Discovering Hidden Patterns in Anesthesia Data Associated with Unanticipated Intensive Care Unit Admissions

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Jessica Jean Peterson

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Bonnie L. Westra, PhD, Adviser and Karen A. Monsen, PhD, Co-adviser

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DEDICATION

The author has dedicated this dissertation to all of the patients that have had surgery with anesthesia and the providers that care for them. Patients rely on anesthesia providers to keep them safe during surgery and deliver effective care that is focused on the human health experience. Anesthesia providers have championed patient safety initiatives for decades. May anesthesia providers continue to partner with hospital administrators, governmental agencies, and patient advocate groups to improve the surgical experience and quality anesthesia care.

ABSTRACT

Unanticipated intensive care unit admissions (UIA) are a metric of quality anesthesia care since they have been associated with intraoperative incidents and nearly four times as likely to die within 30 days of surgery compared to patients that were not admitted to the intensive care unit unexpectedly. Patient age, American Society of Anesthesiology Classification, type of procedure, tachycardia, hypotension, and cardiovascular and neuromuscular blocking drugs administered in the operating room have all been associated with patient UIA. Intraoperative anesthesia data is generated in real-time and can be used to identify patterns in patient care associated with UIA. Knowledge about patterns in intraoperative medication administration and hemodynamic data is important to develop interventions that can be used to prevent intraoperative deterioration. Patterns were defined as two or more characteristics in the line graphs.

This data visualization study discovered, labeled, and tested patterns in intraoperative hemodynamic management for association with patient UIA. Data from 68 adult, inpatient, elective surgical patients were matched to 34 patients with UIA in the University of Minnesota, Academic Health Center, Clinical Data Repository. A prototype line graph was evaluated to identify salient (obvious) patterns in intraoperative hemodynamic management for the data set. Line graphs for patients with and without UIA were created and visualized. Patterns in intraoperative hemodynamic management were discovered using data visualization with line graphs and operationally defined. Odds ratios were used to test categorical patterns and one-way analysis of variance was used to test continuous numeric patterns for association with patient UIA. Seven patterns were significantly associated with patient UIA ($p < .05$).

Patterns included characteristics of time, shape of the lines, and line labels. The patterns of moderate doses of local anesthetics during induction, large doses of neuromuscular blocking drugs during induction, and moderate doses of central nervous system drugs during maintenance anesthesia were more likely to be associated with patient UIA. The patterns of large doses of local anesthetic during induction, anti-infective line, gap in hemodynamic data during emergence, and hypodynamic data during maintenance anesthesia were less likely to be associated with patient UIA.

The researcher in this study encountered challenges with missing data and data redundancy. It was feasible to initiate manual procedures to ensure data quality. The intraoperative hemodynamic data management patterns identified in this study generated new insight into the relative dose and timing of intraoperative medication administration associated with patient UIA. Both the findings from this study and data visualization methods will be advantageous in future research to identify and test more complex patterns for association with patient UIA. Sophisticated intraoperative hemodynamic patterns can be used to tailor interventions aimed to prevent intraoperative deterioration and patient UIA.

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Chapter 1

INTRODUCTION

In 2001 the Institute of Medicine (IOM) reported that a large proportion of healthcare was ineffective, wasteful, or unsafe (Institute of Medicine (US) Committee on Quality of Health Care, in America, 2001). The 2001 IOM report was a catalyst for healthcare redesign and generated numerous initiatives focused on improving patient care. One quality care initiative that has been used to track patient safety and effective patient care is the incidence of unanticipated intensive care unit admissions (UIA), defined as the rate of unplanned patient admissions to an intensive care unit (ICU) within 24 hours of surgery with anesthesia (American Society of Anesthesiology, 2014). Since anesthesia providers are expected to deliver safe anxiolysis, amnesia, akinesia, analgesia, and autonomic stability during surgery to improve the patient's health status, patients with UIA are a valid quality care metric of anesthesia care (AANA Board of Directors, 2005; American Society of Anesthesiology Committee on Surgical Anesthesia, 2011; Haller, Myles, Langley, Stoelwinder, & McNeil, 2008; Haller, Stoelwinder, Myles, & McNeil, 2009).

National healthcare initiatives have also called upon electronic health record (EHR) data and information technology tools to improve quality patient care in an effort to reduce patient morbidity and mortality (The White House, Office of the Press Secretary, 2015; U. S. Department of Health and Human Services, Agency for Health Research and Quality, 2014). Electronic health record data have been described as a rich source of information for quality care initiatives since a large volume and variety of time-dependent data can be used to provide insight into the trajectory of patient care (Bates, Saria, Ohno-Machado, Shah, & Escobar, 2014; Peters & Buntrock, 2014; Simpson, 2015). Anesthesia data is a logical data source for intraoperative health trajectory research as more than 30 demographic and 25 physiologic time-dependent data types are routinely documented in the patients EHR and anesthesia data are a source of real-time intraoperative information (Kadry, Feaster, Macario, & Ehrenfeld, 2012; Peterson, White, Westra, & Monsen, 2014; Shah & O'Reilly, 2008). Intraoperative anesthesia data is the only source of real-time, granular assessment and intervention EHR data that can be used to identify patterns in intraoperative events that are associated with patient UIA. In this study, a large volume and variety of anesthesia data routinely collected on patient's surgical encounters with and without an UIA were analyzed with information technology tools and data visualization using line graphs to generate new insight into how patients deteriorated during routine anesthesia care.

Information technology tools and innovative research methods such as data visualization can be used to effectively analyze complex time-dependent data sets and generate data-driven hypotheses about the sequence and timing of events for quality care initiatives (Berger & Berger, 2004; Krumholz, 2014; Simpson, 2015). Innovative research methods are urgently needed to advance knowledge about how patients deteriorated with an UIA. Despite two decades of research the incidence of patients with UIA has remained unchanged (Haller et al., 2005; Rose, Byrick, Cohen, & Caskennette, 1996; Swann, Houston, & Goldberg, 1993; Wanderer, Anderson-Dam, Levine, & Bittner, 2013). Thus far, research has emphasized demographic variables predictive of or associated with UIA such as advanced age and American Society of Anesthesiology classification status. However, identification of these demographic variables has been ineffective at reducing the incidence of patient UIA. Prior research has also identified intraoperative incidents or near misses were associated with patient UIA and the majority of patients with UIA were diagnosed with acute cardiovascular events (Brunelli et al., 2008; Bui et al., 2011; Cullen, Nemeskal, Cooper, Zaslavsky, & Dwyer, 1992; Haller et al., 2005). This evidence would suggest that there are patterns in intraoperative hemodynamic assessments and interventions in patients with UIA. Research is needed to explore how intraoperative hemodynamic assessments and medication interventions changed during patient care and were associated with patient UIA.

Significance of the Problem

Every year there are more than 50 million anesthetics performed in the United States and in 2014 over 3% of these patients were an UIA (Center for Disease Control and Prevention, April 29, 2015; Kim et al., 2014; Theron et al., 2014). Patients with UIA required prolonged, high-acuity intraoperative and postoperative care (Bates et al., 2014; Haller et al., 2005; Kamath et al., 2012). Specifically, patients with UIA were eight times more likely to have an *intraoperative* incident or near miss, hospitalized 14 days longer, and nearly four times as likely to die within 30 days of surgery compared to patients that were not admitted to the ICU unexpectedly (Haller et al., 2005). In 2014, the cost of intraoperative and postoperative care for patients with UIA was estimated to be over 10 trillion dollars (Center for Disease Control and Prevention, April 29, 2015; Dasta, McLaughlin, Mody, & Piech, 2005; Macario, 2010; Wanderer et al., 2013).

There is an urgent need to mitigate the cost of patient care associated with UIA. In 2015, Centers for Medicare and Medicaid Services (CMS) initiated a negative reimbursement adjustment for injury or illness caused by assessment or treatment provided during hospitalization (Centers for Medicare and Medicaid Services, 2015). The negative reimbursement adjustment meant CMS no longer reimbursed healthcare services when a complication occurred or for healthcare services used to treat hospital acquired complications. Lost revenue due to patient with UIA would threaten the financial viability of healthcare organizations (American Association of Nurse Anesthetists, 2015; Centers for Medicare and Medicaid Services, 2015; Haller et al., 2005; Kamath et al., 2013; Theron et al., 2014). The change to an outcome-based reimbursement system has put tremendous pressure on healthcare organizations to partner with researchers to improve quality care initiatives such as patient UIA.

As in other healthcare research, patients have multiple variables that interact over time to influence clinical decisions, quality care, and patient outcomes (Donabedian, 1988; Donabedian, 1983). Quality care initiatives focused on inpatient readmission, morbidity, or mortality offered insight into how time-dependent EHR data and information technology tools can be incorporated into research designs and generate knowledge to improve patient care. Related research on premature infants and adult depression used time-dependent EHR data and information technology tools to identify patterns in patient care and improve outcomes. Premature infants randomized to have five-day heart rate trends displayed on bedside monitors received interventions to treat early onset of sepsis and were 0.75 times as likely to die within three months (Moorman et al., 2011). A study on adult depression extracted time-dependent demographic, assessment, and intervention EHR data over five years and researchers identified a pattern among medication category, duration of the first episode of depression, and risk of recurrent depression (Li, 2012). This evidence suggested that time-dependent EHR data and information technology tools can be used to improve patient care and may generate new insight into how patients with UIA deteriorated during surgery with anesthesia care.

Prior research on patients with UIA used EHR data and information technology tools to extract and analyze demographic and intraoperative variables predictive of or associated with UIA. However, prior research analyzed univariate dichotomous data. Therefore, it is not known how repeated intraoperative hemodynamic assessments and interventions changed over time in patients with UIA. In prior research, age, American Society of Anesthesiology (ASA) classification, intraoperative vasopressor administration, blood transfusion, heart rate (HR), and systolic blood pressure (SBP) measurements were significantly associated with patient UIA (Brunelli et al., 2008; Haller et al., 2005; Wanderer et al., 2013). However, little is known about how intraoperative hemodynamic data changed over time in a patient with an UIA. Innovative research methods such as data visualization can be used to analyze EHR data with information technology tools and discover knowledge about how intraoperative HR, SBP, and medication administration data changed during surgery with anesthesia. New knowledge about patterns in intraoperative hemodynamic management associated with patient UIA can be used to develop and test early warning/ detection interventions in future research.

Purpose and Specific Aims

The purpose of this study was to discover time-dependent intraoperative hemodynamic management data patterns associated with patient UIA. This study extracted and analyzed time-dependent intraoperative HR, SBP, and medication administration data and used data visualization with line graphs to identify intraoperative hemodynamic management data patterns using visual perception, preattentive reasoning, and human intelligence. The specific aims of this study were:

1) Evaluate the salience of a prototype visualization for the intraoperative anesthesia data set;
2) Discover, label, and define patterns in intraoperative hemodynamic management data for each patient with and without an UIA;
3) Compare patterns identified in Aim 2 for associations with patient UIA.

This study analyzed patients with UIA using data visualization with line graphs and a case-control study design to evaluate the concepts of intraoperative hemodynamic management and quality anesthesia care. Exploratory research on patients with UIA, intraoperative hemodynamic management, and quality anesthesia care may add new insight into the literature that has sought to explain UIA with demographic variables.

Conceptual Framework

Unanticipated intensive care unit admissions have been linked to the constructs of intraoperative hemodynamic management and quality anesthesia care (American Society of Anesthesiology, 2014; Haller et al., 2005; Haller et al., 2008). Quality patient care was not directly observable and has been theorized to be safe, effective, efficient, holistic, and compassionate (Burhans & Alligood, 2010; Donabedian, 1983; Lee, 2013). Therefore, the theory of quality care assessment and the concept of intraoperative hemodynamic management were used to create a conceptual framework for this data visualization study on patient with UIA (Donabedian, 1988).

Theory of quality care assessment. The theory of quality care assessment was used to describe how healthcare providers are expected to deliver competent, knowledgeable care within the standard of their respective discipline to have a positive influence on patients' behavior, social network, physical health, or mental health (Donabedian, 1988; Donabedian, 1978). The theory of quality care assessment was also used to conceptualize how to perform research on quality intraoperative anesthesia care. Based upon the theory of quality care assessment, researchers analyzed how structure and process predictors generated a positive or negative change in the health status (Figure 1.1) (Donabedian, 1988; Donabedian, 1978; Donabedian, 1983). Structure predictors were defined as attributes of the environment or clinician that influenced patient care such as physical space, equipment, or clinician qualifications (Donabedian, 1988; Donabedian, 1983). Patient attributes were de-emphasized in the theory of quality care assessment but other literature about quality patient care included demographic predictors such as patient age or comorbidities to understand a change in patient status (Institute of Medicine Committee on Quality of Health Care in America, 2001; Kreitzer, 2015; Lee, 2013). Process predictors were described as observations or actions involved in giving or receiving care such as performing surgery (Donabedian, 1988). Finally, patient outcomes were described as positive or negative changes in health status attributed to patient care such as measures of morbidity, mortality, or adverse events (Donabedian, 1988).

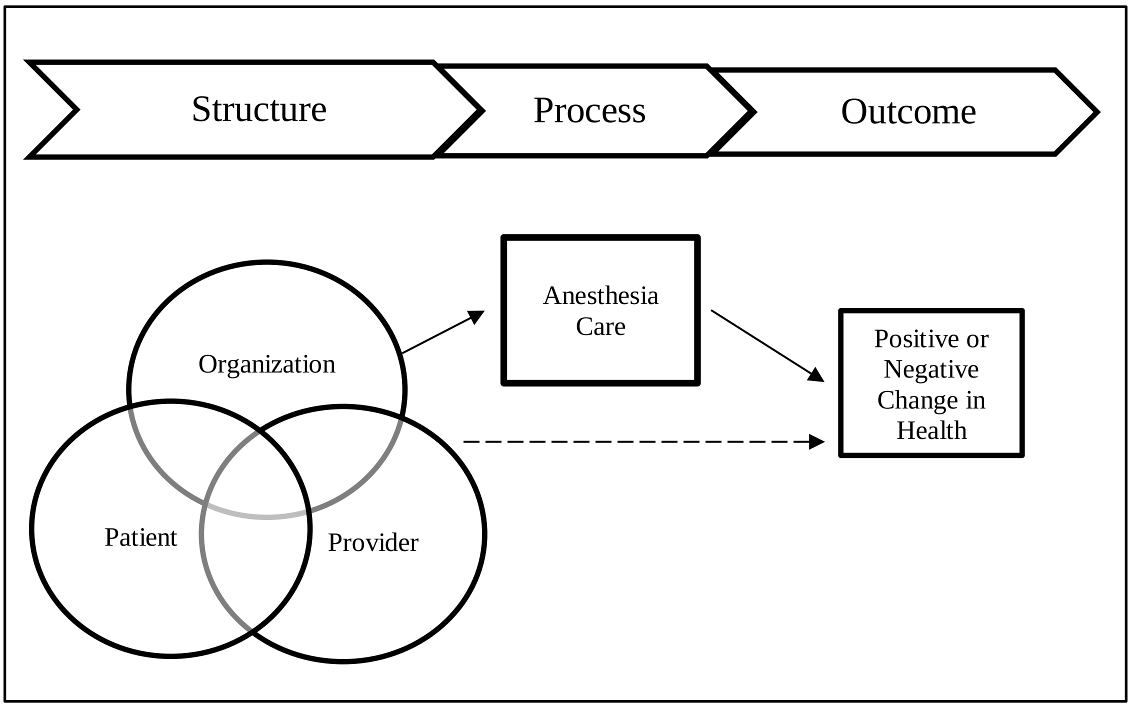


Figure 1.1. Conceptual Model of Quality Anesthesia Care

a. Adapted from the theory of quality care assessment (Donabedian, 1988; Donabedian, 1983).

In the theory of quality care assessment, process variables were used to moderate structure variables and *change* a patient outcome (Donabedian, 1988). Two other fundamental aspects of quality care assessment and research on patients with UIA were time-dependent data and the concept of change over time. Health trajectory research has modeled variables predictive of or associated with an outcome and has the potential to identify dynamic acceleration or deceleration in a patient's health status (Andrienko & Andrienko, 2006; Henly, Wyman, & Findorff, 2011). When structure and process predictors are integrated in health trajectory research, knowledge about patterns in health status over time can be used to identify patients with the greatest risk for adverse outcomes (Donabedian, 1988; Henly et al., 2011).

The theory of quality care assessment has been adapted to anesthesia care and was used to operationalize how patient characteristics were moderated by anesthesia assessments and interventions such as intraoperative medication administration and hemodynamic data to change the patient's health status within 24 hours of surgery with anesthesia. Therefore, the theory of quality care assessment provided the theoretical linkage between patient's demographic variables, intraoperative events such as HR, and SBP assessments and medication administration, and patients with UIA. However, the theory of quality care assessment did not provide the theoretical linkage about how routine surgical encounters deteriorated during routine anesthesia care. To guide selection of variables for knowledge discovery with databases the theory of quality care assessment was combined with the concept of hemodynamic stability and intraoperative hemodynamic management.

Intraoperative hemodynamic management. The conceptual framework of intraoperative hemodynamic management was used to describe the cyclic process of clinical decision-making about intraoperative hemodynamic data and medication administration in patients with and without an UIA (Figure 1.3). This conceptual framework was used to link patient characteristics with anesthesia provider's clinical decision-making which are hypothesized to change a patient's health status during surgery with anesthesia. During surgery, the anesthesia provider is constantly comparing hemodynamic assessments and medication administration to tacit and experiential knowledge about pharmacology and physiology to maintain hemodynamic stability. The conceptual framework of intraoperative hemodynamic management was used to guide the review of the literature and selection of data that was associated with patient UIA.

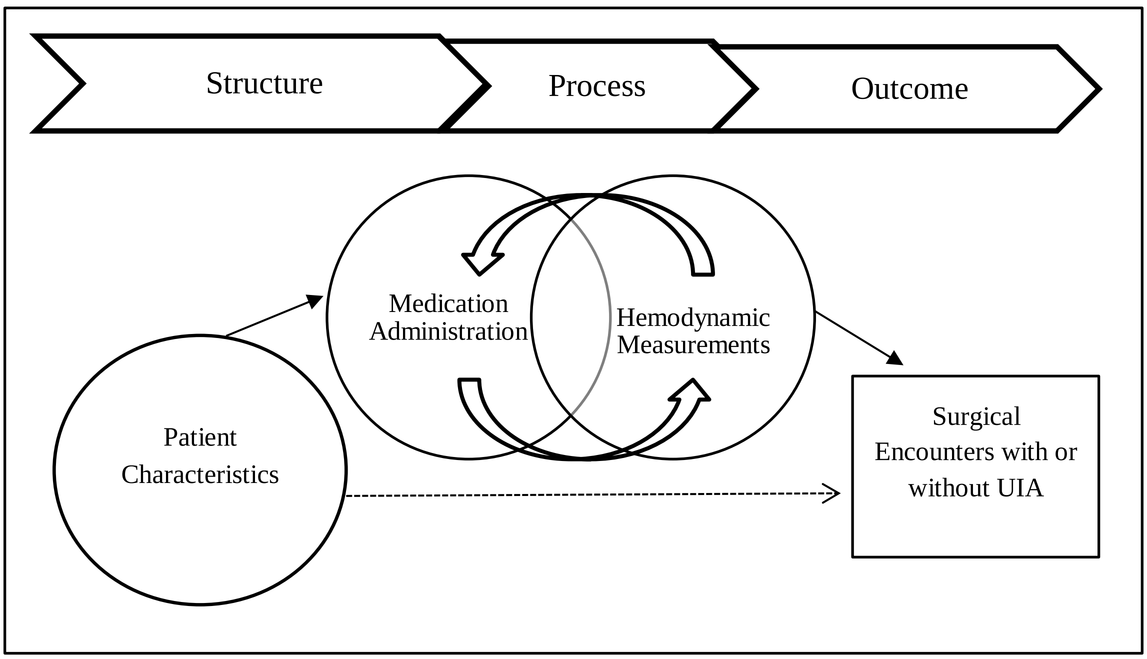


Figure 1.2. Conceptual Model of Intraoperative Hemodynamic Management.

Note. Adapted from the theory of the quality care and the concept of hemodynamic stability (Donabedian, 1988; Peterson, Westra, & Monsen, 2015). Original figure.

Hemodynamic stability. The concept of hemodynamic stability was used to further delineate the process of intraoperative hemodynamic management. There were three attributes for the concept of hemodynamic stability: *blood flow*, *fluctuation within stated parameters*, and *measured or evaluated in the context of time* (Figure 1.3). Blood flow was described as a physiologic function that was assessed by one or more types of measurements. Heart rate (HR) or mean arterial blood pressure (MAP) were the most frequently cited hemodynamic measurements used to assess blood flow (Cillo, 2012; McDonald, Fernando, Ashpole, & Columb, 2011; Vimlati, Larsson, Hedenstierna, & Lichtwarck-Aschoff, 2012; Zhou, Xiao, & Yun, 2013). However, combinations of measurements such as HR and SBP provided a more thorough assessment of hemodynamic stability and were also frequently cited in the literature (Allen, George, White, Muir, & Habib, 2010; Huey-Ling, Chun-Che, Jen-Jen, Shau-Ting, & Hsing-I, 2008; McDonald et al., 2011; Zhou et al., 2013).

The second attribute of hemodynamic stability was fluctuation within stated parameters and often referred to a percent change in a HR, blood pressure (BP), systolic blood pressure (SBP), MAP, or cardiac output from a respective baseline value. The percent increase or decrease from baseline ranged from 5 to 30% in the literature (Smischney, Beach, Loftus, Dodds, & Koff, 2012; Solanki, Puri, & Mathew, 2010; Summers, Harrison, Thompson, Porter, & Coleman, 2011; Vimlati et al., 2012; Zhou et al., 2013). A 20% change from baseline was the most commonly suggested parameter for fluctuation of blood flow (Allen et al., 2010; Chen et al., 2010; Cillo, 2012; de

Barbieri, Frigo, & Zampieron, 2009; McDonald et al., 2011; Smischney et al., 2012; Vimlati et al., 2012; White et al., 2009).

The final attribute of intraoperative hemodynamic management was temporality which described the frequency and duration of blood flow measurements. Measurements were taken at one moment in time or re-evaluated at various time intervals such as every three minutes or continuously (Brady, 2010; Cillo, 2012; Dere et al., 2010; Smischney et al., 2012). The other temporal characteristic was the duration of time used to compare blood flow measurements and the literature described that measurements needed to remain unchanged for minutes or hours to be considered hemodynamically stable (Allen et al., 2010; McDonald et al., 2011; Smischney et al., 2012; Tan, van Stigt, & van Vugt, 2010; Zhou et al., 2013). The concept of hemodynamic stability was used to integrate the attributes of *blood flow*, *fluctuation within stated parameters*, and *measured or evaluated in the context of time* and was defined as a physiological state consisting of circulatory responses to internal or external stimuli where blood flow fluctuated within parameters that were measured or evaluated over time (Peterson et al., 2015).

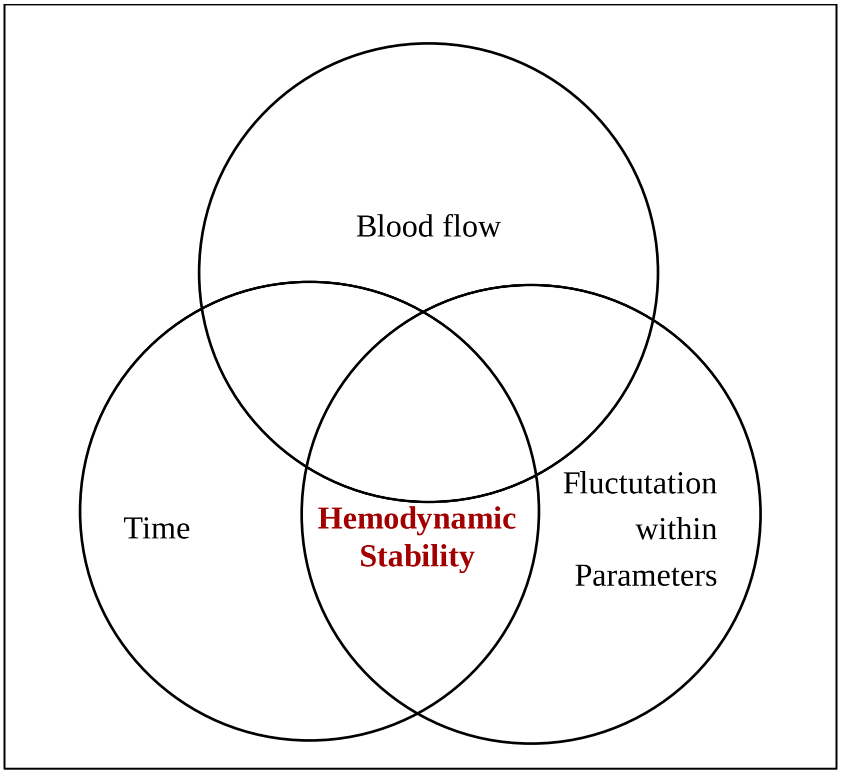


Figure 1.3. Conceptual Model of Hemodynamic Stability

Note. Model to represent how the attributes of blood flow, time, and fluctuation with parameters overlap and are used to define hemodynamic stability. Original figure.

Conclusion

Patients with UIA are a high-risk, high-cost population, and hospitals will no longer be reimbursed for their care. The theory of quality care assessment and concepts of intraoperative hemodynamic management and hemodynamic stability were used to conceptualize and link multiple variables and time-dependent intraoperative data for patients with and without an UIA to study how surgical encounters deteriorated during routine care. Data visualization using line graphs is an innovative research method that was used to discover hidden patterns in patient surgical encounters with and without UIA and advance a research agenda toward reducing the incidence of UIA.

Chapter 2

REVIEW OF THE LITERATURE

The conceptual framework outlined in the previous chapter was used to guide a review of the literature about demographic and clinical variables predictive of or associated with intraoperative hemodynamic management in patients with UIA. The review of the literature was organized around structure and process variables of patients with UIA as outlined from the theory of quality care assessment. First, the search strategy will be outlined. Then the review of the literature will be used to define the concept of patients with UIA as a metric of quality anesthesia care and discuss how patients UIA have been operationalized in prior research. Next, each structure and process variable of a patients UIA are defined and evaluated according to how the variable was reported by researchers in the literature. Finally, implications for future research on UIA will be presented.

Search Strategy

A literature search was conducted with the following electronic databases: PubMed, Cumulative Index to Nursing & Allied Health Literature (CINAHL), and OVID Medline. The following title and abstract search strategy was used for PubMed and CINAHL: (unplanned or unanticipated or unbooked or unintended or unexpected) AND (operating room or postsurgical or postoperative) AND (admission or admit or admissions or admitted) AND Publication Date (MM/DD/YYYY-06/30/2015). The publication date was not restricted and the electronic databases were searched on 07/17/2015. The following keyword search strategy was used for OVID Medline: (unanticipated or unplanned or unexpected or unbooked or unintended) within three words of (admission or admit) AND (operating room or postoperative or postsurgical). Seven hundred forty-three titles and abstracts were reviewed.

Inclusion and Exclusion Criteria

Articles were included if they contained demographic or intraoperative hemodynamic information about an adult (age ≥ 18 years old) patients surgical encounters with UIA. Articles were excluded if they only described a patients UIA that was *more than* 24 hours after surgery or omitted how long after surgery the UIA occurred. After duplicates were removed and the inclusion/ exclusion criteria were applied twenty-one articles remained and two articles were added from a cited reference search.

Quality of the Evidence

Eleven of the studies included in the systematic review of the literature on a patients surgical encounters with UIA were observational study designs and were evaluated according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist (Institute of Social and Preventative Medicine, University of Bern, 2009). Two of the studies were non-randomized experimental study designs and were evaluated according to the Transparent Reporting of Evaluations with Nonrandomized Designs (TREND) checklist (Centers for Disease Control and Prevention, 2014). The remaining studies were either case reports or a review of the literature. Overall the quality of the evidence was good; the average STROBE score was 17.6 out of 22 (range 13-21) and the average TREND score was 18 out of 22 (range 15-21). Next, structure, process, and outcome data were abstracted from each study with the Matrix Method (Garrard, 2011). Twenty-two items to describe the study, nine structure variables, 21 process variables, and 31 admission diagnoses associated with a patient's surgical encounters with UIA were abstracted and placed in the literature matrix. The literature matrix was used to synthesize the evidence how patients with UIA were operationalized; as well as structure and process variables predictive of or associated with UIA.

The first studies that contained statistically significant structure and process variables of adult patients with UIA were published in the 1990s and may have contained measurement error because data were manually collected from hand-written records which adjusted physiologic measurements toward favorable values (Cook, McDonald, & Nunziata, 1989; Cullen et al., 1992; Rose et al., 1996). Despite the potential measurement error, these studies were included in the review of the literature because they established relationships between the structure of American Society of Anesthesiology physical classification (ASA class), process of intraoperative physiologic management, and the outcome of patients with UIA which were used in subsequent research. Beginning in 2005, large cohort studies (N > 40,000 surgical encounters) used electronic health record (EHR) data to analyze predictors of patients with UIA. These studies reduced measurement error and respondent bias with EHR data but large sample sizes were prone to type I error and the statistical strength of quantitative data were analyzed categorically (Ludbrook, 2008; Mosteller, Gilbert, & McPeek, 2006).

The significant structure variables associated with patient UIA were: age, ASA class, comorbidities, elective or emergent procedure, gender, surgical procedure. The significant process variables were: estimated blood loss, intraoperative blood pressure, heart rate, neuromuscular blocking drug administration, packed red blood cell transfusion, pulse oximetry, sympathomimetic administration, and temporality. These were classified into demographic predictors which were characteristics of the patient's surgical encounter that could not be manipulated or intraoperative hemodynamic variables which were independent variables observed or manipulated during intraoperative anesthesia care (Concato, Feinstein, & Holford, 2006).

Outcome Variable: Unanticipated Intensive Care Unit Admissions

Conceptually, patients with UIA have been used to represent unsafe, ineffective anesthesia care during surgery (American Society of Anesthesiology, 2014; Haller et al., 2005). Theoretically, inpatient, elective surgical encounters with UIA had medical conditions optimized prior to surgery, deteriorated unexpectedly, received high acuity intraoperative anesthesia care, and required invasive postoperative cardiopulmonary care (Haller et al., 2005). Since patients received surgery with anesthesia care prior to the negative change in health status their intraoperative anesthesia care theoretically contributed to the patients UIA (Haller et al., 2005). Patients with UIA have been operationalized as a patients surgical encounter with anesthesia care not registered to be admitted to an ICU prior to the start of surgery and admitted to the ICU within 48 hours after surgery (American Society of Anesthesiology, 2014). However, side effects or complications of anesthesia interventions do not exceed 24 hours (American Society of Anesthesiology Committee on Standards and Practice Parameters, 2011; American Society of Anesthesiology Committee on Surgical Anesthesia, 2011; Kwo, 2008).

Researchers in 60% of the studies described how patient's surgical encounters were classified as UIA. Among these studies, researchers described validation of a patients UIA with a second data source or by another data analyst (Bui et al., 2011; Haller et al., 2005; Haller et al., 2008; Harris, Runnels, & Matz, 2001; Jaffer et al., 2005; Kamath et al., 2012; Kamath et al., 2013; Piercy et al., 2006; Swann et al., 1993; Theron et al., 2014). One challenge for researchers was to verify that a patient's surgical encounter was not planned to be an ICU admission prior to surgery and was admitted to an ICU within 24 hours of surgery with anesthesia. Researchers in 26% of the studies used electronic registration data to verify ICU admission (Haller et al., 2005; Haller et al., 2008; Harris et al., 2001; Kamath et al., 2013; Theron et al., 2014; Wanderer et al., 2013). Researchers in one study used electronic time-dependent registration data to determine that the surgical encounter was not registered for ICU at the beginning of surgery and was admitted to the ICU within 24 hours of surgery (Haller et al., 2005). The gap in knowledge about measurement of a patients UIA was the reliability of registration data. Researchers should report the frequency of missing registration data when they report the incidence of patient UIA.

Variables Predictive of or Associated with UIA

A systematic review of the literature was performed on adult patients UIA and included 23 studies from 11 different countries. Researchers in 13 studies described statistically significant variables associated with or predictive of patients UIA (Table 2.1). The remaining studies were case reports, analyzed variables with a count or percentage, or combined variables of UIA with other outcome variables. Demographic and intraoperative hemodynamic variables of patients UIA were extracted from the literature to synthesize evidence about the structure and process of intraoperative deterioration and UIA. Admission diagnoses were also extracted from the literature to evaluate the theoretical linkages between statistically significant variables and a patients UIA.

Table 2.1. *Literature Matrix*

Study	**Design**	**Sample** [a]	**Variables Associated with or Predictive of UIA** (95% Confidence Interval, p-value)
Brunelli et al. (2008)	Observational Retrospective cohort	82/1297 consecutive patients	Age: > 65 LR β 0.04 (SE 0.01, p <. 01) Cardiac Comorbidity: adj MLR β 0.03 (SE 0.01, p = .04) Predicted FEV_1< 65%: adj MLR β .04 (SE .01, p <. 01) Procedure: Pneumonectomy adj MLR β .09 (SE .02, p < .01)
Bui et al. (2011)	Observational Retrospective Cohort	8/394 consecutive patients	Age: mean 68.6 (p = .02) Procedure: Supra vs Infratentorial Craniotomy (p = .83)
Chi et al. (2011)	Observational Retrospective cohort	≤29/141 consecutive ovarian cancer patients	Age: > 60 (p = .57) ASA class: I, II, or III (p = .19) Comorbidity: BMI ≥ 24 (p = .04) Estimated blood loss: ≥ 1 liter (p <.01) Timing of Surgery: ≥ 327 min (p < .01)
Cullen et al. (1992)	Observational Case-control	71/17076 consecutive patients	Age: < 41, 41-65, > 65 adj LR 1.82 (1.54-3.38, p < .01) ASA class: ≥ III adj LR 2.33 (2.18-5.12, p < .01) Intraoperative pulse oximetry (p < .01)
Eichenberger et al. (2011)	Experimental Nonrandomized clinical trial	103/5013 consecutive PACU[b] surgical encounters	ASA class I-II: adj OR 0.71 (0.37-1.35, p = .30) ASA class III-V: adj OR 0.74 (0.51-1.08, p = .12)

Ezri et al. (2004)	Observational Retrospective cohort	1/234	Procedure: Laproscopic vs Open Bariatric Surgery (p = .28)
Grosse-Sundrup et al. (2012)	Observational Case-control	249/18579 consecutive surgical encounters	Intraoperative: NMBD[c] OR 1.4 (1.09-1.80, p < .01)
Haller et al. (2008)	Observational Retrospective cohort	188/188	NA
Haller et al. (2005)	Observational Prospective cohort	201/44130 consecutive surgical encounters, excluded: cardiac, lung, transplant, multi-trauma, and ruptured aortic procedures	Age: < 41 baseline group 41-64 OR 1.17 (0.77-1.78, p < .01) > 64 OR 2.86 (2.00-4.12, p < .01) ASA I: baseline group II: OR 4.12 (1.85-9.17) III: OR 11.15 (5.17-24.04) IV: OR 29.9 (13.63-65.62) V: OR 13.08 (1.59-107.13) Difference (p < .01) Comorbidity: Anemia 2.87 (1.85-4.31, p <.01) CAD OR 2.07 (1.45-2.8, p <.01) CHF OR 2.34 (1.71-3.18, p <.01) CVD OR 3.04 (1.97-4.53, p < .01) HTN OR 2.10 (1.57-2.82, p < .01) Obesity OR 1.91 (1.26-2.82, p <.01) Renal failure OR 1.86 (1.00-3.20, p = .04) Shock OR 4.36 (2.68-6.78, p < .01) Emergent Procedure: OR 2.69 (1.78-3.95, p < .01) Male: OR 1.83 (1.34-2.51, p < .01) Procedure: Derm/ Plastics- baseline Blood forming: OR 4.74 (1.18-18.98) CNS: OR 8.59 (3.04-24.29) Cardiac OR 6.41(2.25-18.26) Digestive: OR 4.53 (1.65-12.40)

			Ear, Nose, Throat: OR 1.93 (.43-8.63) Eye: OR 0 Female breast or genital: OR 0.73 (0.13-4.00) Respiratory: OR 7.04 (2.20-22.5) Difference ($p < .01$) Timing of Surgery: In hours: OR 0.27 (0.20-0.37, $p < .01$) Late hours: OR 5.33 (3.54-7.80, $p < .01$) After hours: OR 2.25 (1.54-3.20, $p < .01$)
Harris et al. (2001)	Observational: Retrospective cohort	16/109 consecutive cervical spine surgical encounters	Age: older mean +/- SEM ($p < .05$) Comorbidity: Alcoholism ($p > .50$) CAD ($p < .05$), DM ($p < .01$) HTN ($p < .02$), Tobacco ($p > .99$), PVD ($p > .99$) Procedure: Anterior decompression ($p > .15$)
Ivic et al. (2011)	Observational Case report	1/1	NA
Jaffer et al. (2005)	Observational Prospective cohort	1/510	NA
Kamath et al. (2013)	Experimental Nonrandom clinical trial	4/175	NA
Kamath et al. (2012)	Observational Prospective cohort	89/1259 consecutive surgical encounters	Age: > 75 OR 2.9 (1.5-2.9, $p < .01$) ASA $\geq$ 3: OR 20.5 (8.7-50.1, $p < .01$) Comorbidity: BMI > 35: OR 2.5 (1.3-10.4, $p = .02$) MI: OR 5.6 (1.8-18.4, $p = .01$) OSA: OR 3.6 (1.3-10.4, $p =.10$) Renal disease: OR 6.1 (2.5-15.1, $p < .01$) Female ($p = .83$)

			Intraoperative: Avg minimum MAP (p = .14) Avg maximum MAP (p = .47) Avg minimum HR (p = .02) Avg maximum HR (p = .10) Estimated blood loss (p < .01) PRBC OR 7.1 (3.1-16.1, p < .01) Sympathomimetics OR 5.9 (1.7-22.4, p = .01)
Karcioglu (2014)	Observational Case report	1/1	NA
Kim et al. (2014)	Observational Prospective cohort	7/275	NA
Piercy et al. (2006)	Observational Retrospective cohort	165/165 consecutive UIA	Age: per year unadj OR 1.01 (0.99-1.04) Number of comorbidities: unadj OR 1.17 (0.81-1.69) ≥1 comorbidity: unadj OR 2.07 (0.85-5.01) Elective: adj OR 4.45 (1.85-10.78) Male: unadj OR 1.28 (1.52-2.99)
Rose et al. (1996)	Observational: Prospective cohort	31/15059 consecutive non-cardiac and non- neurosurgical encounters	Age: > 60 (p < .01) ASA I-III / IV-V: (p < .01) Comorbidity: COPD (p > .01) Heart disease (p > .01) HIV positive (p < .01) Renal disease (p > .01) Smoker (p > .01) Emergent (p < .01) Female (p > .01) Procedure: Abdominal (p < .01) Intraoperative: SBP < 80mmHg >15 min (p < .01) HR: >120 bpm for >10 min (p < .01) Dysrhythmia (p < .01) SpO2: <90% (p < .01) > 6 U PRBCs: (p < .01) Inadequate NMBD reversal (p < .01)

Rose et al. (1994)	Observational Prospective cohort	55/24157 PACU patients	NA
Swann et al. (1993)	Observational Retrospective cohort	34/18555 consecutive surgical encounters	NA
Theron el al. (2014)	Observational Retrospective cohort	1/183 consecutive surgical encounters	NA
Toomtong et al. (2002)	Observational Prospective cohort	80/10231 consecutive surgical encounters	NA
Wanderer et al. (2013)	Observational: Retrospective cohort	4847/71996 consecutive surgical encounters, excluded cardiac, OB/GYN, ECT	Median Age: adj OR 0.99 (0.99-0.99, p =.01) ASA: adj OR 1.51 (1.43-1.59, p < .01) Duration of Surgery: Daytime start: OR 0.22 (0.20-0.23, p < .01) Daytime end: OR 0.20 (0.19-0.22, p < .01) Emergent: adj OR 5.47 (4.97-6.02, p < .01) Intraoperative: # times MAP < 65: OR 1.07 (1.06-1.07, p < .01) # times MAP < 50: OR 1.39 (1.34-1.45, p < .01) Avg HR entire case: OR 1.02 (1.02-1.02, p < .01) EBL: Univariate OR 1.001 (1.001-1.001, p < .01) PRBC: OR 1.10 (1.06 -1.13, p < .01) Sympathomimetics: Norepinephrine: OR 2.50 (2.10-2.98, p < .01) Epinephrine: OR 9.92 (5.23-18.83, p < .01)

Note. a. UIA/ total number or patients in the sample. b. PACU was a the post-anesthesia care unit where patients could stay up to 3 days. c. Cases: ≥ 1 non-depolarizing neuromuscular blocking drug (NMBD), Controls: no NMBD. *Abbreviations:* adj MLR, adjusted multivariate linear regression; ASA, American Society of Anesthesiology classification; Avg, average; BMI, body mass index; CAD, coronary artery disease; CHF, congestive heart failure; CNS, central nervous system; COPD, chronic obstructive pulmonary disease; CRT, Cardiac resynchronization therapy; CVS, cardiothoracic surgery; DM, diabetes mellitus; FEV1, forced expiratory volume in one second, HIV, human immunodeficiency virus; HR, heart rate; HTN, hypertension; LR, logistic regression; MAP, mean arterial blood pressure, MI, myocardial infarction; NA, variables not analyzed for statistical significance or not provided; OR, odds ratio; OSA, obstructive sleep apnea; PRBC, packed red blood cells; PVD, peripheral vascular disease; SE, standard error; SBP, systolic blood pressure.

Demographic Variables. Demographic variables were used to represent the characteristics of the patient and also included ASA class, type of procedure, and type of anesthesia since these variables are frequently reported in anesthesia literature to describe characteristics of the surgical encounter. The following six demographic variables of patients with UIA were identified in the review of the literature: age, ASA classification, comorbidities, elective/ emergence procedure, sex, and type of surgical procedure. For each variable, a historical context, conceptual definition, operational definition, prevalence in the literature, synthesis of the evidence about the variable, discussion about gaps in knowledge, and implications for this study are presented.

Age. Patient age is a common consideration to preoperative and intraoperative anesthesia management. Increased age is associated with increased comorbidities, home medication regimens, and decreased functional capacity which put older adults at an increased risk of preoperative complications (Sweitzer, 2008). Conceptually, patient age was defined as the number of years the person has been alive.

Patient age was analyzed by researchers in 39% of the studies and therefore the most frequently studied variable of a patients with UIA. Patient age greater than or equal to 65 years old was at least twice as likely to be associated with patient UIA (OR 2.9) (Haller et al., 2005; Kamath et al., 2012). However, the likelihood of an UIA dropped to 0.99 (95% CI 0.99-0.99) when age was adjusted for other variables such as blood transfusion, administration of epinephrine, mean blood pressure < 65 millimeters of mercury, and the duration of the surgical procedure with the additive rule of probability (Wanderer et al., 2013). Age was moderated by other variables in patients with UIA.

The gap in knowledge was to understand how age interacted with other variables such as surgical procedure, comorbidities, heart rate and blood pressure measurements, or vasopressor administration to change a patient's response or a clinician's intervention during anesthesia care. For this study, age was used to match patients with and without an UIA and describe the sample of patients. Since age was used to match surgical encounters it was not used to identify and test intraoperative hemodynamic data patterns associated with patients UIA.

American Society of Anesthesiology (ASA) classification. The ASA classification system has been used since 1963 to quantify a patient risk for morbidity and mortality after surgery with anesthesia (Owens, Felts, & Spitznagel, 1978). As shown in Table 2.2, the ASA classification system was a Likert scale value assigned by an anesthesia provider based upon the patients preoperative comorbidities and activity tolerance and has been reported to have an inter-rater reliability of 0.61 (95% CI 0.60-0.62) (Sankar, Johnson, Beattie, Tait, & Wijeysundera, 2014; Sweitzer, 2008). Conceptually, ASA classification was defined as the overall health or illness of a patient prior to anesthesia and operationalized with a whole number between 1 and 6 on the patient's anesthesia preoperative evaluation form (Sweitzer, 2008).

Table 2.2. *American Society of Anesthesiology Classification System*

ASA class	Definition
1	Healthy patient, no physical or psychological diseases.
2	Mild systemic disease/s, unlikely to impact anesthesia care (e.g., controlled hypertension, mild asthma).
3	Systemic disease/s, limited activities of daily living, likely to impact anesthesia care (e.g., class two congestive heart failure, renal failure).
4	Severe systemic disease/s, constant threat to life, major impact on anesthesia care (e.g., acute myocardial infarct, mechanical ventilation).
5	Moribund patient, expected to die within 24 hours with or without surgery (e.g., ruptured abdominal aneurysm).
6	Organ donor.
E	Added to any ASA classes to denote an emergency surgery.

Note. Adapted from "Overview of Preoperative Assessment and Management" (Sweitzer, 2008).

Researchers in 30% of the studies reported the statistical significance of the patients ASA classification and increased ASA classification was associated with increased likelihood of a patients UIA (Chi et al., 2010; Cullen et al., 1992; Eichenberger et al., 2011; Haller et al., 2005; Kamath et al., 2012; D. K. Rose et al., 1996; Wanderer et al., 2013). Patients with an ASA class 3 were more than 11 times as likely to have an UIA (95% CI 5.17-24.04), ASA class 4 were nearly 30 times as likely to have an UIA (95% CI 13.63-65.62), and ASA class 5 were 13 times as likely to have an UIA (95% CI 1.59-107.13) (Haller et al., 2005). When ASA classes were combined, a patient's surgical encounter with ASA classes greater than or equal to 3 were between two and 20 times as likely to be associated with an UIA (Cullen et al., 1992; Kamath et al., 2012). When adjusted for other variables of a patients UIA such as age, duration of surgery, mean intraoperative blood pressure measurements, and blood loss and analyzed with the additive rule of probability the likelihood of a patients UIA dropped to 0.74 and 1.51 for ASA classification (Eichenberger et al., 2011; Wanderer et al., 2013).

The gap in knowledge was to understand how intraoperative management was different based upon ASA classification during patients surgical encounters with UIA. More research is also needed to determine why ASA class 5 patients had a lower likelihood of UIA compared to ASA class 3 or 4 patients. Furthermore, researchers should study why ASA class 3 was the threshold for increased likelihood of an UIA. For this study, one challenge was to identify the reliability of the ASA classification data. In addition to the literature about inter-rater reliability, knowledge about where the ASA classification was documented in the EHR impacted the results of this study. Foremost, ASA classification can be documented as unstructured data in a preoperative anesthesia note or as structured nursing data in the patients EHR (Stonemetz & Ruskin, 2008). In this study, unstructured ASA classification data from the preoperative anesthesia note could not be extracted for research since a de-identified data set was extracted; therefore, ASA classification was extracted from nursing documentation (personal communication, Z. Cohen, personal communication, December 1, 2015).

Comorbidities. Comorbidities have been used by anesthesia providers to assess organ function/ dysfunction and anticipate the patients threshold to tolerate physiologic stress prior to surgery with anesthesia (Kwo, 2008; Sweitzer, 2008). Conceptually, a comorbidity was defined as the presence of two or more chronic diseases or conditions and a patient with more cardiopulmonary comorbidities is considered 'sicker' compared to the patient with fewer comorbidities (American Society of Anesthesiology Committee on Surgical Anesthesia, 2011; Kwo, 2008; Sweitzer, 2008). One challenge in defining comorbidities was the classification scheme used to analyze and report results in research. Both specific comorbidities such as aortic stenosis and hypertension with chronic kidney disease and generalized categories of comorbidities such as valvular heart disorders and hypertensive disease are reported in research (Agency for Healthcare Research and Quality, January 2012). Clinicians and researchers need to determine if results with different classification schemes can be used to change practice or inform future research.

Researchers in 30% of the studies included statistical analysis of comorbidities associated with a patients UIA and established that the body system affected but not the number of comorbidities was associated with patients UIA (Brunelli et al., 2008; Chi et al., 2010; Haller et al., 2005; Harris et al., 2001; Kamath et al., 2012; Kim et al., 2014; D. K. Rose et al., 1996). A comorbidity of anemia, coronary artery disease, obstructive sleep apnea, or shock were more than two times as likely to be associated with a patients UIA (Haller et al., 2005; Kamath et al., 2012). A comorbidity of myocardial infarction was more than five times and renal disease was more than six times as likely to be associated with a patients UIA (Kamath et al., 2012). Mental health comorbidities were not reported in any of the studies.

The gap in research about comorbidities was to identify if different comorbidities were associated with different intraoperative management and patients UIA. In this study, the level of description for comorbidities was assessed. The classification scheme of comorbidities was rolled-up to the highest disease/ condition category to describe the sample and test hypotheses about patterns in intraoperative hemodynamic management associated with patients UIA.

Elective or Emergent Procedure. Procedures have been classified as elective or emergent by anesthesia providers since the 1960's (Owens et al., 1978). Conceptually, elective procedures were defined as procedures scheduled after active medical conditions were optimized and emergent procedures were defined as life-threatening conditions that required immediate surgery (Sweitzer, 2008).

Researchers in 17% of the studies reported the statistical significance of elective or emergent procedures associated with patients UIA. Elective procedures were 4.5 times as likely and emergent procedures were more than 2 times as likely to be associated with patients UIA (range OR 2.69- 9.63) (Haller et al., 2005; Piercy et al., 2006; Wanderer et al., 2013). When emergent surgical encounters were adjusted for other predictors of patient UIA and analyzed with additive probability the OR fell from 9.96 to an adjusted OR of 5.47 (95% CI 4.97-6.02) (Wanderer et al., 2013). However, since both elective and emergent procedures were variables associated with patient UIA researchers suggested that emergent and elective procedures measured different constructs. Researchers that studied differences between elective and emergent procedures reported that elective surgical encounters with complications such as wound infection or postoperative mortality represented poor management of known conditions; whereas emergent surgical encounters with the same complications represented decompensation prior to surgery and were anticipated to have poor outcomes (Haider et al., 2015; Hyder et al., 2015; Kukreja et al., 2015).

The gap in knowledge was to understand differences between elective and emergent surgery predictive of or associated with patient UIA. Future research on quality anesthesia care and patient UIA should use elective and emergent procedures to establish inclusion and exclusion criteria. Patients with elective surgical encounters were included in this study to identify intraoperative hemodynamic data patterns associated with patients that were optimized prior to surgery but were associated with deterioration and UIA.

Sex. Sex was a common demographic variable analyzed by researchers to describe if differences exist among samples or subgroups (Dawson & Trapp, 2004a). Conceptually, sex was defined as male or female sociocultural characteristics and operationalized with EHR data that listed the patients sex as male or female (Haller et al., 2005; Kamath et al., 2012; Piercy et al., 2006; D. K. Rose et al., 1996).

Researchers in 17% of the studies analyzed sex in patients with UIA. However, only one study reported that sex was statistically significant in a patients UIA; with males almost 2 times as likely to be associated with patient UIA compared to females (Haller et al., 2008). However, other literature has linked sex to social habits such as recreational activities or alcohol consumption, trauma, and certain types of procedures such as open abdominal aneurysm repair which would be more specific variables associated with patient deterioration (Kwo, 2008). The gap in knowledge was to understand how sex was associated with a patients UIA. In this study gender was included to describe and match patients with and without UIA.

Type of Surgical Procedure. The first surgical procedure that was performed with anesthesia was documented in 1846 (Robinson & Toledo, 2012). Conceptually, a surgical procedure was defined as an intervention that used instruments to diagnose a medical condition, repair damage, or remove disease (Sweitzer, 2008). Similar to comorbidities, one challenge with surgical procedures was the level of coding. Some studies coded and analyzed surgical procedures based upon the approach or anatomic location of the procedure such as supratentorial or infratentorial craniotomy; whereas other studies rolled-up specific procedures into a generalized category (Bui et al., 2011; Ezri et al., 2004; Haller et al., 2005; Harris et al., 2001).

Researchers in 22% of the studies reported statistical analysis of surgical procedures associated with a patient UIA (Brunelli et al., 2008; Bui et al., 2011; Ezri et al., 2004; Haller et al., 2005; Harris et al., 2001). Abdominal, cardiac, central nervous system, and respiratory procedures were more than 4 times as likely to be associated with a patients UIA (Brunelli et al., 2008; Haller et al., 2005; D. K. Rose et al., 1996). However, ear, nose, or throat, eye, or female organ procedures were less than 2 times as likely to be associated with a patients UIA (Haller et al., 2005). Each surgical procedure has different amounts of physiologic trauma and stress applied to the patient which are managed differently by the anesthesia provider (American Society of Anesthesiology Committee on Surgical Anesthesia, 2011; Sweitzer, 2008).

The gap in the research was to understand how patients with UIA were managed during routine care and generate hypotheses about how intraoperative hemodynamic management was different based upon the type of procedure. The type of surgical procedure was included in this study to describe the sample and match patients with and without an UIA. If an exact match based upon the type of surgical procedure could not be identified the surgical procedure was rolled-up to the systems level (Agency for Healthcare Research and Quality, January 2012).

Intraoperative Hemodynamic Management Variables

Variables associated with intraoperative hemodynamic management in patients with UIA were used to represent the processes of giving or receiving care. Estimated blood loss, blood pressure, heart rate, neuromuscular blocking drug administration, packed red blood cell administration, pulse oximetry, sympathomimetic drug administration, and temporality were predictors of intraoperative hemodynamic management that were extracted from the literature on patients with UIA.

Estimated blood loss. Documentation of estimated blood loss (EBL) is a standard of anesthesia practice that is used to review intraoperative management according to practice guidelines (AANA Board of Directors, 2005; American Society of Anesthesiology Committee on Standards and Practice Parameters, 2008; American Society of Anesthesiology Committee on Surgical Anesthesia, 2011). Conceptually, EBL was defined as an imprecise measurement of blood on the surgical field, absorbed into surgical sponges, or suctioned from the body during surgery (American Society of Anesthesiology Committee on Standards and Practice Parameters, 2008; American Society of Anesthesiology Committee on Surgical Anesthesia, 2011).

Researchers in 13% of the studies analyzed EBL for statistical significance (Chi et al., 2010; Kamath et al., 2012; Wanderer et al., 2013). Researchers in one study reported EBL more than 1000 ml was significantly associated with UIA ($p < .01$) (Kamath et al., 2012). However, a different study reported EBL did not increase the likelihood of UIA (OR 1.00, 95% CI 1.00-1.00) and almost half of the surgical encounters had missing data

(Wanderer et al., 2013). Researchers in obstetrical care have reported visual estimates of blood loss overestimated EBL when there was 300 ml or less and underestimated EBL when there was more than 1000 ml (Schorn, 2010).

The gap in research was to generate evidence that EBL was an accurate and consistent measure of blood loss. Without valid and reliable EBL data the variable would create visual interference and mislead human intelligence to identify patterns in intraoperative hemodynamic management. Since the validity and reliability of EBL data has been questioned in the literature, EBL was not included in this study.

Blood pressure. Blood pressure has been measured and documented on the intraoperative anesthesia record since 1895 and is used to make clinical decisions about how the patient tolerated surgery with anesthesia (Molnar, Nemes, Szabo, & Fulesdi, 2008). Conceptually, blood pressure was defined as the force of blood flow within the cardiovascular system (International Hemodynamic Society, 2000). One challenge for researchers that included blood pressure as a variable in patient UIA was the threat of instrumentation. In other studies, non-invasive blood pressure monitoring underestimated SBP by an average of 9.7 millimeters of mercury (mmHg) (95% CI 6.5-13.0) compared to arterial SBP monitoring devices which are routinely calibrated prior to patient care (Manios et al., 2007).

Researchers in 13% of the studies reported MAP or SBP measurements that were statistically significant in patients with UIA. Mean arterial blood pressure was the dominant blood pressure value associated with patient UIA (Kamath et al., 2012; Wanderer et al., 2013). In one study, MAP measurements averaged over the duration of surgery were not statistically significant (Kamath et al., 2012). However, SBP less than

80 mmHg, MAP less than 65 mmHg, and MAP less than 50 mmHg were all statistically significant in patient with UIA ($p < .01$) (D. K. Rose et al., 1996; Wanderer et al., 2013). Furthermore, lower MAP measurements were more strongly associated with increased likelihood of patient UIA (MAP < 65 OR 1.07, MAP < 50 OR 1.39) (Wanderer et al., 2013). When MAP less than 65 mmHg was adjusted for other variables associated with patient UIA and analyzed with additive probability the adjusted odds ratio was 1.02 (95% CI 1.01-1.03); however, an adjusted OR for MAP less than 50 mmHg was not reported (Wanderer et al., 2013).

The gap in knowledge was to understand what blood pressure parameters are safe for certain comorbidities and surgical procedures. Patients with a comorbidity of congestive heart failure need to maintain a lower SBP compared to patients with a comorbidity of ischemic stroke to maintain adequate blood flow to vital organs during surgery (Kwo, 2008). When all surgical encounters are expected to have the same range blood pressure measurements researchers and clinicians failed to consider individual homeostatic mechanisms and normal intra-individual variability. In this study, intra-arterial blood pressure measurements were used to minimize the threat of instrumentation and identify accurate patterns among intraoperative hemodynamic data associated with patient UIA.

Heart rate. Heart rate (HR) has also been measured and recorded on the intraoperative anesthesia record since 1895 and is used by the anesthesia provider to make clinical decisions about titrating medication to maintain amnesia, immobility, and analgesia during surgery (Molnar et al., 2008). Heart rate was defined as the number of beats per unit of time, usually expressed as beats per minute (bpm) (International Hemodynamic Society, 2000).

Researchers in 13% of the studies reported the statistical significance of intraoperative HR associated with patient UIA. Researchers in two studies reported average minimum HR and HR greater than 120 bpm were statistically significant in patients UIA ($p = .02$, $p < .01$, respectively) (Kamath et al., 2012; D. K. Rose et al., 1996). Researchers in another study reported the average intraoperative HR for patients surgical encounters with UIA (OR 1.03, 95% CI 1.03-1.03) and when adjusted for other variables associated with patient UIA the average HR dropped slightly (adjusted OR 1.02, 95% CI 1.02-1.02) (Wanderer et al., 2013). The findings from these studies should be interpreted cautiously. Other researchers have studied differences between anesthesia data documented by hand and actual measurement values; hand-written anesthesia records which have been identified to contain terminal digit preference and regression to the mean (Cook et al., 1989).

The gap in knowledge was to understand how HR measurements compromised patient safety when tachycardia is only one sign of patient deterioration and low cardiac output. In this study, intraoperative heart rate data was combined with SBP data to explore the concept of hemodynamic stability which was defined as concurrent HR and SBP measurements within 20% of baseline (Allen et al., 2010; McDonald et al., 2011; Peterson et al., 2015). Knowledge about HR and SBP managements within 20% of baseline can be used to generate insight into inadequate hemodynamic responses or interventions associated with patient UIA.

Neuromuscular blocking drug (NMBD) administration. Neuromuscular blocking drugs (NMBDs) have been used since 1942 to improve operating conditions and have direct and indirect effects on hemodynamic status (Robinson & Toledo, 2012). Intraoperative NMBD administration was defined as medications that are administered to paralyze muscle contractions (Neuromuscular-blocking drugs. 2006). Neuromuscular blocking drugs are theoretically linked to changes in HR and blood pressure. When a patient is extubated and NMBDs are still active the patient can experience labored respiratory effort and/ or respiratory failure which activate the sympathetic nervous system. Tachycardia and hypertension are early signs of respiratory distress and bradycardia and hypotension are signs of prolonged respiratory failure (Neuromuscular-blocking drugs. 2006). Neuromuscular blocking drugs can also indirectly change hemodynamic status by three different mechanisms:

- Some NMBDs release histamine and other NMBDs release catecholamines which respectively create hypotension and tachycardia or hypertension and tachycardia (Neuromuscular-blocking drugs. 2006).
- Neuromuscular blocking drugs are reversed with medications that increase HR and blood pressure (Neuromuscular-blocking drugs. 2006).
- Deep NMBD administration cannot be reversed and the patient must remain intubated. When a patient remains intubated sedatives are routinely administered to synchronize ventilation which depress the patients HR and blood pressure (Neuromuscular-blocking drugs. 2006).

Researchers in two of the studies reported the statistical significance of NMBDs in patients with UIA (Grosse-Sundrup et al., 2012; D. K. Rose et al., 1996). Patients that were administered NMBDs were 1.4 times as likely to be have inadequate reversal, be re-intubated, and admitted unexpectedly to an ICU compared to surgical encounters that did not receive NMBDs (Grosse-Sundrup et al., 2012). However, this study excluded ultra-short acting and long acting NMBDs which can also lead to residual neuromuscular blockade and reintubation (Neuromuscular-blocking drugs. 2006).

The gap in knowledge was to understand how repeated or cumulative dosages of any NMBDs were associated with HR and blood pressure changes in patients with UIA. In this study, the cumulative dosage of NMBDs were analyzed with HR and SBP data to generate knowledge about patterns in intraoperative hemodynamic management in patients with and without an UIA. Knowledge about how NMBDs are administered to patients can be used to identify and test patterns in intraoperative hemodynamic management associated with patients UIA.

Packed red blood cell transfusion. Human blood transfusions were first administered in the early 1800s as a life-saving intervention to treat postpartum hemorrhage (Baskett, 2002). Conceptually, packed red blood cell (PRBC) transfusion was defined as blood that has been collected, processed, and administered back into circulation (Welsby & Bredehoeft, 2008). When blood volume is low the sympathetic nervous system is activated and HR and blood pressure increase in an attempt to deliver oxygen rich hemoglobin to tissues (Nielsen, Dahl, Johansson, Henneberg, & Rasmussen, 2012).

Researchers in 13% of studies reported the statistical significance of intraoperative PRBC transfusion in patients with UIA. All of the studies analyzed PRBC transfusion as a dichotomous variable in patients with UIA. Two of the studies used any

PRBC transfusion as the criteria for the predictor and the other study used more than six PRBC transfusions (Kamath et al., 2012; D. K. Rose et al., 1996; Wanderer et al., 2013). Two of the studies reported the odds of PRBC transfusion. There was a wide range of odds of PRBC transfusion associated with patients UIA (range OR 1.10 to 7.10) (Kamath et al., 2012; D. K. Rose et al., 1996; Wanderer et al., 2013). Researchers in related fields have reported intraoperative PRBC transfusion was associated with inadequate fluid resuscitation, hemodynamic instability, and complications such as hypothermia, infection, and myocardial infarction which prompted transfusion triggers of 8 grams per deciliter (g/dl) and 10 g/dl for critically ill and health patients respectively (Ejaz, Spolverato, Kim, Frank, & Pawlik, 2014; Nielsen et al., 2012).

The gap in knowledge was to understand how PRBC transfusion was associated with intraoperative medication administration and hemodynamic data in patients with UIA. In this study medication administration record data was extracted; however, there was no PRBC transfusion data. Hypotheses about patterns in the quantity and timing of PRBC transfusion associated with a patients UIA should be tested in future research.

Pulse oximetry. Beginning in 1987, general anesthetics were required to use pulse oximetry to guide clinical decision-making about oxygen and medication administration to prevent adverse outcomes (Cooper et al., 1987). Intraoperative pulse oximetry (SpO2) was defined as the measure of oxygen bound to hemoglobin (American Society of Anesthesiology Committee on Standards and Practice Parameters, 2008; American Society of Anesthesiology Committee on Standards and Practice Parameters, 2011). Pulse oximetry is a measurement of cardiac and pulmonary system function. Decreased pulse oximetry measurements can be caused by low inspired oxygen, impaired diffusion thru the lungs, or increased or decreased heart rate, preload, or afterload (Hess & Kacmarek, 2008).

Researchers of one study reported statistical analysis of intraoperative pulse oximetry in their results (Cullen et al., 1992). Researchers in both studies reported intraoperative SpO2 was significantly associated with a patients UIA ($p < .01$) (Cullen et al., 1992; D. K. Rose et al., 1996). The aim of one study was to identify if using pulse oximetry was associated with a patients UIA; whereas the other study analyzed the association between a SpO2 of < 90% and UIA (Cullen et al., 1992; D. K. Rose et al., 1996). Researchers have studied differences between documentation of physiologic data such as SpO2 in hand-written and electronic documentation and reported hand-written SpO2 values overestimated the trend in SpO2 (Lerou, Dirksen, van Daele, Nijhuis, & Crul, 1988).

The review of the literature did not cite intraoperative SpO2 data as valid, reliable, or correlated to intraoperative hemodynamic status. The gap in research was to generate evidence about valid and reliable intraoperative SpO2 data in a patients surgical encounters with UIA. Furthermore, researchers should identify if intraoperative SpO2 measurements are correlated to direct measures of intraoperative hemodynamic status such as HR, MAP, and SBP. Therefore, intraoperative SpO2 was not included in this study to identify patterns in intraoperative hemodynamic status associated with a patients UIA.

Sympathomimetic drug administration. Sympathomimetic drugs were first administered in the early 1900s to treat life threatening conditions such as asthma exacerbation or anaphylaxis (Runciman, 1980). Conceptually, sympathomimetic drug administration was defined as a medication that was given to a patient to release dopamine, norepinephrine, or epinephrine into the blood stream (Sympathomimetics. 2006). Catecholamines are used in the body to increase the diffusion of oxygen in the blood stream and delivery of blood to tissues (Sympathomimetics. 2006; Runciman, 1980).

Researchers in 8% of the studies reported the statistical significance of sympathomimetic drug administration associated with patient UIA. The odds ratio of any sympathomimetic drug administered in patients with UIA was 5.9 (95% CI 1.7-22.4); whereas phenylephrine, norepinephrine, dopamine, and epinephrine were respectively 2.66, 27.01, 35.59, and 91.14 as likely to be associated with patient UIA (Kamath et al., 2012; Wanderer et al., 2013). When adjusted for other variables of a patients UIA and analyzed with additive probability norepinephrine and epinephrine had an OR of 2.50 and 9.92 respectively; neither phenylephrine nor dopamine had an adjusted OR reported (Wanderer et al., 2013).

The gap in knowledge was to understand how sympathomimetic drug administration was associated with hemodynamic measurements and other pharmacologic classes of drug administration. Specifically, the sequence of sympathomimetic drug administration with other hemodynamic data. In this study, the cumulative dosage of sympathomimetic drug administration was analyzed for patients with and without an UIA. Sympathomimetic administration was analyzed with range HR or SBP data and other therapeutic classes of intraoperative medication administration to identify how sympathomimetic drug administration changed over time in patients with UIA. Patterns in sympathomimetic drug administration can be used to generate hypotheses about the sequence of events and timing of deterioration associated with patient UIA.

Temporality. In 1895, a line graph of HR, respiratory rate, and temperature measurements was the first formal documentation of the relationship between anesthesia care and time (Molnar et al., 2008). Temporality was defined as the relationship between an event and a time scale and is one feature that can be used to move observational data closer to a causal inference (Henly et al., 2011; Hill, 1965).

Researchers in 13% of the studies described the statistical significance of temporal relationships associated with patient UIA. The duration of surgery, procedures that occurred late in the day or afterhours, or procedures with sustained tachycardia (HR > 120 beats per minute) or hypotension (SBP < 80 mmHg) were analyzed as dichotomous variables and significantly associated with patient UIA ($p < .01$) (Chi et al., 2010; Haller et al., 2005; D. K. Rose et al., 1996). Researchers in two studies analyzed temporality with an odds ratio and reported surgical encounters that started between 7 a.m. and 3 p.m. were 0.27 and 0.23 times as likely to be associated with patient UIA (Haller et al., 2005; Wanderer et al., 2013). The relationship between HR, MAP, or SBP measurements, parameters, and temporality was also significantly associated with patients UIA ($p < .01$) (D. K. Rose et al., 1996).

The gap in knowledge was to understand the relationship among time and a large volume and variety of hemodynamic data in patient UIA. In this study, temporality was used to identify patterns in intraoperative hemodynamic data management associated with patients UIA. The time when intraoperative HR and SBP measurements were documented and medication were administered were used to establish a relationship between actions involved in giving or receiving hemodynamic care and patients UIA. The time scale was in hours and minutes from the start of anesthesia care and used to establish how patients with UIA changed from being optimized for surgery to requiring high acuity postoperative cardiovascular care. Hypotheses about the sequence of events or timing associated with intraoperative hemodynamic deterioration can be used to develop early detection/ warning systems for UIA in future research.

Intensive Care Unit (ICU) Admission Diagnosis

Historically, ICU admission diagnoses have been used as the criteria to determine who would benefit from intensive medical and nursing care, invasive monitoring, advanced oxygen deliver, or sympathomimetic drug administration (Guidelines for intensive care unit admission, discharge, and triage task force of the American College of Critical Care Medicine, Society of Critical Care Medicine, 1999). Conceptually, admission diagnoses were defined as the primary reason why the patient is being admitted for care (Agency for Healthcare Research and Quality, January 2012).

Researchers in 78% of the studies reported the narrative description for admission diagnosis associated with a patients UIA. Atelectasis and pneumonia were the only statistically significant ($p < .05$) reasons for ICU admission in surgical encounters with UIA (Rose et al., 1996). However, more than 25% patients with UIA were admitted for acute cardiovascular events such as bleeding, myocardial infarction, or decreased level of consciousness (Brunelli et al., 2008; Bui et al., 2011; Cullen et al., 1992).

The gap in knowledge was to identify if there is an association among demographic data, intraoperative events, ICU admission diagnoses, and patients UIA. In this study, admission diagnoses in UIA were not be collected. However, admission diagnoses reported by prior researchers were used to refine the purpose of this study from all physiologic intraoperative data patterns to intraoperative hemodynamic data patterns association with patients UIA.

Gaps in Knowledge

There were six demographic and eight intraoperative hemodynamic variables associated with or predictive of patient UIA reported in the literature. The strongest variables (OR > 2.0, 95% CI > 1.0, p < .01) of patients UIA were: age greater than 64 years old, ASA class greater than or equal to three, a comorbidity of anemia, cerebral vascular disease, coronary artery disease, congestive heart failure, hypertension, myocardial infarction, or obstructive sleep apnea, type of procedure, and intraoperative vasopressor administration (Haller et al., 2005; Wanderer et al., 2013). Some researchers validated a patients UIA and analyzed variables with odds ratios which strengthened the relationship between a variables and patients UIA. However, several investigators analyzed variables of patient UIA with univariate techniques or additive probability for interactions between two variables. Furthermore, several researchers used longitudinal study designs but analyzed repeated measurements with an average value. Finally, temporality was parsimoniously used as dimension of care to evaluate how patients unexpectedly.

Based upon this review of the literature three areas that may be fruitful for future research include:

- Use inductive research methods to evaluate demographic and intraoperative medication administration data to generate knowledge about relevant hemodynamic variables associated with patients UIA.
- Explore interactions among mutually inclusive events to identify patterns in demographic and hemodynamic assessment and intervention data in a patients UIA.
- Study time-dependent events in patient's surgical encounters with UIA.

Inductive Approach to Research on UIA

Prior investigators selected variables based upon theoretical or experiential knowledge of information that may contribute to unexpected patient deterioration. Researchers that used deductive approaches added to the body of knowledge about patient UIA by testing hypotheses or interventions for statistical significance (Berger & Berger, 2004). Inductive approaches offer different insight into a body of knowledge by analyzing a large volume and variety of data to generate hypotheses about meaningful patterns for subsequent research (Berger & Berger, 2004). Inductive approaches take in variables with known and unknown relationships to discover and test which variables are meaningful (Berger & Berger, 2004).

One gap in the literature was to use inductive approaches to discover which time-dependent intraoperative hemodynamic management patterns were associated with patients UIA. Specifically, the gap in the research was to analyze the dose of all medications administered to patients to discover patterns among intraoperative medication administration and hemodynamic data in patients with UIA. Data-driven hypotheses about intraoperative medication administration to manage hemodynamic stability in patients with UIA will provide a direction for future clinical trials aimed to prevent patient UIA. An inductive approach to research on UIA has the potential to add to a body of knowledge about variables associated with patient UIA and/ or generate new, potentially stronger variables associated with patients UIA.

Mutually Inclusive Events

Another gap in research about quality anesthesia care and patients with UIA was data analyzed according to the additive rule of probability which assumed mutually *exclusive* events. Research on patients with UIA rarely analyzed the likelihood that two events occurred simultaneously. Furthermore, none of the researchers in this review of the literature reported the likelihood that more than two events occurred simultaneously or that one event preceded another event. Researchers that studied patient UIA relied upon the additive rule of probability which stated that *either* of the two events would occur in patients surgical encounters with UIA (Dawson & Trapp, 2004b). This body of knowledge on individual variables or mutually exclusive events in patients with UIA contradicted the theory of quality care assessment which acknowledged how variables can occur at the same time to change patients health status (Donabedian, 1988; Donabedian, 1978).

Prior research identified estimated blood loss, intraoperative blood pressure, intraoperative heart rate, neuromuscular blocking drug administration, packed red blood cell transfusion, *or* sympathomimetic administration increased the likelihood of a patients UIA. However, literature on patients with UIA omitted assessment of collinearity or interaction terms which assumed independent variables (Concato et al., 2006). The assumption of independent variables and mutually exclusive events in patients with UIA was flawed; the human body shares systemic circulation. A change in local metabolic conditions in one area of the body is known to create compensatory mechanisms or graded responses which vary by age and comorbidities in different organ systems to maintain homeostasis (Donina, 2011; Solopov, Gorbaneva, Vlasov, & Voskresenskii, 2012). The gap in the literature was to study events that occurred simultaneously and how one event preceded a different intraoperative event to advance knowledge about how patients with UIA deteriorated.

Time-dependent Events

Finally, prior research on patients with UIA collected longitudinal data but implemented analytic techniques that averaged all intraoperative physiologic assessment and intervention data into a single value (Chi et al., 2010; Grosse-Sundrup et al., 2012; Kamath et al., 2012; Wanderer et al., 2013). Prior researchers minimized the role of temporality in data analysis which constrained knowledge about the trajectory of a patients UIA (Designing quantitative studies, 2004; Concato et al., 2006; Henly et al., 2011; Hill, 1965). Researchers investigating patients with UIA had the opportunity to use longitudinal study design to analyze time-dependent data. Intraoperative physiologic assessment and intervention data are documented at least every five minutes for the duration of anesthesia care (American Society of Anesthesiology Committee on Standards and Practice Parameters, 2008; Peterson, Mathiason Moore, & Monsen, IRB approval 04/2014). The gap in the literature was to retain time-dependent intraoperative hemodynamic assessment and intervention data to generate models that can be used to identify an associated between critical time-dependent events and a patients UIA.

Conclusion

Critical barriers to research on patients with UIA have included the complex combination among variables associated with or predictive of quality patient care, selecting some predictors within a category while ignoring others, and the lack of electronically available time-dependent data; all of which can influence results. Knowledge about a patient's UIA should be advanced with studies that analyze multivariate time-dependent intraoperative data sets to generate knowledge about how patients deteriorated during routine care. Furthermore, researchers should use inductive and deductive methods that are robust for identifying meaningful interactions among dynamic categorical and numeric hemodynamic variables.

Longitudinal study designs with intensive time-dependent intraoperative data would contribute knowledge about the sequence of events, rate of change, and timing of intraoperative deterioration in patients with UIA. Knowledge discovery with databases and innovative research methods such as data visualization can explore a large volume and variety of time-orientated hemodynamic data to identify patterns in intraoperative hemodynamic management in patients with UIA (Berger & Berger, 2004; Kirk, 2012).

Data visualization with line graphs is a new approach to research on patients with UIA. Time-dependent intraoperative hemodynamic anesthesia assessment and intervention data can be explored with information technology tools and human intelligence to generate and test hypotheses about patterns anesthesia care associated with patients UIA. Patterns in intraoperative hemodynamic management that are statistically significant can be used to develop and test early warning systems in future research.

Chapter 3

METHODOLOGY

In this chapter, the systematic approach to data visualization using line graphs and study design will be outlined. Data visualization is an advanced research methodology that is used to study mutually inclusive and time-dependent data and generate insight into how variables changed over time. Then, the sample of patients with UIA will be described. This chapter will end with a description of the analytic plan and ethical considerations.

Data Visualization Methods

In data visualization methods, statistical techniques and information technology tools are used to transform large and complex data sets into visual representations for exploratory data analysis with human intelligence (Dzemyda, Kurasova, & Žilinskas, 2013; Kirk, 2012; Tufte, 2001e). Anscombes quartet (Figure 3.1) was published in 1973 and generated compelling evidence about the value of data visualization to explore data sets. Anscombe analyzed four different data sets with generalized linear regression and identified the same mean, general linear regression coefficient, regression line equation, and estimated standard error. However, data visualization with line graphs determined that the data sets were not identical and had four distinct relationships: linear, curvilinear, linear with one outlier, and a single outlier with high leverage (Anscombe, 1973). The results of Anscombe's research reported that traditional statistical analysis alone could mask significant relationships that were salient with data visualization.

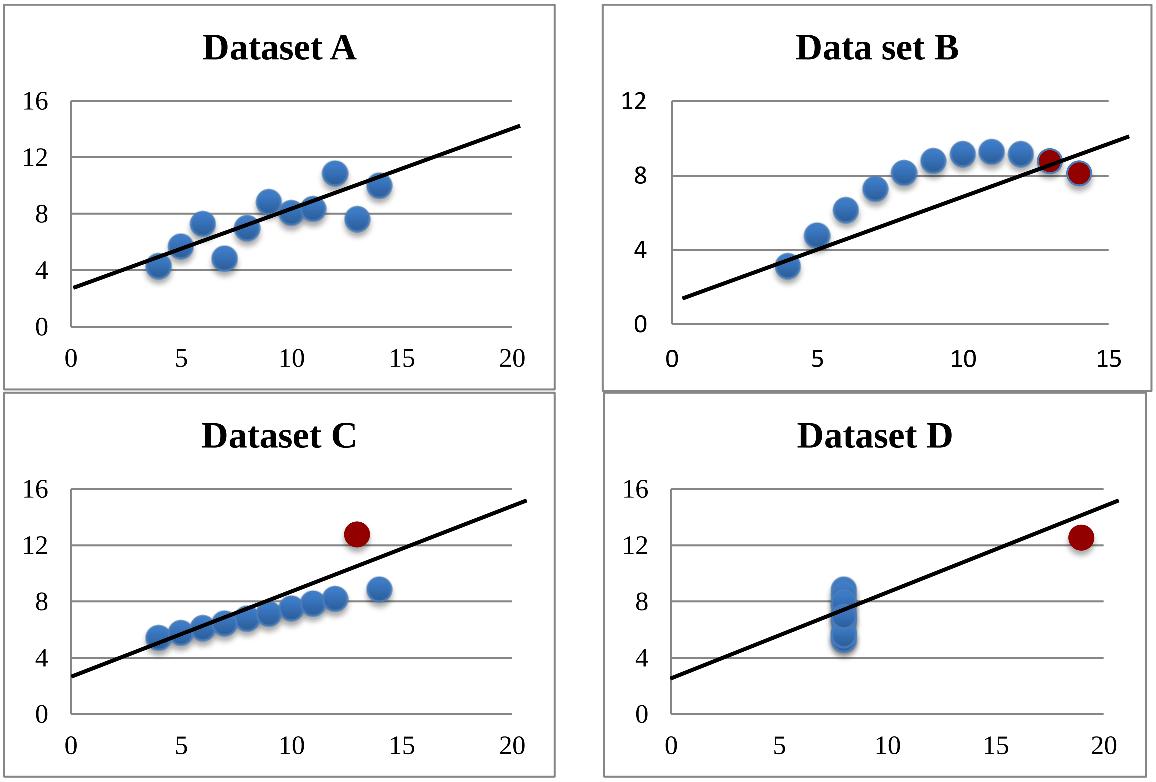


Figure 3.1. Visualization of Anscombe's Quartet (Anscombe, 1973).
Note. Adapted from *Graphs in Statistical Analysis* (Anscombe, 1973).

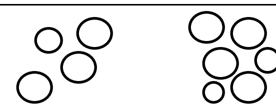
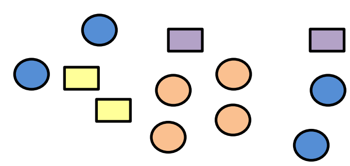
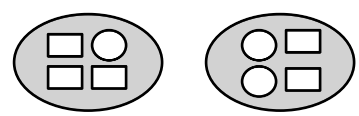
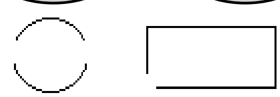
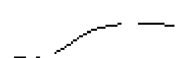
Since the 1800s, data visualization methods have been recognized as the most effective and efficient analytic tools to explore, describe, and summarize large data sets. In the mid-1800s, Florence Nightingales area chart conveyed how mortality changed over time in the British army and her Coxcomb diagram displayed the cause of death in British military hospitals during the Crimean War (1854-1856) (Small, 1998). Data visualization methods have expanded since the 1800s and are now used to systematically represent complex healthcare data sets with lines and code data with shape and color hue on Cartesian coordinates to simultaneously detect patterns, outliers, and relationships with human intelligence (Kirk, 2012; Tufte, 2001d; Tufte, 2001e). Hospital databases have linked a large volume of dimensions to multiple patient and clinician features to generate large and complex data sets (Andrienko & Andrienko, 2006; Dzemyda et al., 2013). Dimensions are different variables and features are the description, value, parameter, location, and/ or time associated with each variable (Dzemyda et al., 2013).

A classification scheme for data visualization methods has been described by Kirk (Kirk, 2012). There are more than forty-three different data visualization methods nested under the following five categories: assess part-to-whole relationships, compare categories, show change over time, plot connections and relationships, and map data (Kirk, 2012). A specific data visualization method is selected based upon the number of variables to be analyzed, the types of variable (nominal, ordinal, interval, or ratio), and the purpose of the study. Common data visualization methods include: bar charts which are used to compare absolute or relative sizes, pie charts which are used to assess part-to-whole relationships, parallel coordinates which are used to plot associations, line graphs which are used to show change over a continuous time period, and choropleth maps which are used to determine geo-spatial relationships (Kirk, 2012).

Visual Perception

Visual perception, preattentive reasoning, and the cerebral cortex are used in data visualization methods for human intelligence to analyze and interpret complex data sets. Visual perception is the process of seeing, analyzing, and giving meaning to visual information (Conway, 2009; Few, 2002). The visual stimuli of lines, shapes, and color hues were reflected onto the researcher's retina and transmitted through the optic chiasm into the primary visual cortex (also known as the striate cortex, V1, and Brodmanns area 17) in the occipital lobe in the brain (Hubel & Wiesel, 1977; Ropper, Samuels, & Klein, 2014). The neurons in the primary visual cortex were then activated by the lines, proximity of data, and color hues (Conway, 2009; Lorteije et al., 2015; Talsma, Senkowski, Soto-Faraco, & Woldorff, 2010). Next, information was transmitted to the parietal and temporal lobes in the brain and organized according to the Gestalt Laws of Visual Perception (Table 3.1) (Ali & Peebles, 2013; Conway, 2009; Cooke, Ali, & Peebles, 2013; Hubel & Wiesel, 1977; Lorteije et al., 2015; Ropper et al., 2014).

Table 3.1. *Gestalt Laws of Visual Perception.*

Gestalt Law	Definition	Example
Proximity	Objects that are close together are perceived as having similar characteristics.	
Similarity	Objects that share dimensions such as color or shape are perceived as having similar characteristics.	
Enclosure	Objects that have a boundary around them are perceived as a group.	
Closure	Open objects are perceived as closed when lines are in sequence.	
Continuity	Objects that are aligned appear to be a continuation of one group.	

Note. Selected Gestalt Laws of Visual Perceptions adapted from *Data Visualization for Human Perception* (Few, 2002).

Preattentive Reasoning

After visual stimuli are organized by the temporal lobes, information is transmitted to the cerebral cortex for higher order executive functioning to develop knowledge which is referred to as preattentive reasoning (Hubel & Wiesel, 1977; Ropper et al., 2014; Seger, Braunlich, Wehe, & Liu, 2015; Talsma et al., 2010). The frontoinsular and medial frontal cortex are subconsciously activated when the brain is confronted with new information. These two areas of the brain form a salience network where new information is subconsciously compared and categorized to existing knowledge (Seger et al., 2015). Once activated the salience network is used to reconcile different or conflicting information and is highly accurate at identification of prominent, obvious, and significant information (Ropper et al., 2014; Seger et al., 2015; Talsma et al., 2010). Data visualization and preattentive reasoning have developed over thousands of years to interpret up to 254 data points per square inch and analyze information in less than 200 microseconds which is much more effective and efficient than cognitive perception of tabular data (Few, 2002; Tufte, 2001c).

Human Intelligence

The final step in data visualization methods is to apply human intelligence (Dzemyda et al., 2013; Seger et al., 2015; Talsma et al., 2010). The temporal lobe, parietal lobe, and inferior frontal gyrus located in the frontal lobe are used to consciously think about data visualization to discover knowledge about data clusters, outliers, and patterns (Conway, 2009). The temporal lobe is used to recognize representations of data and the parietal lobe is used to apply mathematical and analytic skills to interpret the visualization. Finally, the inferior frontal gyrus is used to think about information creatively, compare information to existing knowledge, and generate new insight into information (Conway, 2009; Dzemyda et al., 2013; Kirk, 2012). Data clusters, outliers, and patterns identified with preattentive reasoning are critically evaluated in the context of the data set and clinical expertise is used to generate data-driven knowledge about multivariate, multidimensional, dependent data, and an outcome.

This data visualization study utilized the primary visual cortex and preattentive reasoning to identify salient patterns among patient characteristics, intraoperative medication administration, and a smoothed hemodynamic trend line by comparing color coded line graphs of patients surgical encounters with and without UIA. Line graph methods have been used to effectively localize and discriminate data patterns with human intelligence from multivariate data sets (Ali & Peebles, 2013; Javed, McDonnel, & Elmqvist, 2010). Data density in the line graphs is interpreted by the primary visual cortex and frontal lobe as prominent features in a data set (Dzemyda et al., 2013; Kirk, 2012). In this data visualization study, the time of intraoperative anesthesia care was plotted on the x-axis and the normalized values for smoothed hemodynamic data and intraoperative medication administration were plotted on the y-axis. Preattentive reasoning was used to identify intraoperative hemodynamic data patterns and human intelligence was used to generate data-driven hypotheses about patterns in the sequence of events and timing of intraoperative hemodynamic management. The data patterns were then tested for statistical significance.

Theoretical Principles of Data Visualization

Line graphs were selected to systematically retain the structure of data for visual perception, preattentive reasoning, and human intelligence to perform data analysis. There are two main theoretical principles for data analysis with data visualization methods. Foremost, choices about data transformation for quality and analysis must be guided by logical and deliberate decisions to support visual perception and preattentive reasoning (Berman & Berman, 2013; Feng, Kwock, Lee, & Taylor, 2010; Seger et al., 2015; Talsma et al., 2010). The structure of the data should be maintained with procedures for handling implausible values or unrecognized characters and data transformation should preserve the distribution of the data. Procedures to clean and transform data should be clearly outlined, consistently applied, and accurate; otherwise the visualization could mislead visual perception and preattentive reasoning (Berman & Berman, 2013; Dzemyda et al., 2013; Few, 2015).

The second theoretical principle for data visualization methods is the importance of data representation and presentation. Each element of representation and presentation was guided by knowledge from cognitive science, cognitive psychology, and graphic design about how human intelligence is used to recognize and understand patterns (Conway, 2009; Cooke et al., 2013; Feng et al., 2010; Seger et al., 2015). The application of color hue, shape, position, and transparency should be evaluated to determine that visual perception and preattentive reasoning are possible with data representations (Cooke et al., 2013; Feng et al., 2010; Few, 2002). When principles of visual perception are violated, patterns may be distorted (Feng et al., 2010).

Study Design

A 1:2 case-control study design was selected to identify intraoperative hemodynamic management associated with adult patients UIA. The cases were patient surgical encounters with UIA and the controls were patient surgical encounters without UIA. The case-control study design was an efficient design to set up data collection procedures to explore the relationships among a large number of predictor variables and useful for generating and testing hypotheses about a rare outcome (Newman, Browner, Cummings, & & Hulley, 2013; S. Rose & Laan, 2009). Two times as many controls were selected to mitigate the threat of bias from unknown confounders in the control group without increasing the variance in predictor variables, which may occur with 1:3 or 1:4 matching (Newman et al., 2013; S. Rose & Laan, 2009).

Description of the Data set (Sample)

The targeted population was adult (18 and older), inpatient, elective surgical encounters that received anesthesia care. Adult, inpatient, elective surgical encounters that received anesthesia were selected to represent a population that was optimized prior to surgery and therefore at less risk of adverse events. A consecutive sample of all adult, inpatient, elective surgical encounters were extracted from the University of Minnesota, Academic Health Center Clinical Data Repository (AHC- CDR) from January 1, 2012 through June 30, 2015. This sample was used to discover hidden patterns in intraoperative hemodynamic management and test patterns for association with a patients UIA.

Sample size estimation. A minimum of three units of analysis per object or predictor visualized are required to recognize salient patterns with data visualization (Seger et al., 2015). The unit of analysis for this study was a set of one case and two control surgical encounters. The variables in this data visualization study were therapeutic class of intraoperative medication administration and a smoothed hemodynamic trend line. Ten therapeutic classes of medication are routinely administered during surgery with anesthesia (Pharmacology & physiology in anesthetic practice, 2006). Therefore, a minimum of 30 cases and 60 controls were needed to create data visualization using lines graphs.

Inclusion criteria. Patients surgical encounters with and without UIA were included in this study if the surgical encounter had:

1. Data in the AHC-CDR between January 1, 2012 and June 30, 2015.
2. An age greater than or equal to 18 years old.
3. Inpatient, elective surgery with anesthesia

Date range. The date range was selected to collect reliable anesthesia data from the AHC-CDR and obtain the minimum number of patients with an UIA that are required for data visualization. Foremost, the AHC- CDR contains EHR data from a single instance of intraoperative anesthesia care for six Fairview Health Service hospitals since January 1, 2012 (personal communication, Kurt Johnson, Fairview Perioperative Clinical Informatics Operations Lead, 06/12/2015). Therefore, January 1, 2012 was selected as the start date for data extraction to increase the completeness and reliability of anesthesia data for this study. Additionally, June 30, 2015 was selected as the end date for data extraction to balance the number of patients with an UIA that were needed to identify patterns with the timeline for this study.

Age range. A patient with an age greater than or equal to 18 years old on the date of the surgical encounter was included in this study. Age was operationalized with registration data on the date of the patient's surgical encounter in years. The age range was selected to align with the purpose of the study. Children have different hemodynamic parameters that guide clinical decision-making (Brierley et al., 2009). Therefore, intraoperative medication administration and hemodynamic data patterns may be different in children compared to adults. Patients aged greater than 90 was coded as 90 to protect patient confidentiality.

Inpatient, elective surgery with anesthesia. Patient surgical encounters with anesthesia registered as elective and inpatient were included in this study to represent patients that had been evaluated and optimized prior to the start of anesthesia and therefore at less risk for an adverse event (Sweitzer, 2008). Inpatient surgical encounters represented patients that planned to be admitted to a hospital unit after surgery. Both elective and inpatient status were operationalized with registration data from the date of the surgical encounter. Finally, the start and stop time of anesthesia was extracted with inpatient, elective registration data to confirm the patient had surgery with anesthesia.

Exclusion criteria. If the patients surgical encounter was emergent, outpatient, or null the patient was excluded from this study. Patient's surgical encounters with non-invasive intraoperative SBP measurements were also excluded from this study. Non-invasive blood pressure measurements are not routinely calibrated in non-research settings and are less accurate compared to arterial line measurements (Greenberg, Murphy, & Vender, 2009; Manios et al., 2007). Therefore, arterial SBP measurements were used to increase precise intraoperative SBP measurements. Precise blood pressure measurement strengthened the association between intraoperative hemodynamic management data patterns and patients surgical encounters with UIA.

Variables

Demographic Characteristics

Seventeen demographic characteristics were extracted from the AHC-CDR to describe patients' surgical encounters with and without UIA and the overall data set. Age on the date of a patient's surgical encounter, gender, race, ethnicity, active primary problem, active medical history, social history, elective surgery, patient class, type of procedure, type of anesthesia, ASA class, patient weight, weight units, height, height units, and body mass index (BMI) were the demographic characteristics extracted. Age, gender, race, ethnicity, type of procedure, and type of anesthesia were the patient characteristics that were used to describe the data set and patients surgical encounters with and without UIA. Characteristics such as weight, height, and BMI were used to operationalize weight-based dosing of intraoperative medication administration. Other characteristics such as age, ASA classification, gender, type of procedure, and type of anesthesia were used to match a patients' surgical encounter with and without UIA. Finally, active primary problem, active medical history, and social history were used to generate and test hypotheses about intraoperative hemodynamic data patterns associated with patients UIA. The operational definitions and plausible values for the demographic characteristics are provided in Table 3.2.

Table 3.2. *Demographic Characteristics*

Variable	Operational Definition	Plausible Values
Age	Patient age in years on the date of the surgical encounter extracted from the encounter services table.	≥ 18- ≤ 89, Null
Gender	Description of patient gender on the date of the surgical encounter extracted from the patient demographic table.	Male, Female, Null
Race	Description of race on the date of the surgical encounter extracted from the patient demographic table.	White, Native Hawaiian or Other Pacific Islander, Asian, Black or African American, Hispanic or Latino, American Indian or Alaska Native, Multiracial, Declined/ Unknown, Null
Ethnicity	Description of ethnicity on the date of the surgical encounter extracted from the patient table.	Hispanic or Latino, Non-Hispanic or Latino, Declined/ Unknown, Null
Active Primary Problem	Description of active primary problems on the date of the surgical encounter extracted from the patient problem list table.	e.g. Abdominal pain, Null
Active Medical History	Description of the active medical diagnoses/ comorbidities on the date of the surgical encounter extracted from the encounter diagnosis table.	e.g. CHF, COPD, Diabetes Mellitus Type II, Null
Social History	Description of and value for the alcohol use, illicit drug use, and tobacco use on the date of the surgical encounter extracted from the encounter social history table.	e.g. Yes, No, Not asked, Quit, Never, Passive, Current user, Former User, Unknown, Null 0,1,2,3,4,1-4
Elective Surgery Status	Description of elective procedure on the date of the surgical encounter extracted from the encounter admission table.	Elective, Routine, Standard, Null

Patient Class	Description of patient class on the date of the surgical encounter extracted from the encounter admission table.	Inpatient, Outpatient, Observation, Null
Type of Procedure	Description of the procedure code name of the surgical procedure on the date of the surgical encounter extracted from the encounter procedure table.	e.g. Excision of pilonidal cyst or sinus, Cesarean delivery, Null
Type of Anesthesia	Description of the final type of anesthesia listed on the intraoperative anesthesia flowsheet record on the date of the surgical encounter extracted from the observation table.	General, Regional, or Local Monitored Anesthesia Care, Null
American Society of Anesthesiology (ASA) Classification	Value for the ASA class documented on the intraoperative anesthesia flowsheet record on the date of the surgical encounter extracted from the observation table.	1, 1E, 2, 2E, 3, 3E, 4, 4E, 5, 5E, 6, 6E, Null
Weight	Value for the weight of the patient on the date of the surgical encounter extracted from the encounter vitals table.	10-1200, Null
Weight unit	Description of the unit for the weight	e.g. pounds, kilograms, Null
Height	Value for the height of the patient on the date of the surgical encounter extracted from the encounter vitals table	48-240, Null
Height unit	Description of the unit for height	e.g. centimeters, inches, feet, Null
Body mass index	Weight in kilograms divided by the height in meters squared on the date of surgical encounter extracted from the encounters vitals table	10-150, Null

Intraoperative Hemodynamic (Independent) Variables

The intraoperative variables of patients with UIA were therapeutic classes of intraoperative medication administration and a smoothed hemodynamic trend line. All of the intraoperative hemodynamic variables were new variables that were created during data preparation for the purpose of this study.

Therapeutic class of intraoperative medication administration. Conceptually, a therapeutic class of intraoperative medication administration was the medication administered to the patient by the anesthesia provider and had the potential to change hemodynamic responses. The therapeutic classes of intraoperative medication administration were defined as the cumulative dose by therapeutic class of intraoperative medications documented on the intraoperative medication administration record (MAR). Crystalloid intravenous fluid was not included in the AHC-CDR data dictionary therapeutic classes of medication administration. However, other categories of IV fluid such as PRBCs and albumin were included. Therefore, for the purpose of this study IV fluid was added to the therapeutic class of 'nutritional products'.

The therapeutic classes of intraoperative medication administration were operationalized with time-dependent, cumulative dosage of intraoperative classes of medications administration by therapeutic class (Table 3.4). Specifically, anesthesia start and end time, medication therapeutic class, medication dose, medication dose unit, route, and time of administration were the data types extracted from the AHC-CDR and were used to transform data into the therapeutic class of intraoperative medication administration.

Table 3.3. *Intraoperative Medication Administration Variables*

Variable	Operational Definition	Plausible Values
Anesthesia Start Time	Value for the start time of anesthesia care on the date of the surgical encounter extracted from the encounter observation table.	00:00-23:59, Null
Anesthesia End Time	Value for the end time of anesthesia care on the date of the surgical encounter extracted from the encounter observation table.	00:00-23:59, Null
Medication Pharmacologic Class	Pharmacologic class of medication administered on the date of the surgical encounter extracted from the encounter SVC medication administration table.	Analgesics-narcotics, Analgesics-nonnarcotic, Anti-rheumatics, Antianginal agents, Antianxiety agents, Antiarrhythmic, Antiasthmatics, Anticoagulants, Antidiabetics, Antiemetics, Antihistamines, Antihypertensives, Antimyasthenic agents, Beta blockers, Cardiotonics, Cephalosporins, Corticosteroids, Diuretics, General anesthetics, Hypnotics, Local anesthetics-parenteral, Misc antiinfectives, Misc endocrine, Mineral & electrolytes, Misc hematologicals, Neuromuscular blockers, Oxytocics, Penicillins, Pressors, Thyroid, Ulcer drugs, NULL
Medication Therapeutic Class	Therapeutic class of medication administered on the date of the surgical encounter extracted from the encounter medication administration table.	Analgesics, Antiinfective agents, Cardiovascular agents, Central nervous system drugs, Endocrine metabolic drugs, Gastronintestinal agents, Hematological agents,

		Local Anesthetics, Misc products, Neuromuscular drugs, Nutritional products, Respiratory agents, NULL
Medication Name	Description of the name of the medication administered on the date of the surgical encounter extracted from the surgical encounter medication administration table.	Acetaminophen, Albumin, Amiodarone, Aspirin, Atropine, Bupivicaine, Calcium Chloride, Cefazolin, Cisatracurium, Clindamycin, Dexamethasone, Dexmedetomidine, Diphenhydramine, Dopamine, Droperidol, Ephedrine, Ephedrine, Epinephrine, Ertapenem, Esmolol, Etomidate, Fentanyl, Glycopyrolate, Heparin, Hetastarch, Hydralazine, Hydromorphone, Ketamine, Ketorolac, Labetalol, Lidocaine, Magnesium, Mannitol, Metoprolol, Midazolam, Milrinone, Mineral oil, Morphine, Neostigmine, Nitroglycerin, Norepinephrine, Ondansetron, Oxytocin, Phenylephrine, Piperacillin, Potassium Chloride, Promethazine, Propofol, Protamine, Regular insulin, Remifentanil, Rocuronium, Ropivicaine, Scopolamine, Sodium bicarbonate, Sodium chloride, Succinylcholine, Vancomycin, Vasopressin, Vecuronium
Medication Dose	Value for the dosage of medication administered on the date of the surgical encounter	0.01-4000, Null

	extracted from the encounter medication administration table.	
Medication Dose Unit	Description of the units for the dose of medication administered on the date of the surgical encounter extracted from the encounter medication administration table.	Micrograms (mcg) Milligrams (mg) Grams (g) Milliliters (ml) Cubic centimeters (cc), Null
Intravenous (IV) Fluid	Description of and volume for the IV fluid administered on the date of the surgical encounter extracted from the encounter observation table.	e.g. normal saline (NS), lactated ringers (LR), 5% dextrose lactated ringers (D5LR), 0-6000, 1 liter, Null

Smoothed hemodynamic trend line. Conceptually, a smoothed hemodynamic trend line was hemodynamically stable or unstable measurements assessed during anesthesia care. A smoothed hemodynamic trend line was defined as the concurrent HR or blood pressure measurement that was the furthest from baseline. During data preparation, each patients intraoperative HR and aSBP measurements were transformed into a percentage of the median value of the first three respective measurements which served as the baseline. Next, the concurrent intraoperative HR or aSBP measurement that was the furthest from baseline was used to operationalize hemodynamic data. Finally, the concurrent HR or aSBP measurement that was the furthest from baseline was averaged with data in the prior two minutes to create a smoothed hemodynamic trend line. Anesthesia start time, anesthesia end time, intraoperative HR measurements, and intraoperative aSBP measurements were the variables extracted from the AHC-CDR. The operational definition and plausible values for intraoperative hemodynamic data are provided in Table 3.4.

Table 3.4. *Intraoperative Hemodynamic Data Variables*

Variable	Operational Definition	Plausible Values
Anesthesia Start Time	Value for the start time of anesthesia care on the date of the surgical encounter extracted from the encounter observation table.	00:00-23:59, Null
Anesthesia End Time	Value for the end time of anesthesia care on the date of the surgical encounter extracted from the encounter observation table.	00:00-23:59, Null
Systolic Blood Pressure	Value of systolic blood pressure measurements on the date of the surgical encounter extracted from the encounter vitals table.	Within 2 standard deviations from the patients mean SBP, Null
Blood Pressure Measurement Device	Description of the device used to measure blood pressure on the date of the surgical encounter extracted from the encounter vitals table.	Noninvasive blood pressure (NIBP) cuff, Arterial blood pressure (ABP), Null
Heart Rate	Value for heart rate in beats per minute within 7 days of the date of the surgical encounter and on the date of the surgical encounter extracted from the encounter vitals table.	Within 2 standard deviations from the patients mean HR, Null

Outcome (Dependent) Variable

The outcome variable for this study was patients with UIA. Patients UIA were defined as patients unplanned surgical encounter admissions to an intensive care unit (ICU) within 24 hours of surgery with anesthesia. Registration data were used to calculate and validate a patients' surgical encounter with an UIA. The department name, date and time arrived and discharged from the department, and room number were extracted from the AHC-CDR. Planned postoperative admission unit was not available in the AHC-CDR at the time of data extraction. Therefore, to be classified as an UIA the patient was required to have an anesthesia start and stop time within the date and time of surgery, then be discharged to a unit other than the post anesthesia care unit or intensive care unit (ICU) prior to transferring into to an ICU within 24 hours of perioperative care. The operational definition and plausible values for UIA are provided in Table 3.4. The primary investigator classified patients as UIA. Twenty percent of the ICU admissions were randomly selected to validate their classification by two independent reviewers. There was 90% agreement in classification in UIA status. Discrepancies were reviewed and resolved with group consensus.

Table 3.5. *Definition and Plausible Values for Outcome Variables*

Variable	Operational Definition	Plausible Values
Department Name	Name of the department where the patient was admitted, transferred, or discharged during their surgical encounter.	Surgery, Phase I Pool Room, Surgery, PACU, ICU
In Date/ Time Out Date/ Time	Date and time when the patient was admitted, transferred, or discharged in and out of a department during their surgical encounter.	DD/MM/YYYY 00:00-23:59
Anesthesia Start/ Stop Time	Start and stop time for the patients anesthesia encounter was admitted, transferred, or discharged in and out of a department during their surgical encounter.	DD/MM/YYYY 00:00-23:59
Unanticipated Intensive Care Unit Admission	Description of if a surgical encounter was not registered to be admitted to an intensive care unit at the start of anesthesia care and was admitted to an intensive care unit within 24 hours of the end of anesthesia care extracted from the encounters admission/ discharge table.	Yes, No, NA

Summary

Demographic characteristics, intraoperative hemodynamic predictor variables, and UIA variables were the data types extracted by the AHC-CDR research and development staff for this study. Verbal and written correspondence with the AHC-CDR staff was used to determine that data collection was accurate. Descriptive statistics for all demographic characteristics, intraoperative, and outcome variables were used to determine if data collection was accurate and/ or consistent.

Data Analysis Plan

First, data was analyzed with exploratory data visualization using line graphs, then statistically analyzed with Odds Ratios and one-way analysis with variance to identify intraoperative hemodynamic management data patterns associated with adult, inpatient, elective surgery patients UIA. Exploratory data visualization is a method with specific steps and procedures to explore complex data sets with the speed and accuracy of visual perception, preattentive reasoning, and human intelligence to generate data-driven hypotheses that can be tested for statistical significance (Andrienko & Andrienko, 2006; Kirk, 2012). For exploratory data visualization with line graphs to support inference of quantitative information visual integrity must be maintained in the line graphs (Dzemyda et al., 2013; Tufte, 2001f). Visual integrity is inhibited by data or design distortion (Feng et al., 2010; Tufte, 2001f).

Assumptions in Data Visualization

Data visualization using line graphs has three assumptions to mitigate data and design distortion and promote accurate data analysis using human intelligence. The three assumptions in data visualization were: 1) data and mathematical accuracy, 2) visualization accuracy, 3) annotation accuracy. After the assumptions of data visualization were verified, data was accurately and efficiently analyzed for patterns among multivariate data (Harter et al., 2012; Javed et al., 2010; Pieczkiewicz & Finkelstein, 2010; Tufte, 2001f).

Data and mathematical accuracy. The primary assumption in data visualization was data and calculations were accurate (Kirk, 2012; Tufte, 2001e). The assumption of data and mathematical accuracy was imperative to guide preattentive reasoning and human intelligence about data in this study. Procedures for data preparation, cleaning, data transformations, and statistical analysis were evaluated to maintain the structure of the data and mathematical accuracy. Foremost, procedures for handling missing data, erroneous values, outliers, data transformation, and statistical analysis were audited and congruent with the purpose of the study (Kirk, 2012; Soley-Bori, 2013). For example, missing data can be coded or imputed if the purpose of the study is to generate insight into how missing data influenced an outcome but missing data can be deleted if data or visual distortion is generated (Andrienko & Andrienko, 2006; Kirk, 2012; Soley-Bori, 2013). In this study, missing data was deleted to remove visual distortion from the line graphs. Additionally, mathematical calculations used to describe or transform the data set were verified to ensure the visualization accurately represented the concepts inherent to the study (Dzemyda et al., 2013; Kirk, 2012; Tufte, 2001e).

Visual accuracy. The second assumption in data visualization was visual accuracy. Visual accuracy was determined by the number of units in data analysis, the visualization technique, and representation of quantitative information (Dzemyda et al., 2013; Tufte, 2001e). The assumption of visual accuracy was verified with the number of units in data analysis (a set of one patients surgical encounter with an UIA and two patient's surgical encounters without an UIA) which did not exceed the number of features visualized (value, time, and category) (Dzemyda et al., 2013). Visual accuracy was also determined by aligning the purpose of the study with appropriate data visualization methods (Dzemyda et al., 2013; Kirk, 2012). Line graphs are used to explore change over time and explore patterns among categories with a broad range of values which is in alignment with the purpose of this study to discover time-dependent intraoperative hemodynamic management data patterns associated with patients UIA (Kirk, 2012).

Finally, visual accuracy was determined by accurate representation of quantitative information (Kirk, 2012; Tufte, 2001e). Quantitative data represented with visual variables such as shape or transparency was proportional to the distribution of the data (Kirk, 2012; Tufte, 2001a). The assumption of visual accuracy was verified by evaluating the selection of shape, color hue, and location of data representations according to principles of visual perception and preattentive reasoning (Santos & Dillenseger, 2005; Tufte, 2001a) In this study, two data visualization experts evaluated a prototype line graph with the Quality Data Visualization Scale to validate data representation. The procedure for evaluating visual accuracy of the prototype line graph along with the description of the visualization scale are provided in the data analysis plan under Aim 1.

Annotation accuracy. The final assumption in data visualization was annotation accuracy (Tufte, 2001b). The assumption of annotation accuracy was used to ensure the context of data is included in data analysis. The title, axis labels, and units of measure were standardized, grammatically correct, and concise (Kirk, 2012; Tufte, 2001a). Furthermore, the typography style, font, and color hue were legible to support human intelligence of data representations (Kirk, 2012; Tufte, 2001a). The assumption of annotation accuracy was also verified by evaluating the titles and axis labels according to principles of visual perception and preattentive reasoning (Santos & Dillenseger, 2005; Tufte, 2001a). In this study, two data visualization experts evaluated the prototype line graph with the Quality Data Visualization Scale to validate annotation accuracy. The procedures for evaluating the line graph along with the description of the visualization scale are provided in the data analysis plan under Aim 1.

Summary. The assumptions of data and statistical accuracy, visual accuracy, and annotation accuracy are essential for visual perception, preattentive reasoning, and human intelligence data analysis of multivariate data. These assumptions were verified to identify the sequence and timing of events in intraoperative hemodynamic management associated with a patients UIA with data visualization using line graphs. If these assumptions were violated, then visual distortion would have occurred and human intelligence would not have been able to localize or discriminate patterns in multidimensional data.

Data Analysis and Software

The steps in data analysis included: data selection, data preparation, data transformation, and human intelligence (Kirk, 2012). Data preparation evaluated the structure of the data and data transformation created new variables for visualization of intraoperative hemodynamic management. The final steps in data visualization used visual proprioception, preattentive reasoning, and human intelligence to identify salient intraoperative hemodynamic patterns associated with a patient's surgical encounter with UIA.

Data Selection

First data were selected from the AHC-CDR data mart. Patient data was extracted using SQL® software. Queries were created using each patient's unique identification number to extract encounter data from admission/discharge, demographic, event, medication, observation, patient, and service tables within the AHC-CDR data shelter. Data were saved in Microsoft Excel© and imported into analytic software.

Data Preparation

The first step in the data visualization method was data preparation which entailed analyzing the structure of the data set and handling implausible, duplicate, or missing data. First, the data set was assessed for uncommon characters, implausible values, and duplicate data using Microsoft Excel©. No uncommon characters (e.g. >, #) were identified in the data set.

Implausible values and duplicate data. Implausible values are defined as illogical measurements for data elements (or variables) (Tables 3.1-3). Heart rate, aSBP, and medication values were assessed for implausible values with descriptive statistics and line graphs. First, a mean and standard deviation were calculated for each patients HR and aSBP values. The mean and standard deviation were also calculated for each drug name in the entire data set. Outlier values greater than two standard deviations from the mean were visually inspected with line graphs. Values that did not follow the patients trend in the three values immediately before and after the suspected outlier were considered implausible and coded as missing since the value would impair statistical and visual accuracy (Kirk, 2012). The procedure of using six data points to establish a data pattern and identify implausible values was established from health trajectory research and a pilot study on intraoperative HR and SBP data (Henly, Wyman, & Findorff, 2011; Peterson, Mathiason Moore, & Monsen, IRB approval 04/2014). Duplicate data are two values for the same observation (e.g. two aSBP values with the same time-stamp). There were no duplicate HR, aSBP, or medication values in the data set.

Missing data. Data missing at random are considered part of the visualization model but data not missing at random cannot be used to model data (Baur et al., 2015; Soley-Bori, 2013). Patients with UIA were evaluated for missing data using the Standard Query Language server in the University of Minnesota data shelter. Patients with UIA had ASA classification or aSBP data missing at random. The AHC-CDR research and development staff manually extracted ASA classification data on 11 patients with UIA. Patients with UIA also had missing aSBP data. There was no pattern among patient age, ASA class, or date of surgery for missing aSBP data. Patients with missing aSBP data were excluded from this study since there was no procedure to extract the missing data.

Matching patients. The sample of a patients with an UIA were matched with two patients without UIA. The criteria used to match patient's surgical encounters with (cases) and without (controls) UIA is described in Table 3.6. Based upon the review of the literature patient age, ASA classification, gender, and type of surgical procedure were characteristics used to create comparable groups in anesthesia research (Newman et al., 2013).

The type of surgical procedure for each case was matched as closely as possible using the name and International Classification of Diseases, ninth revision (ICD-9) code. If there was not an exact match for the type of surgical procedure the procedure was rolled-up to the next highest ICD-9 level using the Agency for Healthcare Research and Quality clinical classification criteria (Agency for Healthcare Research and Quality, July, 2016). Type of anesthesia would also be a logical criterion to create comparable groups and is included in other anesthesia research. The type of anesthesia can alter pharmacologic and procedural interventions that could have contributed to intraoperative hemodynamic management and patients UIA (Pharmacology & physiology in anesthetic practice, 2006; Sweitzer, 2008). The list of patients with (cases) and without (controls) UIA were cross checked. No case or control patients' surgical encounters were duplicated. Once comparable groups were established the variability in intraoperative predictors were analyzed for association with UIA.

Table 3.6. *Matching Criteria for Cases and Controls*

Criteria	Matching Procedure
Age	Age range: 18-39, 40-64, 65-75, 76-89
American Society of Anesthesiology (ASA) Classification	ASA classification 1-2 ASA classification ≥ 3
Gender	Male, Female
Type of Surgical Procedure	Name and ICD-9 code of the primary surgical procedure
Type of Anesthesia	General anesthesia General with a block Spinal anesthesia Local monitored anesthesia care

Note. The age range for matching a patient's surgical encounter with and without an UIA was selected from sociologic literature to separate differences in middle and older adulthood (Rice University, 2016).

Finally, the structure of the combined case and control patients surgical encounters were analyzed by classifying each variable as nominal, ordinal, interval, or ratio. Then descriptive statistics were calculated for each data type with R statistical packages. Descriptive statistics included: count, percentage for nominal variables, median and range for ordinal variables, and mean, standard deviation, and range for interval and ratio variables. Descriptive statistics are required to describe the sample, data transformations, and to code the data set with visual variables (e.g. shape and color hue).

Data transformation. The next step in the data visualization method was data transformation (Andrienko & Andrienko, 2006; Kirk, 2012). Data were transformed to into new concepts such as the smoothed hemodynamic trend line and cumulative dose by therapeutic class of intraoperative medication administration. The time of intraoperative

HR, aSBP, and medication administration were transformed into the time from the start of anesthesia. Then, concurrent intraoperative HR and aSBP measurements were transformed using the Locus algorithm© (Peterson, Mathiason, & Monsen, 2015). The Locus algorithm© used the median value of the first three intraoperative HR or SBP measurements to establish a baseline and all HR and aSBP values were converted into a percentage of the patient's baseline. Next, the concurrent HR or aSBP percentage that was the furthest from baseline was retained and averaged with the percentages in the prior two minutes to create a smoothed hemodynamic trend line. The Locus algorithm © and procedure for smoothed hemodynamic trend line were piloted with intraoperative HR and non-invasive SBP data from 50 patients' surgical encounters (Peterson et al., 2015).

Finally, intraoperative medication administration data were transformed into a cumulative equivalent dose by therapeutic class and labeled with the name of the therapeutic class. The intraoperative medication administration conversion dosages and normalization ratio are provided in Table 3.7. The therapeutic classes of intraoperative medication administration and a smoothed hemodynamic trend line were visualized as variables in each patient's line graph.

Table 3.7. *Therapeutic Class Conversion Chart*

Therapeutic Class	Medication Name	Equivalent Dose
Analgesics	Acetaminophen	500 mg
	Alfentanil	0.1 mg
	Aspirin	81 mg
	Fentanyl	0.01 mg
	Hydromorphone	7 mg
	Ketorolac	0.3 mg
	Meperidine	0.1 mg
	Morphine	1 mg
	Remifentanil	0.02 mg
	Sufentanil	0.001 mg
Anti-Infective Agents	Cefazolin	1000 mg
	Cefotetan	1000 mg
	Clindamycin	600 mg
	Ertapenum	1000 mg
	Metronidazole	250 mg
	Vancomycin	1000 mg
Cardiovascular Agents	Atropine	0.07mg
	Dobutamine	0.002 mg
	Esmolol	0.5 mg
	Ephedrine	10 mg
	Epinephrine	0.001 mg
	Furosemide	0.1 mg
	Hydralazine	2.5 mg
	Labetalol	0.1 mg
	Mannitol	0.25 mg
	Metoprolol	1 mg
	Nitroglycerin	.05
	Norepinephrine	0.004 mg
	Phenylephrine	.05 mg
	Vasopressin	0.04 units
Central Nervous System Drugs	Dexmedetomidine	10 mg
	Etomidate	0.2 mg
	Ketamine	1 mg
	Midazolam	0.15 mg
	Propofol	1.5 mg
Endocrine Metabolic Drugs	Dexamethasone	25 mg
	Insulin	0.1 units
	Oxytocin	1 unit

Gastrointestinal Agents	Droperidol	1.25 mg
	Edriophonium	0.5 mg
	Glycopyrolate	0.06 mg
	Neostigmine	0.04 mg
	Ondansetron	4 mg
	Promethazine	25 mg
	Scopolamine	0.07 mg
Hematologic Agents	Heparin	100 units
	Protamine	1.3 mg
Local Anesthetics	Bupivacaine	4 mg
	Lidocaine	1 mg
	Ropivicaine	4 mg
Neuromuscular Blocking Agents	Cisatracurium	.05 mg
	Pancuronium	0.07 mg
	Rocuronium	0.3 mg
	Succinylcholine	1 mg
	Vecuronium	.05 mg
Nutritional Products	Albumin	250 ml
	Calcium Chloride	1000 mg
	Potassium Chloride	10 mEq
	Sodium Bicarbonate	2 mEq

Note. Adopted from Pharmacology & Physiology in Anesthetic Practice (*Pharmacology & physiology in anesthetic practice*, 2006). *Abbreviations*. mg, milligrams; ml, milliliters.

Linking the Aims to Data Analysis

In this section, the data analysis method will be linked to the aims.

Aim 1. *Evaluate the salience of a prototype visualization for the intraoperative anesthesia data set,*

A prototype line graph was designed with R Studio® version 1.0.136 using an unmatched patients' intraoperative hemodynamic and medication administration data. The x-axis of the Cartesian coordinates was the time in minutes from the start of anesthesia and the y-axis was a normalization scale. Descriptive statistics were calculated for each feature in the unmatched patients' data set and a normalization scale was created to fit the range of values. Next, each cumulative dosage by therapeutic class of intraoperative medication administration and the smoothed hemodynamic trend line were plotted on the Cartesian coordinates. The smoothed hemodynamic trend line was a solid red line and each therapeutic class of intraoperative medication was a distinct color hue. All lines on the visualization were a solid line type. Visual variables such as color hue and shape (e.g. dashed line) were applied to differentiate the smoothed hemodynamic trend line from the therapeutic classes of medication administration.

The prototype line graph was evaluated by two experts in data visualization for salient data representation and presentation. A Quality Data Visualization Scale (Appendix A) was developed for the data visualization experts to evaluate salience in the data visualization prototype. Salience is defined as visual information that is identified as prominent, obvious, or significant with visual proprioception and preattentive reasoning (Feng et al., 2010; Seger et al., 2015; Talsma et al., 2010). The Quality Data Visualization Scale was developed from a published questionnaire on evaluation of effective data visualization (Santos & Dillenseger, 2005).

Copies of the Quality Data Visualization Scale were given to each data visualization expert, then each expert independently evaluated the line graph prototype. Next, the items on the completed scale were averaged and any item that averaged less than an eight was followed up with qualitative feedback. Eight was selected as the threshold for passing an item on the Quality Visualization Scale to correspond to a high level of salience (DeVellis, 2012; Santos & Dillenseger, 2005). Qualitative feedback provided by the data visualization experts on low scoring items was incorporated into the next iteration of the prototype. The prototype line graph visualization was evaluated and re-evaluated until all seven items on the scale scored greater than or equal to an eight. The Quality Data Visualization Scale results and qualitative feedback were logged in an audit trail along with design decisions about the visualization prototypes. The results of the prototype visualization are the percent agreement of the two data visualization experts for all of the items in the Quality Data Visualization Scale.

Aim 2. *Discover, label, and define patterns in intraoperative hemodynamic management data for each patient with and without UIA,*

Salient intraoperative hemodynamic management data patterns in a patient's surgical encounter with and without an UIA were discovered using visual perception, preattentive reasoning, and human intelligence of the set line graphs. Line graphs were created for the entire data set based upon the final prototype using R. The line graphs were professionally printed and analyzed with visual perception, preattentive reasoning, and human intelligence. The set line graphs underwent constant comparative analysis to identify salient intraoperative hemodynamic management patterns (Aigner, 2011; Polit & Beck, 2012). Constant comparative analysis entailed visualizing the line graphs, coding the attributes of data patterns in Microsoft Excel ©, visualizing additional set line graphs, and recoding attributes until no new attributes were identified. Each attribute was given an operational definition.

Next an intraoperative hemodynamic management pattern matrix (Table 3.8) was created using Microsoft Excel ©. Each line graph was numbered. The first column in the pattern matrix was numbered for the line graphs and the remaining columns contained the label of the intraoperative hemodynamic attributes. Next, the line graphs of patients with and without UIA were visualized and the attributes marked in the pattern matrix. Finally, the pattern matrix was organized according to line graphs with the same attributes. The attributes were used to label and establish an operational definition for intraoperative hemodynamic management data patterns. A threshold for the quantity of patterns to be defined was determined after the attributes were finalized. Intraoperative hemodynamic management data patterns were labeled and defined at an intermediate level of abstraction which is desirable for theory-based advanced nursing practice (Kenny, 2006). The results included a narrative description of all of the attributes of the salient intraoperative hemodynamic management data patterns and descriptive statistics.

Table. 3.8. *Intraoperative Hemodynamic Management Data Pattern Matrix*

Line Graph Number	Attribute 1	Attribute 2	Attribute …	Attribute n
1				
2				
3				
4				
5				
.				
.				
.				
n				

Aim 3. *Compare patterns identified in Aim 2 for associations with patient UIA.*

Salient intraoperative hemodynamic management data patterns identified in Aim 2 were compared for associations with patients UIA using Odds Ratios (ORs) or one-way analysis of variance (ANOVA) statistical tests. First counts of patient surgical encounters with and without UIA for each data pattern was determined from the descriptive statistics calculated in Aim 2. Then, ORs were calculated for categorical patterns and one-way ANOVA was used to analyze continuous numeric patterns using Statistical Package for the Social Sciences (SPSS)®. A p-value $< .05$ was used to determine statistical significance of intraoperative hemodynamic management data patterns associated with a patients UIA. The results include the frequency, test statistic, standard error, p-value, OR, and 95% confidence interval for categorical patterns and mean, standard deviation, mean square, F statistic, and p-value for continuous numeric patterns.

Ethical Issues

The data set was acquired from the University of Minnesota, AHC-CDR which has established procedures to protect patient health record data for inclusion in research. Foremost, the AHC-CDR has an opt-out procedure where patients can have their health record information excluded from research. The AHC-CDR staff has estimated 2-4% of patients have opted to exclude their health care information from research (personal communication, Matt Larson, CDR staff, 08/12/2015). Women and minorities will be included in this study unless they opted out of their data to be included in research. As mentioned under the inclusion criteria, data from children will be excluded from this study based upon knowledge about different thresholds for 'normal' HR and aSBP measurements.

The AHC-CDR also established procedures to maintain confidentiality and security. Data will be fully de-identified by the AHC-CDR staff prior to providing it to the investigator to promote confidentiality (personal communication, Zohara Cohen, CDR staff, 01/11/2015). The AHC-CDR has also established procedures to secure healthcare data. Health information is maintained in a firewall and password protected environment (data shelter) with data analysis tools (personal communication, Matt Larson, CDR staff, 08/12/2015). Finally, the research protocol that will be used to collect and analyze data has been reviewed and granted approval by the University of Minnesota Institutional Review Board.

Conclusion

Intraoperative deterioration during routine anesthesia care has been described as a complex quality care initiative. Prior research used quantitative methods to explain demographic and *selective* intraoperative medication as predictors of UIA. This study used data visualization with line graphs to perform exploratory data analysis on intraoperative medication administration and hemodynamic data. All therapeutic classes of intraoperative medication administration and a smoothed hemodynamic trend line were analyzed with visual proprioception, preattentive reasoning, and human intelligence to discover patterns in intraoperative hemodynamic management in patients with UIA. Intraoperative hemodynamic management data patterns discovered with data visualization were then tested for statistical significance.

Chapter 4

RESULTS

Introduction

This case-control study design used data visualization with line graphs and discovered time-dependent intraoperative hemodynamic management data patterns associated with patient unanticipated intensive care unit admission (UIA). Sixty-eight patients without UIA (controls) were matched to 34 patients with UIA (cases). First, a prototype line graph was developed from one of the unmatched patient's intraoperative data and evaluated for salience. Next, the prototype line graph was used to format line graphs for the entire data set. Then, intraoperative hemodynamic data patterns were discovered, labelled, and operationally defined using data visualization and a pattern matrix. Finally, associations between intraoperative hemodynamic management data patterns and patients with UIA were identified with odds ratios and one-way analysis of variance statistical tests.

Description of the Data set

Description of the sample. There were 29,080 inpatient, elective surgical encounters that had anesthesia care in the Academic Health Center, Clinical Data Repository (AHC- CDR) between January 1, 2012 and June 30, 2015. Time-stamped admission data classified patients as UIA and was audited for accuracy. Patients were classified as UIA when their registration data documented they were admitted to any hospital unit other than intensive/ critical care, transferred into the operating room, then transferred to a postoperative hospital unit other than an intensive/ critical care unit, and were transferred into an intensive/ critical care unit within 24 hours from the time they transferred into the operating room. Overall, 122 patients were classified as UIA in the AHC-CDR; therefore, the incidence of a patients with UIA was 0.4%. Thirty-four of the patients classified as UIA had intraoperative arterial systolic blood pressure measurements and were included in this study.

Description of the matched controls. Patient age, American Society of Anesthesiology (ASA) classification, sex, type of procedure, and type of anesthesia were the criteria used to match patients with and without UIA. Characteristics of patients with and without UIA were analyzed with descriptive statistics to validate comparability of groups. There were no statistically significant differences in patient age, ASA classification, sex, type of procedure, and type of anesthesia in patients with and without UIA since Fischer's exact test was > .05 (Table 4.1).

Table. 4.1. *Descriptive Analysis of Matching Criteria*

Characteristic	**Patients with UIA** Percentage (count) *n = 34*	**Patients without UIA** Percentage (count) *n = 68*
Age		
18-39	6% (2)	6% (4)
40-64	59% (20)	59% (40)
65-75	15% (5)	15% (10)
76-89	20% (7)	21% (14)
ASA Classification		
1-2	9% (3)	9% (6)
≥ 3	91% (31)	91% (62)
Sex		
Male	53% (18)	53% (36)
Female	47% (16)	47% (16)
Type of Procedure		
Cardiovascular	15% (5)	15% (10)
Central Nervous System	9% (3)	9% (6)
Digestive	15% (5)	15% (10)
Endocrine	3% (1)	3% (2)
Female Reproductive	9% (3)	9% (6)
Integumentary	3% (1)	3% (2)
Musculoskeletal	29% (10)	29% (20)
Respiratory	9% (3)	9% (6)
Urinary	9% (3)	9% (6)
Type of Anesthesia		
General	94% (32)	94% (64)
General with a Block	3% (1)	3% (2)
Spinal	3% (1)	3% (1)
Local Monitored Care	0% (0)	0% (0)

*Fischer's Exact Test p-value < .05

Note. None of the matching criteria were statistically significant.

Excluded patients. Seventy-two percent (88/122) of patients that were classified as UIA were excluded from this study since they did not have non-invasive arterial blood pressure (NIBP) measurements. These patients were excluded to minimize the threat of instrumentation and visual distortion. Non-invasive and arterial blood pressure measurements have different intervals between measurements and are calibrated differently in clinical practice. Non-invasive blood pressure measurements are documented less frequently; often every three to five minutes during anesthesia care compared to arterial blood pressure measurements which are documented every minute. Furthermore, NIBP measurement devices are not calibrated prior to routine anesthesia care.

Descriptive Analysis

In addition to the aforementioned criteria used to match patients, demographic characteristics such as patient weight, height, body mass index (BMI), race, ethnicity, and tobacco use were used to describe the data set (Table 4.2). Demographic characteristics such as alcohol use and illicit drug use were not included in descriptive analysis of the data set since more than 75% of data were missing. Based upon descriptive data available for analysis patients with UIA had significantly more missing height and ethnicity data compared to patients without UIA and were nonhispanic ($p < .05$). Average weight, height, and body mass index were comparable for patients with and without UIA; as were race and tobacco use ($p > .05$).

Table 4.2. *Descriptive Analysis of Demographic Characteristics*

Characteristic	**Entire Data set** Mean/ Frequency (SD/count) *n = 102*	**Patients with UIA** Mean/ Frequency (SD/count) *n = 34*	**Patients without UIA** Mean/ Frequency (SD/count) *n = 68*
Missing Weight	24% (24)	21% (7)	25% (17)
Weight in pounds	217.2 (56.8)	211.4 (66.6)	220.0 (52.4)
Missing Height	12% (12)	21% (7)*	7% (5)
Height in inches	68.7 (5.2)	70.2 (4.8)	67.3 (5.6)
Missing BMI	38% (39)	35% (12)	40% (27)
BMI (SD)	31.4 (9.5)	27.0 (7.9)	35.2 (10.3)
Race			
Missing	70% (72)	65% (22)	74% (50)
African American	11% (11)	11% (4)	10% (7)
White	8% (8)	9% (3)	7% (5)
Hispanic or Latino	6% (6)	6% (2)	6% (4)
Asian	3% (3)	6% (2)	1% (1)
Pacific Islander	2% (2)	3% (1)	1% (1)
Hawaiian/ Other	0% (0)	0% (0)	0 % (0)
Ethnicity			
Missing	60% (61)	44% (15)*	67% (46)
Declined/ unknown	20% (21)	26% (9)	18% (12)
Non-Hispanic	17% (17)	26% (9)*	12% (8)
Hispanic or Latino	3% (3)	3% (1)	3% (2)
Tobacco Use			
Missing	73% (74)	65% (22)	76% (52)
Not asked	10% (10)	9% (3)	11% (7)
Former	8% (8)	12% (4)	6% (4)
Current	7% (7)	9% (3)	6% (4)
Never	2% (3)	5% (2)	1% (1)

*Chi-square test statistically significant ($p < .05$)

** Chi-square test statistically significant ($p < .001$)

Aim One: Evaluate the Salience of a Prototype Visualization

A prototype (example) line graph was created from one unmatched patient's intraoperative hemodynamic and medication administration data using R Studio® version 1.0.136. A qualitative color scheme was applied to the line graph to discriminate between the different therapeutic classes of medication administration and the hemodynamic data trend line. The first prototype line graph had dashed line types and was evaluated by two data visualization experts using the Quality Data Visualization Scale (Appendix A). All items on the Quality Data Visualization Scale (QDVS) scored greater than or equal to eight; however narrative feedback recommended a solid line instead of the dashed line type. A second prototype line graph was created using R Studio® version 1.0.136 with solid line types and evaluated by the same data visualization experts. Percent agreement means that all items on the QDVS also scored greater or equal to eight. The score and percent agreement for each prototype line graph are presented in Table 4.2 and Table 4.3.

Table. 4.3. *Percentage Agreement for Prototype 1.*

Quality Data Visualization Scale	***Rater 1***	***Rater 2***	***Percent Agreement*** (≥ 8)
Item 1	8	10	100
Item 2	9	10	100
Item 3	8	9	100
Item 4	9	10	100
Item 5	10	8	100
Item 6	10	10	100
Item 7	10	10	100

Table. 4.4. *Percentage Agreement for Prototype 2.*

Quality Data Visualization Scale	***Rater 1***	***Rater 2***	***Percent Agreement*** (≥ 8)
Item 1	8	10	100
Item 2	9	10	100
Item 3	9	8	100
Item 4	9	9	100
Item 5	10	8	100
Item 6	10	10	100
Item 7	10	10	100

Since both prototype line graphs resulted in 100% agreement for all items on the QDVS expert opinion was used to determine which prototype would be used to identify salient patterns for the entire data set. Expert opinion determined that the solid line types on Prototype 2 (Figure 4.1) created a more prominent visualization which would be advantageous for human intelligence to identify salient patterns.

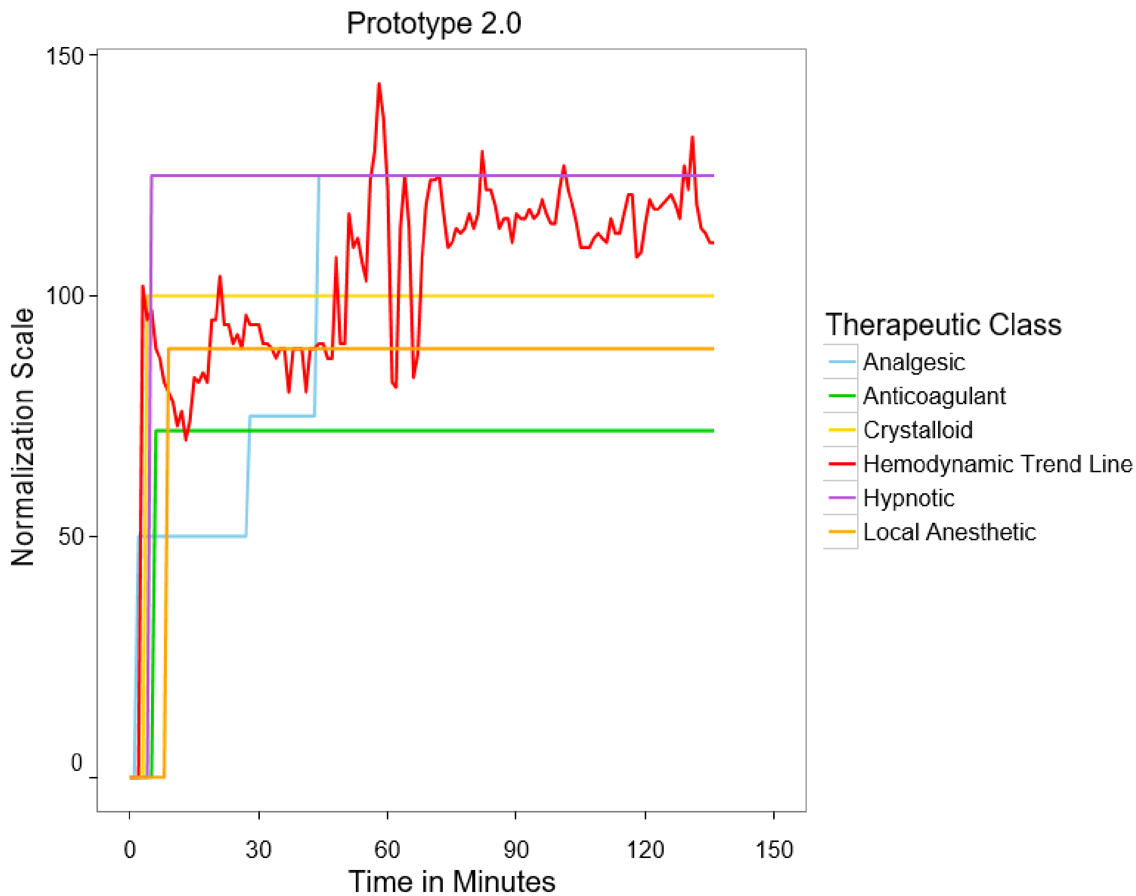


Figure 4.1. Prototype 2 Line Graph.

Aim Two: Discover, Label, and Define Patterns in Intraoperative Hemodynamic Management

Line graphs for the entire data set were created with R Studio® version 1.0.136 using prototype 2 to format the axis labels, color scheme, and normalization scale. Line graphs were created for each patient in the entire data set (Appendix B Data Set Line Graphs). All of the lines graphs in the data set were visualized, salient attributes were recorded in a journal, and the attributes were refined until no new obvious characteristics were visualized. Attributes were single characteristics in the line graph and data patterns were two or more attributes in the line graph. Thirty-five intraoperative hemodynamic data patterns were discovered using data visualization, labelled, and given an operational definition that was clinically meaningful (Table 4.4).

Table. 4.5. *Operational Definitions of Intraoperative Hemodynamic Data Patterns*

Pattern Label	Operational Definition
Induction Flat	No increase in the therapeutic class normalization value in the first 30 minutes.
Induction Gradual Steps	The therapeutic class normalization value increased more than once by less than or equal 50 in the first 30 minutes.
Induction Gradual Single Step	The therapeutic class normalization value increased once by less than or equal to 50 in the first 30 minutes.
Induction Large Steps	The therapeutic class normalization value increased more than once by greater than or equal to 51 in the first 30 minutes.
Induction Large Single Step	The therapeutic class normalization value increased once by greater than or equal to 51 in the first 30 minutes.
Maintenance Flat	No increase in the therapeutic class normalization value after the first 30 minutes or prior to the last 30 minutes.
Maintenance Gradual Steps	The therapeutic class normalization value increased more than once by less than or equal to 50 after the first 30 minutes or prior to the last 30 minutes.
Maintenance Gradual Single Step	The therapeutic class normalization value increased once by less than or equal to 50 after the first 30 minutes or prior to the last 30 minutes.
Maintenance Large Steps	The therapeutic class normalization value increased more than once by greater than or equal to 51 after the first 30 minutes or prior to the last 30 minutes.
Maintenance Large Single Step	The therapeutic class normalization value increased once by greater than or equal to 51 after the first 30 minutes or prior to the last 30 minutes.
Emergence Flat	No change in the therapeutic class normalization value in the last 30 minutes.
Emergence Gradual Steps	The therapeutic class normalization value increased more than once by less than or equal to 50 in the last 30 minutes.

Emergence Gradual Single Step	The therapeutic class normalization value increased once by less than or equal to 50 in the last 30 minutes.
Emergence Large Steps	The therapeutic class normalization value increased more than once by greater than or equal to 51 in the last 30 minutes.
Emergence Large Single Step	The therapeutic class normalization value increased once by greater than or equal to 51 in the last 30 minutes.
Induction Hypodynamic	At least one hemodynamic trend line normalization value was less than 80 in the first 30 minutes.
Maintenance Hypodynamic	At least one hemodynamic trend line normalization value was less than 80 after the first 30 minutes and prior to the last 30 minutes.
Emergence Hypodynamic	At least one hemodynamic trend line normalization value was less than 80 in the last 30 minutes.
Induction Hyperdynamic	At least one hemodynamic trend line normalization value was more than 120 in the first 30 minutes.
Maintenance Hypodynamic	At least one hemodynamic trend line normalization value was less than 80 after the first 30 minutes and prior to the last 30 minutes.
Emergence Hypodynamic	At least one hemodynamic trend line normalization values were less than 80 in the last 30 minutes.
Induction Normodynamic	All hemodynamic trend line normalization values were between 80-120 in the first 30 minutes.
Maintenance Normodynamic	All hemodynamic trend line normalizations values were between 80-120 after the first 30 minutes and prior to the last 30 minutes.
Emergence Normodynamic	All hemodynamic trend line normalization values were between 80-120 in the last 30 minutes.
Induction Coarse	More than half of the hemodynamic trend line normalization values increased or decreased by more than 50 in the first 30 minutes.
Maintenance Coarse	More than half of the hemodynamic trend line normalization values increased or decreased by more than 50 after the first 30 minutes and prior to the last 30 minutes.
Emergence Coarse	More than half of the hemodynamic trend line normalization values increased or decreased by more than 50 in the last 30 minutes.
Induction Fine	More than half of the hemodynamic trend line normalization values increased or decreased by less than or equal to 50 in the first 30 minutes.

Emergence Fine	More than half of the hemodynamic trend line normalization values increased or decreased by less than or equal to 50 in the last 30 minutes.
Induction Fine	More than half of the hemodynamic trend line normalization values increased or decreased by less than or equal to 50 in the first 30 minutes.
Maintenance Fine	More than half of the hemodynamic trend line normalization values increased or decreased by less than or equal to 50 after the first 30 minutes and prior to the last 30 minutes.
Emergence Fine	More than half of the hemodynamic trend line normalization values increased or decreased by less than or equal to 50 in the last 30 minutes.
Induction Gap	Values for the hemodynamic trend line were missing for more than 25 minutes in the first 30 minutes.
Maintenance Gap	Values for the hemodynamic trend line were missing for more than 25 minutes after the first 30 minutes and prior to the last 30 minutes.
Emergence Gap	Values for the hemodynamic trend line were missing for more than 25 minutes in the last 30 minutes.

Descriptive statistics of the therapeutic classes of medication were calculated for the entire data set and separately for patients with and without UIA (Table 4.6 and Table 4.7). A therapeutic class of medication is the name representing individual medications that have a similar chemical structure and bind to the same receptors. The frequency among the different therapeutic classes ranged from 7-100% for the entire data set, 3-100% for patients with UIA, and 9-100% for patients without UIA. Endocrine metabolic, nutritional products, and respiratory agents were present in less than 25% of the patients' line graphs and more than 75% of the line graphs contained analgesic, cardiovascular, central nervous system, gastrointestinal, local anesthetic, or neuromuscular blocking drugs. Every patient in the data set received central nervous system medication during anesthesia care.

Table. 4.6. *Descriptive Analysis of Therapeutic Classes*

Attribute	**Entire Data set** Percentage (Count) *n = 102*	**Cases** Percentage (Count) *n = 34*	**Controls** Percentage (Count) *n = 34*
Central Nervous System Line	100% (102)	100% (34)	100% (68)
Analgesic Line	98% (100)	97% (33)	99% (67)
Neuromuscular Blocking Line	94% (96)	88% (30)	97% (66)
Gastrointestinal Line	91% (93)	97% (33)	94% (60)
Cardiovascular Line	87% (89)	88% (30)	87% (59)
Local Anesthetic Line	76% (78)	71% (24)	79% (54)
Anti-infective Line	27% (28)	38% (13)	22% (15)
Hematologic Line	27% (28)	21% (7)	31% (21)
Nutritional Line	20% (20)	9% (3)	25% (17)
Endocrine Metabolic Line	11% (11)	9% (3)	23% (8)
Respiratory Line	7% (7)	3% (1)	9% (6)

Next descriptive statistics were calculated for the 35 intraoperative hemodynamic data patterns. The frequency of data patterns ranged from 0-45% and was similar for the entire data set and for patients with and without UIA. Emergence flat was the most common data pattern for patients with and without UIA. Induction, maintenance, and emergence large steps represented 0% of the data patterns and in patients with UIA 23 of the data patterns had a frequency of less than or equal to 5%.

Table. 4.7. *Descriptive Analysis of Hemodynamic Data Patterns*

Attribute	**Entire Data set** Percentage (Count) *n = 1224*	**UIA** Percentage (count) *n = 408*	**Controls** Percentage (count) *n = 816*
Emergence Flat	45% (545)	42% (172)	46% (373)
Maintenance Gradual Steps	23% (280)	22% (88)	24% (192)
Induction Flat	21% (253)	17% (70)	22% (183)
Induction Gradual Single Step	20% (244)	21% (86)	19% (158)
Maintenance Flat	17% (208)	17% (68)	17% (140)
Maintenance Gradual Single Step	11% (131)	11% (45)	11% (86)
Maintenance Fine	7% (90)	7% (29)	7% (61)
Induction Gradual Steps	6% (79)	6% (26)	6% (53)
Induction Large Single Step	6% (77)	7% (27)	6% (50)
Maintenance Large Step	5% (61)	4% (17)	5% (44)
Maintenance Hypodynamic	5% (66)	4% (17)	6% (49)
Induction Fine	5% (64)	5% (21)	5% (43)
Emergence Fine	5% (66)	6% (26)	5% (40)
Emergence Gradual Single Step	4% (57)	4% (18)	4% (33)
Maintenance Hyperdynamic	4% (52)	5% (19)	4% (33)
Emergence Hyperdynamic	3% (41)	4% (17)	3% (24)
Emergence Large Single Step	3% (32)	2% (9)	3% (23)
Induction Gap	3% (36)	3% (14)	3% (22)
Emergence Gap	3% (32)	1% (6)	3% (26)
Emergence Gradual Steps	2% (26)	2% (10)	2% (16)
Induction Hypodynamic	2% (30)	2% (8)	3% (22)
Emergence Hypodynamic	2% (19)	1% (6)	2% (13)
Induction Hyperdynamic	2% (24)	1% (6)	2% (15)
Induction Normodynamic	2% (29)	3% (12)	2% (17)
Maintenance Large Steps	1% (9)	1% (3)	1% (6)
Maintenance Normodynamic	1% (9)	1% (5)	0% (4)
Emergence Normodynamic	1% (18)	2% (7)	1% (11)
Induction Coarse	1% (13)	0% (2)	1% (11)
Maintenance Coarse	1% (10)	1% (4)	1% (6)
Emergence Coarse	1% (9)	1% (4)	1% (5)
Induction Large Steps	0% (4)	0% (1)	0% (3)
Emergence Large Steps	0% (2)	0% (1)	0% (1)
Maintenance Gap	0% (5)	0% (0)	1% (5)

Aim Three: Compare Patterns for Associations with Patients UIA

Patterns discovered in Aim 2 were either categorical or continuous data and were analyzed with odds ratios or one-way analysis of variance (ANOVA) respectively. One hundred eighty-five patterns were compared for association with UIA and a p-value of $\leq .05$ was used to determine if a data pattern was statistically significant (Appendix C Statistical Analysis of Data Patterns).

Odds ratios (ORs) are the ratio of the probability of a binary event to occur in one group compared to the probability of the same binary event to occur in another group. An ORs of 1 would indicate that both groups have the same likelihood of having an event. In this study OR were used to compare the probability of a data pattern in patients with UIA to the probability of that same data pattern in patients without UIA. Odds ratios were calculated for 181 categorical data patterns discovered in Aim 2 and eight of the patterns were associated with UIA (Table 4.8). Patients with UIA were at least two times as likely to have local anesthetic gradual single step during induction, neuromuscular blocking large single step during induction, and central nervous system gradual single step during maintenance patterns compared to patients without UIA. Patients with UIA were also 2.5 times less likely to have local anesthetic large single step during induction, anti-infective line, to be hypodynamic during maintenance, or have gap in hemodynamic data during emergence patterns compared to patients without UIA.

Table. 4.8. *Statistical Analysis of Categorical Patterns*

Pattern	UIA % (count) *n = 34*	Match % (count) *n =68*	Coefficient β	SE	p-value	Odds Ratio	95% Confidence Interval
Local anesthetic Induction Gradual single step	29% (10)	7% (5)	1.9	0.6	0.002	6.7	2.0-22.5
Neuromuscular blocking drug Induction Large single step	21% (7)	6% (4)	1.6	0.7	0.021	4.7	1.3-17.6
Central nervous system drug Maintenance Gradual single step	35% (12)	16% (11)	1.0	0.5	0.033	2.8	1.1-7.3
Local anesthetic Induction Large single step	38% (13)	60% (41)	-0.9	0.4	0.049	0.4	0.1-0.9
Had Anti-infective line during Induction, Maintenance, or Emergence	41% (14)	22% (15)	-0.9	0.5	0.047	0.4	0.2-0.9
Gap in hemodynamic data during Emergence	18% (6)	32% (26)	-1.1	05	0.039	0.4	0.1-0.9
Hypodynamic during Maintenance	50% (17)	72% (49)	-0.9	0.4	0.030	0.4	0.2-0.9

One-way analysis of variance (ANOVA) is used to assess the relationship between a single categorical variable that has at least three values and a continuous numeric outcome. In this study, ANOVA was selected to compare patterns for association with UIA since there were two groups of matched patients. The number of flat, gradual steps, large steps, and therapeutic classes were the patterns assessed with ANOVA (Table 4.6). None of the aforementioned continuous numeric patterns were associated with UIA since all patterns had a p-value > .05.

Table. 4.9. *Statistical Analysis of Continuous Numeric Patterns*

Pattern	UIA Mean (SD)	Match Mean (SD)	Mean Square	F Statistic	p-value
Number of Flats	9.1 (2.9)	10.2 (2.9)	27.574	3.707	.058
Number of Gradual Steps	8.2 (2.0)	7.9(2.2)	0.176	0.038	.846
Number of Large Steps	2.0 (1.1)	2.0 (1.1)	0.044	0.034	.855
Number of Therapeutic Classes	6.2 (1.3)	6.5 (1.3)	1.961	1.296	.259

Conclusion

In this chapter, the data set was described and the results were presented by aim. The interrater agreement for the prototype line graphs and an image of the second prototype line graph were provided to justify the design of the line graphs for the entire data set. The line graphs for the entire data set, labels, and operational definitions of the patterns of intraoperative hemodynamic data management were provided along with descriptive statistics of the data patterns. Finally, odds ratios and one-way analysis of variance statistical tests were used compare patterns for association with UIA. The descriptive characteristics of patients with and without UIA had a large percentage of missing data since more than 40% of each characteristic had missing data. Data available for analysis would describe patients with UIA as middle-aged, Black or African American, and non-Hispanic. Patients with UIA also had moderate to severe systemic disease that limited their activities of daily living, were overweight, and were former or current smokers. There were seven distinct patterns associated with UIA and pattern of large bolus of neuromuscular blocking drug during induction, gradual bolus of central nervous system drug during maintenance, and less likely for hypodynamic data in maintenance anesthesia may suggest that patients with UIA are managed differently during surgery with anesthesia. Intraoperative hemodynamic data patterns suggested the dose and timing of medication administration may influence hemodynamic data warrants additional research. Significant intraoperative hemodynamic data patterns associated with UIA have implications for data science, education, and future research.

CHAPTER 5

DISCUSSION

Introduction

The purpose of this study was to discover time-dependent intraoperative hemodynamic management data patterns associated with patient unanticipated intensive care unit admission (UIA). This data visualization student had three aims:

Aim 1: Evaluation the salience of a prototype visualization for the intraoperative data set,

Aim 2: Discover, label, and define patterns in intraoperative hemodynamic management data for each patient with and without UIA,

Aim 3: Compare patterns identified in Aim 2 for association with patient UIA.

Data visualization with line graphs was used to localize and discriminate data patterns from a multivariate data set that may not be apparent in prior research that relied upon statistical analysis alone (Ali & Peebles, 2013; Javed, McDonnel, & Elmqvist, 2010; Haller et al., 2005; Wanderer et al., 2013). Patterns of intraoperative hemodynamic management are essential knowledge about intraoperative events associated with patient UIA and imperative to healthcare research since patient UIA has remained an indicator of quality patient care (AANA, 2006; Agency for Healthcare Research and Quality, 2012; American Society of Anesthesiology Committee on Surgical Anesthesia, 2011; Centers for Medicare and Medicaid Services, 2015).

Based upon an extensive critical review of the literature, the strongest variables identified in patients with UIA were age greater than or equal to 64 years old, American Society of Anesthesiology (ASA) classification greater than or equal to three, comorbidity of anemia, cerebral vascular disease, coronary artery disease, congestive heart failure, hypertension, myocardial infarction, and obstructive sleep apnea, intraoperative vasopressor administration, and central nervous system, cardiac, or digestive procedure. The gap in the literature was to incorporate inductive research methods to explore patterns in how patients changed over time in the operating room. This study used data visualization with line graphs to explore intensive time-dependent intraoperative hemodynamic data and medication administrations to identify the sequence of events, rate of change, and timing of patterns associated with patient UIA. Data obtained from the University of Minnesota, Academic Health Center, Clinical Data Repository (AHC-CDR) compared 34 patients with UIA to 68 patients without UIA that were matched on age, American Society of Anesthesiology classification, type of procedure, and type of anesthesia.

A conceptual framework was developed to guide variables selection since no conceptual frameworks existed in the literature. The conceptual framework of intraoperative hemodynamic management was developed to propose that the cyclic process of medication administration and hemodynamic data could change the strength or direction of patient characteristics to influence patient UIA. Demographic characteristics as well as intraoperative hemodynamic and medication administration data were extracted from the AHC-CDR. Data were transformed into a cumulative dose of intraoperative medication administration by therapeutic class and a hemodynamic trend line. Patient data were plotted on line graphs and visualized to identify salient patterns in intraoperative hemodynamic data management. Patterns were then analyzed with odds ratios and one-way analysis of variance to identify patterns associated with UIA. Seven patterns were statistically significant in patient UIA ($p < .05$). Local anesthetic gradual single step during induction, neuromuscular blocker large single step during induction, and central nervous system gradual single step during maintenance were all at least 2.8 times as likely to be associated with UIA. Local anesthetic large single step, ant-infective therapy, gap in hemodynamic data during emergence, and hypodynamic during maintenance were all 2.5 times less likely to be associated with UIA.

In the following sections the sample demographics and results from this study are discussed in light of findings from prior research. Both strengths and limitations of the study design are also described. The findings are linked to the conceptual framework and theoretical background that grounded this study. Finally, implications for clinical practice, policy, and future research will be discussed.

Sample Demographics

Data from adult patients that had inpatient, elective surgery between January 1, 2012 and June 30, 2015 were included in this study. Overall, 29,080 patients meet the inclusion criteria and the incidence of adult, inpatient, elective surgical patients with UIA was 0.4%. The incidence of patient UIA in this study is similar to 0.4-6% incidence found in the literature (Cullen et al., 1992; Haller et al., 2005; Wanderer et al., 2013). Only 34 of these patients had arterial blood pressure measurements and were included in this study. The majority of patients with UIA were between 40-64 years old, had American Society of Anesthesiology classification 3 and above, and had a cardiovascular, digestive, or musculoskeletal surgical procedure with general anesthesia. On average, patients with UIA were also 211 pounds (SD 66.0), height of 70 inches (SD

4.8), and had a body mass index of 27 kilograms per meters squared (SD 7.); however, 21% of patients with UIA had missing data. There also was considerable missing data for race (65%), ethnicity (44%), and tobacco use (65%). Among demographic characteristics age, ASA classification, and type of procedure were similar to findings in previous research (Brunelli et al., 2006; Haller et al., 2005; Wanderer et al., 2013). None of the studies described the type of anesthesia. Therefore, it is unknown if the sample of patients with UIA in this study differed from patients with UIA in prior research.

Patterns Compared to the Literature

Analysis of patterns discovered with data visualization using line graphs revealed that seven patterns were associated with patient UIA; however, the vast majority of patterns were not. It was rare to find significant patterns using intraoperative anesthesia data in patients with UIA. There were patterns representing therapeutic medication classes. There were also patterns representing hemodynamics, which are fluctuations in heart rate and blood pressure measurements. Several of the patterns associated with UIA were supported in the literature while other patterns discovered with data visualization did not align with the literature. The pattern of neuromuscular blocking drug induction large single step, was supported in the literature. Pattern of anti-infective medication administration, central nervous system maintenance gradual single step, a single gradual local anesthetic dose, a large single step during induction, hypodynamic data during maintenance, and gap in hemodynamic data during emergence were not substantiated in the literature. In the next sections, patterns will be compared to the literature, an alternative explanation will be stated, and suggestions will be proposed for further evaluation.

Significant Patterns Substantiated in the Literature

There was only one pattern identified in this study that was supported in the literature. Patients with UIA were 4.7 times as likely to have a large single bolus of a neuromuscular blocking drug during the induction of anesthesia. The pattern of neuromuscular blocking drug administration is substantiated in the literature. Prior research described patients with UIA that received neuromuscular blocking drugs were 1.36 times as likely to have a postoperative desaturation event and 1.4 times as likely to be reintubated (Grosse-Sundrup et al., 2012). However, researchers did not describe the dose or timing of neuromuscular blocking drug administration in patients with UIA. Data visualization with line graphs was able to generate new, more in-depth insight into the association between neuromuscular blocking drug administration and a patient UIA. The pattern of neuromuscular blocking drug during induction of anesthesia should be evaluated in future research with postoperative pulse oximetry, respiratory rate, oxygen delivery device, and depth of neuromuscular blockade (train-of-four) data. Additional data types would generate new insights into clinical decision-making surrounding neuromuscular blocking drug administration in patient UIA.

Significant Patterns Unsubstantiated in the Literature

The following six patterns were statistically significant in this study but not supported in prior research about a patient UIA. Patients with an anti-infective line, a large single step of local anesthetic during induction, hypodynamic data during maintenance, and gap hemodynamic data during emergence were less likely to have an UIA. Patients with a gradual single step of local anesthetic during induction, central nervous medication during maintenance were more likely to have an UIA.

Patients with a pattern of an anti-infective line and large single step of local anesthetic medication administered during induction were associated with a decreased likelihood of an UIA. Foremost, patients with an UIA were 2.5 times less likely to have a pattern of anti-infective line. Previously, researchers had not described anti-infective (antibiotic) medication administration to be associated with or predictive of a patient UIA (Brunelli et al., 2008; Chi et al., 2011; Haller et al., 2005; Harris et al., 2001; Kamath et al., 2012; Wanderer et al., 2013). An alternative explanation for a pattern of less anti-infective lines associated with patient UIA is infection. Some researchers reported patients that received antibiotics were less likely to develop a postoperative surgical site infection (Antimicrobials, 2006; Tantigate et al., 2017; Chandranath et al., 2016). The pattern of anti-infective lines should be investigated with additional data types such as laboratory data and intensive care unit admission diagnoses to generate additional insight into the implication of the pattern on patient outcome.

A pattern of local anesthetic administration was also less likely to be associated with a patient UIA. Patients with an UIA were 2.5 times *less likely* to have a large single bolus and 6.7 times *more likely* to have a gradual single bolus of local anesthetic medication administered during induction of anesthesia. Local anesthetic administration was not reported in prior research associated with an UIA (Brunelli et al., 2008; Chi et al., 2011; Haller et al., 2005; Harris et al., 2001; Kamath et al., 2012; Wanderer et al., 2013). An alternative explanation for both local anesthetic patterns would be the association between increased pain and under dosing local anesthetics (Chinachoti & Makarasara, 2012; Local anesthetics, 2012; Yang, Abrahams, Hurn, Grafe, & Kirsch, 2011). Patterns of local anesthetic administration during induction of anesthesia cannot be further evaluated with a pain scale data since patients are unconscious during anesthesia and hemodynamic data used in this study did not support the alternative explanation. Further data types such as clinician assessment of patient pain would need to be added to documentation systems to evaluate these patterns.

Additionally, the pattern of central nervous system (CNS) medication administration was not supported in the literature about a patient UIA. A moderate dose of CNS medication during the middle of surgery was 2.8 times as likely to be associated with UIA. An alternative explanation for a pattern of CNS medication associated with a patient UIA is a light plane of anesthesia in the presence of increased surgical stimulation. Related research described providing intravenous sedation administered throughout general anesthesia reduced postoperative pain during intense surgical procedures (Fan et al., 2017; Nielsen et al., 2017). The pattern of a CNS medication in the middle of surgery should be evaluated further with intraoperative surgical data such as surgical incision, surgical closure, operative notes, and planned and performed surgical procedure codes.

Two of the significant patterns in this study were related to the hemodynamic trend line. Patients with UIA were less likely to be associated with hypodynamic data during the middle of surgery and less likely to have a gap in hemodynamic data at the end of surgery. Foremost, patients with UIA were 2.5 times less likely to have pattern of hypodynamic data during maintenance anesthesia. This is counter intuitive and inconsistent with previous research. Hemodynamic data were classified as hypodynamic in this study if one concurrent heart rate or blood pressure value was more than 20% below baseline. Prior research suggested that low blood pressure and high heart rates were statistically significant in patients with UIA (Rose et al., 1996; Wanderer et al., 2013). Researchers have also reported that intraoperative blood pressure measurements more than 30% below baseline were associated with increased risk of organ damage (Bijker et al., 2012). An alternative explanation for pattern of hypodynamic data during maintenance anesthesia would be patients benefit from mild hypotension but exaggerated or prolonged hypotension may impair vital organ function. This pattern should be further evaluated with intraoperative data that measured end organ function such as urine output or ST segments.

The last significant pattern that was not supported in the literature is a gap in hemodynamic data. In this study, patients with an UIA were 2.5 times *less likely* to have heart rate and blood pressure data missing for more than 25 minutes at the end of surgery. Prior research on a patient UIA described intraoperative heart rate or blood pressure values were associated with an UIA; however, gaps in hemodynamic data were not described in the literature (Rose et al., 1996; Wanderer et al., 2013). It may be that a gap in hemodynamic data during emergence is that unstable patients are monitored more closely during transitions in patient care. Related research on intraoperative hemodynamic data identified gaps in hemodynamic data longer than 5 minutes were not clinically relevant since values were within 10 mmHg (Epstein & Dexter, 2011). The pattern of gap hemodynamic data associated with patient UIA should be further evaluated with intraoperative data about patient positioning and registration data to determine if the gap in data was associated with transitions in patient care. Root cause analysis for the prolonged gap in data would support interventions to reduce missing data.

Non-significant Patterns Previously Substantiated in the Literature

Researchers in one study reported cardiovascular medication administration was 5.9 times as likely to be associated with patient UIA (Kamath et al., 2012). Patients with an UIA were more likely to receive cardiovascular medications in prior research (Kamath et al., 2012; Wanderer et al., 2013). A pattern of cardiovascular medication administration was not statistically significant ($p > .05$) in this study. This was an unexpected finding, especially since patients with an UIA were associated with a pattern of less hypodynamic data during maintenance anesthesia. It is possible that the lack of a cardiovascular medication pattern would be increased surgical stimuli during the middle of surgery. The lack of pattern should be further evaluated with data that describe the level of surgical stimuli.

Limitations

This study was a retrospective case-control study design that used data visualization with line graphs to identify intraoperative hemodynamic management patterns associated with UIA. There were seven patterns associated with UIA; however, the finding from this study are limited by the retrospective observational study design, measurements used to establish a baseline for the hemodynamic data trend line and the number of statistical tests used to identify patterns associated with patient UIA.

This study may be limited by bias common to all case-control designs since data collection occurred prior to the study. Foremost, the sample may not be representative of the population (Song & Chung, 2011). Additionally, findings from case-control studies may contain bias from differential measurement (Song & Chung, 2011). Ultimately, the sample of patients with UIA was narrowly defined and significant patterns associated with patient UIA may be limited by the frequency of missing data. Therefore, the patterns associated with patient UIA identified in this study may not be generalizable.

This study may also have been limited by using the first three intraoperative heart rate and blood pressure measurements to establish baseline values that were used during data transformation. The heart rate and blood pressure measurements that were taken in the operating room and used to establish a respective baseline value may not have been representative of typical heart rate or blood pressure values for the patient. Intraoperative measurements were used to establish baseline values based upon work that pilot tested the method and the lack of research to justify other methods.

Finally, this study may be limited by the number of odds ratios that were performed to identify patterns associated with UIA. Given the randomness of data and the probability of a 5% chance of finding a statistically significant result when there is not one (Type I error); the statistically significant patterns identified to have association with UIA may be a spurious finding. Any pattern with a p-value close to .05 should be considered to have limited significance due to the large number of statistical tests performed in this study. Future research should include the use of false discovery rates which provide a measure of chance to improve confidence in results (Benjamini et al., 2010; Subramanian et al., 2005; Charchar et al., 2012).

Education, Policy, and Future Research Implications

This study used innovative research methods to discover and test patterns for association with patient UIA. Prior to the study the research hypothesized that patterns of large analgesic, large neuromuscular blocking medication, and gradual central nervous system drug administration, and hypodynamic trend line would be associated with patient UIA. Pattern of neuromuscular blocking medication was statistically significant in patients with UIA; however, six patterns identified using data science and data visualization were new. Data science is an interdisciplinary field that uses diverse methods to extract and analyze structured and/ or unstructured data to generate knowledge (Berger & Berger, 2004; Simpson, 2015). Data visualization methods use concepts from data science to extract and transform data for analysis (Monsen et al., 2015).

In this data visualization study 31 data types were extracted from a large clinical data repository, analyzed to determine which data types could be used in research, transformed to create new variables, and represented with lines and color hues to discover patterns in patient care. Based upon procedures to deal with missing data, implausible values, and redundant data there are implications for nursing education, policy, clinical practice, and future research.

Implications for Nursing Education

The ultimate goal of nurse educators is to educate all levels of nurses to understand and apply diverse research methods to advance patient care (American College of Nursing, 2006). At the baccalaureate level, nurses apply research in their clinical practice; masters prepared nurses implement evidence-based practice guidelines; doctoral in clinical practice doctorate nurses translate evidence into interventions; and nurse researchers advance knowledge and test interventions on patient outcomes. This data visualization study demonstrated the value of data visualization methods to explore large and complex data sets to identify and test new data driven hypotheses. Nurses at all levels of education need knowledge of these cutting-edge research methods.

Data visualization methods include more than 45 different techniques that are used to compare categories, assess part-to-whole relationships, analyze associations, determine change over time, and map geo-spatial differences (Monsen et al., 2015). Scientific rigor is established in each technique as data are transformed, visual variables applied, salient patterns identified with human proprioception, and patterns tested for statistical significance (Monsen et al., 2015; Monsen et al., 2017). Data visualization should be included into each level of nursing curriculum to advance discovering new knowledge about patients, nursing care, and health systems and apply new insights into clinical practice to change patient outcomes.

Implications for Policy and Clinical Practice

Data standards have been developed to standardize language that is used to describe anesthesia practice and determine minimum data that are included in anesthesia documentation (Peterson, White, Westra, & Monsen, 2014). Missing demographic and hemodynamic data does not align with the data standard to document heart rate and blood pressure at a minimum of every 5 minutes during anesthesia care (American Society of Anesthesiology Committee on Standards and Practice Parameters, 2011). Findings from this study should be used by policy makers, hospital administrators, and bedside anesthesia providers to reduce the amount of missing data in anesthesia documentation. Policy makers and hospital administrators should enforce the minimum standard of documentation for demographic and hemodynamic data to improve complete data for patient use and research. Anesthesia providers verify complete documentation prior to closing the patient record and use scanning software with "pop-up" reminders to minimize missing data. Anesthesia data sets that are complete and accurate are essential to serve as an objective account of intraoperative events and identify trends in patient care.

Implications for Future Research

In this study, data visualization with line graphs was used to discover and test patterns in adult, inpatient, intraoperative hemodynamic management. Seven of those patterns were associated with patient UIA ($p < .05$). Procedures used to discover and test patterns associated with UIA identified that assumptions used to operationalize patients with UIA and baseline hemodynamic status were poorly delineated in research. Additionally, frequency of missing data and solid line graphs would pose barriers in larger data visualization studies. Finally, findings from this data visualization study should be expanded to identify and test more complex patterns associated with patient UIA.

Operationalization of UIA and Baseline hemodynamic status. Two concepts that were important in this study were patient UIA and hemodynamic stability. Patient UIA was operationalized as time-stamped admission data to a unit other than the operating room (OR) prior to surgery, admission to the OR, admission to a unit other than an intensive care unit (ICU), and admission to an ICU within 24 hours of surgery. Hemodynamic stability was operationalized with time-stamped heart rate and blood pressure data that was within 20% of baseline. Future research should study the criteria that are used to operationalize these two concepts.

Specifically, future research should study the 24-hour limit to define patient UIA since data granularity can influence operationalization of the measurement. Time-stamped data captures the hour, minute, and second that patients were admitted to a unit. Future research should analyze if there are meaningful differences in patients classified as UIA that were one hour, 12, 24, and 48 hours after surgery. Research questions about the proximity of time used to classify patient UIA could help discriminate patients that experienced intraoperative deterioration. Future research on patient UIA should also include planned admission unit as a variable to improve accurate classification of patient UIA. Planned admission unit data would let researchers know what unit a patient was intended to be admitted to. Data currently available for research only generated insight into where the patient was admitted. This likely resulted in under classification of patients with UIA.

Patterns of intraoperative hemodynamic management were also founded upon the concept of hemodynamic stability which was defined as circulatory responses to internal or external stimuli where blood flow fluctuated within parameters that were measured or evaluated over time (Peterson, Westra, & Monsen, 2015). In the review of the literature patients were classified as hemodynamically stable if their blood pressure and heart rate values were within 20% of baseline (Peterson et al., 2015). Anecdotal conversation with anesthesia providers suggests that measurements recorded to a week before surgery are mentally averaged to establish baseline; other providers use measurements taken immediately before surgery (personal communication, Wisconsin Association of Nurse Anesthetists Spring Meeting; 04/12/2015). Even more precarious is the situation where heart rate or blood pressure measurements are not documented prior to anesthesia care. Future research should systematically evaluate what heart rate and blood pressure measurements are used to establish patient baseline and inform intraoperative clinical decision-making. Research to clearly delineate the parameters for patient baseline is an important topic in future healthcare research since studies have used hemodynamic stability as an outcome variable (Smischney, Beach, Loftus, Dodds, & Koff, 2012; Solanki, Puri, & Mathew, 2010; Summers, Harrison, Thompson, Porter, & Coleman, 2011; Vimlati et al., 2012; Zhou et al., 2013).

Data visualization research. Both missing data and redundant data are common in data visualization research since data are collected from uncontrolled sources (Biswas et al., 2013; Soley, 2013; Tufte, 2001c).). In this study procedures to extract missing data or verify data obscured by the solid lines in the line graphs were implemented since the sample size was small. In this study an original sample of 29,080 patients were reduced to a sample of 34 patients with UIA. Of the 34 patients with UIA, five patients had missing American Society of Anesthesiology (ASA) classification data which was an essential data type to match patients. Researchers obtained unstructured ASA classification data on all five patients by manually reading perioperative clinical notes. The amount of missing data precluded this procedure from being repeated for alcohol use, ethnicity, body mass index, illicit drug use, and race. The solid lines in the line graphs occasionally obscured the line of another therapeutic class of medication. Twelve lines overlapped in the line graphs and all were manually verified with the raw data set since data represented more than once impair precision of relationships (Biswas et al., 2013; Tufte, 2013c). However, in larger studies these procedures would not be feasible to deal with missing or redundant data since each procedure required manual verification.

Data science has alternative approaches that are well suited to handle missing or redundant data in massive data sets. Data scientists are evaluating methods such as multiple imputation, maximum likelihood, and Bayesian simulation to identify best practices for dealing with missing data (Soley, 2013). Methods that retain some randomness in data are advantageous since data visualization experts require large volumes of quality data to generate models that can accurately predict patient outcomes. Furthermore, as the volume, variety, and velocity of data continue to expand the dilemma of redundant data can threaten meaningful results. Transparency is one technique where a percentage of data are suppressed to allow more prominent information to be presented in a narrower field (Elliott et al., 2015). Researchers that use data visualization will need to expand tools and techniques in future research to work with more diverse and large quantities of data to provide estimates that are meaningful for clinical practice. Finally, data visualization with line graphs should be used in future research for other outcomes. The method was effective for identifying hidden patterns in a large, complex data set and added new insight into variables associated with a rare outcome. Data visualization methods can use used to advance knowledge about other rare quality care outcomes such as anaphylaxis, wrong site surgeries, transfusion reactions, and operating room fires.

Complex pattern recognition. Data visualization methods are uniquely positioned to discover patterns in patient care from large, complex data sets since data are transformed into images that allow the speed and accuracy of visual perception and preattentive reasoning to identify salient information (Conway, 2009; Few 2002). Knowledge about patterns in patient care are important to determine what aspects of patient care should be enhanced or avoided. The findings from this study may suggest that large single doses of neuromuscular blocking drugs during the beginning of surgery, large single doses of local anesthetic drugs during the beginning of surgery, or smaller single doses of central nervous system drugs during the middle of surgery may need to be avoided to prevent UIA. The findings from this study may also suggest that heart rate and blood pressure values near 20% below baseline may be protective against UIA. These are simple patterns associated with UIA. Future research on patient UIA should re-evaluate definitions of patterns used in this study and combine variables from theory, clinical expertise, and findings from this study to discover complex patterns associated with patient UIA.

Foremost, the operational definitions used to identify patterns in this study may need to be adjusted in future research. Patterns in this study were defined by phase of anesthesia, ‘large’ versus ‘gradual’ doses of intraoperative medication administration, therapeutic class of medication administration, or the hemodynamic trend line. Patterns were narrowly defined. Future research on patterns associated with patient UIA may benefit from less granular definitions to add new insight into associations between intraoperative hemodynamic data and medication administration.

Future research should also combine variables in more complex ways to identify patterns associated with patient UIA. Data visualization techniques are robust for multivariate multidimensional pattern recognition (Monsen et al., 2015). Data visualization methods are uniquely positioned to identify complex patterns associated with patient UIA since preattentive reasoning and the salience network can interpret more than 250 data points per square inch (Few, 2002; Tufte, 2001c). Data visualization techniques can combine many types of demographic, intraoperative assessment, and intraoperative intervention data to identify more complex patterns associated with patient UIA. Knowledge about complex patterns associated with patient UIA are needed to develop algorithms that can accurately warn providers about intraoperative deterioration and recommend interventions to prevent patient UIA.

Summary

Data visualization using line graphs is an innovative research method to study patterns in intraoperative anesthesia care. Scientific rigor was incorporated into the procedures that were used to extract and analyze a large volume and variety of rapidly changing intraoperative medication and hemodynamic data. Data visualization was a successful method to identify six novel intraoperative hemodynamic management data patterns that were not identified in prior research. These six new patterns will contribute new knowledge about the association between intraoperative medication administration, hemodynamic data, and patient UIA to the existing literature. Additionally, the pattern on neuromuscular blocking drugs generated new insight into the timing of intraoperative medication administration associated with patient UIA. Data visualization using line graphs generated new knowledge that can be used to explore these patterns more explicitly in future research.

Conclusion

A critical review of the literature demonstrated a gap in knowledge about the sequence and timing of medication administration and hemodynamic data in elective surgery adult patients with UIA. Several authors reported that cardiovascular and neuromuscular blocking drugs were more likely to be administered in patients with UIA compared to patients that were not UIA. Other authors reported demographic variables such as age greater than 64 years, ASA classification greater than or equal to 3, and type of surgical procedure were associated with patient UIA (Haller et al., 2005; Wanderer et al., 2013). One of the largest gaps in the literature was to use inductive research methods to discover which intraoperative medications were associated with UIA when all data were included in analysis.

A 1:2 case-control study was designed with data visualization using line graphs and included 34 inpatient adult elective surgery patients with arterial blood pressure measurements that had UIA between January 1, 2012 and June 30, 2015. These patients were matched to 68 patients without UIA on age, ASA classification, type of procedure, and type of anesthesia to create comparable groups. Descriptive statistics on the aforementioned matching criteria were used to determine that the cases and controls were comparable.

Three research aims were addressed in this data visualization study. Foremost, the salience of a prototype line graph was established with interrater agreement of 100%. Next, patterns of intraoperative hemodynamic management were discovered, labeled, and operationally defined using data visualization with line graphs and descriptive statistics. Finally, intraoperative hemodynamic management data patterns were compared for association with UIA using odds ratios and one-way analysis of variance statistical tests. There were 185 intraoperative hemodynamic management data patterns tested for association with UIA and seven patterns were statistically significant ($p < .05$). Six of those patterns were identified to be meaningful. Pattern of large single dose of local anesthetic during induction of anesthesia, large single dose of neuromuscular blocking drug during induction of anesthesia and gradual single dose of central nervous system drug during maintenance anesthesia were new patterns discovered with data visualization that were relevant for anesthesia practice. Pattern of less likely to have anti-infective therapeutic classes of medication and hypodynamic during maintenance anesthesia were also new findings that can be added to the knowledge about patient UIA.

Increased attention to the patterns associated with adult UIA should be more fully developed in future research. Data visualization methods are powerful techniques for future research since more complex patterns can be identified and tested for association with patient UIA. Researchers aimed at reducing the incidence of healthcare associated complications such as patient UIA cannot be satisfied with the simple patterns discovered in this study. Additional data types from diverse data sources offer a rich source of information for data visualization and the potential to generate new, more meaningful patterns associated with UIA. Much more knowledge needs to be added to the literature on patient UIA before interventions can be developed to treat specific patient, clinician, and procedural indicators and reduce the incidence of patient UIA.

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Appendix A. Quality Data Visualization Scale

1. Data transformation(s) represented the physical phenomenon of interest

1	2	3	4	5	6	7	8	9	10
Poorly				Average					Very Well

2. Design fit the data types

1	2	3	4	5	6	7	8	9	10
Poorly				Average					Very Well

3. Shape(s) represented data

1	2	3	4	5	6	7	8	9	10
Poorly				Average					Very Well

4. Color(s) represented data

1	2	3	4	5	6	7	8	9	10
Poorly				Average					Very Well

5. Annotation enhanced human intelligence

1	2	3	4	5	6	7	8	9	10
Poorly				Average					Very Well

6. Human intelligence localized intraoperative hemodynamic data patterns

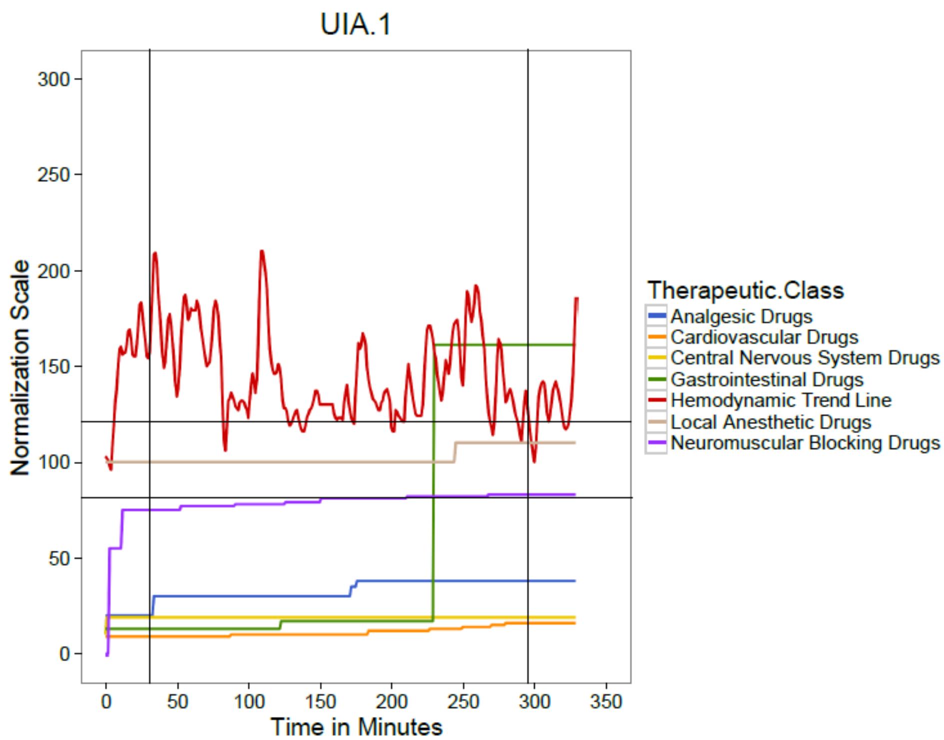
1	2	3	4	5	6	7	8	9	10
Poorly				Average					Very Well

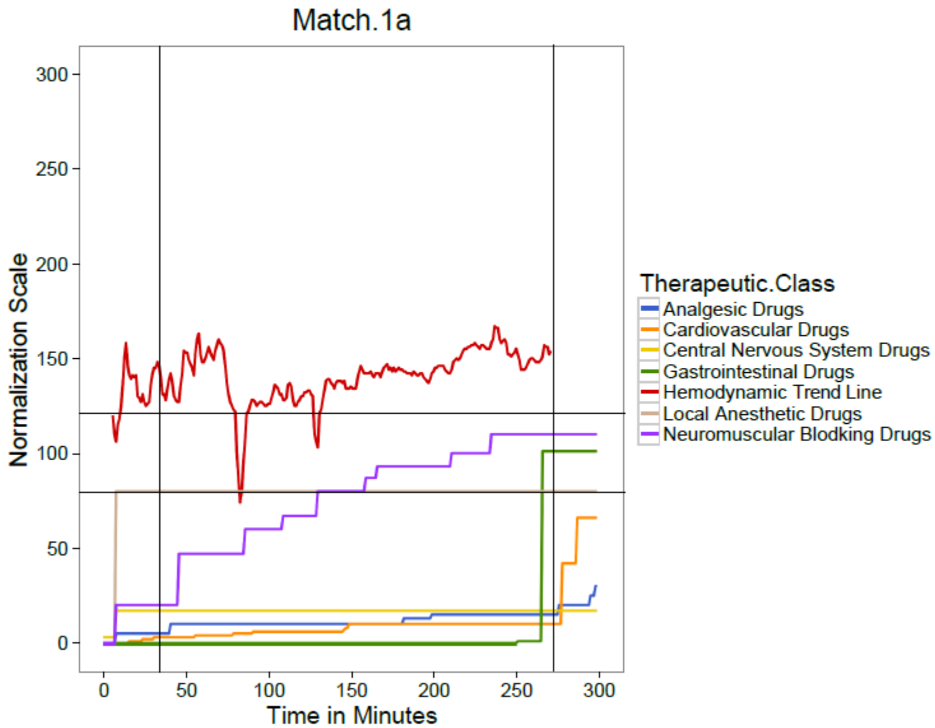
7. Human intelligence discriminated intraoperative hemodynamic data patterns in Unanticipated Intensive Care Unit Admissions

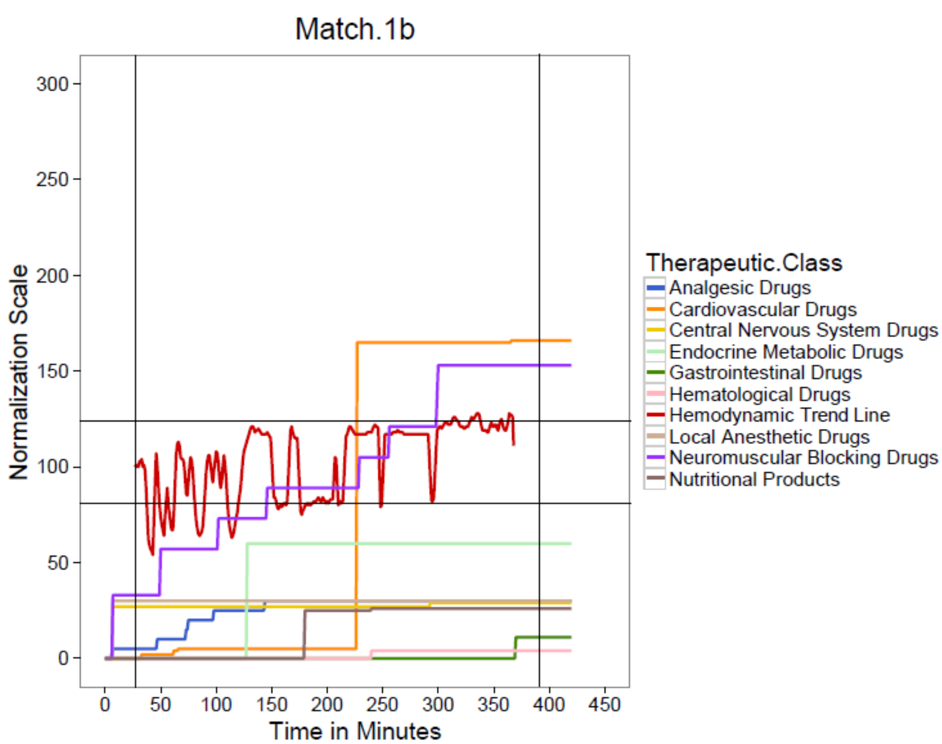
1	2	3	4	5	6	7	8	9	10
Poorly				Average					Very Well

Note. Adapted from "Quality evaluation in medical visualization: Some issues and a taxonomy of methods" by B. S. Santos and J. Dillenseger, 2005, *Proceedings from the International Society for Optics and Photonics, 5744.*

Appendix B. Sample of Data Set Line Graphs




Match.1a
Normalization Scale
300
250
200
150
100
50
0
0 50 100 150 200 250 300
Time in Minutes
Therapeutic.Class
Analgesic Drugs
Cardiovascular Drugs
Central Nervous System Drugs
Gastrointestinal Drugs
Hemodynamic Trend Line
Local Anesthetic Drugs
Neuromuscular Blodking Drugs


Match.1b
Normalization Scale
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250
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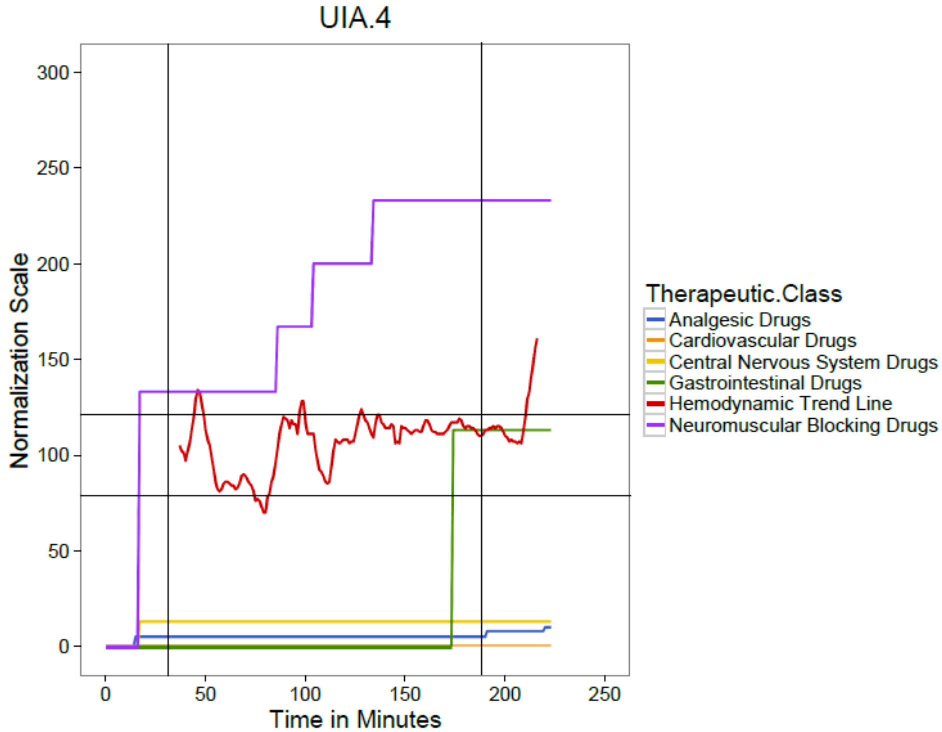
0 50 100 150 200 250 300 350 400 450
Time in Minutes
Therapeutic.Class
Analgesic Drugs
Cardiovascular Drugs
Central Nervous System Drugs
Endocrine Metabolic Drugs
Gastrointestinal Drugs
Hematological Drugs
Hemodynamic Trend Line
Local Anesthetic Drugs
Neuromuscular Blocking Drugs
Nutritional Products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Normalization Scale
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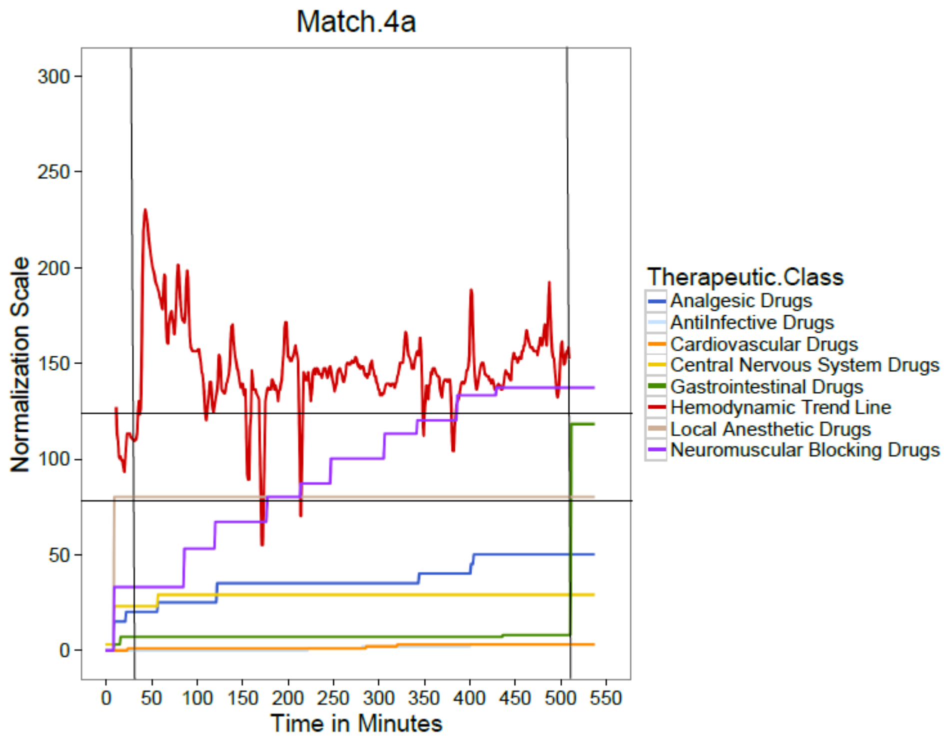
Time in Minutes
Therapeutic.Class
Analgesic Drugs
Cardiovascular Drugs
Central Nervous System Drugs
Gastrointestinal Drugs
Hemodynamic Trend Line
Neuromuscular Blocking Drugs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Normalization Scale
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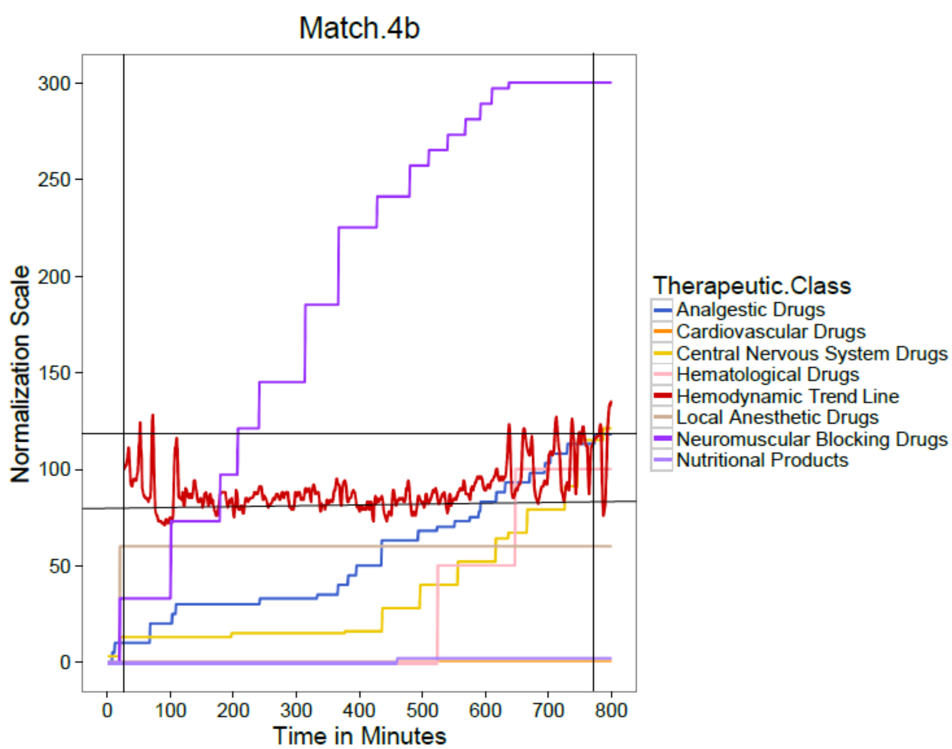
Analgesic Drugs
AntiInfective Drugs
Cardiovascular Drugs
Central Nervous System Drugs
Gastrointestinal Drugs
Hemodynamic Trend Line
Local Anesthetic Drugs
Neuromuscular Blocking Drugs


Match.4b
Normalization Scale
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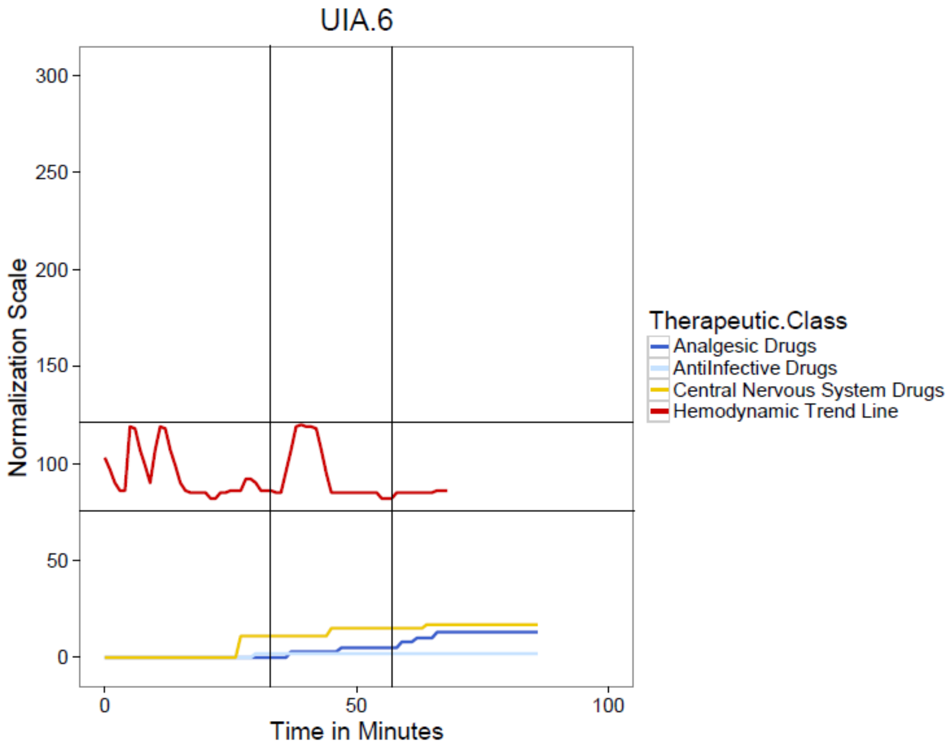
Time in Minutes
Therapeutic.Class
Analgesic Drugs
Cardiovascular Drugs
Central Nervous System Drugs
Hematological Drugs
Hemodynamic Trend Line
Local Anesthetic Drugs
Neuromuscular Blocking Drugs
Nutritional Products



UIA.6
Normalization Scale
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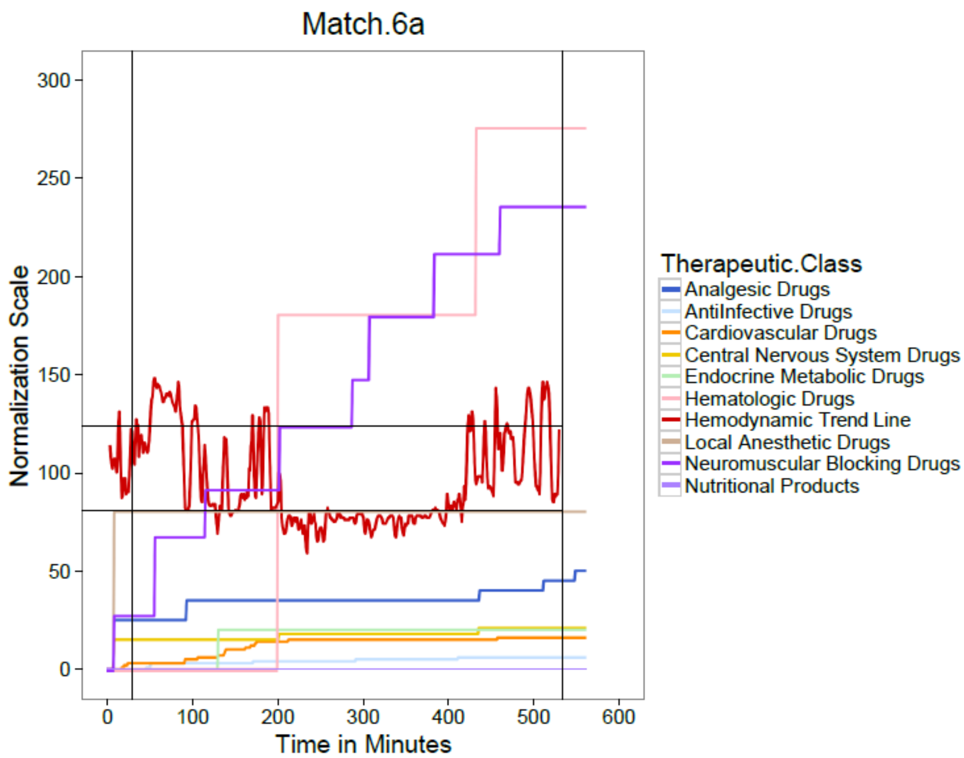
Time in Minutes
Therapeutic.Class
Analgesic Drugs
AntiInfective Drugs
Central Nervous System Drugs
Hemodynamic Trend Line


Match.6a
Normalization Scale
Time in Minutes
Therapeutic.Class
Analgesic Drugs
AntiInfective Drugs
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Endocrine Metabolic Drugs
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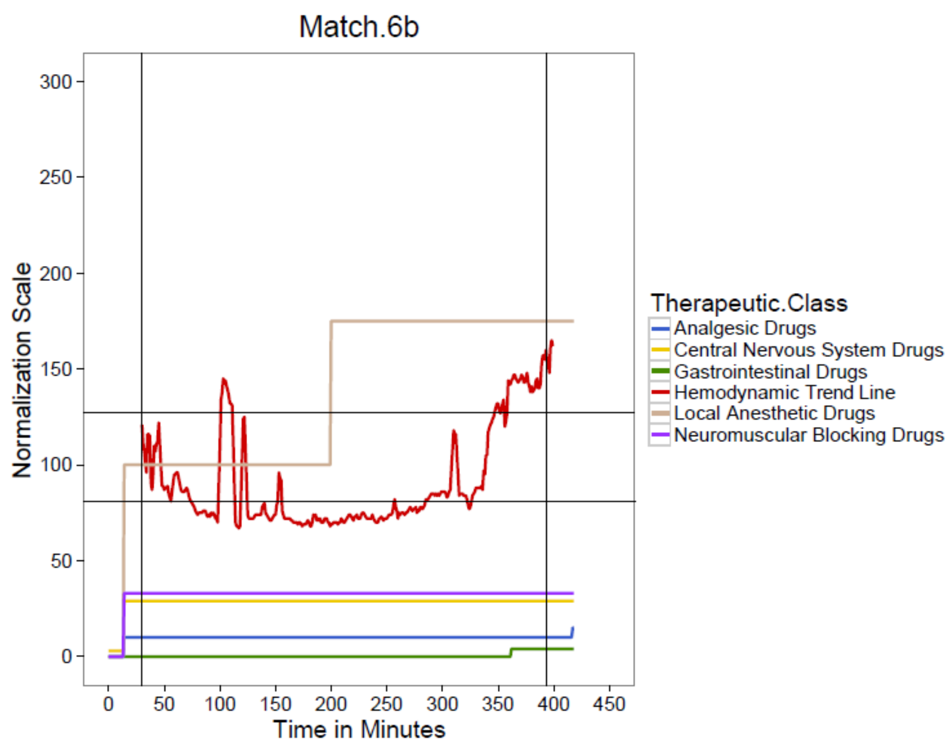
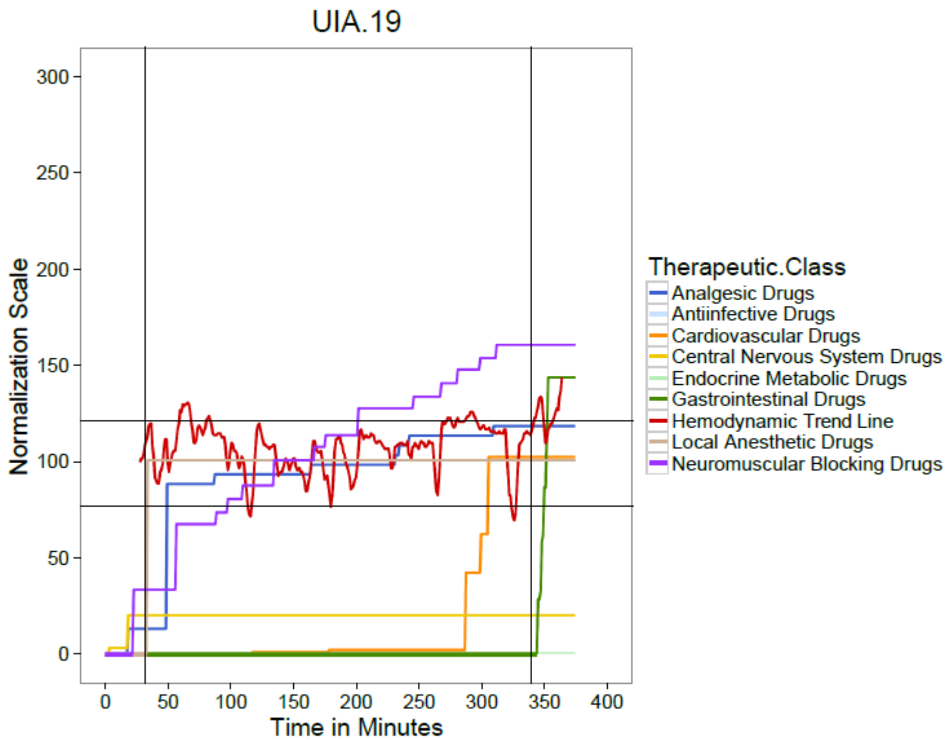
Local Anesthetic Drugs
Neuromuscular Blocking Drugs
Nutritional Products


Match.6b
Normalization Scale
Time in Minutes
Therapeutic.Class
Analgesic Drugs
Central Nervous System Drugs
Gastrointestinal Drugs
Hemodynamic Trend Line
Local Anesthetic Drugs
Neuromuscular Blocking Drugs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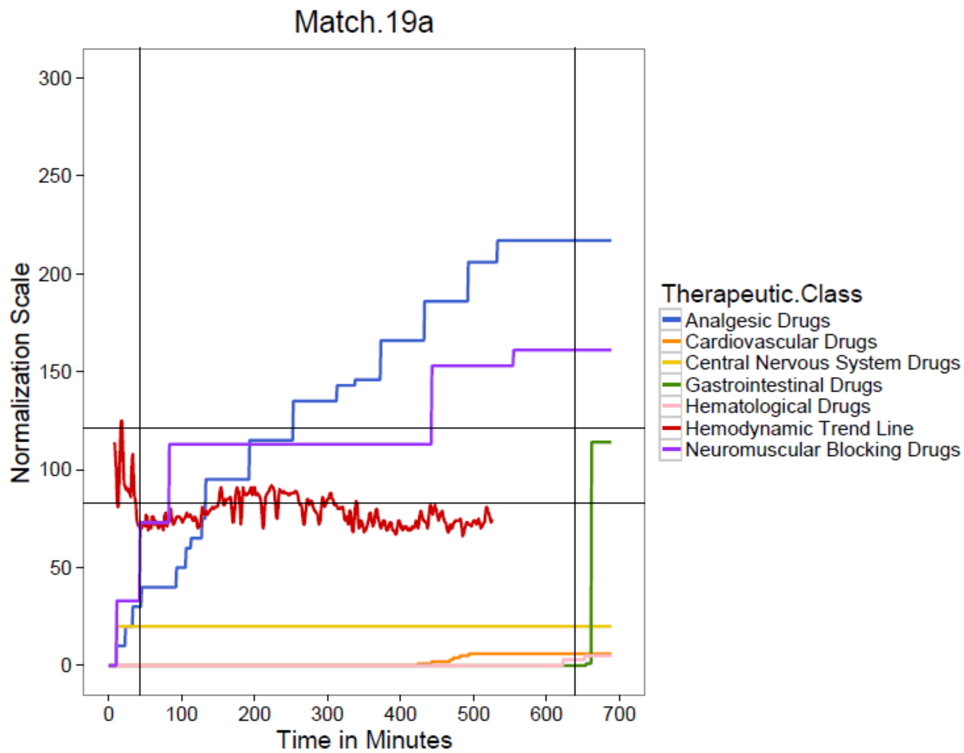
Time in Minutes
Therapeutic.Class
Analgesic Drugs
Antiinfective Drugs
Cardiovascular Drugs
Central Nervous System Drugs
Endocrine Metabolic Drugs
Gastrointestinal Drugs
Hemodynamic Trend Line
Local Anesthetic Drugs
Neuromuscular Blocking Drugs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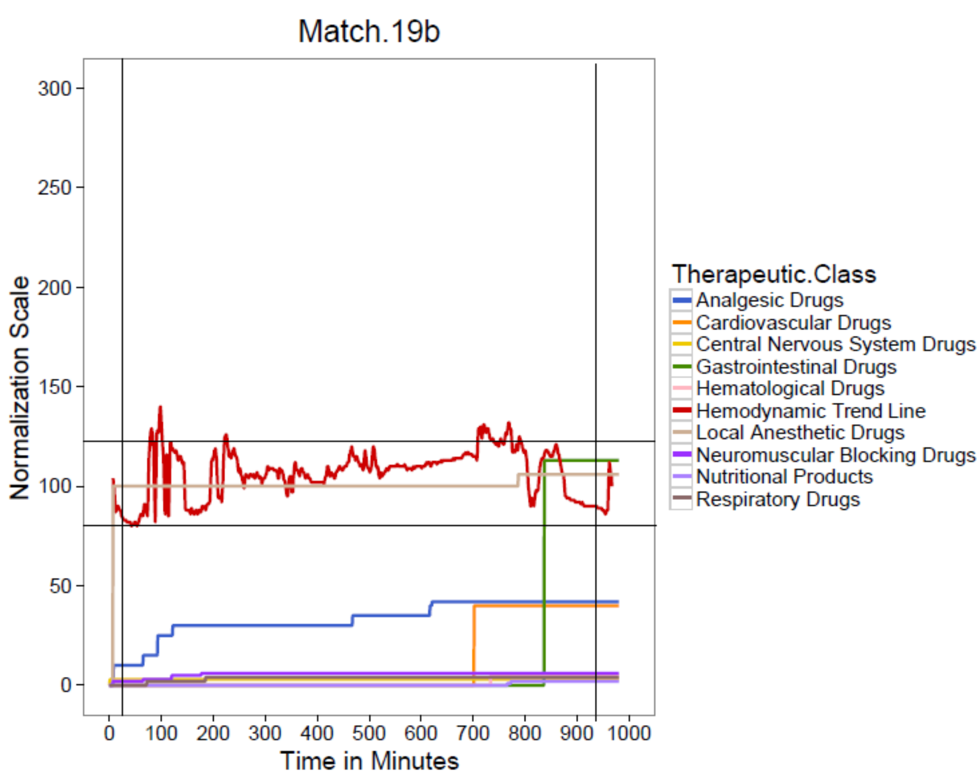
Time in Minutes
Therapeutic.Class
Analgesic Drugs
Cardiovascular Drugs
Central Nervous System Drugs
Gastrointestinal Drugs
Hematological Drugs
Hemodynamic Trend Line
Neuromuscular Blocking Drugs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Time in Minutes
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Cardiovascular Drugs
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Gastrointestinal Drugs
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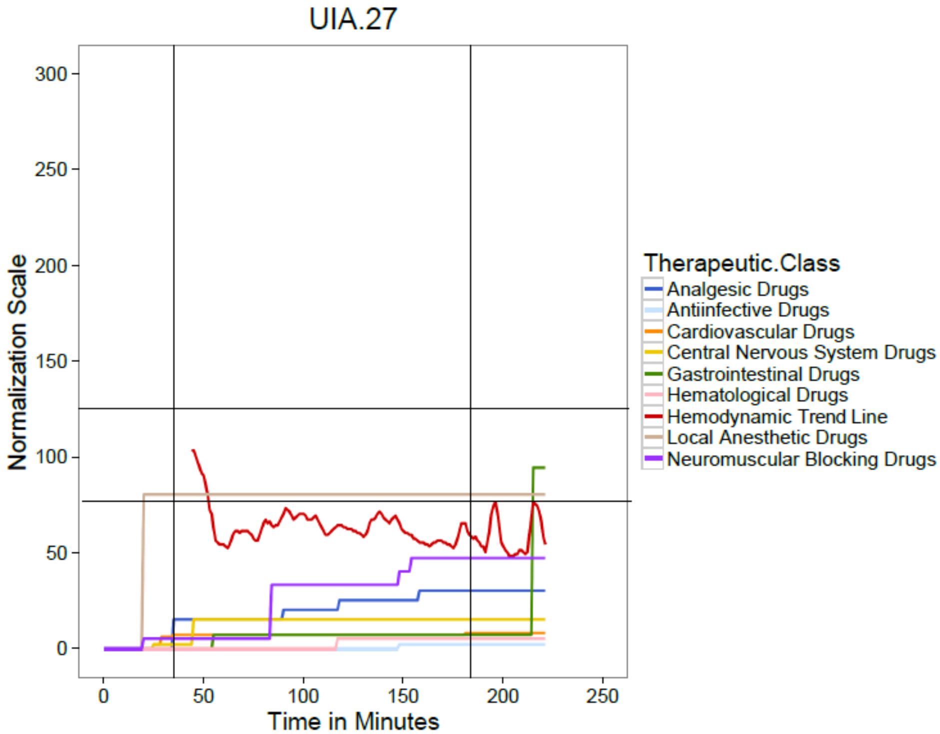
Hemodynamic Trend Line
Local Anesthetic Drugs
Neuromuscular Blocking Drugs
Nutritional Products
Respiratory Drugs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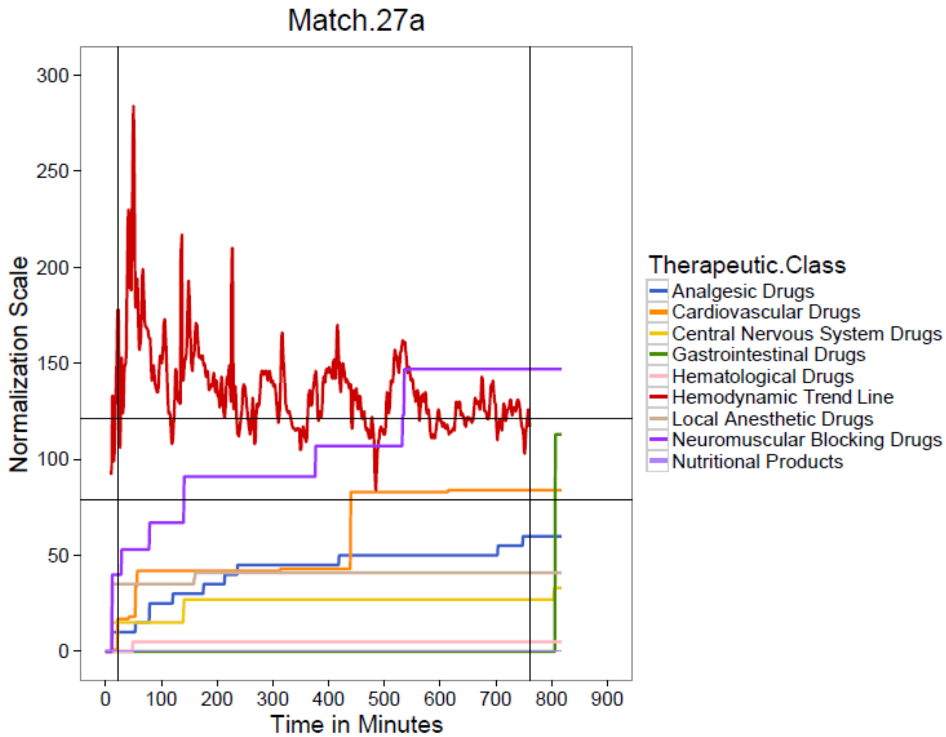
Cardiovascular Drugs
Central Nervous System Drugs
Gastrointestinal Drugs
Hematological Drugs
Hemodynamic Trend Line
Local Anesthetic Drugs
Neuromuscular Blocking Drugs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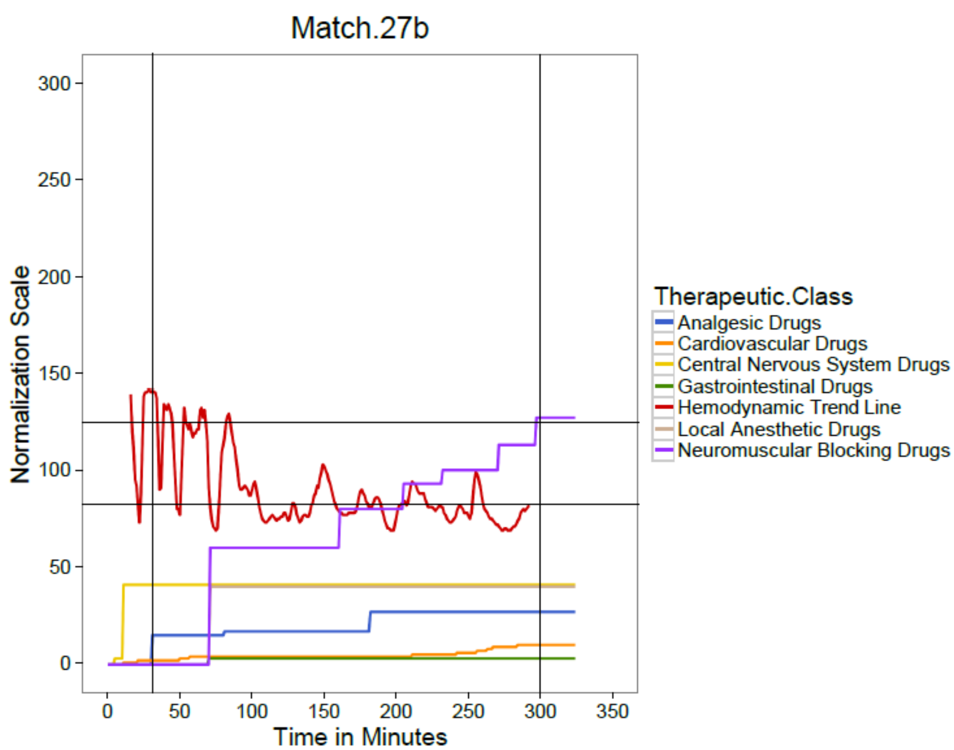
800
900
Time in Minutes
Therapeutic.Class
Analgesic Drugs
Cardiovascular Drugs
Central Nervous System Drugs
Gastrointestinal Drugs
Hematological Drugs
Hemodynamic Trend Line
Local Anesthetic Drugs
Neuromuscular Blocking Drugs
Nutritional Products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300
350
Time in Minutes
Therapeutic.Class
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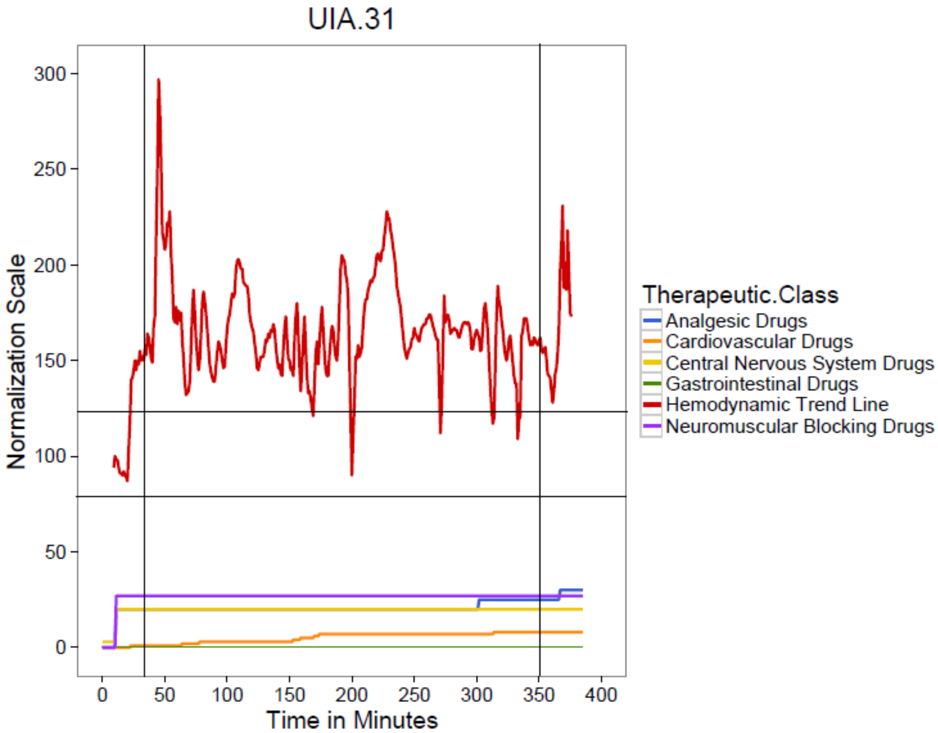
Cardiovascular Drugs
Central Nervous System Drugs
Gastrointestinal Drugs
Hemodynamic Trend Line
Local Anesthetic Drugs
Neuromuscular Blocking Drugs



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300
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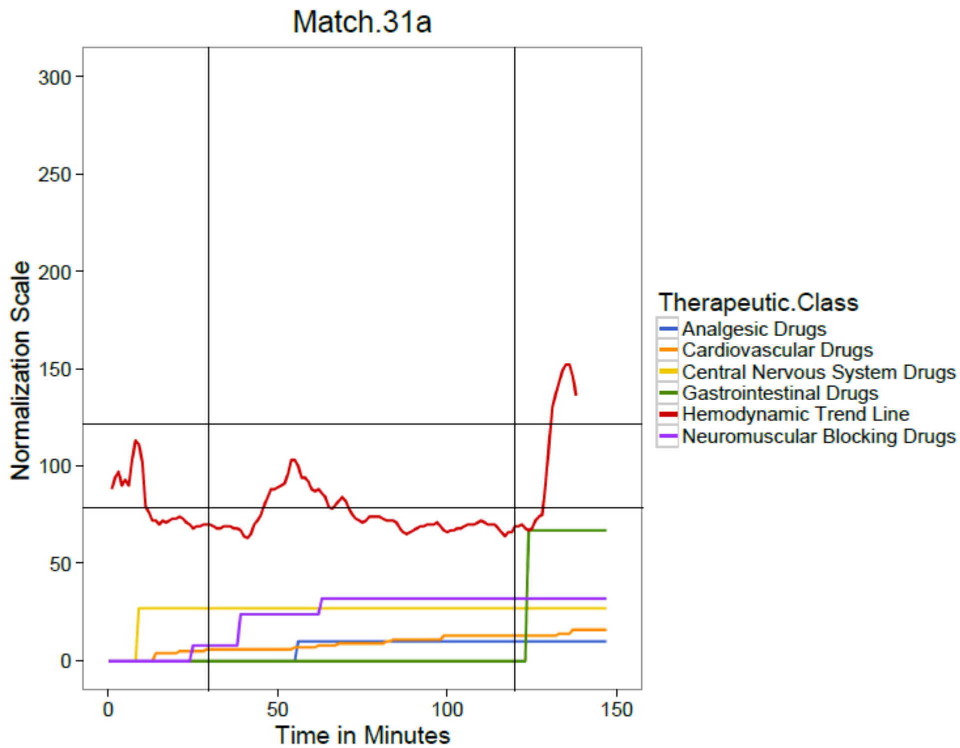
Time in Minutes
Therapeutic.Class
Analgesic Drugs
Cardiovascular Drugs
Central Nervous System Drugs
Gastrointestinal Drugs
Hemodynamic Trend Line
Neuromuscular Blocking Drugs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200
150
100
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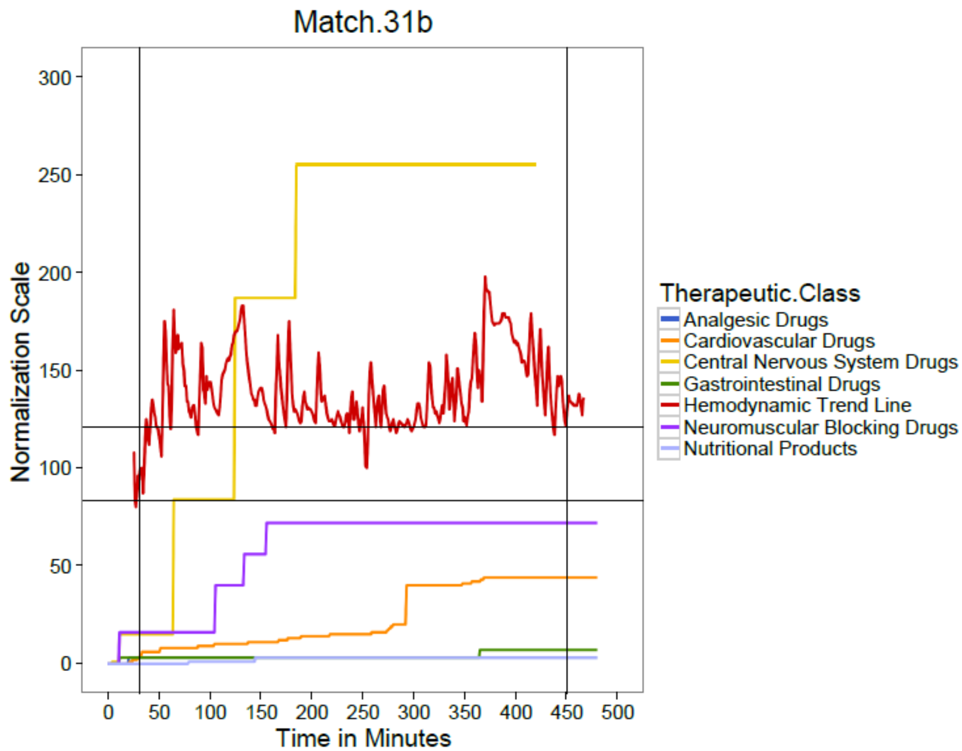
100
150
Time in Minutes
Therapeutic.Class
Analgesic Drugs
Cardiovascular Drugs
Central Nervous System Drugs
Gastrointestinal Drugs
Hemodynamic Trend Line
Neuromuscular Blocking Drugs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Normalization Scale
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250
200
150
100
50
0
0
50
100
150
200
250
300
350
400
450
500
Time in Minutes
Therapeutic.Class
Analgesic Drugs
Cardiovascular Drugs
Central Nervous System Drugs
Gastrointestinal Drugs
Hemodynamic Trend Line
Neuromuscular Blocking Drugs
Nutritional Products

Appendix C Statistical Analysis of Data Patterns

Table 1. Had Line Pattern Odds Ratios

Therapeutic Class	**UIA** % (count) *n = 34*	**Match** % (count) *n = 68*	**Coefficient β**	**SE**	**p-value**	**Odds Ratio**	**95% Confidence Interval**
Had Anti-infective line	41% (14)	22% (15)	-0.9	0.5	.047	0.4	0.2-0.9
Had Neuromuscular Blocking line	88% (30)	97% (66)	1.5	0.9	.097	4.4	0.8-25.4
Had Respiratory line	3% (1)	10% (7)	1.3	1.1	.222	3.8	0.4-32.1
Had Nutritional line	9% (3)	25% (17)	1.2	0.7	.063	3.4	0.9-12.7
Had Analgesic line	97% (33)	98% (67)	0.7	1.4	.620	2.0	0.1-33.5
Had Hematological line	21% (7)	32% (22)	0.6	0.5	.218	1.8	0.7-4.9
Had Endocrine line	9% (3)	15% (10)	0.6	0.7	.406	1.7	0.5-7.0
Had Local Anesthetic line	74% (25)	81% (55)	0.4	0.5	.719	1.5	0.6-4.0
Had Cardiovascular line	88% (30)	85% (58)	-0.3	0.6	.685	0.7	0.2-2.7
Had Gastrointestinal line	94% (32)	87% (59)	-0.9	0.8	.272	0.4	0.1-2.0

Table 2. Induction Flat Pattern Odds Ratios

Therapeutic Class	**UIA %** (count) *n = 34*	**Match %** (count) *n = 68*	**Coefficient β**	**SE**	**p-value**	**Odds Ratio**	**95% Confidence Interval**
Cardiovascular	50% (17)	51% (35)	-0.2	0.5	0.739	0.9	0.4-2.1
Anti-infective	29% (10)	18% (12)	-0.5	0.9	0.591	0.6	0.1-3.5
Central Nervous System	9% (3)	10% (7)	-0.2	0.7	0.814	0.8	0.2-3.5
Endocrine	6% (2)	12% (8)	-0.7	1.5	0.634	0.5	0.1-8.7
Neuromuscular Blocking	6% (2)	12% (8)	-0.7	0.8	0.424	0.5	0.1-2.6
Gastrointestinal	71% (24)	78% (53)	-1.1	0.6	0.069	0.3	0.1-1.1
Hematological	18% (6)	31% (21)	-1.3	1.5	0.254	0.3	0.1-5.3
Local Anesthetic	3% (1)	10% (7)	-1.3	1.1	0.254	0.3	0.1-2.5
Analgesic	3% (1)	15% (10)	-1.7	1.1	0.107	0.2	0.1-1.5
Nutritional	0% (0)	0% (0)	--	--	--	--	--
Respiratory	3% (1)	7% (5)	--	--	--	--	--

Table 3. Induction Gradual Steps Pattern Odds Ratios

Therapeutic Class	**UIA %** (count) *n = 34*	**Match %** (count) *n = 68*	**Coefficient β**	**SE**	**p-value**	**Odds Ratio**	**95% Confidence Interval**
Gastrointestinal	3% (1)	1% (1)	0.6	1.4	.662	1.9	0.1-30.9
Analgesic	26% (9)	25% (17)	0.1	0.5	.771	1.2	0.4-3.0
Neuromuscular Blocking	9% (3)	9% (6)	0.1	0.7	.887	1.1	0.3-4.8
Cardiovascular	9% (3)	10% (7)	-0.2	0.7	.772	0.8	0.2-3.4
Central Nervous System	26% (9)	32% (22)	-0.8	0.5	.543	0.8	0.3-1.9
Endocrine	0% (0)	0% (0)	--	--	--	--	--
Hematological	0% (0)	0% (0)	--	--	--	--	--
Anti-infective	0% (0)	0% (0)	--	--	--	--	--
Local Anesthetic	3% (1)	0% (0)	--	--	--	--	--
Nutritional	0% (0)	0% (0)	--	--	--	--	--
Respiratory	0% (0)	0% (0)	--	--	--	--	--

Table 4. Induction Gradual Single Step Pattern Odds Ratios

Therapeutic Class	**UIA %** (count) *n = 34*	**Match %** (count) *n =34*	**Coefficient β**	**SE**	**p-value**	**Odds Ratio**	**95% Confidence Interval**
Local Anesthetic	29% (10)	7% (5)	1.9	0.6	.002	6.7	2.0-22.6
Gastrointestinal	18% (6)	6% (4)	1.2	0.7	.093	3.2	0.8-12.2
Analgesic	65% (22)	59% (40)	0.3	1.4	.613	2.1	0.1-34.1
Cardiovascular	3% (8)	22% (15)	0.1	0.5	.935	1.0	0.4-2.7
Central Nervous System	53% (18)	56% (38)	-0.1	0.4	.778	0.9	0.4-2.0
Neuromuscular Blocking	59% (20)	71% (48)	-0.3	0.5	.5	0.8	0.3-1.9
Anti-infective	6% (2)	4% (3)	-0.4	0.5	.685	0.7	0.1-4.7
Endocrine	0% (0)	3% (2)	--	--	--	--	--
Hematological	0% (0)	1% (1)	--	--	--	--	--
Nutritional	0% (0)	0% (0)	--	--	--	--	--
Respiratory	3% (1)	11% (7)	--	--	--	--	--

Table 5. Induction Large Steps Pattern Odds Ratios

Therapeutic Class	**UIA %** (count) *n =34*	**Match %** (count) *n = 68*	**Coefficient β**	**SE**	**p-value**	**Odds Ratio**	**95% Confidence Interval**
Central Nervous System	3% (1)	1% (1)	-0.7	1.4	.620	2.0	0.1-33.5
Analgesic	0% (0)	0% (0)	--	--	--	--	--
Anti-infective	0% (0)	0% (0)	--	--	--	--	--
Cardiovascular	0% (0)	0% (0)	--	--	--	--	--
Endocrine	0% (0)	0% (0)	--	--	--	--	--
Gastrointestinal	0% (0)	0% (0)	--	--	--	--	--
Hematological	0% (0)	0% (0)	--	--	--	--	--
Local Anesthetic	0% (0)	1% (1)	--	--	--	--	--
Neuromuscular Blocking	0% (0)	1% (1)	--	--	--	--	--
Nutritional	0% (0)	0% (0)	--	--	--	--	--
Respiratory	0% (0)	0% (0)	--	--	--	--	--

Table 6. Induction Large Single Step Pattern Odds Ratios

Therapeutic Class	**UIA % (count)** *n =34*	**Match % (count)** *n = 68*	**Coefficient β**	**SE**	**p-value**	**Odds Ratio**	**95% Confidence Interval**
Neuromuscular Blocking	0% (0)	1% (1)	1.6	0.7	.021	4.7	1.3-17.6
Local Anesthetic	0% (0)	1% (1)	-1.0	0.5	.049	0.4	0.1-1.0
Central Nervous System	3% (1)	1% (1)	1.0	0.7	.151	2.8	0.7-11.0
Analgesic	0% (0)	0% (0)	0.7	1.4	.613	2.1	0.1-34.0
Anti-infective	0% (0)	0% (0)	--	--	--	--	--
Cardiovascular	0% (0)	0% (0)	--	--	--	--	--
Endocrine	0% (0)	0% (0)	--	--	--	--	--
Gastrointestinal	0% (0)	0% (0)	--	--	--	--	--
Hematological	0% (0)	0% (0)	--	--	--	--	--
Nutritional	0% (0)	0% (0)	--	--	--	--	--
Respiratory	0% (0)	0% (0)	--	--	--	--	--

Table 7. Maintenance Flat Pattern Odds Ratios

Therapeutic Class	UIA % (count) *n = 34*	Match % (count) *n = 68*	Coefficient β	SE	p-value	Odds Ratio	95% Confidence Interval
Gastrointestinal	32% (11)	21% (14)	0.5	0.5	.280	1.7	0.7-4.3
Analgesic	12% (4)	9% (6)	0.3	0.7	.621	1.4	0.4-5.4
Endocrine	3% (1)	4% (3)	0.2	1.4	.913	1.2	0.1-18.3
Local Anesthetic	62% (21)	66% (45)	0.2	0.6	.812	1.2	0.3-4.2
Anti-infective	12% (4)	10% (7)	0.1	0.7	.858	1.1	0.3-4.9
Central Nervous System	50% (17)	53% (36)	-0.2	0.4	.779	0.9	0.4-2.0
Cardiovascular	12% (4)	13% (9)	-0.2	0.6	.785	0.8	0.2-3.0
Neuromuscular Blocking	9% (3)	16% (11)	-0.6	0.7	.396	0.6	0.1-2.2
Hematological	0% (0)	1% (1)	--	--	--	--	--
Nutritional	0% (0)	25% (17)	--	--	--	--	--
Respiratory	0% (0)	3% (2)	--	--	--	--	--

Table 8. Maintenance Gradual Steps Pattern Odds Ratios

Therapeutic Class	**UIA % (count)** *n = 34*	**Match % (count)** *n = 68*	**Coefficient β**	**SE**	**p-value**	**Odds Ratio**	**95% Confidence Interval**
Endocrine	3% (1)	1% (1)	1.5	1.6	.352	4.5	0.2-106.8
Cardiovascular	71% (24)	56% (38)	0.7	0.5	.163	2.1	0.7-6.0
Gastrointestinal	18% (6)	9% (6)	0.7	0.6	.255	2.0	0.6-6.9
Nutritional	6% (2)	13% (9)	0.6	1.3	.662	1.8	0.1-23.5
Anti-infective	0% (0)	0% (0)	0.5	0.9	.591	1.6	0.3-8.9
Neuromuscular Blocking	62% (21)	69% (47)	-0.1	0.5	.904	0.9	0.4-2.4
Analgesic	74% (25)	82% (56)	-0.5	0.5	.351	0.6	0.2-1.8
Central Nervous System	12% (4)	29% (20)	-1.1	0.6	.056	0.3	0.1-1.0
Hematological	3% (1)	12% (8)	-1.2	1.2	.291	0.3	0.03-2.9
Local Anesthetic	0% (0)	1% (1)	--	--	--	--	--
Respiratory	0% (0)	4% (3)	--	--	--	--	--

Table 9. Maintenance Gradual Single Step Pattern Odds Ratios

Therapeutic Class	**UIA %** (count) *n = 34*	**Match %** (count) *n = 68*	**Coefficient β**	**SE**	**p-value**	**Odds Ratio**	**95% Confidence Interval**
Central Nervous System	9% (3)	15% (10)	1.0	0.5	.033	2.8	1.1-7.3
Hematological	18% (6)	18% (12)	1.6	1.2	.166	5.0	0.5-48.8
Neuromuscular Blocking	18% (6)	10% (7)	0.7	0.6	.219	2.1	0.6-6.9
Analgesic	12% (4)	7% (5)	0.5	0.7	.448	1.7	04-6.8
Endocrine	3% (1)	6% (4)	-0.3	1.4	.835	0.8	0.0-11.3
Local Anesthetic	6% (2)	9% (6)	-0.3	0.9	.689	0.7	0.1-3.8
Gastrointestinal	24% (8)	31% (21)	-0.5	0.5	.303	0.6	0.2-1.6
Cardiovascular	9% (3)	9% (6)	-0.6	07	.370	0.5	0.1-2.1
Anti-infective	6% (2)	9% (6)	-1.4	0.9	.135	0.3	0.0-1.5
Nutritional	0% (0)	4% (3)	--	--	--	--	--
Respiratory	3% (1)	1% (1)	--	--	--	--	--

Table 10. Maintenance Large Steps Pattern Odds Ratios

Therapeutic Class	**UIA %** (count) *n = 34*	**Match %** (count) *n = 68*	**Coefficient β**	**SE**	**p-value**	**Odds Ratio**	**95% Confidence Interval**
Neuromuscular Blocking	3% (1)	1% (1)	0.8	1.4	.573	2.2	0.1-37.1
Gastrointestinal	3% (1)	1% (1)	0.6	1.4	.662	1.9	0.1-30.9
Analgesic	0% (0)	1% (1)	--	--	--	--	--
Anti-infective	0% (0)	0% (0)	--	--	--	--	--
Cardiovascular	3% (1)	0% (0)	--	--	--	--	--
Central Nervous System	0% (0)	3% (2)	--	--	--	--	--
Endocrine	0% (0)	0% (0)	--	--	--	--	--
Hematological	0% (0)	1% (1)	--	--	--	--	--
Local Anesthetic	0% (0)	0% (0)	--	--	--	--	--
Nutritional	0% (0)	0% (0)	--	--	--	--	--
Respiratory	0% (0)	0% (0)	--	--	--	--	--

Table 11. Maintenance Large Single Step Pattern Odds Ratios

Therapeutic Class	**UIA % (count)** *n = 34*	**Match % (count)** *n = 68*	**Coefficient β**	**SE**	**p-value**	**Odds Ratio**	**95% Confidence Interval**
Neuromuscular Blocking	3% (1)	7% (5)	0.8	1.4	.573	2.2	0.1-37.1
Gastrointestinal	38% (13)	37% (25)	0.6	1.4	.662	1.9	0.1-30.9
Analgesic	0% (0)	0% (0)	--	--	--	--	--
Anti-infective	0% (0)	0% (0)	--	--	--	--	--
Cardiovascular	0% (0)	4% (3)	--	--	--	--	--
Central Nervous System	0% (0)	1% (1)	--	--	--	--	--
Endocrine	0% (0)	3% (2)	--	--	--	--	--
Hematological	0% (0)	4% (3)	--	--	--	--	--
Local Anesthetic	6% (2)	7% (5)	--	--	--	--	--
Nutritional	3% (1)	0% (0)	--	--	--	--	--
Respiratory	0% (0)	0% (0)	--	--	--	--	--

Table 11. Emergence Flat Pattern Odds Ratios

Therapeutic Class	**UIA %** (count) *n = 34*	**Match %** (count) *n = 68*	**Coefficient β**	**SE**	**p-value**	**Odds Ratio**	**95% Confidence Interval**
Cardiovascular	68% (23)	57% (39)	0.5	0.5	.360	1.6	0.6-4.4
Central Nervous System	82% (28)	81% (55)	0.1	0.5	.857	1.1	0.4-3.2
Neuromuscular Blocking	82% (28)	97% (66)	-0.1	0.9	.910	0.9	0.2-5.2
Analgesic	68% (23)	76% (52)	-0.4	0.5	.392	0.7	0.3-1.7
Gastrointestinal	53% (18)	62% (42)	-0.6	0.5	.154	0.5	0.2-1.3
Anti-infective	38% (13)	22% (15)	--	--	--	--	--
Endocrine	9% (3)	15% (10)	--	--	--	--	--
Hematological	21% (7)	31% (21)	--	--	--	--	--
Local Anesthetic	74% (25)	81% (55)	--	--	--	--	--
Nutritional	9% (3)	25% (17)	--	--	--	--	--
Respiratory	3% (1)	7% (5)	--	--	--	--	--

Table 12. Emergence Gradual Steps Pattern Odds Ratios

Therapeutic Class	**UIA %** (count) *n = 34*	**Match %** (count) *n = 68*	**Coefficient β**	**SE**	**p-value**	**Odds Ratio**	**95% Confidence Interval**
Analgesic	12% (4)	7% (5)	0.5	0.7	.448	1.7	0.4-6.8
Central Nervous System	6% (2)	4% (3)	0.3	0.9	.747	1.4	0.2-8.5
Cardiovascular	9% (3)	10% (7)	-0.2	0.7	.772	0.8	0.2-3.4
Anti-infective	0% (0)	0% (0)	--	--	--	--	--
Endocrine	0% (0)	0% (0)	--	--	--	--	--
Gastrointestinal	3% (1)	0% (0)	--	--	--	--	--
Hematological	0% (0)	0% (0)	--	--	--	--	--
Local Anesthetic	0% (0)	0% (0)	--	--	--	--	--
Neuromuscular Blocking	0% (0)	1% (1)	--	--	--	--	--
Nutritional	0% (0)	0% (0)	--	--	--	--	--
Respiratory	0% (0)	0% (0)	--	--	--	--	--

Table 13. Emergence Gradual Steps Pattern Odds Ratios

Therapeutic Class	**UIA %** (count) *n = 34*	**Match %** (count) *n = 68*	**Coefficient β**	**SE**	**p-value**	**Odds Ratio**	**95% Confidence Interval**
Central Nervous System	12% (4)	9% (6)	0.3	0.7	.639	1.4	0.4-5.3
Gastrointestinal	9% (3)	6% (4)	0.4	0.8	.659	1.4	0.3-6.8
Analgesic	18% (6)	24% (10)	0.2	0.6	.677	1.3	0.4-3.8
Cardiovascular	12% (4)	9% (6)	0.3	0.7	.676	1.3	0.3-5.1
Neuromuscular Blocking	3% (1)	6% (4)	-0.6	1.1	.5	0.5	0.1-5.0
Anti-infective	0% (0)	0% (0)	--	--	--	--	--
Endocrine	0% (0)	0% (0)	--	--	--	--	--
Hematological	0% (0)	1% (1)	--	--	--	--	--
Local Anesthetic	0% (0)	0% (0)	--	--	--	--	--
Nutritional	0% (0)	0% (0)	--	--	--	--	--
Respiratory	0% (0)	3% (2)	--	--	--	--	--

Table 14. Emergence Large Steps Pattern Odds Ratios

Therapeutic Class	**UIA % (count)** *n = 34*	**Match %** (count) *n = 68*	**Coefficient β**	**SE**	**p-value**	**Odds Ratio**	**95% Confidence Interval**
Gastrointestinal	3% (1)	1% (1)	-0.6	1.4	.662	1.9	0.1-31.0
Analgesic	0% (0)	0% (0)	--	--	--	--	--
Anti-infective	0% (0)	0% (0)	--	--	--	--	--
Cardiovascular	0% (0)	0% (0)	--	--	--	--	--
Central Nervous System	0% (0)	0% (0)	--	--	--	--	--
Endocrine	0% (0)	0% (0)	--	--	--	--	--
Hematological	0% (0)	0% (0)	--	--	--	--	--
Local Anesthetic	0% (0)	0% (0)	--	--	--	--	--
Neuromuscular Blocking	0% (0)	0% (0)	--	--	--	--	--
Nutritional	0% (0)	0% (0)	--	--	--	--	--
Respiratory	0% (0)	0% (0)	--	--	--	--	--

Table 15. Emergence Large Single Step Pattern Odds Ratios

Therapeutic Class	**UIA %** (count) *n = 34*	**Match %** (count) *n = 68*	**Coefficient β**	**SE**	**p-value**	**Odds Ratio**	**95% Confidence Interval**
Gastrointestinal	26% (9)	19% (13)	0.3	0.5	.518	1.4	0.5-3.7
Analgesic	0% (0)	0% (0)	--	--	--	--	--
Anti-infective	0% (0)	0% (0)	--	--	--	--	--
Cardiovascular	0% (0)	7% (5)	--	--	--	--	--
Central Nervous System	0% (0)	6% (4)	--	--	--	--	--
Endocrine	0% (0)	0% (0)	--	--	--	--	--
Hematological	0% (0)	0% (0)	--	--	--	--	--
Local Anesthetic	3% (1)	0% (0)	--	--	--	--	--
Neuromuscular Blocking	0% (0)	0% (0)	--	--	--	--	--
Nutritional	0% (0)	0% (0)	--	--	--	--	--
Respiratory	0% (0)	0% (0)	--	--	--	--	--

Table 16. Hemodynamic Trend Line Pattern Odds Ratios

Therapeutic Class	**UIA %** (count) *n = 34*	**Match %** (count) *n = 68*	**Coefficient β**	**SE**	**p-value**	**Odds Ratio**	**95% Confidence Interval**
Maintenance Hypodynamic	50% (17)	72% (49)	-0.9	0.4	.030	0.4	0.2-0.9
Emergence Gap	18% (6)	38% (26)	-1.0	0.5	.039	0.3	0.1-0.9
Maintenance Normodynamic	15% (5)	6% (4)	1.0	0.7	.151	2.8	0.7-11.0
Emergence Fine	76% (26)	59% (40)	-0.8	0.5	.083	2.3	0.9-5.8
Emergence Hyperdynamic	50% (17)	35% (24)	0.6	0.4	.155	1.8	0.8-4.2
Emergence Coarse	12% (4)	7% (5)	0.5	0.7	.463	1.7	0.4-6.7
Induction Normodynamic	35% (12)	25% (17)	0.5	0.5	.279	1.6	0.7-4.0
Induction Gap	41% (14)	32% (22)	0.4	0.4	.380	1.5	0.6-3.4
Maintenance Coarse	12% (4)	9% (6)	0.3	0.7	.639	1.4	0.4-5.3
Emergence Normodynamic	21% (7)	16% (11)	0.3	0.5	.582	1.3	0.5-3.8
Maintenance Hyperdynamic	56% (19)	49% (33)	0.3	0.4	.484	1.3	0.6-3.1
Emergence Hypodynamic	18% (6)	19% (13)	-0.1	0.5	.9	0.9	0.3-2.6
Induction Fine	62% (21)	63% (43)	-0.1	0.4	.885	0.9	0.4-2.2
Induction Hyperdynamic	18% (6)	22% (15)	-0.2	0.5	.653	0.8	0.3-2.3
Maintenance Fine	6% (29)	90% (61)	-0.4	0.6	.516	0.7	0.2-2.3
Induction Hypodynamic	24% (8)	32% (22)	-0.2	0.5	.358	0.6	0.3-1.6
Induction Coarse	6% (2)	16% (11)	-1.1	0.8	.159	0.3	0.1-1.6
Maintenance Gap	0% (0)	7% (5)	--	--	--	--	--