CDSS instances included and excluded from dose analysis. IIT CDSS misidentified 27 instances as overrides that had actual doses equal to calculated doses. We analyzed dosing for the remaining 179,452 IIT CDSS values.

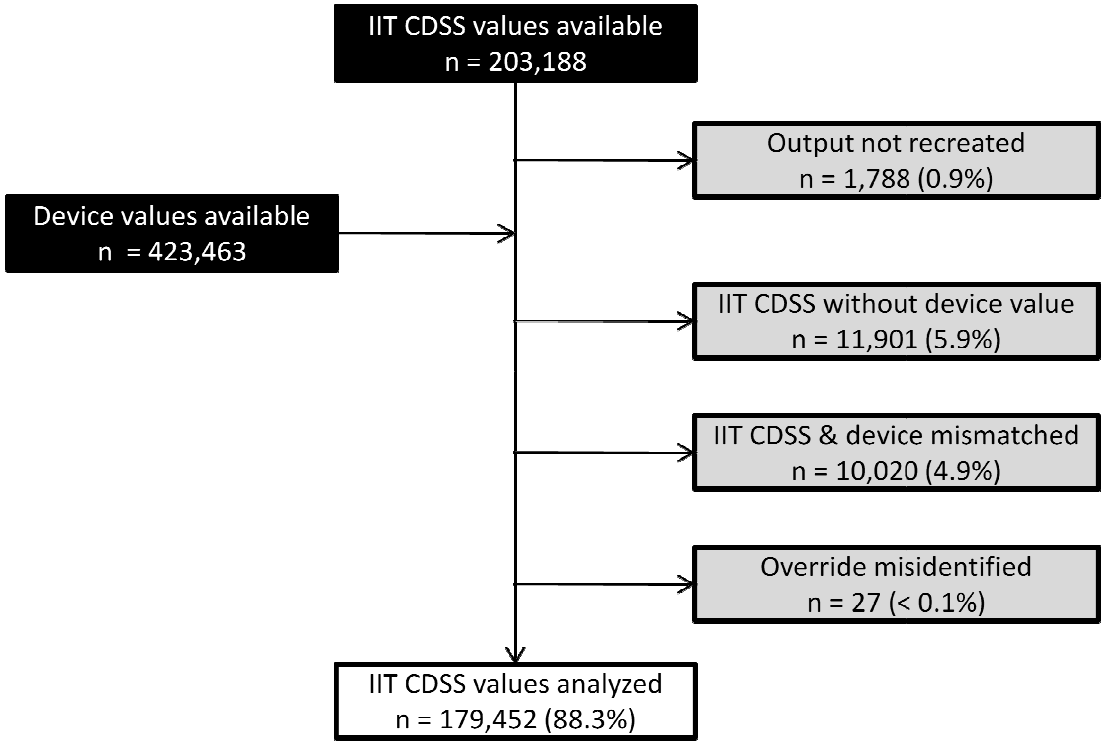


Figure 5. IIT CDSS instances excluded and included for analysis. Data sources (black), instances excluded from dose analysis (gray), and instances included for dose analysis (white). To reliably determine doses that nurses elected not to administer, we excluded 23,736 (11.7%) of 203,188 IIT CDSS doses.

Overrides accounted for 5.1% of IIT CDSS activity of which 83.4% of override doses were LTR and the remainder GTR (Table 10). The majority of GTR doses differed from calculated doses by a small deviation whereas the plurality of LTR doses differed from calculated doses by a large deviation.

Table 10. Frequency and direction of nurse overrides

	N	%
Orders (N = 179,452)		
Recommended	170,377	94.9%
Override	9,075	5.1%
Direction of override doses (N = 9,075)		
Greater than recommended	1,505	16.6%
Less than recommended	7,570	83.4%
Degree of deviation for override doses		
Greater than recommended (N = 1,505)		
Small deviation (≤ 25%)	1,188	78.9%
Medium deviation (26% - 49%)	202	13.4%
Large deviation (≥ 50%)	115	7.6%
Less than recommended (N = 7,570)		
Small deviation	2,778	36.7%
Medium deviation	1,347	17.8%
Large deviation	3,445	45.5%
Total (N = 9,075)		
Small deviation	3,966	43.7%
Medium deviation	1,549	17.1%
Large deviation	3,560	39.2%

Nurses chose to override 5.1% of IIT CDSS recommended insulin doses, and more than four out of five override doses were amounts less than recommended by IIT CDSS.

When examining insulin administration by BG band (Table 11), nurses administered the highest proportion of recommended doses when BG < 60 mg/dL and the lowest proportion when BG was 60-80 mg/dL. The number of LTR doses exceeded the number of GTR doses in every BG band, including when BG exceeded 110 mg/dL, except when BG was less than 60 mg/dL and the protocol instructs nurses not to administer insulin.

Table 11. Blood glucose (BG) values by band at the time of insulin administration

	BG < 60	BG 60-80	BG 80-110	BG 110-150	BG 150-200	BG >200
Recommended, n (%)	2,113 (99.8%)	9,262 (87.0%)	73,045 (96.0%)	64,543 (95.5%)	16,521 (93.2%)	4,893 (92.4%)
Greater than Recommended	4 (0.2%)	66 (0.6%)	411 (0.5%)	489 (0.7%)	336 (1.9%)	199 (3.8%)
Less than Recommended	0 (0%)	1,321 (12.4%)	2,639 (3.5%)	2,531 (3.7%)	873 (4.9%)	206 (3.9%)

Percentages are based on column total and BG values ranges are presented in mg/dL. The protocol specifies nurses to not administer insulin when BG < 60 mg/dL.

Nurses administered the highest proportion of LTR doses when BG 60-80 mg/dL and GTR doses when BG > 200 mg/dL. However, the number of LTR doses exceeded the number of GTR doses when BG > 200 mg/dL.

Blood glucose values differed before, during, and after each insulin administration for recommended, greater than recommended, and less than recommended doses (Table 12). As shown in Figure 6, recommended doses showed a gradual trend of BG values toward the protocol target range, and the BG value following a recommended dose was lower than those following GTR and LTR doses. GTR doses showed a pronounced downward blood glucose trend with hyperglycemic BG levels preceding and at the time of dose followed by a continued downward trend.

Table 12. Blood glucose variability for recommended (R), greater than recommended (GTR), and less than recommended (LTR) insulin doses

	Recommended	Greater than Recommended	Less than Recommended	R vs. GTR	R vs. LTR
BG (mg/dL), mean ± SD before (BG_{n-1})	118 ± 37	150 ± 55	103 ± 32	**< 0.001**	**< 0.001**
BG mean ± SD during (BG_n)	117 ± 36	143 ± 54	115 ± 38	**< 0.001**	**< 0.001**
BG mean ± SD after (BG_{n+1})	115 ± 33	132 ± 46	122 ± 35	**< 0.001**	**< 0.001**
BG change before (BG_{n-1} - BG_n)	-2.43 ± 32.92	-9.91 ± 36.05	11.09 ± 42.24	**< 0.001**	**< 0.001**
BG change after (BG_n - BG_{n+1})	-2.17 ± 33.19	-10.96 ± 37.47	7.19 ± 38.53	**< 0.001**	**< 0.001**
Hypoglycemia, n (%)	1,872 (1.1%)	12 (0.8%)	64 (0.8%)	0.257	**0.033**
Hyperglycemia	1,411 (0.8%)	23 (1.5%)	118 (1.6%)	**0.003**	**< 0.001**

Blood glucose variability differed for nearly every measure, including blood glucose change before and after insulin administration for recommended ($p < 0.001$) and LTR ($p < 0.001$) but not GTR ($p=0.621$).

GTR insulin administration appears to have reduced elevated BG levels on average and at the high end (Figure 6, panels A and B) and maintained levels in the target range at the low end (Figure 6, panel C). BG values following administration of a GTR dose were mostly higher than those following recommended and LTR doses. LTR doses showed a pronounced upward trend with lower BG values preceding and at time of dose compared to recommended and GTR doses. A continued upward trend followed and resulted in BG values both out of range (Figure 6, panels A and B) and in range (Figure 6, panel C). BG values following LTR doses were higher than those following recommended doses.

Nearly all measures of blood glucose variability differed between recommended, greater than recommended, and less than recommended doses (Table 4). Additionally, successive blood glucose change before and after each insulin administration differed for recommended ($p < 0.001$) and LTR doses ($p < 0.001$) but not for GTR doses ($p = 0.621$). The proportion of hypoglycemia was significantly greater for recommended doses than for LTR doses ($p = 0.033$); however, the proportion of hypoglycemia was not significantly greater for recommended doses than for GTR doses ($p = 0.257$). The proportion of hyperglycemia was significantly lower for recommended doses compared to GTR doses ($p = 0.003$) and LTR doses ($p < 0.001$).

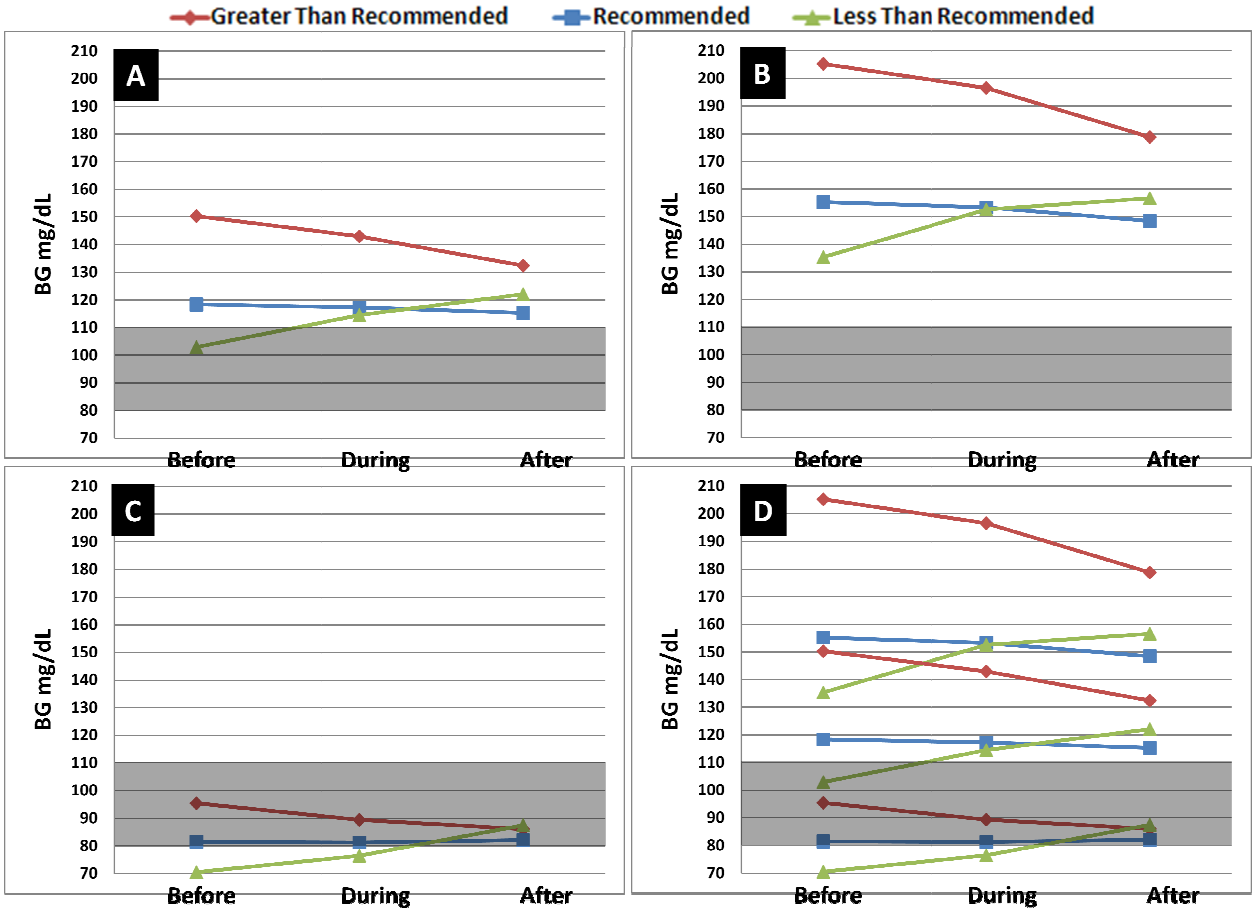


Figure 6. Blood glucose (BG) levels (mean ± SD) before, during, and after insulin administration for recommended, greater than recommended (GTR), and less than recommended (LTR) doses differed across all comparisons ($p < 0.001$). Shaded area indicates BG target range of 80-110 mg/dL. Panel A shows the average case (mean values), Panel B the high end (+SD), Panel C the low end (-SD), and Panel D all combined.

Table 13 summarizes insulin resistance parameters. Comparing overall calculated insulin dose, recommended differed significantly from GTR ($p < 0.001$) and LTR ($p = 0.002$) doses. Hypoglycemia and hyperglycemia occurred infrequently, and some insulin parameters differed for these conditions between recommended, GTR, and LTR doses. When nurses administered LTR doses overall and in the event of hyperglycemia, the multiplier was significantly elevated compared to recommended doses.

Table 13. Insulin parameters for recommended (R), greater than recommended (GTR), and less than recommended (LTR) doses overall and in the event of subsequent hypoglycemia and hyperglycemia

	Recommended	Greater than Recommended	Less than Recommended	R vs. GTR	R vs. LTR
Overall, n (%)	170,377 (94.94%)	1,505 (0.84%)	7,570 (4.22%)		
Actual dose	3.9 (1.7-6.1)	6.0 (3.1-9.0)	2.5 (0.4-4.6)	**< 0.001**	**< 0.001**
Calculated dose		4.8 (2.3-7.4)	3.7 (0.8-6.7)	**< 0.001**	**0.002**
Multiplier	0.068 (0.042-0.110)	0.066 (0.029-0.102)	0.080 (0.043-0.118)	**< 0.001**	**< 0.001**
Hypoglycemia, n (%)	1,872 (1.04%)	12 (0.01%)	64 (0.04%)		
Actual dose	5.1 (1.8-6.8)	5.1 (2.4-7.8)	2.0 (0-4.5)	0.696	**< 0.001**
Calculated dose		3.3 (1.1-5.5)	2.45 (0-5.0)	0.164	**0.001**
Multiplier	0.080 (0.045-0.115)	0.065 (0.024-0.106)	0.057 (0.030-0.084)	0.461	**0.004**
Hyperglycemia, n (%)	1,411 (0.79%)	23 (0.01%)	118 (0.07%)		
Actual dose	4.1 (1.8-6.5)	5.0 (2.8-7.3)	2.25 (0-5.3)	0.741	**< 0.001**
Calculated dose		3.0 (1.1-4.9)	4.55 (0-8.9)	**0.024**	0.625
Multiplier	0.060 (0.026-0.095)	0.030 (0.019-0.041)	0.085 (0.053-0.116)	**< 0.001**	**< 0.001**

Percentages reflect total number of insulin doses as denominator. Actual and calculated doses differed in all comparisons ($p < 0.002$).

Discussion

By administering less than recommended doses in 83% of IIT CDSS overrides, critical care nurses encouraged hypoglycemia prevention at the expense of hyperglycemia control, reflecting the "fear of hypoglycemia" in intensive care units [30]. For override doses, the rate of hypoglycemia was lower and the rate of hyperglycemia higher compared to recommended doses. When nurses administered LTR doses overall, patients required more insulin as estimated by the multiplier than when nurses administered recommended and GTR doses. This suggests that nurses considered the amount of a recommended dose, not the trend of past insulin resistance, when overriding IIT CDSS with LTR doses. The effect of LTR doses on BG levels was mostly favorable. At the low end (Figure 6, Panel C), blood glucose levels increased into the protocol target range; in the average case (Figure 6, Panel A), BG increased within an acceptable range.[6]

[6] Some researchers advocate a high blood glucose target of 140 to 150 mg/dL instead of 110 mg/dL [91]

However, at the high end (Figure 6, Panel B), BG levels following LTR doses continued above 150 mg/dL after increasing prior to the dose. Both recommended and LTR doses at the high end occurred when BG was 153 mg/dL, which was greater than the BG level for GTR doses in the average case. Administration of greater than recommended doses lowered BG levels (Figure 6, Panel D), and administration of recommended doses in lieu of LTR when BG exceeded 150 mg/dL and increased from the previous dose might have improved hyperglycemia control.

Nurse education, interface modification, and algorithm changes may potentially improve hyperglycemic control while limiting hypoglycemia. Current IIT CDSS recommendations may be sufficient and require user training to encourage nurses to more frequently administer recommended doses instead of LTR doses when BG increases from below to above 150 mg/dL. Additionally, a passive text alert encouraging users to administer a recommended insulin dose instead of a LTR dose when BG increases from below to above 150 mg/dL may help improve protocol compliance and hyperglycemia control. Implementing these changes may be challenging given hypoglycemia concerns. Showing the multiplier value on screen might also provide another form of decision support regarding patients' insulin resistance and prevent nurses from administering LTR doses as frequently. However, displaying this parameter may also create visual clutter and confusion. This investigation has focused on IIT CDSS using a linear equation [51, 52], and more sophisticated quadratic or model-based approaches might lead to better performance [25, 95]. However, the algorithm studied may be tweaked to incorporate LTR doses in the average case and on the low end.

This study has strengths and limitations. We analyzed a large dataset that reflects actual practice in an institution with cultural acceptance of clinical information systems. Several institutions [14, 23, 28, 50] use a similar dosing equation [51, 52] to the one studied, so results may be generalizable to similar critical care unit settings. Limitations include conclusions not being generalizable to other settings due to high clinical informatics commitment at the study institution; the unit of analysis being the data point, not the patient; and results showing correlation, not causation, between insulin doses and blood glucose levels. Additionally, we excluded almost 12% of IIT CDSS instances from dose analysis and recognize the override rate could be greater than reported. Missing data, failure to reproduce log data, and incorrectly marked system overrides can occur due to device malfunction, data transfer failure, undocumented code changes, and other process errors inherent to the ecology of clinical information systems. Mismatched BG data affects IIT CDSS recommendations [92], and we encourage investigators to similarly control for data discrepancies when conducting clinical research. Our current work, informed by this and previous studies [39, 92], uses qualitative methods to understand how IIT CDSS affects and is affected by other care processes, clinical information systems, and personnel. Future work will examine override trends over time.

Conclusion

Nurse override of clinical decision support system dosing recommendations is a source of intensive insulin therapy variability in critical care settings. Nurses elected to override 5.1% of dosing recommendations generated using a commonly adopted algorithm, and 83.4% of override doses were less than recommended by CDSS; 45.5% of

these doses were ≥ 50% less than recommended. Nurse overrides encouraged hypoglycemia prevention but occasionally interfered with hyperglycemia control. Administration of recommended doses instead of less than recommended doses when blood glucose is greater than 150 mg/dL could lead to tighter blood glucose control and reduced risk of infection. IIT CDSS nurse education, interface design, and dosing algorithm modifications can potentially improve hyperglycemia control while limiting hypoglycemia. Qualitative study of IIT CDSS is necessary to understand why nurses override recommendations, how IIT CDSS functions in clinical practice, and whether other workflow features affect intensive insulin therapy.

CHAPTER V

BARRIERS AND FACILITATORS TO THE USE OF COMPUTER-BASED INTENSIVE INSULIN THERAPY

Introduction

Intensive insulin therapy (IIT) is the standard of critical care, but recent studies raise questions about the therapy's mortality benefit and risk to patients [72, 79, 89, 90]. To maintain tight blood glucose (BG) control, the treatment requires nurses to perform frequent BG measurements, usually using handheld testing devices [91], and adjust insulin infusion pumps according to protocol logic [1]. Increasingly nurses deliver IIT using computerized clinical decision support systems (CDSSs) [82], which studies have deemed effective for controlling hyperglycemia and safe for achieving low rates of hypoglycemia [83]. Researchers have identified sources of variability affecting IIT performance—patient populations, blood glucose target ranges, nutrition sources, nurse staffing, and genetic factors [91]—and the impact of paper-based IIT protocols on nurse workflow [31, 70]. However, few investigations have formally assessed the workflow complexity introduced by IIT CDSS [83] or how nurses perceive the technology's role in patient care [26, 71].

Previous studies have quantified the effect of nurse workflow on IIT CDSS performance. Researchers have identified relationships between late timing of BG measurements and hyper- [39] and hypoglycemic episodes [10, 39] as well as between blood glucose variability and mortality [40]. In a prior investigation, we showed that

5.3% of blood glucose values manually transcribed to IIT CDSS did not match corresponding source values from handheld testing devices, which affected CDSS alerts and dosing recommendations as well as blood glucose variability [92]. Investigators have reported rates of nurse IIT CDSS override, or deviation from system recommendations, ranging from 2% to 23% [10, 53, 71, 93, 96]. Previously we demonstrated that 83.9% of IIT CDSS override doses were less than recommended [96], quantifying nurse "fear of hypoglycemia" [30]. Additionally, categorization of IIT CDSS free text comments at one institution showed that nurses chose to override system recommendations due to fear of hypoglycemia [71], dose disagreement [71, 93], and workflow factors [71]. Timing, mismatched data, and overrides affect IIT CDSS performance.

Although these findings describe IIT CDSS use, they do so using system log data that may not fully capture the "assumptions, norms, values, choices, and interactions" involved in decision making [43]. Computer-based intensive insulin therapy is a combination of people, process, and technology, and examining social, organizational, and contextual characteristics of IIT CDSS can potentially lead to process and algorithm improvements [83]. In particular, few studies of IIT CDSS [83], and CDSS in general [17], have evaluated interventions with respect to other clinical information systems and care processes. A descriptive, exploratory approach is appropriate for investigating these types of issues [97]. Using naturalistic methods [97], the goal of this study was to illuminate barriers and facilitators to use of IIT CDSS.

Methods

We conducted a qualitative study of IIT CDSS by directly observing and interviewing clinical personnel in the 21-bed surgical intensive care unit (SICU) and 31-bed trauma intensive care unit (TICU) at Vanderbilt University Hospital, an urban tertiary care academic facility in Nashville, Tennessee. For nearly two decades, researchers and staff at Vanderbilt University Hospital have developed, tested, and implemented clinical information systems to facilitate quality improvement (Figure 7). As a result, use of clinical information systems has become an established part of clinician culture. Although other intensive care units at the institution treat patients using IIT CDSS, we focused our study on SICU and TICU due to common management by Division of Trauma and Surgical Critical Care faculty. 35.1% (n=1,883) SICU patients and 26.3% (n=2,152) TICU patients received IIT CDSS between 11/2004 and 2/2009 [92].

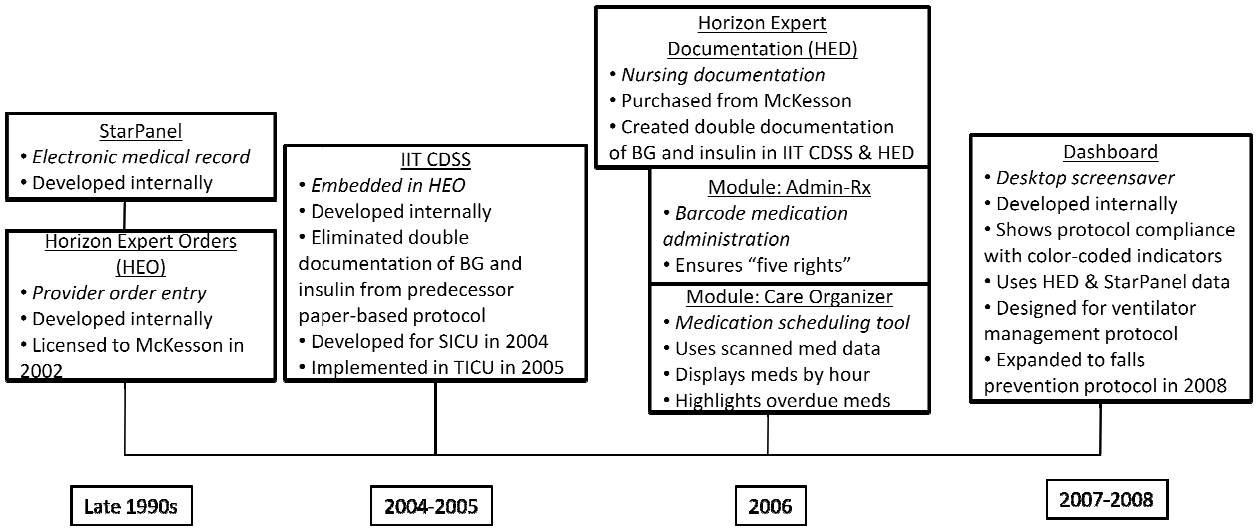


Figure 7. Timeline of clinical information systems development and implementation for SICU and TICU at Vanderbilt University Hospital. Dashboard indicators include green for compliant, yellow for action required to remain compliant, and red for non-compliant. For implementation details, see [83] for IIT CDSS and [98] for dashboard. Workstations connected to the hospital network are located on mobile carts, at nursing stations, and in patient rooms at the bedside.

IIT CDSS description

After a patient's blood glucose level exceeds 110 mg/dL and a physician initiates the intensive insulin therapy protocol, a nurse uses IIT CDSS embedded in the provider order entry system to maintain tight glucose control between 80 and 110 mg/dL by default (Figure 8). IIT CDSS requires a nurse to enter a blood glucose value obtained from a handheld testing device via keyboard, select a dextrose source, and specify the site and method of blood draw in order to calculate a recommendation. IIT CDSS calculates insulin rates using a linear equation [51, 52] based on current and previous BG input as well as current insulin rate.

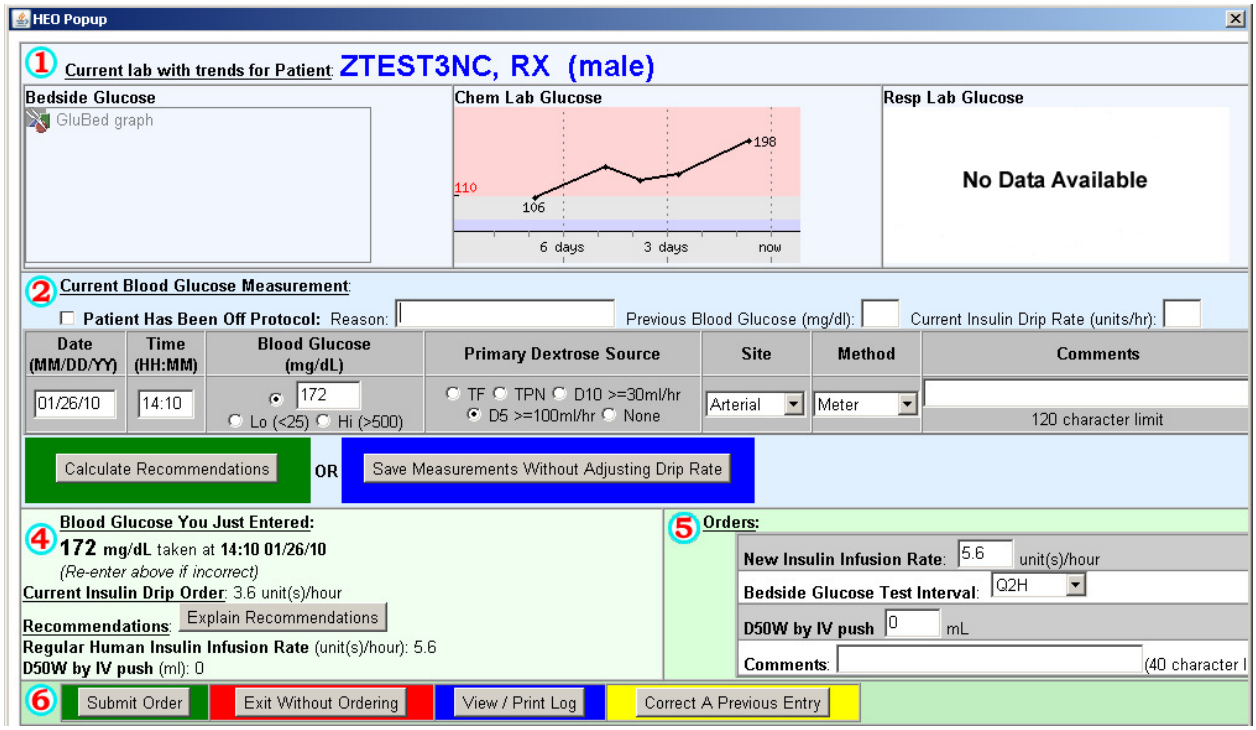


Figure 8. IIT CDSS interface used by nurses. Similar to interfaces of other decision support modules in the provider order entry system, IIT CDSS displays colorful numbers to guide users through a sequence of operations.

To control hyperglycemia, nurses perform IIT CDSS every two hours, but timing can be early or late in practice [39]. Blood glucose values less than 80 mg/dL trigger an order for 50% dextrose (D50W) and checking of blood glucose in thirty minutes [21]. Additionally, BG values less than 60 mg/dL generate instructions for nurses to suspend insulin administration for thirty minutes [21]. A nurse can view IIT CDSS's rationale by clicking the "Explain Recommendations" button. If a nurse wishes to override an insulin recommendation, he or she replaces the numerical figure next to "New Insulin Infusion Rate" with a different sum. IIT CDSS logs all on screen input including designation of override doses. Using the values recorded by IIT CDSS, a nurse adjusts an Alaris infusion pump and/or administers D50W via injection. Infusion pumps are capable of exporting data electronically but the feature was not enabled during the study. IIT CDSS does not remind nurses to perform blood glucose tests or administer insulin.

Under certain circumstances the care team may wish to temporarily regulate a patient's blood glucose through other means (e.g. during an operating room procedure according to surgery protocol) but not discontinue orders for IIT CDSS. When a patient returns to BG control through IIT CDSS, a nurse clicks the "Patient Has Been Off Protocol" checkbox and provides a reason as well as the previous BG and current insulin infusion rate used in the alternate BG regulation strategy. IIT CDSS then uses these figures and a current BG value to calculate recommendations.

Data collection

A researcher trained in ethnographic methods (TRC) collected data by observing nurse workflow and conducting unstructured interviews with nurses and other clinicians

between 2/16/2010 and 3/18/2010. Prior to observations and interviews, the researcher briefly explained the project and obtained verbal assent from clinicians, patients, and families as necessary. Participation was voluntary and responses were confidential. The Vanderbilt University Institutional Review Board approved this study.

The researcher recorded de-identified notes using a pen and paper before transcribing them electronically for further analysis. Notes consisted of narrative text describing observations as well as direct quotes from clinical personnel. Data collection started in SICU because it was the original IIT CDSS implementation site, moved to TICU, and then shifted between the two as needed. Informed by pilot study experience [83], a typical data collection session lasted two-to-three hours to account for nurses performing IIT CDSS at two hour intervals by default. The goal of each session was to follow one nurse who performed at least two IIT CDSS iterations. In some sessions the researcher followed multiple nurses. The researcher observed nurses on weekdays between 9:00am and 7:00pm as well as on one weeknight and one weekend day. In total the researcher observed 49 hours of SICU and TICU workflow in which nurses used IIT CDSS 47 times (Table 14). As described elsewhere [92], we also had access to a database of 38 months of retrospectively collected IIT CDSS records for quantitatively examining trends seen in observations.

Table 14. Characteristics of study observations.

	SICU	TICU
Time	25 hours 25 minutes	23 hours 35 minutes
Sessions	11	9
Nurses observed (unique)	16 (13)	14 (12)
Patient:nurse ratio 2:1 (1:1)	11 (1)	8 (1)
Nurses interviewed but not observed	2	5
Patients observed (on IIT CDSS)	25 (16)	21 (16)
IIT CDSS iterations observed	22	27

The scope of study was intentionally broad to account for interactions between people, process, and technology in IIT CDSS delivery. In conducting observations, the researcher examined all activities encountered by a nurse: direct patient care; computer use; supply retrieval; laboratory specimen transport; new patient admission; and interactions with families, nursing assistants, resident physicians, fellows, attending physicians, medical students, respiratory therapists, nutritionists, imaging personnel, nurse practitioners, charge nurses, and medical receptionists. The researcher performed unstructured interviews to clarify observations and in response to prompts volunteered by clinicians. The protocol interval provided an opportunity to explore the breadth of clinical activities influencing and influenced by each IIT CDSS iteration.

Data analysis

Informed by grounded theory [99], the researcher inductively examined observation and interview notes using the constant comparative method to allow themes to emerge from data. Using NVivo 8, a software package for qualitative analysis, the researcher scrutinized, or coded, transcribed notes line-by-line by labeling concepts, distinguishing the properties and dimensions of concepts, comparing and relating concepts, and questioning associations between concepts. As part of the analysis process, the researcher recorded memos to reflect on observations, the coding process, and emergent themes. Coding and memoing occurred immediately following each data collection session. Concepts that emerged from data analysis informed the direction of future data collection sessions, a process called theoretical sampling. Through an iterative process, data analysis developed concepts and the relationships between them

while also addressing the variation across observations. Data collection and analysis ceased when no new data emerged, a point called data saturation.

This study ensured analytical rigor by employing standard techniques of naturalistic inquiry [100]. Throughout the study the researcher confirmed observations and emerging concepts through opportunistic interviews with nurses in the study sites, a process called member checking. Additionally, the researcher met with a peer debriefer, an informatician trained in ethnography who was not involved in the study, to confer on data emergence and alternative approaches to data collection and analysis. The researcher also triangulated data sources—the multiple nurses observed across two ICUs; critical care personnel not observed including a nurse manager, an attending, a fellow, and a pharmacist; and retrospective database records—and methods—direct observation, unstructured interviews, and database queries—in order to verify IIT CDSS findings from multiple perspectives. Finally, the researcher maintained reflexivity, or awareness of self and bias in collecting data, through regular journaling exercises in order to limit interference with data collection and analysis.

Results

We identified four barriers and four facilitators to IIT CDSS use based on analysis of observation and interview data. Examination of retrospective database records confirmed observations when needed.

Barrier 1: workload tradeoffs between computer use and direct patient care

Time and effort demands of electronic nursing documentation

Nurses expressed concern about the amount of time required for documentation in HED, the electronic nursing documentation system, and cited system use as an occasional detriment to patient care. Depending on patient acuity, nurses prioritized patient care ahead of computer system usage. However, nurses recognized HED usage as a necessary activity for regulatory and legal purposes but questioned the utility of perfunctory documentation. Nurses spent a considerable amount of time "backcharting" care they provided in the past due to ongoing patient care demands. HED hindered nurse efficiency by requiring double documentation of data points unrelated to IIT within and across individual flow sheets, a source of complaints from nurses. Although infusion pumps and pulmonary artery catheter monitors were capable of electronic data output, nurses manually entered values from these devices into HED, which increased time spent documenting. Nurses appreciated the automatic data transfer of vital signs from bedside monitors to HED; the safety provided by Admin-Rx, the barcode medication administration system, despite additional time required; and the display of hour-by-hour medications in Care Organizer, the medication scheduling tool.

Nurse suspicion of dashboard

The dashboard is a desktop screensaver displaying color-coded protocol compliance indicators based on nursing documentation system and electronic medical record data. Initially well-received by nurses, the dashboard became viewed as a managerial surveillance tool promoting documentation compliance at the occasional expense of patient care. Skepticism of the dashboard increased after the addition of falls

prevention parameters to the display. Complaining of alert fatigue, one nurse said, "we're near the breaking point where people stop paying attention to [the dashboard] and it loses its functionality." Nurses felt the benefit of the dashboard accrued to unit and hospital management rather than nurses and patients. Instead of the system providing beneficial reminders, nurses said the dashboard prompted charge nurses to constantly monitor compliance and urge floor nurses to complete tasks to avoid being "in the red" on the dashboard. Over time nurse perceptions of the dashboard as a platform for care reminders changed from helpful to intrusive.

Time and effort demands of IIT CDSS

Occurring at two hour intervals or less, computer-based intensive insulin therapy occupied a significant portion of nurses' time. Treating hypoglycemia required more time from nurses to administer D50W and monitor patients. While preparing to administer D50W and recheck BG in thirty minutes according to IIT CDSS recommendations following a blood glucose level of 79 mg/dL, a nurse remarked "I'll soon enough be chasing my tail the other way" when the protocol would resume its regular schedule and focus on hyperglycemia control. With care tasks adding up, nurses often remarked, "I wish someone would do my sugars!" On several occasions we observed an idle nurse offer to help another nurse with blood glucose testing for IIT CDSS. Additionally, when nurses deemed other care needs more pressing than blood glucose regulation (e.g. for patients with stable blood glucose levels), IIT CDSS usage became less of a priority. Nurses attempted to balance direct patient care with electronic nursing documentation and IIT CDSS usage.

Double documentation in electronic nursing documentation and IIT CDSS

IIT CDSS stored blood glucose, insulin, D50W, and dextrose source data in the electronic medical record for each therapy iteration based on nurse input, but nurses also manually recorded these parameters in HED, a form of double documentation. Furthermore, nurses recorded insulin data twice in HED—once for rate and once for volume.

Barrier 2: lack of IIT CDSS reminders

Insulin and D50W doses generated by IIT CDSS appeared in Care Organizer after their administration because Care Organizer used the most recently processed medication orders to populate the list. In its current configuration, Care Organizer displays medications scanned using the Admin-Rx barcode medication administration system. Nurses scan intravenous infusions, like the insulin infusions used for IIT, only when they are first administered.

Table 15 presents a case where Care Organizer did not accurately display IIT CDSS orders. In this example, nurse resilience maintained intensive insulin therapy compliance despite clinical information system rigidity. However, the researcher also observed a nurse almost forget to recheck a patient's blood glucose 30 minutes after administering D50W and another nurse nearly fail to check BG after three hours, the definition of overdue for the standard two hour interval [39]. Both times the researcher inquired about IIT CDSS to jog the nurses' memory, which led the nurse to carry out the therapy.

Table 15. Example demonstrating lack of reminders through Care Organizer configuration

After using IIT CDSS at 10:02am, an order for insulin for the amount recorded by IIT CDSS appeared in Care Organizer. When the nurse checked Care Organizer at 10:59am for 11:00am medications to administer, the nurse acknowledged the 10:02am IIT CDSS order because it had already been given, removing it from the list. At 11:55am the nurse accessed Care Organizer to check the list of medications to administer at 12:00pm. An order for heparin injection appeared but not insulin. Knowing the two hour interval for intensive insulin therapy required a 12:00pm dose, the nurse used IIT CDSS at 12:05pm and generated insulin and D50W orders due to the patient's blood glucose falling slightly below 80 mg/dL. The nurse immediately administered D50W and planned to perform IIT CDSS in thirty minutes per protocol for hypoglycemia risk. At 12:37pm the nurse performed IIT using CDSS and the patient's BG had increased above 80 mg/dL. At 1:00pm the nurse accessed Care Organizer and acknowledged insulin orders from 12:05pm and 12:37pm as well as the 12:05 D50W dose because they had already been given. IIT CDSS use at two hour intervals resumed at 2:00pm.

Barrier 3: user interface design assumptions

Unintended use of "off protocol" functionality

In one instance, the researcher observed unintended and potentially harmful use of IIT CDSS's "Patient Has Been Off Protocol" functionality (Box 16). Review of IIT CDSS database records from 11/2004 through 2/2009 indicated that other nurses may have similarly used IIT CDSS to incorrectly administer overrides in less than one percent of cases.

Table 16. Example demonstrating improper use of patient off protocol functionality

Uncomfortable with a current high insulin rate for a patient treated with IIT, a nurse clicked the "Patient Has Been Off Protocol" checkbox and entered the current BG result and an insulin rate of his choosing less than that currently being administered. Asked to explain this behavior, the nurse described his intent to override, which led the researcher to describe the override procedure he had seen in previous observations of replacing the recommended rate text. The nurse stated he was unaware that administering an override via the "Patient Has Been Off Protocol" functionality was incorrect and continued to administer the dose in this fashion.

Dextrose source selection

Although IIT CDSS required nurses to select a dextrose source in order to calculate recommendations, patients frequently received dextrose from multiple sources simultaneously. This led nurses to select the greatest of dextrose sources to satisfy IIT

CDSS requirements and then fully document multiple dextrose sources in HED. Despite partial double documentation, IIT CDSS log data did not fully reflect patient nutrition.

Blood draw source selection

Most of the blood tests we observed used blood drawn from capillary sources (e.g. finger stick) rather than arterial sources that yield more accurate results [91]. "Arterial" is the default blood source selection in IIT CDSS, and we observed instances where nurses performed a test using capillary blood but did not select "capillary" in the system. Review of retrospectively collected IIT CDSS data indicated that nurses selected "capillary" for 39% of blood sources, and we suspect that the percentage might underestimate the true occurrence of tests performed using capillary blood. Use of capillary blood may prevent IIT CDSS from using accurate blood glucose readings to calculate recommendations, and the IIT CDSS interface may facilitate incorrect documentation of blood sources.

Barrier 4: potential for error in operating medical devices

Insulin infusion pump adjustment

IIT CDSS recommends insulin infusion rates and allows nurses to override recommendations, but the protocol relies on a nurse to manually adjust a patient's infusion pump. Although infusion pumps can transfer insulin adjustment data to other systems, this feature was not enabled during the study. In one instance we observed a nurse enter a rate of 2.6 units per hour on the pump after accepting IIT CDSS's recommendation of 2.7 units per hour. We are unsure whether this occurred deliberately or by chance. In another instance a nurse failed to adjust an infusion pump after

accepting IIT CDSS recommendations due to an emergent patient care situation at another bedside.

Handheld testing device use and physical layout

When treating patients under isolation precautions, nurses did not bring handheld testing devices into patient rooms in order to prevent device contamination according to hospital policy. Instead nurses leaned through doorways to conduct tests on devices positioned on nearby surfaces. In one instance, a nurse conducted the test outside the patient room before returning to a computer workstation at the isolation patient's bedside to enter the value into IIT CDSS and administer care. She did not use a paper sheet to keep notes and instead relied on memory. The value entered by the nurse, 224, did not equal the value from the testing device, 226. In another instance, we observed a nurse caring for a non-isolation patient located in an isolation room conducting blood glucose tests outside the patient room although the device could have been used at the bedside. One nurse stated a preference for conducting BG testing and computer usage in the patient room in order to avoid making mistakes.

Facilitator 1: trust in IIT CDSS combined with clinical judgment

Nurses said they trusted IIT CDSS because it was evidence-based and made appropriate recommendations. Nurses recognized the cumulative impact of blood glucose and insulin data on IIT CDSS output, and one respondent said he needed to trust the previous shift nurse's use of IIT CDSS in order to feel comfortable using the system. Usually nurses transcribed BG values, selected other required parameters, clicked the calculate button, and accepted recommendations quickly and without argument.

However, when electing to override, nurses appeared sensitive (e.g. wincing facial expressions) to recommended insulin rates, which were generally high (e.g. ten units per hour), and subsequently administered doses less than recommended. Asked to explain these decisions, nurses cited blood glucose trends, nutrition sources, general intuition, and a desire to prevent patients' blood glucose levels from "bottoming out" in hypoglycemia. One nurse said, "I would never give more [insulin]; I would only give less. I wouldn't feel comfortable giving more. I don't want [patients] becoming hypoglycemic." Nurses accepted 94.9% of recommended insulin doses between 11/2004 and 2/2009, and BG values following override doses were within acceptable ranges in most cases [96]. Nurses appear to have appropriately exercised clinical judgment by compensating for glycemia-influencing factors beyond IIT CDSS algorithm parameters.

Despite trust in recommendations, nurse understanding of IIT CDSS's dosing algorithm varied. Several nurses described the system as a "black box" that "learns the patient," and nurse explanations of IIT CDSS algorithm inputs—current blood glucose and dextrose source; the average of two blood glucose values; and a combination of patient's height, weight, blood glucose, previous insulin, and dextrose source—were not accurate. One nurse stated that he or she clicked the "Explain Recommendations" once but found the description confusing and closed the window. Regardless of their reported IIT CDSS algorithm understanding, nurses' "feel" for IIT CDSS recommendations appeared appropriate.

Facilitator 2: IIT CDSS adds value to blood glucose data entry

IIT CDSS added value to the otherwise rote documentation of blood glucose values through the calculation of insulin and D50W doses. Prior to HED implementation, IIT CDSS also reduced documentation requirements compared to a paper-based protocol. Overall the system prevented nurses from making mathematical errors in drug dosing. IIT CDSS data also populated a view in StarPanel helpful for examining blood glucose and insulin trends. In contrast to IIT CDSS, documentation of blood glucose values in HED provided nurses with legal assurance rather than immediate value for patient care.

Facilitator 3: nurse resilience

Nurses adapted to myriad changes in order to perform IIT CDSS. Without any systematic reminders, nurses remembered to perform IIT CDSS at two hour intervals. In the event of hypoglycemic events, nurses successfully altered their work schedules to obtain D50W doses and recheck blood glucose measurements in thirty minutes before reverting to the default two hour interval. Despite competing care tasks and workplace interruptions, nurses diligently adjusted insulin pumps after using IIT CDSS. Additionally, nurses regularly dismissed insulin and D50W doses that no longer applied from Care Organizer in order to clarify medication scheduling.

Facilitator 4: paper documentation

For most nurses paper served as the conduit between bedside readings and HED and IIT CDSS. Although this practice amounted to triple documentation, the majority of

nurses would have relied solely on memory in a disruptive work environment and potentially forgotten or misremembered data points critical to patient care (Barrier 4). Nurses used blank paper sheets, pre-specified forms of their or a colleague's creation, or improvised scraps and bandage wrappers to record parameters from devices, physical assessments, and computer systems. Nurses frequently recorded BG measurements on paper sheets and referred to these notes when using IIT CDSS.

Discussion

This investigation is the first field study of IIT CDSS and reveals sociotechnical interactions affecting protocol performance not addressed by previous research. The relationship between IIT CDSS and nursing documentation and reminder systems implemented after IIT CDSS shows how the whole of clinical information systems, greater than the sum of its parts, affects computer-based intensive insulin therapy. Use of and attitudes toward the systems studied suggest opportunities for IIT CDSS improvement that other institutions may find useful.

A tradeoff in critical care nurse workload exists between direct patient care and computer system use, and attitudes toward IIT CDSS and HED underscore the importance of adding value to clinical documentation. Nurses often felt that nursing documentation system requirements hindered their ability to administer patient care but regarded IIT CDSS, which recommended drug doses based on nurse data input, as a clinical process benefit. Both activities occupied significant portions of nurses' time. Researchers have recognized the opportunity to provide decision support through electronic documentation systems, and provision of such "Smart Forms" [101] for ICU

documentation may improve nurse perception, data quality, workflow, and patient outcomes. Figure 9 depicts a possible workflow improvement leveraging streamlined documentation for dosing recommendations and drug safety. Future study can investigate the change's impact on data accuracy, safety, and nurse satisfaction. Capturing more parameters in IIT CDSS could also facilitate use of more sophisticated dosing algorithms that incorporate dextrose sources [95]. Due to the varying degrees of algorithm understanding expressed by nurses in this study, changes to the underlying dosing algorithm may go unnoticed, which can be of potential value in a blinded study. However, changing the dosing algorithm without notifying nurses could also have deleterious effects on nurses' mental models of IIT CDSS and thus their clinical judgment and patients' safety.

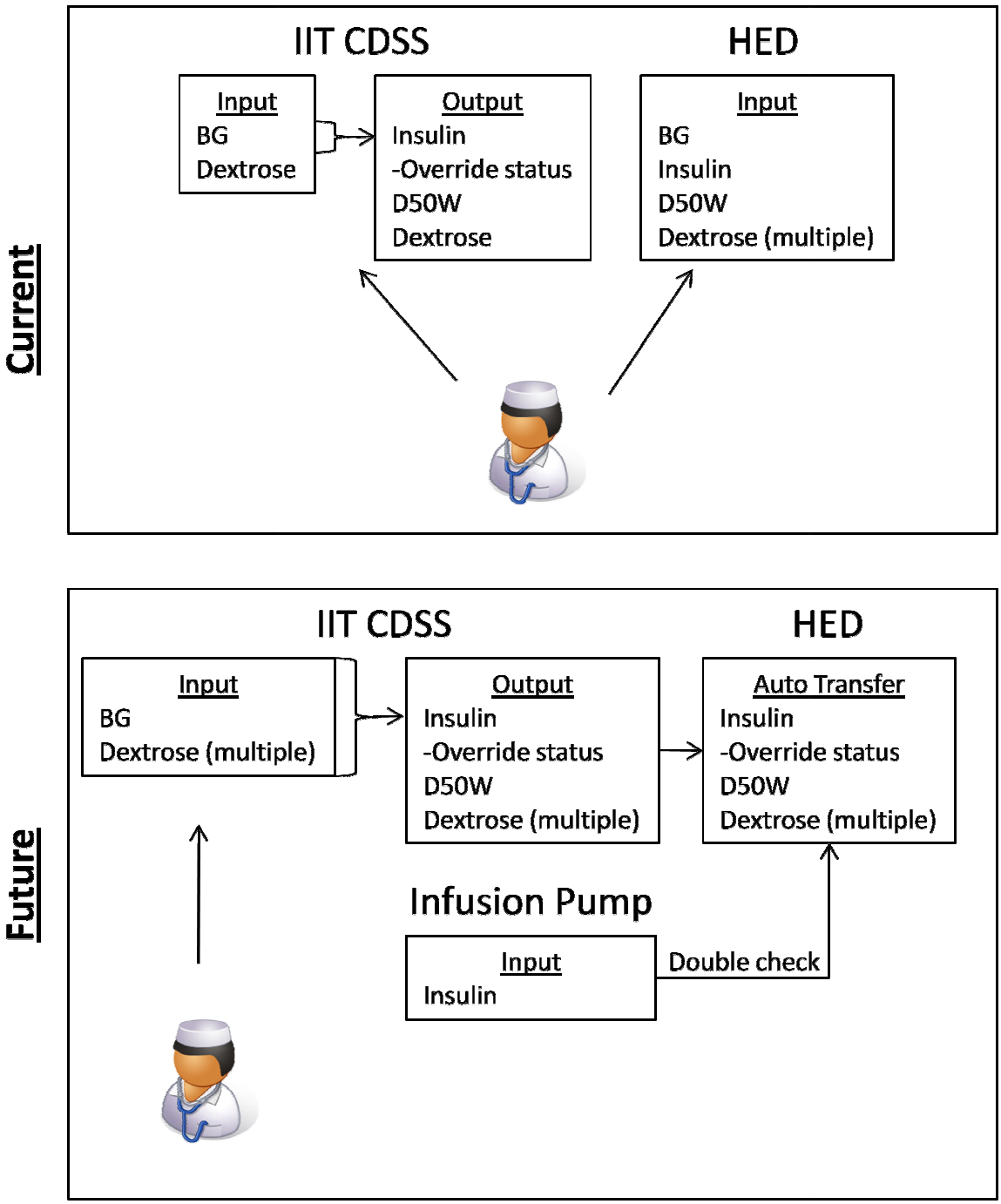


Figure 9. Current and future IIT CDSS documentation workflow. Currently nurses record data for each protocol iteration in IIT CDSS and HED. In the future, nurses could record these data in IIT CDSS, which could then transfer the data to HED to eliminate double documentation and save nurses time. Automatic transfer of infusion pump data to HED could also save time and help nurses double check that administered insulin rates match orders to improve safety.

Timing of IIT CDSS affects protocol performance [10, 39], and some implementations actively remind nurses to perform IIT CDSS using popup alerts [23, 53]. Alert fatigue is a concern in clinical informatics [102], and the passive alerts observed in this study, provided through the nurse medication scheduling tool and dashboard, appeared effective to varying degrees for non-IIT nursing tasks. However, due to a limitation in the medication scheduling tool's current configuration, insulin and D50W did not appear correctly alongside other hourly medications. A code change can likely improve the display. Alternatively, color-coded indicators for blood glucose and insulin administration timing could fit the existing dashboard motif and remedy the situation, but staff attitudes toward the dashboard may pose a barrier to general system use. Regardless, the absence of reminders for IIT and presence of reminders for all non-IIT tasks may adversely affect nurses' perception of IIT compliance necessity, which in turn can worsen protocol performance and outcomes. Additional research is needed.

Developers' software design assumptions can profoundly impact user behavior and effectiveness of clinical software interventions [47]. Assumptions in the IIT CDSS design process did not bear out as evidenced by users improperly overriding recommendations by using functionality intended for patients off protocol, relying on the default instead of selecting the correct blood source, and improperly transcribing blood glucose values from handheld testing devices to IIT CDSS. Interface changes including explicit language describing intended use, dropdown menus presenting multiple options without default selections, and larger data input fields may potentially alleviate these issues, respectively. Regular IIT CDSS data auditing and nurse training may also reduce

unintended use. Accuracy of IIT CDSS data collection can affect secondary research uses as well as new dosing algorithms that rely on parameters beyond blood glucose.

Patterson [103], Militello [104], and Saleem [102] previously identified barriers and facilitators to use of computerized reminders in outpatient settings, and we have extended this line of inquiry to intensive care units for IIT CDSS. Scholars have noted the paucity of theory in biomedical informatics research [18], but the common themes identified by previous studies and this investigation—limiting the number of reminders, reducing the perception that management benefits more from system use than end users, eliminating double documentation, and integrating CDSS into workflow—may indicate the beginning of an empirically derived theory for computerized clinical decision support systems to promote high performance of clinical protocols. Additional research is required.

Nurses and healthcare institutions in the aggregate expend considerable time and resources to perform intensive insulin therapy [105] while debate continues about the treatment's effectiveness and safety. IIT may not deliver the benefits observed in the landmark Leuven study, but controlling hyperglycemia while limiting hypoglycemia remain important goals [89, 91]. We recognize the capacity for human error in manually transcribing blood glucose values from testing devices to IIT CDSS [92] and in adjusting insulin pumps. However, given the controversy surrounding IIT, we do not advocate replacing these technologies with integrated devices that measure blood glucose and adjust insulin due to cost concerns and unexplored unintended consequences.

Limitations

This study has limitations. In 49 hours of observation we did not observe protocol initiation or patient travel to the operating room, MRI, or x-ray. We conducted this study at a single academic medical center with high informatics commitment that may not exist in other settings. We also did not examine IIT CDSS in other intensive care units, operating rooms, or other units at the study site. As a result, findings may not transfer to other settings. Due to resource constraints, a single researcher conducted observations, interviews, and data analysis. However, ethnographic studies conducted by single researchers have previously contributed to informatics [106-108]. The researcher's presence during observations may have affected clinicians' actions [109], but prolonged engagement [100] in the study sites may have mitigated this behavior.

Conclusion

By evaluating a clinical decision support system for intensive insulin therapy with respect to other clinical information systems and care processes, we identified nurse attitudes, data processing gaps, design assumptions, and nurse resilience that affected system use. Findings suggest opportunities for improvement involving documentation, reminders, and user interface changes. Researchers and practitioners of clinical decision support systems should consider these oft overlooked aspects in system design and evaluation.

CHAPTER VI

CONCLUSION

Summary of Research Findings

The critical care community is in a state of flux due to concerns about the safety and effectiveness of intensive insulin therapy [89, 91]. Although previous studies of intensive insulin therapy recognized the additional effort required of nurses to implement the treatment [91], few investigated workflow as a source of computer-based IIT variability [10, 39], and none fully addressed the "assumptions, norms, values, choices, and interactions" [43] affecting computer-based intensive insulin therapy. This research used a mixed methods approach informed by institutional theory to investigate social, organizational, and contextual factors influencing adoption and everyday use of computer-based IIT.

This dissertation makes two primary contributions: 1) identification of novel sociotechnical interactions affecting computer-based intensive insulin therapy and 2) demonstration of the value of an informatics evaluation approach combining social theory, quantitative methods, and qualitative methods. The explicit understanding of computer-based IIT workflow generated by this research provides opportunities to improve existing implementations in order to potentially yield outcomes observed in the Leuven study and prevent investment in costly and unproven replacement technologies. Researchers and practitioners of biomedical informatics and implementation science may

find the approach used in the dissertation helpful for managing and evaluating other interventions.

This research began with an organizational analysis of intensive insulin therapy adoption using institutional isomorphism [6] as a lens of inquiry. This portion of the dissertation examined assumptions and norms at the macro-level of the critical care community to position the research within a larger context. Through the influence of peers, regulators, and professions, healthcare organizations implemented intensive insulin therapy and became more similar but not necessarily more efficient: although critical care settings implemented IIT, the organizational changes required might not have produced intended effects as safety and effectiveness concerns increased [105]. The organizational analysis identified the problem investigated in this dissertation—that rules, policies, and procedures of IIT were disseminated without consideration of people, process, and technology interactions—as well as the hypothesis—that understanding IIT's people, process, and technology interactions will help hospitals achieve the benefits of the Leuven study.

The dissertation proceeded with a literature review and case study of clinical decision support systems for intensive insulin therapy [83]. Using institutional theory as a guide, the literature review demonstrated the inconsistent reporting of workflow and care process execution across published investigations, and the case study showed how the implementation of computer-based IIT required considerable organizational change and produced complexity as well as unintended consequences. From this analysis, three unexplored sources of variability emerged: opportunity for error involved in manually transcribing blood glucose values from testing devices to IIT CDSS, nurse perspectives

of system use, and the influence of site-specific clinical information systems and care processes on IIT CDSS. These three areas informed the remainder of the research.

The next phase of the dissertation involved a quantitative analysis of IIT CDSS in two parts. Objectives were to quantify the frequency and effect of blood glucose data mismatches and determine the characteristics and effects of nurse overrides on IIT CDSS performance. As identified in the literature review and case study, most IIT CDSS implementations assume the blood glucose value entered by a clinician into a computer to generate a protocol recommendation matches the corresponding value on a testing device [83]. This portion of the dissertation tested that assumption. After gathering 51 months of retrospective IIT CDSS and laboratory system data for two intensive care units at one teaching hospital, system output was recalculated for each IIT CDSS instance. Surprisingly, of the 189,499 IIT CDSS instances available for analysis, 11,901 lacked a device value and 1,788 failed to reproduce log output. Manual process error, undocumented code changes, and other technical and process issues may explain the discrepant data and illustrate the need for investigators to scrutinize clinical information system data for research and operational purposes. After excluding these data, 10,020 (5.3%) of 179,479 pairs of BG values were mismatched [92]. Overall insulin dosing appeared to not have been affected by mismatched data, but instances of hypo- and hyperglycemia may have been prevented had BG mismatches not occurred. Expert panel chart review is required to determine whether these instances represent preventable adverse events. Regardless, this analysis supported the claim that BG data entry is a "critical safety issue" for IIT [82] and established mismatched blood glucose data as a source of variability in IIT CDSS.

Using the same data set, the second part of the quantitative analysis examined a nurse's decision to accept or override an insulin dose recommended by IIT CDSS. Per the literature review and case study, nearly all published approaches assume nurses appropriately elect to override system recommendations. This part of the dissertation tested the assumption and evaluated nurse choices. Of the 179,452 IIT CDSS instances evaluated, 9,075 (5.1%) were overrides. More than four out of five overrides were less than recommended by IIT CDSS, and these doses usually differed by ≥25% from system recommendations. In contrast, greater than recommended doses were likely to differ by ≤25%. The decision to administer recommended and override doses resulted in appropriate changes in BG levels except for less than recommended administrations following BG increases from below to above 150 mg/dL. Findings indicated nurses used IIT CDSS recommendations and overrides to effectively treat hyperglycemia and prevent hypoglycemia. However, nurse "fear of hypoglycemia" [30] occasionally interfered with blood glucose control. Together these findings quantified nurse overrides as a source of IIT CDSS variability.

To understand why data mismatches and overrides occurred and how non-IIT CDSS activities affected and were affected by IIT CDSS, the final phase of the dissertation was an ethnographic study of nurses using IIT CDSS in two intensive care units at one academic medical center. This part of the dissertation investigated "…norms, values, choices, and interactions" [43] involved in system use. Objectives of the ethnography were to evaluate IIT CDSS with respect to other clinical information systems and processes and identify barriers and facilitators to system use. Notes from 49 hours of direct observation and interviews were analyzed inductively for themes to

emerge. Barriers included a tradeoff between computer use and patient care, especially related to use of a separate nursing documentation system; a lack of IIT CDSS reminders; user interface design assumptions; and potential for error in using medical devices. Facilitators included nurse trust in IIT CDSS combined with clinical judgment; value added to BG data entry by IIT CDSS; nurse resilience; and paper documentation. Together findings show that IIT CDSS is greater than the sum of its parts: systems and processes added before and after IIT CDSS affected protocol performance and directions for future improvement. Additionally, results corroborated findings from other CDSS studies and may contribute toward an empirically derived theory of CDSS.

As the debate over intensive insulin therapy's effectiveness and safety continues, researchers and practitioners can use the results of this dissertation to better define delivery of computer-based approaches. This research evaluated IIT CDSS use in two intensive care units, and results of this dissertation may not generalize to other institutions due to organizational and technological factors. Future work should address IIT CDSS use in other ICUs and non-ICU settings including imaging and surgery as well as alternative blood glucose regulation strategies in and patient transfer techniques between these sites. Data mismatches, override behavior, and IIT CDSS's relationship with other systems and care processes suggest that systematic improvements are possible through algorithm and interface changes.

Algorithm Changes

Similar to many institutions, the algorithm studied in this dissertation is based on a linear equation developed by Bode and White [51, 52] that uses blood glucose values as

input. Dissertation findings suggest the algorithm can be adjusted or replaced to improve glycemic control. In the quantitative analysis, nurses appropriately overrode IIT CDSS recommendations with the exception of administering less than recommended doses when BG increased from <150 mg/dL to >150 mg/dL prior to dosing. An adjusted algorithm can issue an alert encouraging users to administer the recommended dose in order to encourage glycemic control. In the ethnography, nurses cited nutrition sources as a reason to override IIT CDSS recommendations. Salience of nutrition sources suggests that the Bode and White linear equation might be at its limit and that algorithms incorporating nutrition sources, such as model predictive control [95], may be superior. Future work should address the development, validation, and implementation of next generation IIT CDSS algorithms that incorporate parameters beyond blood glucose values and nutrition sources. Machine learning techniques can be potentially helpful in identifying factors predicting hypoglycemia and new models for dosing based on a patient's genotype and phenotype. Basic science discoveries may also influence the future course of IIT CDSS algorithms, and translation of these findings into practice through informatics and workflow adjustment will be necessary. Regardless of the algorithm used, dissertation findings underscored the importance of allowing nurses to exercise clinical judgment and override system recommendations due to parameters falling outside the purview of computerized models.

Interface Changes

This dissertation established blood glucose data mismatches between handheld testing devices and manual entry as a source of IIT CDSS variability. Mismatched data

may have contributed to hypo- and hyperglycemic episodes [92], and several workflow modifications can potentially reduce the likelihood of data mismatches. Institutions can require two nurses to enter BG values into IIT CDSS for each instance to provide reliability. Such a change may overburden nurses in an already stressful environment. Glucometers capable of wirelessly transferring data to IIT CDSS may also be of benefit. However, in addition to the cost of replacing existing devices, ensuring a correct BG value transfers to the correct computer for the correct patient in a timely fashion may be a challenge. Installing docking stations at each patient bedside or nurse workstation would provide a direct link between BG testing devices and computers. Issues of transfer time across the hospital network initially led to the decision for nurses to manually enter blood glucose values [83], and the tradeoff of time for manual entry versus accuracy for automatic transfer demonstrates the real world advantage of manual transcription of BG values. In addition to mismatches, missing device BG data noted in this study suggests that docking may not always result in data transfer. Improved device and docking usability by manufacturers may improve the likelihood of transferring data from devices to clinical data repositories. The field of human computer interaction may also provide insight for designing user interfaces for manual transcription that reduce the likelihood of data entry error. One might argue that manual transcription is worth the risk until chart review can confirm mismatched data caused adverse drug events. At present, the overall benefit of IIT CDSS versus paper protocols—timelier, more accurate recommendations—appears to ultimately outweigh the risk of data mismatches caused by manual transcription.

By automatically capturing and storing insulin rates from infusion pumps in clinical data repositories, institutions can potentially monitor compliance between IIT CDSS and actual dosing to improve patient safety. The ethnography showed that IIT CDSS insulin rates may occasionally not be entered into pumps due to emergent care situations, typographical error, and nurse forgetfulness. Alerts based on pump-CDSS rate mismatch may help clinicians ensure proper insulin dosing. Although devices that constantly measure blood glucose and suggest insulin infusion rates are entering the market, they are costly and require integration with existing clinical information systems and workflow. Findings of this dissertation indicate that existing combinations of technology be adjusted before investing in replacement technology.

Intensive insulin therapy patient care and documentation consumes a considerable portion of a nurse's time, and IIT CDSS approaches should minimize time spent documenting while ensuring data accuracy. In the ethnography, nurses identified double documentation of IIT data between IIT CDSS and an electronic nursing documentation system as an unnecessary expenditure of effort. Transfer of data between systems or integration of decision support capabilities in nursing documentation systems can alleviate this concern. The ethnography also showed unintended and inaccurate use of interface features. Some nurses provided overrides using an interface portion intended for returning patients to the protocol after a temporary stoppage. To reduce the risk of improper use, interfaces should clearly identify the purpose of functions intended for occasional use (e.g. return from being off protocol, routine override). Although patients often received nutrition from multiple sources, the system only allowed nurses to select one source. Expected choices for blood glucose testing site and method were the

system's default selections, and nurses occasionally failed to change system selections when using alternate techniques. To ensure accurate collection of IIT CDSS data for secondary research and next generation algorithms, interfaces should enable selection of multiple nutrition sources and remove default site and method selections in favor of rapid pick lists (Figure 10).

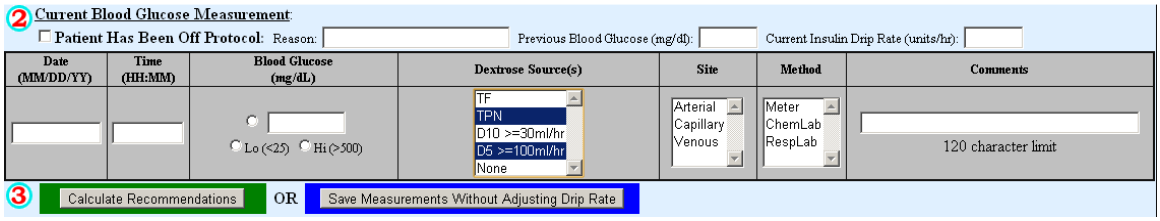


Figure 10. IIT CDSS interface modification enabling selection of multiple dextrose sources and removing blood glucose testing site and method in favor of rapid selection.

Improved visualization of blood glucose and insulin trend data may assist clinicians in making decision for IIT CDSS. As demonstrated in the quantitative analysis and ethnography, nurses appeared to administer less than recommended doses due to the dose amount and independent of the multiplier, an estimate of insulin resistance. Displaying the multiplier and other insulin resistance trends on screen is an area of future research. Additionally, displaying BG variability data such as number of hypoglycemic and hyperglycemic events may also assist clinical decision making. Interface changes, especially those involving new insulin resistance and blood glucose variability displays, will require appropriate training of nurses.

Dissertation Value for Different Stakeholders

This investigation of social, organizational, and contextual characteristics of computer-based intensive insulin therapy has implications for nurses, patients, healthcare institutions, informaticians, researchers, and managers. Nurses stand to benefit from software improvements based on dissertation findings that streamline workflow, save time, provide better decision support, and potentially increase job satisfaction. Through improved work processes, patients may receive better care as well as experience more time with care givers at the bedside instead of documenting on computers. For healthcare institutions, the effect of workflow modifications can potentially improve protocol compliance, care outcomes, and return on investment. Findings also provide guidance for informaticians developing IIT CDSS and point to data quality concerns that all clinical investigators should consider. For informaticians, researchers, and managers, explicit consideration of "assumptions, norms, values, choices, and interactions" [43] in planning, implementing, and evaluating clinical information systems can provide a perspective that improves the likelihood of project success. Social, organizational, and contextual interactions are critical to the success and failure of other clinical decision support systems and electronic medical record applications [17, 18]. Researchers and practitioners can use the approach from this dissertation for a variety of clinical interventions.

This research identified evidence of institutional isomorphism—the tendency for organizations to become more similar but not necessarily more efficient—in intensive insulin therapy adoption [105], and we have separately investigated the phenomena in the adoption of provider order entry, barcode medication administration, and health

information exchange [110]. Coercive forces through the American Recovery and Reinvestment Act will speed adoption of health information technology in the United States [110], and consideration of workflow, unintended consequences, and process changes related to new technologies in individual care settings [111] will be critically important for providers to achieve meaningful use of systems and taxpayers to receive return on investment.

A June 2010 study by the Leapfrog Group showing the continued prevalence of medication errors in 214 hospitals with provider order entry underscored the need for "monitoring and improvement at implementation and on a long-term basis" [112]. Prospective evaluation of clinical interventions using quantitative process measurement and qualitative workflow analysis has the potential to help institutions achieve intended efficiencies of IT-driven organizational changes and prevent ceremonial conformity to institutionalized forms that unintentionally have adverse operational effects [5]. Rigorous analysis and publication of findings from prospective mixed methods studies can fill a gap in the literature for detailed implementation strategies of clinical inventions that improve patient outcomes. The following illustrates this concept using computer-based intensive insulin therapy.

Explicit understanding of computer-based IIT workflow produced by this dissertation and nascent studies from other institutions can provide a blueprint for healthcare institutions with varying degrees of informatics resources. Institutions with robust informatics initially implementing computer-based intensive insulin therapy should prospectively monitor process variability (e.g. data mismatches and overrides) and outcomes (e.g. blood glucose variability, achievement of target ranges, mortality,

morbidity) through electronic dashboards in order to determine improvements to therapy delivery and overall care value. In order to rapidly identify and respond to protocol execution issues related to other systems and processes not detected by quantitative measurement, institutions should simultaneously perform qualitative analysis of the intervention using direct observation of workflow and clinician interviews. The combination of methods enables practitioners and researchers to identify discrepancies in data and work processes and to understand whether they interfere with intended care delivery (e.g. determining if data entry error appears to adversely affect insulin dosing). If after extensive workflow modifications an institution does not meet intended outcome goals, the organization should consider other options.

Institutions without the ability to rapidly audit clinical performance may choose to wait for new randomized studies and meta-analyses showing therapy effectiveness before implementing necessary process changes. Healthcare organizations lacking solid informatics foundations should guide IIT CDSS implementation with respect to process variability sources, user interface issues, and nurse workflow concerns identified in this research. If development of quantitative measurement tools is too expensive in certain settings, qualitative analysis of workflow impact may suffice by providing a means to identify and resolve workflow issues interfering with intended care delivery. For clinical process changes mandated by government and other oversight agencies, ongoing qualitative analysis and process refinement is critical. Sources of coercive influence, such as government, should consider the availability of detailed process understanding before requiring other organizations to adopt new therapies.

Closing Words

Workflow is an often taken-for-granted assumption in clinical investigations, and this dissertation demonstrated the importance of considering workflow as a dynamic rather than as a static entity for computer-based intensive insulin therapy. Detailed description in the literature of the methods of computer-based intensive insulin therapy—or any intervention—can help healthcare organizations achieve the results of exemplar institutions.

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ROLE OF STUDENT IN CO-AUTHORED MANUSCRIPTS

Mr. Campion was responsible for concept formulation, literature review, case study formulation, experimental design, programming, statistical analysis, ethnographic data collection and analysis, and general authorship in all manuscripts. Dr. Gadd supervised Mr. Campion throughout these phases, and Drs. Lorenzi, May, Ozdas, and Waitman provided critical revisions. Additionally, Dr. May provided Mr. Campion access to the study site and data.

This dissertation includes work published or submitted for publication in academic journals. At the time of this writing, Chapter I [105] (with exception of "specific aims" section), Chapter II [83], and Chapter III [92] have been accepted for publication while Chapter IV and Chapter V are under review. The following paragraph presents copyright permission in the parlance of each publisher's license.

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mismatches on a computer-based intensive insulin therapy protocol, 2010, Epub ahead of print DOI:10.1007/s00134-010-1868-7, Campion TR Jr, May AK, Waitman LR, Ozdas A, Gadd CS.