5-8-2024

Potential Impact of Proposed Medical Device on Hospital Acquired Anemia

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Potential Impact of Proposed Medical Device on Hospital Acquired Anemia

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A Thesis Submitted to the Graduate Faculty of

GRAND VALLEY STATE UNIVERSITY

In

Partial Fulfillment of the Requirements

For the Degree of

Master's of Science in Engineering

Padnos College of Engineering and Computing

April 2024

GRAND VALLEY
STATE UNIVERSITY

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Abstract

Evacuated tubes are the industry standard for drawing blood and have improved phlebotomist and patient safety as well as paved the way for laboratory automation. Current practices using evacuated tubes do not allow caregivers to control the volume of blood drawn, leading to blood waste in hospital settings. This overdrawing of blood has led to the prevalence of iatrogenic anemia, or hospital acquired anemia (HAA). HAA represents a significant risk to patients, leading to increased adverse conditions, and a higher consumption of hospital resources. This study seeks to model the efficacy of a potential new medical device. The proposed device would interface with standard evacuated tubes to control the volume of blood drawn at the point of care to limit blood waste. Blood draw orders for 433 patients were acquired from a local hospital system. This study models changes in patient risk for developing HAA, rates of transfusions, and mortality for the proposed medical device. Patients' average daily phlebotomy, the adjusted odds ratios based on surplus blood drawn, and potential cost savings per patient treated were calculated for various draw conditions. Adjusted odds ratios for the proposed medical device were compared to those reported in the literature and odds ratios calculated for patient risk when using small volume tubes, another potential blood saving technology.

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Chapter 1: Introduction

Introduction

Physicians in Intensive Care Unit (ICU) settings must be able to quickly diagnose and continuously monitor patient conditions. One of the most important tools for rapid diagnosis is blood sample analysis which utilizes blood drawn from patients to identify anomalies in a patient's condition to aid in the determination of the best direction of care. While historically blood was collected manually using needles and syringes, industry standard has moved towards evacuated blood collection tubes [1]. Evacuated blood collection tubes are plastic tubes containing a vacuum and capped with a porous membrane. Evacuated tubes for blood collection were introduced in 1949 by Becton Dickinson with other companies developing their own versions in the early 1970s [1]. Evacuated blood collection tubes provide a safer, more consistent method of blood collection which limits healthcare professionals' exposure to bloodborne pathogens. Examples of evacuated tubes from Becton Dickinson are shown in Figure 1.

Figure 1. Evacuated tubes from Becton Dickinson [2].

Evacuated tubes for blood collection are offered in a variety of sizes from 1.8 mL to 10 mL. Most evacuated tubes inner surfaces are coated by manufacturers with additives during the manufacturing process, thus eliminating the need for healthcare providers to prepare their own sample additives. Additives include anticoagulants, such as sodium citrate, heparin, and potassium mixtures, glycolysis inhibitors like fluoride, and clot

activators [3]. The use of standardized evacuated collection tubes also enables laboratory automation.

While evacuated collection tubes have helped to improve the efficiency and safety of laboratory and phlebotomy activities, the lack of control over the volume of blood drawn by these tubes is a concern. Evacuated tubes are negatively pressurized by the manufacturer and are based on the principle that fluids accelerate from high pressure regions to low pressure regions. During venipuncture, the difference between the positive pressure of the penetrated blood vessel and the negatively pressurized tube draws blood from the vessel to fill the container until equilibrium is achieved. Because these containers fill based on a pressure differential, it is impossible for healthcare professionals to control the drawn volume of blood by any other means than tube size selection. This lack of volume control leads to unnecessary amounts of blood being drawn compared to what is required by laboratory technology for analysis. The difficulty of storing and maintaining blood samples means that excess drawn blood often cannot be kept long-term for testing. Some analytical measurements of blood are stable up to 72 hours after collection when stored at 4 °C but longer storage times can alter sample characteristics such as platelet morphology and white blood cell count [4]. The potentially volatile nature of patient conditions in emergency care also means that long-term samples may no longer representative of a patient's current condition.

Overdrawing of blood for diagnostic testing can result in iatrogenic anemia, commonly referred to as Hospital Acquired Anemia (HAA), and increased rates of negative patient outcomes including increased need for packed red blood cell transfusions and mortality rates. HAA is defined as anemia which develops in a patient who was not admitted into the hospital with anemia [5]. Anemia is the condition of having a reduced proportion of haemoglobin (Hb), haematocrit (HCT), or red blood cells (RBC), and is caused by the imbalance in production to removal or destruction of RBC [6]. Hb and HCT are used more commonly than RBC for determination of anemia in day-to-day clinical practice [7]. Anemia is defined numerically as a reduction in Hb below 13.5 g/dL in men, 12.0 g/dL in women, or an HCT less than 41% in men, 36% in women. While anemia can be identified with either Hb concentrations or HCT values, Hb has been found to correlate

better with the diagnosis of anemia and be more specific than HCT [8]. Anemia is correlated with increased rates of negative surgical outcomes, increased time spent in hospital care, increased rates of admission to intensive care units, and higher demand of hospital resources [9]. An estimated 20% to 40% of patients develop HAA during their time in ICU settings [9, 5]. In the elderly, anemia is more likely to have negative effects due to multiple comorbidities and can lead to myocardial infarction, angina heart failure, and other cardiac complications such as the development of arrhythmia and cardiac hypertrophy. Researchers and healthcare professionals agree that excessive diagnostic testing is detrimental to patient health and that more actions need to be taken to reduce blood waste and overdrawing of blood for diagnostic testing.

Typically, phlebotomy will be initiated per a physician's request for a suite of blood diagnostic testing. The hospital's laboratory will input the request into the Laboratory Information System (LIS) which will then return the required number and type of evacuated tubes required to complete the order. The LIS will group compatible tests of the same tube type together and use this to determine the size of tube that should be used. The order will then be sent back to a trained phlebotomist who will draw the blood from the patients. Current practices for drawing blood using vacuum tubes involves inserting a double-sided needle adaptor, often called a hub, into the patient's blood vessel and then connecting a vacuum tube onto the other side of the adaptor [10]. When the tube is filled, depending on the volume of blood requested by the testing lab, additional tubes may be swapped in for collection. Figure 2 shows the phlebotomy setup when drawing directly from the blood vessel.

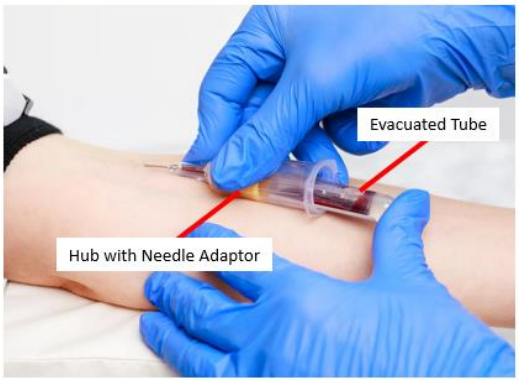

Figure 2. Blood drawing using an evacuated tube for sample collection [11].

Some patients may have a Peripheral Access Device (PAD), or a Central Venous Access Device (CVAD). These devices are generally reserved for use in patients with specific drug delivery needs [12]. An example of a phlebotomy setup using a CVAD is illustrated in Figure 3.

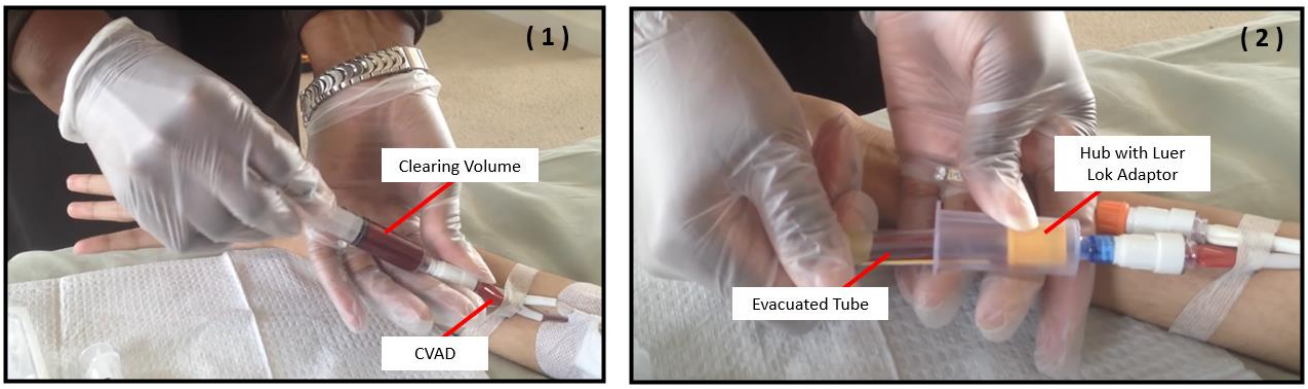

Figure 3. Blood drawing from an arterial device. (1) Drawing clearing volume to flush the device. (2) Drawing blood sample for analysis [13].

When using a PAD or CVAD, it is necessary to draw a clearing volume of blood before samples are collected. These devices are generally flushed with heparinized saline to keep or maintain patency tubing of blood when not in use [14]. The presence of saline or residual fluids may contaminate samples and cause error during laboratory analysis. A clearing volume of 5 mL is standard practice, however, clearing volumes vary from 4 mL to 25 mL depending on the testing being conducted. A study of children receiving routine bloodwork through central venous catheters found that clearing volumes of 3 mL was sufficient to avoid contamination of samples by residual fluids [15]. It's estimated that discarded clearing volumes account for 24% to 30% of patients' blood loss during their hospital stay [14].

The use of a proposed medical device to allow caregivers to capture clearing volumes and set the volume of blood collected in vacuum tubes could help to mitigate the concerns of using evacuated tubes while only minimally changing current blood drawing practice. The proposed device would interface with the hub adaptor or CVAD / PAD. The changed phlebotomy process would involve inserting an evacuated tube into the device then connecting the device to a hub for venipuncture or a CVAD / PAD for drawing from existing lines. If using a CVAD / PAD, the clearing volume would be captured before the

sample was collected using an integrated syringe. The user would then set the desired draw volume before opening the valves to allow for blood to be collected. This could be achieved using a second integrated syringe on the non-patient side of the fluid valves. Once collection is completed, the captured clearing volume could be returned to the patient using the integrated syringe. This proposed device would have three primary benefits compared to the use of syringes and current evacuated tube procedures. First, the device could be connected to a PAD or CVAD, reducing patients' and nurse practitioners' risk of needlestick injuries during venipuncture. Second, the use of the medical device could allow for captured clearing volumes to be returned to the patient rather than discarded, limiting blood waste. Third, the medical device would allow caregivers to set the volume of blood drawn based on the minimum amount required for testing. By limiting the surplus volume of blood drawn and reducing the discarded clearing volumes, the proposed medical device could have a significant impact on rates of HAA.

Purpose

The purpose of this study is to investigate the impact of a proposed medical device which would allow the caregiver to draw precise volumes of blood with evacuated tubes for diagnostic testing on rates of iatrogenic anemia and volumes of surplus blood drawn. This study also aims to estimate the reduction in patient risk of needing a packed red blood cell (PRBC) transfusion and risk of mortality based on blood drawing activities during care. Cost reduction through elimination of unnecessary transfusions is also estimated. It is desired to determine the volume and variability of the average blood drawn per patient per day using data obtained from a local hospital system. Models will be built using the data for comparison of patients' average daily phlebotomy volumes to those reported in the literature. The potential impact of using pediatric sized tubes on patient risk of adverse outcomes related to diagnostic testing will also be investigated.

Scope

The scope of this study is limited by the collected blood draw data from the local hospital system. The obtained dataset does not include patient demographic or medical

information such as age, race, or patient condition at admission. Additionally, the data does not discuss whether patients developed HAA or required a PRBC transfusion during their stay. Due to the limited information on patient outcomes, analysis conducted relies on changes in patient risk based on the volumes of blood drawn compared to estimated draw volumes using the proposed medical device.

Some containers have been removed from the dataset prior to analysis to refine the scope of the data. Blood draws completed using a syringe were omitted due to the irrelevance to the current study. The proposed medical device to control blood drawn is intended to reduce the volume of blood drawn with evacuated tubes. Syringes which already provide manual control over the volume drawn are considered outside the scope of the current study. Clearing volumes which are typically drawn using syringes were also not considered as a part of the study. While clearing volumes are a source of blood waste that the proposed medical device seeks to address, no information about the use of CVADs or PADs for patients in the dataset is available and as such it is difficult to realistically estimate the potential clearing volumes wasted.

Several orders in the dataset pertained to non-blood collection activities including urine, stool, and tissue orders. Any tubes pertaining to non-blood orders were not included for analysis as these had no impact on patients' risk of HAA or transfusion. Several orders were also seemingly used as placeholders with tests ordered including "Feedback Requested" or 0 mL draw volumes. These placeholders were not considered during analysis. Tube types which required 100% fill or a specific fill volume like blood culture tubes were also not considered for analysis as the implementation of the proposed medical device would have no effect on the draw volumes of these tubes. Several tubes ordered had required test volumes greater than the capacity of the tubes listed in the order. To prevent over-estimating the current practices volume of blood drawn, these tubes were omitted rather than assuming multiple tubes were used and not recorded in the order.

Assumptions

Several key assumptions were made to allow for analysis of the blood draw data. It was assumed that the current method for drawing blood using evacuated tubes drew the

full tube volume. This assumption was required as the actual drawn volume for each order was not reported. The assumption that the full evacuated tube volume was drawn also serves as a worst-case estimate of current practices. For comparison to the proposed medical device, it was also assumed that the nursing staff would correctly use the proposed device to draw the requested volume of blood every time.

For generalization of conclusions to other patient populations, the patient population for the local hospital system was assumed to be similar to other hospital systems in the United States. Similarly, it was assumed that values reported in the literature like the odds ratios for developing HAA, requiring a transfusion, and mortality, the probability of requiring a transfusion, and the cost of transfusions per unit of blood, which were collected from separate multi-center and single center studies, were applicable to the current study.

Hypothesis

It was hypothesized that the application of the proposed medical device would significantly reduce patient risk of developing HAA, transfusions, and mortalities based on the reduction of surplus average daily phlebotomy. This reduction in adverse events is expected to provide direct cost savings for the hospital. It is also believed that the proposed device will have significant benefits over other methods of reducing average daily phlebotomy such as the use of small volume tubes.

Significance

This study will assist with the development and implementation of technology to improve patient outcomes by reducing blood waste in hospital settings. Analysis of changes in patient risk for developing HAA, requiring transfusions, and mortality when using a medical device which allows caregivers to draw exact volumes of blood will help to determine the potential benefits of such technology. Estimation of cost reduction due to elimination of unnecessary RBC transfusions could help with determining whether development and adoption of the device is financially feasible by providing hospital purchasing departments a foundation for cost-benefit analysis.

Definitions

Hospital Acquired Anemia (HAA): Anemia which develops in a patient who was not admitted into the hospital with anemia. Also referred to as iatrogenic anemia as it is commonly associated with diagnostic testing.

Evacuated Tubes (Blood Diagnostics): Plastic tubes containing a vacuum and capped with a porous membrane. Used commonly in blood diagnostics as a way to standardize laboratories and improve technicians and phlebotomist safety.

Hemoglobin (Hb): Protein contained in blood. Responsible for the transport of oxygen throughout the body. Hemoglobin concentrations can be used for determination of anemia.

Hematocrit (HCT): Percentage of total blood volume that is made up of red blood cells. Excludes white blood cells, platelets, and plasma.

Packed Red Blood Cells (PRBC): Also referred to as red blood cells, packed red blood cells are prepared samples from which all plasma has been removed. Packed red blood cells are used in transfusions to improve patients' hemoglobin concentrations.

Odds (Statistics): An expression of relative probabilities. Odds describe the ratio of probability that an event will occur to the probability that an event will not occur.

Odds Ratio (Statistics): An expression of association between a treatment and an event. The ratio of a set of odds in which the same event occurs in both groups, but one group has been exposed to some treatment.

Chapter 2: Manuscript in PLOS One Format

Abstract

Evacuated tubes are the industry standard for drawing blood and have paved the way for laboratory automation. Current practices using evacuated tubes do not allow caregivers to control the volume of blood drawn, leading to blood waste in hospital settings. This overdrawing of blood has led to the prevalence of iatrogenic anemia, or hospital acquired anemia (HAA). HAA represents a significant risk to patients, leading to increased adverse conditions and higher consumption of hospital resources. This study evaluates the efficacy of a potential new medical device. The proposed device would interface with standard evacuated tubes to control the volume of blood drawn at the point of care to limit blood waste. Blood draw orders for 433 patients were acquired from a local hospital system. This study models changes in patient risk for developing HAA, rates of transfusions, and mortality for the proposed medical device. Patients' average daily phlebotomy, the adjusted odds ratios based on surplus blood drawn, and potential cost savings per patient treated were calculated for various draw conditions. Adjusted odds ratios for the proposed medical device were compared to those reported in the literature and odds ratios calculated for patient risk when using small volume tubes, another potential blood saving technology.

Introduction

Physicians in Intensive Care Unit (ICU) settings must be able to quickly diagnose and continuously monitor patient conditions. One of the most important tools for rapid diagnosis is blood sample analysis which utilizes blood drawn from patients to quickly identify anomalies in a patient's condition to aid in the development of patient specific intervention strategies. Industry standard for phlebotomy activities has moved towards evacuated blood collection tubes to address concerns with manual drawing of blood using syringes [1]. Evacuated blood collection tubes are plastic tubes containing a vacuum and capped with a porous membrane introduced in 1949 by Becton Dickinson [1]. Evacuated blood collection tubes provide a safer, more consistent method of blood collection which limits healthcare professionals' exposure to bloodborne pathogens. The use of

manufactured tubes also eliminates the need for healthcare providers to prepare their own sample additives and makes laboratory automation possible. While evacuated tubes have helped to improve the efficiency and safety of laboratory and phlebotomy activities, the lack of control over the volume of blood drawn by these tubes is a concern. The lack of control has two deleterious effects. First, the overdrawing of blood leads to increased patient risk of poor outcomes such as developing anemia. Second, the amount of blood drawn may not meet test requirements. This study is focused on the issue of increased patient risks due to large volumes of blood drawn.

During venipuncture, the difference between the positive pressure of the penetrated blood vessel and the negatively pressurized tube draws blood from the vessel to fill the container until equilibrium is achieved. Because these containers fill based on a pressure differential, it is impossible for caregivers to control the drawn volume of blood by any other means than tube size selection and tubes generally fill to full volume. This lack of volume control leads to unnecessary amounts of blood being drawn compared to what is required by laboratory technology for analysis. It is estimated that on average, 2 mL of blood is discarded for every blood draw with an evacuated tube [2]. The difficulty of storing and maintaining blood samples means that excess drawn blood often cannot be kept long-term for testing. Some analytical measurements of blood are stable up to 72 hours after collection when stored at 4 °C but longer storage times can alter sample characteristics such as platelet morphology and white blood cell count [3]. The potentially volatile nature of patient conditions in emergency care also means that long-term samples may not be viable as they are no longer representative of a patient's current condition. Blood waste is further exacerbated through the use of Peripheral Access Devices (PAD) and Central Venous Access Devices (CVAD) which require the clearing volumes to be drawn prior to sample collection. It is estimated that discarded clearing volumes account for 24% to 30% of patients' blood loss during their hospital stay [4]. Additionally, clearing volumes are often pulled using syringes and discarded rather than being reintroduced to the patient due to the risks of introducing air and contaminants into patients' bloodstream.

Overdrawing of blood for diagnostic testing can result in iatrogenic anemia, commonly referred to as Hospital Acquired Anemia (HAA), and increased rates of negative patient outcomes including a greater need for packed red blood cell transfusions and higher

mortality rates. HAA is defined as anemia which develops in patients who experience blood loss during hospitalization [2]. An estimated 20% to 40% of patients develop HAA during their time in ICU settings [2, 5].

There are several types of anemia besides HAA. In general, anemia is the condition of having a reduced hemoglobin (Hb) concentration, hematocrit (HCT), or red blood cells (RBC), and is caused by the imbalance in production to removal or destruction of RBC [6]. Anemia is defined numerically as a reduction in Hb concentrations below 13.5 g/dL in men, 12.0 g/dL in women, or an HCT less than 41% in men, 36% in women. While anemia can be identified with either Hb concentrations or HCT values, Hb concentration has been found to correlate better with the diagnosis of anemia and be more specific than HCT values [7]. Anemia is correlated with increased rates of negative surgical outcomes, increased time spent in hospital care, increased rates of admission to intensive care units, and higher demand of hospital resources [5]. Anemia disproportionately affects women and the elderly as well as infants and neonates. Anemia reduces the oxygen carrying capacity of blood and can lead to tissue hypoxia if left untreated [8]. Patients who develop anemia prior to undergoing a surgical operation have higher in-hospital mortality rates than patients with normal preoperative Hb concentrations [5]. Anemia has also been linked to increased hospital length of stay and higher hospital resource consumption per patient. Patients who undergo surgery are even more at risk of developing HAA post-operation as many patients have depressed bone marrow, and RBC production, post-operation [5]. In pregnant women, premature labor and increased blood loss can occur as well as birth defects such as low birth weight or anemia in the baby [6]. Treatment for HAA typically requires transfusions of packed RBCs which can add significant costs to patient care. It is also well known that blood transfusions can cause other complications which may put patients at risk unnecessarily.

Small volume tubes (SVT) have been proposed as a potential solution to address the surplus of blood drawn for testing. However, the use of SVTs may not be feasible for some hospitals where smaller tubes are not compatible with the available analytical equipment [9]. SVTs also do not address the blood waste resulting from discarding clearing volumes which may explain why some studies have found no significant long-term improvements in PRBC transfusion rates or long term Hb concentrations [10, 11].

In this study, a potential medical device which would interface with evacuated tubes to control the pressure differential between evacuated tubes and blood vessels in a closed system is evaluated. This device would allow nurses to limit the volume of blood drawn during phlebotomy and be capable of capturing and returning clearing volumes. The device would interface with needle hubs commonly used in current practice to allow for seamless introduction into the current process for drawing blood for diagnostic testing. The potential impact of the proposed device was evaluated using data collected from a local hospital system for 433 patients. Changes in patient risk for developing HAA, requiring a transfusion, and mortality were compared between the current procedures and updated procedure with the proposed medical device to determine the cost vs benefits for such a device.

Methodology

Blood draw orders were obtained from a local hospital system for 433 patients. The data includes a de-identified list of patients, physician-initiated blood draws for each patient, size of tube used for each blood draw, unique identifiers for each tube, tests run on each tube, the volume of blood required by the testing lab for a given test, and how many days each patient was in the hospital when a blood draw order was given.

The local hospital system utilizes SoftLab, a laboratory information systems suite developed by [SCC Soft Computer, Florida], for its blood sample ordering. SoftLab takes physicians' requests for blood tests and calculates the volume of blood required for testing. Lab technicians assign two values to each blood test in the system; a test volume and an add-up volume. When an order for a set of blood tests is received, SoftLab takes the first test in the list for a given tube type and set this as the initial draw volume. SoftLab then compares the test volume to the next test with the same tube type. If the next test volume is greater than the initial volume, it is then set as the new calculated volume. If the next test has a test volume less than the initial volume, the add-up volume is added to the running total. The running total is then compared to all subsequent tests for the same tube type in a similar manner. An example of this process is shown in Table 1.

Table 1. Example of calculation for blood required for testing based on physician order.

Test	Test Volume (mL)	Add-Up Volume (mL)	System Calculation	Running Total (mL)
T1	10	2	System uses test volume	10
T2	4	0	RT* > Test Vol., add RT and add-up volume	10 + 0 = 10 10 > 4, keep 10
T3	3	2	RT > Test Vol., add RT and add-up volume	10 + 2 = 12 12 > 3, keep 12
T4	5	1	RT > Test Vol., add RT and add-up volume	12 + 1 = 13 13 > 5, keep 13

*RT – Running Total

In Table 1, a physician has ordered four tests to be completed, T1 – T4, all using the same tube type. The first test has a test volume of 10 mL which is set as the initial volume. The initial volume is added to the add up volume of T2 prior to comparing to the test volume. T2's test volume of 4 mL is less than the current running total of 10 mL meaning its test volume is not taken as the new running total. Adding the add up volume for T3 and comparing the running total to T3's test volume, 12 mL is greater than 3 mL, so the test volume is not taken as the new running total. The add-up volume for T4 is now added to the running total and compared to T4's test volume. Again, the running total of 13 mL is greater than the test volume of 5 mL and the test volume is not taken as the new running total. This means that a final volume of 13 mL is required to complete the suite of tests in this example.

From the calculation of the running total blood required for an order, the minimum required blood volume for each tube can be calculated. It is assumed that the minimum required volume is the actual volume drawn using the proposed medical device. Once the minimum required blood volume for each tube is determined, average daily phlebotomy for a given patient can be determined by dividing the drawn volume by the number of days spent in the hospital. This can then be expanded to determine the average daily draw per patient by dividing average daily phlebotomy for each patient by the total number of patients in the dataset as shown in Equation 1.

$$BDPD = \frac{\sum_{i=1}^{n} V_{Daily,i}}{n} \quad (1)$$

Where $BDPD$ is the volume of blood drawn per patient per day, $V_{Daily,i}$ is the average daily draw volume for a given patient i, and n is the number of patients. BDPD was calculated assuming the current practices drew full tube capacities every time and the proposed medical device only drew the volume required for testing. Additionally, the BDPD for the proposed device under minimum draw volume requirements was calculated. Laboratories may impose minimum draw conditions to reduce the likelihood of testing error or sample contamination.

Increases in odds ratios (OR) for developing HAA, in-hospital mortality, and requiring blood transfusions based on changes in average daily phlebotomy are discussed in Bodley [12]. Bodley states that the odds ratios for HAA, transfusion, and mortality due to an increase in average daily phlebotomy of 5 mL are 1.18, 1.17, and 1.10 respectively. An odds ratio is a measure of association between the odds of an event occurring in a group that is and a group that is not exposed to a treatment or event [13]. The odds ratio is related to logistic regression. For a single, continuous predictor variable, the logit for the probability of an event occurring is given in Equation 2.

$$\log_e\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 x \quad (2)$$

Where p is the probability of an event occurring for a given predictor variable x, β_0 is the model intercept, and β_1 is the difference in the log odds per unit of x. The odds ratio equation is given in Equation 3.

$$\text{OR} = \frac{Odds_R}{Odds_T} \quad (3)$$

Where OR is the odds ratio between the odds of an event occurring in a reference group, $Odds_R$, and treatment group, $Odds_T$. Taking the natural log of both sides of Equation 3 gives

$$\log_e(\mathrm{OR}) = \log_e(\frac{Odds_R}{Odds_T})$$

According to the properties of the natural log, it is known that this is equivalent to,

$$\log_e(\mathrm{OR}) = \log_e(Odds_R) - \log_e(Odds_T)$$

Using the definition that β_1 is the difference in the log odds per unit of x,

$$\log_e(\mathrm{OR}) = \beta_1$$

This means that for a change in the predictor variable x, the adjusted odds ratio is given in Equation 4.

$$\mathrm{OR_{adj}} = e^{\beta_1 x} = e^{\log(\mathrm{OR})x} = \mathrm{OR^x} \tag{4}$$

Where $\mathrm{OR_{adj}}$ is the increase in odds of an event occurring between a reference and treatment group for a change in the predictor variable x. Using estimates of the OR for the occurrence of HAA, PRBC transfusion, and mortality from the literature, adjusted OR for use of the proposed medical device were calculated. Bodley [12] identified that for every 5 mL increase in average daily blood drawn, the odds ratio for Hb concentrations below 8.0 g/dL was 1.18, the odds ratio for needing an RBC transfusion was 1.17, and the odds ratio for mortality was 1.10 based on a case study review of 424 ICU patients.

Equation 4 was compared to odds ratios calculations available in the literature. Bodley [12] reports that the odds ratio for nadir Hb < 8.0 g/dL per 1 mL increase in daily average phlebotomy is 1.033. For an increased average daily phlebotomy of 5 mL, the adjusted odds ratio is calculated as:

$$\mathrm{OR_{adj}} = 1.033^5 = 1.18$$

Bodley [12] reports the odds ratio for increased daily phlebotomy of 5 mL as 1.18. This example shows that Equation 4 for calculations of adjusted odds ratios for increased daily phlebotomy are in agreement with methods found in the literature.

The equation to determine the odds of an event occurring based on its probability can be defined as shown in Equation 5.

$$Odds_n = \frac{p}{1-p} \tag{5}$$

where p is the probability of an event occurring in some group n. The odds equation in Equation 5 can be considered with the ratio of odds as shown in Equation 3. When comparing the odds of an event occurring in a reference and a treatment group, the probability of the event occurring in the treatment group can be defined as shown in Equation 6:

$$p_{Treatment} = \frac{p_{Reference}}{\mathrm{OR}(1-p_{Reference})+p_{Reference}} \tag{6}$$

where $p_{Treatment}$ is the probability of an event occurring in a treatment group, $p_{Reference}$ is the probability of an event occurring in the reference group with no controls, and OR is the ratio between the two groups' odds of the event occurring. Using Equation 6, and the known probability of transfusions without interventions, the likelihood of patients requiring a transfusion when medical devices are introduced into the phlebotomy process can be determined.

Results

For the 433 patients included in the dataset, a total of 750,324 tests were ordered from 30 departments of the local hospital system. The distribution of tests between the departments is shown in Figure 1.

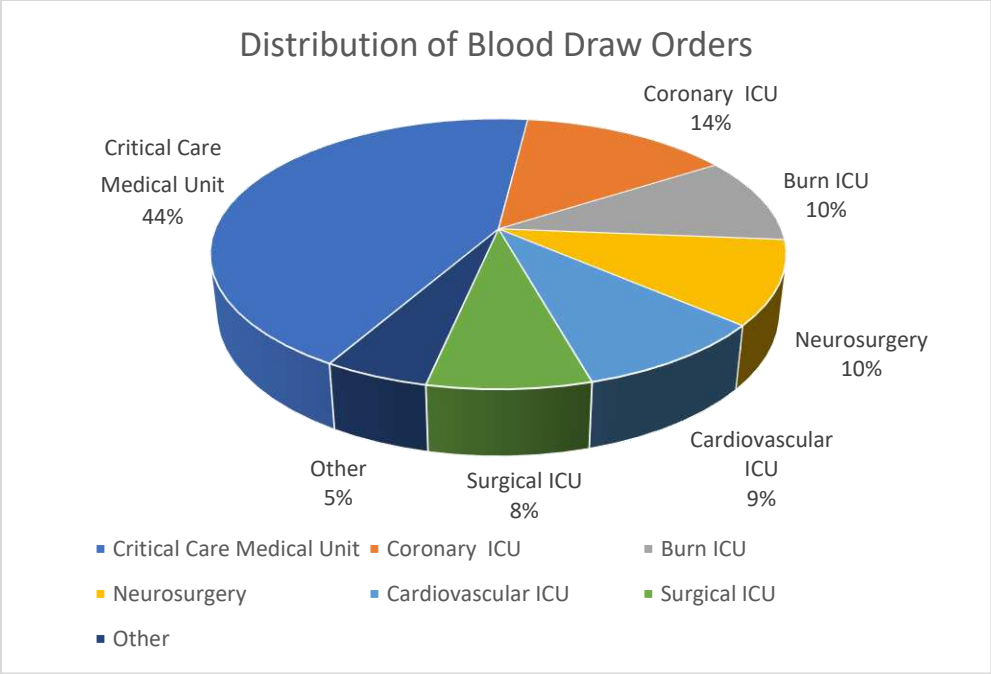

Figure 1. Distribution of blood draw orders across ordering departments of local hospital system for 433 patients.

The greatest number of tests ordered came from the Critical Care Medical Unit, followed by the Coronary ICU, the Burn ICU, the Neurosurgery ICU, the Cardiovascular ICU, and the Surgical ICU. All other departments accounted for less than 5% of the total number of tests ordered. Arterial Blood Gas (ABG), Complete Blood Count (CBC) with differential, Venous Blood Gas, and CBC with No Differential were the four most common groups of tests ordered. For the 750,324 tests ordered, 50,240 individual tubes were collected for analysis.

Average daily phlebotomy was calculated for the 433 patients. Figure 2 shows a box and whisker plot of average daily phlebotomy PD using current methods side by side with estimated average daily phlebotomy using the proposed medical device. Outliers are not displayed in this plot for improved readability. Outliers are defined using the 1.5 x IQR rule.

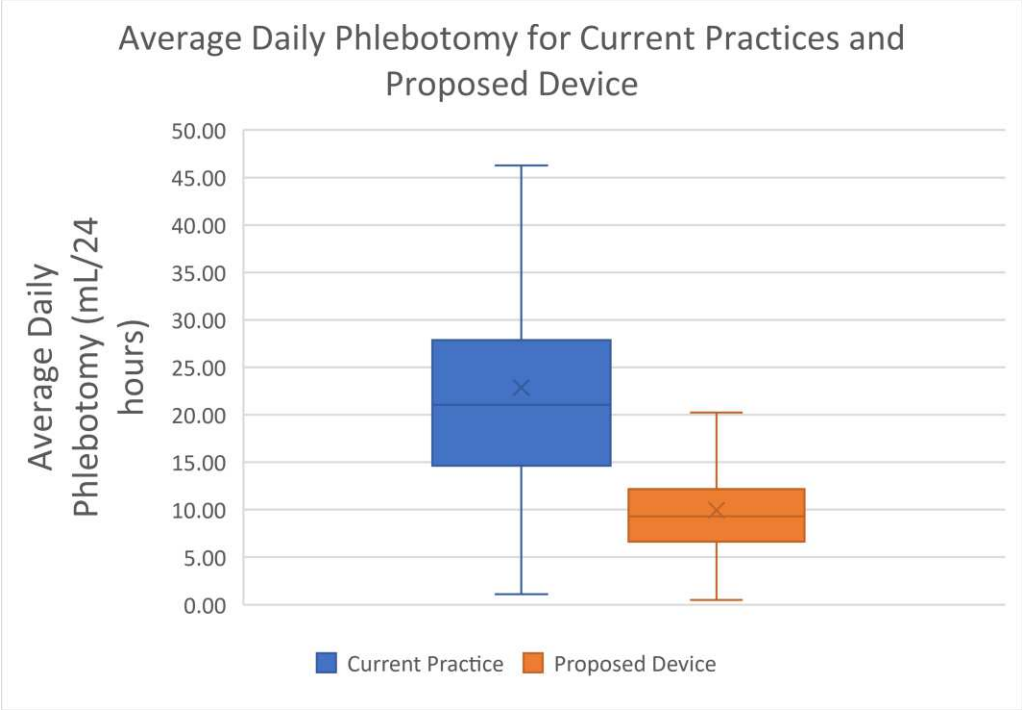

Figure 2. Average volume of blood drawn per patient per day using current and controlled conditions.

As shown in Figure 2, the estimated volume of blood drawn on average per patient per day using the proposed medical device is reduced from the volume of blood drawn under current conditions assuming the full tube volume is drawn. Volume of blood drawn under current conditions ranges from 1.10 to 91.49 mL/day/patient while the volume drawn using the estimated controlled conditions ranges from 0.48 to 30.35 mL/day/patient. Table 2 shows a summary of average volumes of blood drawn.

Table 2. Summary of BDPD and average daily phlebotomy using current methods and with the proposed medical device.

	Current Practices	Proposed Device
Average (mL/day/patient)	22.88	9.96
Maximum (mL/day)	91.49	30.35
Minimum (mL/day)	1.10	0.48
Standard Deviation (mL/day)	11.54	4.60

Table 2 shows that the proposed medical device also reduces the estimated average volume of BDPD from 22.88 mL/day/patient to 9.96 mL/day/patient. The estimated average BDPD for the proposed medical device was calculated assuming only the volume of blood required for a given suite of tests was collected. Figure 3 shows a box and whisker plot of the average daily phlebotomy using the proposed medical device if minimum draw volumes were instituted ranging from 0.5 mL per tube to 3.0 mL per tube. Tubes whose volumes were less than the required minimum draw volume were assumed to have been filled only to the tube capacity. Outliers again have been removed from the plot to improve readability.

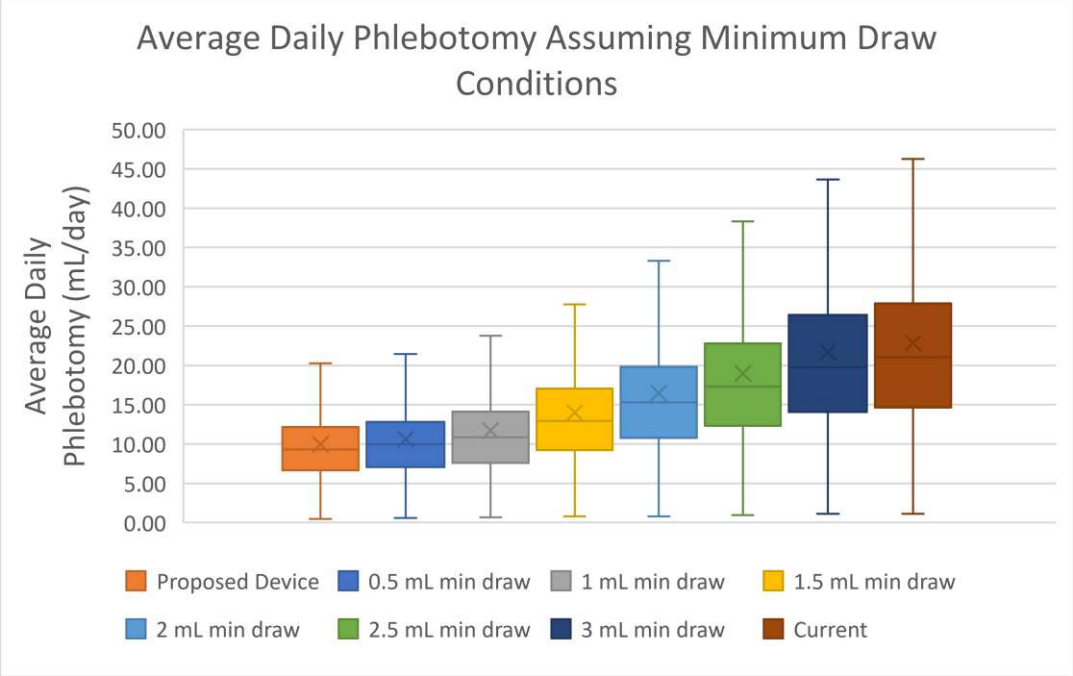

Figure 3. Average daily phlebotomy using the proposed device with minimum draw conditions.

Figure 3 shows that as the required minimum draw volume per tube increases, the range of average daily phlebotomy increases until the 3 mL minimum draw condition which extends a similar range as the current draw practices average daily phlebotomy. Table 3 shows a summary of the estimated average daily phlebotomy for dataset when minimum draw conditions are imposed.

Table 3. Summary of average daily phlebotomy using a proposed medical device with minimum draw conditions.

	0.5 mL Minimum	1 mL Minimum	1.5 mL Minimum	2 mL Minimum	2.5 mL Minimum	3 mL Minimum
Average (mL/day/patient)	10.62	11.69	13.99	16.49	18.95	21.71
Maximum (mL/day)	33.75	38.98	49.86	62.23	72.65	82.69
Minimum (mL/day)	0.58	0.68	0.78	0.80	0.95	1.10
Standard Deviation (mL/day)	5.00	5.58	6.75	8.07	9.33	10.65

As seen in Table 3, average BDPD increases with increasing minimum required draw volumes from 10.62 mL/day/patient for the 0.5 mL minimum condition to 21.71 mL/day/patient for the 3 mL minimum condition. The range of average daily phlebotomy similarly increases with increasing minimum draw volumes with the maximum average daily phlebotomy increasing from 33.75 to 82.69 mL/day/patient. The minimum average daily phlebotomy also increases with increasing minimum draw volumes; however, the change is less dramatic with minimum average daily phlebotomy increasing from 0.58 to only 1.10 mL/day/patient.

Table 4 shows a summary of the surplus BDPD between the required test volumes and the current practices. Each of the controlled draw regimes was also included for comparison to the no-minimum draw condition.

Table 4. Surplus in average daily phlebotomy between current practices and controlled draw regimes with proposed medical device.

	Current Practice	0.5 mL Minimum	1 mL Minimum	1.5 mL Minimum	2 mL Minimum	2.5 mL Minimum	3 mL Minimum
Average (mL/day/patient)	12.93	0.66	1.73	4.03	6.54	8.99	11.76
Maximum (mL/day)	61.14	3.93	9.34	19.51	31.89	42.30	52.34
Minimum (mL/day)	0.62	0.00	0.00	0.30	0.32	0.47	0.62
Standard Deviation (mL/day)	7.47	0.57	1.38	2.69	4.13	5.37	6.55

Table 4 shows that the surplus in average daily phlebotomy increases as the minimum draw volume requirements increase, with the current draw practices having the largest difference in average daily phlebotomy when compared to the required test volumes.

Non-parametric statistical analysis was conducted to compare average daily phlebotomy for the different draw regimes. A Kruskal-Wallis rank sum test showed that there is a statistically significant difference between median daily average phlebotomy for at least one pair of the eight draw regimes ($p < 2.2 \times 10^{-16}$). Table 5 shows a summary of pairwise comparisons using Dunn's test, to current phlebotomy practices. P-values were adjusted using the Benjamini-Hochberg method.

Table 5. Comparisons between average daily phlebotomy using current practices and the proposed medical device with minimum draw conditions.

	Z Score	Adjusted P-value	Significance ($p < 0.05$)
Proposed Device	20.298	3.773×10^{-90}	Significant
0.5 mL Minimum	19.491	1.825×10^{-83}	Significant
1.0 mL Minimum	17.756	1.076×10^{-69}	Significant
1.5 mL Minimum	13.549	2.492×10^{-41}	Significant
2.0 mL Minimum	8.951	7.039×10^{-19}	Significant
2.5 mL Minimum	5.319	1.462×10^{-7}	Significant
3.0 mL Minimum	1.821	7.382×10^{-2}	Non- Significant

As shown in Table 5, it was found that for all but the 3 mL minimum draw condition, statistically significant differences at the 95% confidence level ($p < 0.05$) exist between population medians for average daily phlebotomy using the current practices and the proposed medical device.

Using the average daily phlebotomies determined for patients with the eight different draw regimes, adjusted odds ratios were calculated for each patient based on surplus average daily phlebotomy and odds ratios reported in Bodley [12] for risk of HAA, transfusion, and mortality for increases in average daily phlebotomy. Table 6 shows a summary of adjusted odds ratios for the risk of developing HAA.

Table 6. Adjusted odds ratio for risk of developing HAA using current practices and the proposed medical device.

	Proposed Device	0.5 mL Minimum	1 mL Minimum	1.5 mL Minimum	2 mL Minimum	2.5 mL Minimum	3 mL Minimum
Average	1.593	1.550	1.486	1.363	1.245	1.143	1.040
Maximum	7.568	6.763	5.687	3.967	2.679	1.915	1.388
Minimum	1.021	1.017	1.014	1.011	1.010	1.005	1.000
Standard Deviation	0.585	0.514	0.422	0.282	0.171	0.098	0.046

Table 6 shows that on average, the odds that patients develop HAA are 1.593 times greater for the current practices than if the proposed medical device were used. Patient odds of developing HAA under the current practices are always greater than with the proposed medical device as the minimum odds ratio for the no minimum draw condition is greater than 1.000. As the minimum draw condition increases, the average adjusted odds ratio for the risk of developing HAA decreases until there is only a 4% difference in odds for the 3 mL minimum draw condition. Table 7 shows adjusted odds ratios for the risk of requiring a transfusion.

Table 7. Adjusted odds ratio for risk of requiring a transfusion using current practices and the proposed medical device.

	Proposed Device	0.5 mL Minimum	1 mL Minimum	1.5 mL Minimum	2 mL Minimum	2.5 mL Minimum	3 mL Minimum
Average	1.552	1.513	1.454	1.340	1.231	1.135	1.038
Maximum	6.820	6.130	5.201	3.696	2.547	1.852	1.365
Minimum	1.020	1.017	1.013	1.010	1.009	1.005	1.000
Standard Deviation	0.526	0.464	0.383	0.259	0.159	0.092	0.043

Table 7 shows that on average, the odds that patients require a transfusion are 1.552 times greater for the current practices than if the proposed medical device were used. Similar to the risk of developing HAA, the adjusted odds ratio decreases as the minimum required volume increases until approximately 1.038 for the 3 mL minimum condition. Table 8 shows the adjusted odds ratios for the risk of patient mortality. The 95% confidence interval for adjusted odds ratio for patient mortality is 1.502 to 1.601.

Table 8. Adjusted odds ratio for risk of patient mortality using current practices and the proposed medical device.

	Proposed Device	0.5 mL Minimum	1 mL Minimum	1.5 mL Minimum	2 mL Minimum	2.5 mL Minimum	3 mL Minimum
Average	1.294	1.276	1.248	1.190	1.132	1.079	1.023
Maximum	3.207	3.006	2.721	2.211	1.764	1.454	1.208
Minimum	1.012	1.010	1.008	1.006	1.006	1.003	1.000
Standard Deviation	0.224	0.203	0.174	0.127	0.083	0.051	0.025

Table 8 shows that on average the odds of patient mortality are 1.294 times greater than for the current practices than if the proposed medical device were used. Again, like the odds ratio for developing HAA and requiring a transfusion, the adjusted odds of mortality decrease with increasing minimum draw volumes. The minimum average adjusted odds of mortality of 1.023 occurs for the 3 mL minimum draw condition. The 95% confidence interval for adjusted odds ratio for patient mortality is 1.273 to 1.315. Tables 6, 7, and 8 are represented graphically in Figure 4.

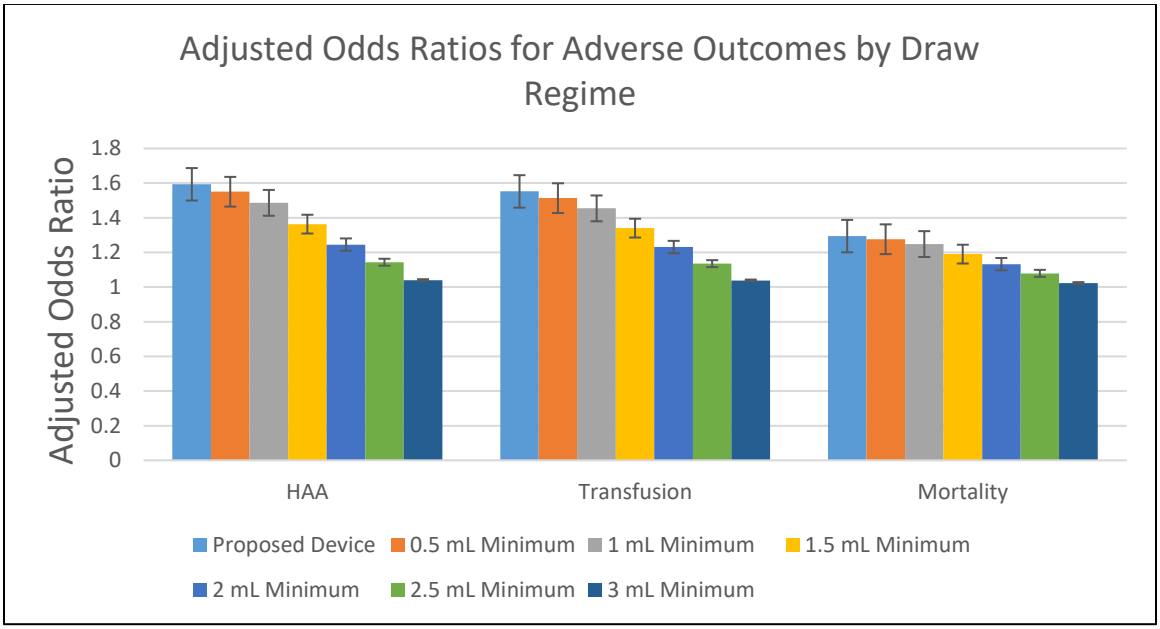

Figure 4. Average adjusted odds ratios with standard error for a proposed blood drawing device with and without minimum draw conditions.

Since the odds ratio is a ratio of patient risk without the proposed device relative to a group of patients who use the proposed device, the adjusted odds ratios shown in Figure 4

represent a decrease in risk of negative patient outcomes using the proposed device. For example, patients whose blood is drawn without the proposed device on average have a 1.593 times greater risk of developing HAA compared to patients using the device. The closer the odds ratio is to 1.0, the less benefits are expected to be obtained through the treatment. For the 3 mL minimum draw condition, which was not significantly different from the current practices when considering average daily phlebotomy, the average adjusted odds ratio is relatively close to 1.0 and almost no benefits are expected from using the device with this large of a minimum draw requirement.

Discussion

Based on the simulated use of the proposed medical device, the potential benefits of a device which allows caregivers to limit the volume of blood drawn with evacuated tubes is readily apparent. The proposed device significantly reduces average daily phlebotomy compared to current practices even without considering the volume of blood saved by capturing clearing volumes. The device also shows potential benefits over small volume tubes although there is some disagreement between this model and the literature on the changes to risk when using small volume tubes. The proposed medical device can be used with buffer volumes without a significant reduction in benefits up to 2.5 mL minimum volume conditions compared to current practices.

The adjusted odds ratios for the risk of requiring a transfusion were used to estimate the cost savings of the proposed medical device as a basis for the economics of the device. Assuming the probability of requiring a transfusion is 0.475 and each patient receiving a transfusion requires three units of PRBC, as discussed in the 7,000-patient multicenter study Chornenki et al. [14], Table 9 shows the average estimated cost savings due to reductions in unnecessary transfusions using the proposed medical device in terms of USD per patient.

Table 9. Probability of requiring a transfusion based on adjusted odds ratios and estimated cost of transfusions per patient treated.

Draw Regime	Current Practices	Proposed Device	0.5 mL Minimum	1 mL Minimum	1.5 mL Minimum	2 mL Minimum	2.5 mL Minimum	3 mL Minimum
Average Probability of Transfusion	0.475	0.360	0.363	0.370	0.387	0.408	0.427	0.448
Estimated Cost for 3 units of PRBC per Patient Treated (USD/patient)	1,539	1,193	1,213	1,243	1,306	1,373	1,437	1,509
Average Cost Reduction per Patient (USD/patient)	--	346	326	296	233	166	102	30
Estimated Device Price (USD)	--	115	109	99	78	55	34	10

The no-minimum draw condition has the lowest probability of patients requiring a transfusion and the greatest amount of cost reduction when compared to current practices. The probability of requiring a transfusion increases with increasing minimum draw volume requirements from 0.360 to 0.448. Figure 5 shows the estimated costs of transfusions per 433 patients for the eight draw regimes.

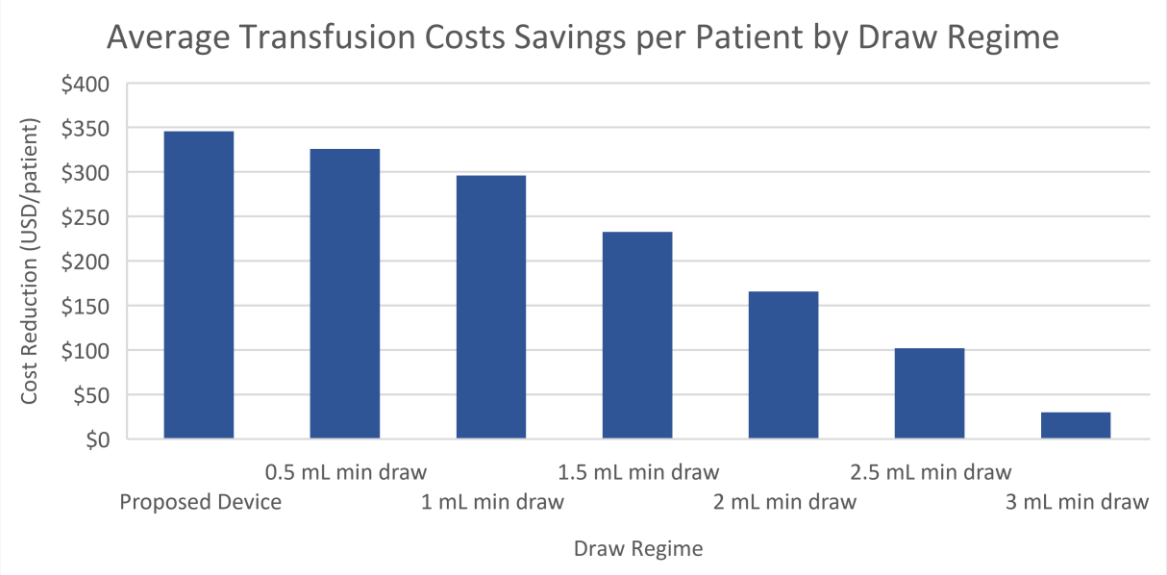

Figure 5. Estimated cost reductions of transfusions per patient for eight draw regimes.

The estimated cost of transfusions for the no minimum draw volume condition is approximately a 23% reduction in total costs. Estimated savings decrease to approximately a 5.68% reduction in cost when increasing the required minimum volume per tube to 3 mL as shown in Figure 5. Assuming hospitals would purchase a device for 1/3 of the cost savings provided per patient, hospitals could be willing to pay between $10 and $115 for the proposed medical device depending on whether buffer volumes will be required.

Small volume tubes are potential competitors to the proposed medical device. Garcia et. al [15] compared rates of hemoglobin level decline between groups of adult ICU patients who were treated using either pediatric or adult sized evacuated tubes. Pediatric tube sizes used were 0.5 mL for hematology, 0.6 mL for chemistries, 2.5 mL for coagulation tests, 1 mL for arterial blood gases, and 10 mL for blood cultures. This study's model for calculating average daily phlebotomy for current practices was recalculated assuming pediatric tube sizes based on the group of tests ordered. For suites of tests requested which exceed the small volume tubes' capacity, additional tubes of the same type were added until the total tube capacity allowed for the suite of tests to be collected. Figure 6 shows a box and whisker plot comparing the estimated average daily phlebotomy using the proposed medical device and the small volume tubes.

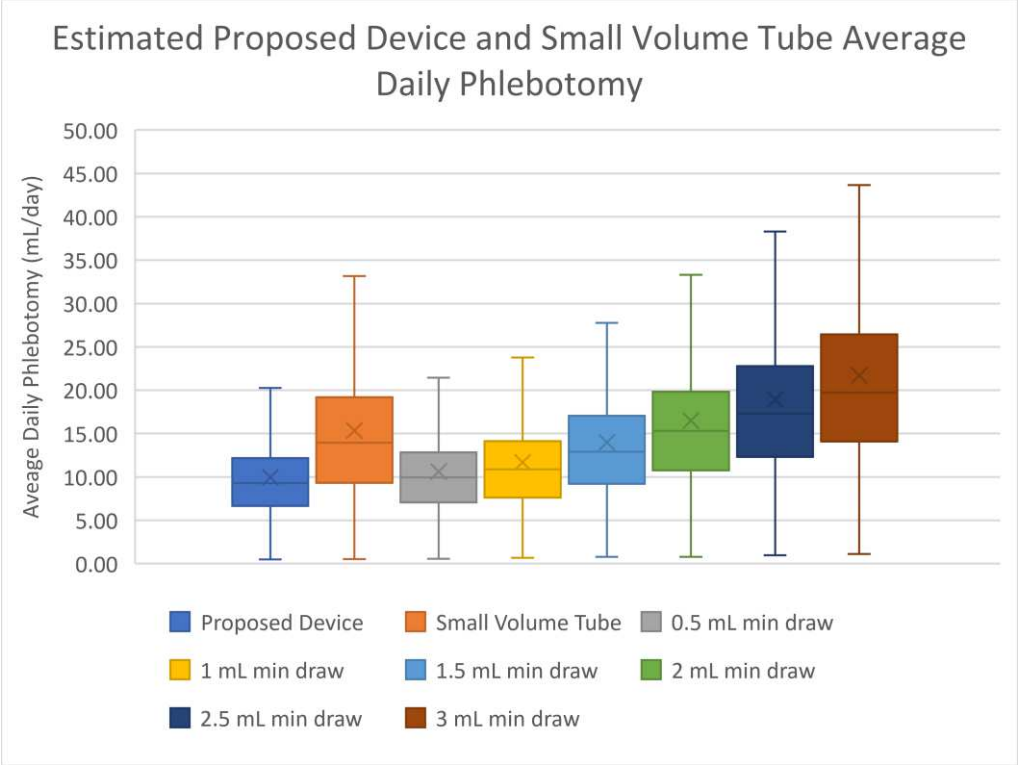

Figure 6. Average daily phlebotomy using the proposed medical device and pediatric sized tubes.

Figure 6 shows that the proposed medical device has a greater effect on reducing average daily phlebotomy than the pediatric tubes used in the SVT model. When considering the blood draw orders using the small volume tubes, BDPD is 15.36 mL/patient/day (95% CI 14.603 – 16.126) compared to the proposed device's BDPD of 9.96 mL/patient/day (95% CI 9.526 – 10.392). Using a pairwise Wilcoxon rank test to compare the two datasets, the difference in average daily phlebotomy of patients using the device and small volume tubes is statistically significant at the 95% confidence level. ($p < 2.2 \times 10^{-16}$). In actual use, it is likely the difference between average daily phlebotomy for SVTs and the proposed device would increase further due to the loss of clearing volumes that the proposed device can capture and return that SVTs on their own cannot. There are additional downsides to using SVTs such as the need to transfer blood to a larger tube in the event laboratory equipment cannot handle the smaller tube sizes. While some benefits have been seen utilizing SVTs in the short term, some studies have found no significant improvements in PRBC transfusion rates or long term Hb concentrations [10, 11]. When comparing the SVT

average daily phlebotomy to the minimum draw conditions, the SVT average daily phlebotomy is between the 1.5 mL and 2.5 mL per tube minimum draw conditions.

The BDPD calculated for small volume tubes in this study is in relative agreement with the BDPD identified in Garcia et al [15] which found that adult participants who were subjected to the pediatric size evacuated tubes had BDPD of 8.6 mL/patient/day. The surplus blood between the estimated current practices and small volume tube average daily phlebotomies was determined and the odds ratios for risk of developing HAA, requiring a transfusion, and patient mortality was calculated using the relationship described in Bodley [12] for increases in average daily phlebotomy. Table 10 shows a summary of these adjusted odds ratios.

Table 10. Adjusted odds ratios for decreases in average daily phlebotomy between small volume tubes and current practices.

	OR HAA	OR Transfusion	OR Mortality
Average	1.30	1.28	1.16
Max	3.65	3.41	2.11
Min	1.02	1.02	1.01
Standard Deviation	0.23	0.21	0.11

Average adjusted ORs shown in Table 10 are similar but represent a lesser reduction in risk than those shown in Tables 6 – 8 for the proposed medical device. This is expected as there is a statistically significant reduction in average daily phlebotomy between the two draw methods.

Table 11 shows the number of patients per 100 patients treated that are expected to require a transfusion (develop hemoglobin < 7g/dL) or experience mortality for pediatric and adult tube conditions as reported in Garcia et al [15]. Also shown are the calculated odds ratios for these events in the pediatric versus adult tube groups.

Table 11. Calculated odds ratios for probability of events occurring, adapted from Garcia et al [15].

Condition	Number of Patients Using Pediatric Tubes (n=100)	Number of Patients Using Adult Tubes (n=100)	Odds Ratio
Transfusion (Hb < 7g/dL)	6	11	1.94
Mortality	9	10	1.12

The odds ratios calculated for the risk of transfusion and risk of mortality between adult and pediatric tube sizes shown Table 11 do not fall within the 95% confidence intervals calculated for the current study (1.502 – 1.601 for transfusions, 1.273 – 1.315 for mortality), with the odds ratio for requiring a transfusion exceeding the estimate study and the odds ratio for patient mortality underestimating compared to the current study. This may be due to the relatively small sample size of Garcia et al [15]. The disagreement between the two sets of odds ratios may also be due to the adjusted odds for increased average daily phlebotomy reported in Bodley [12]. Larger sample size studies encompassing multiple centers should be evaluated to determine the generalizability of the odds ratios reported in Bodley [12] for increased risks per 5 mL increases in average daily phlebotomy.

Salisbury et al. [16] investigated diagnostic blood loss from phlebotomy and the incidence rate of HAA in a large, multicenter case review study of 17,676 patients who suffered from acute myocardial infarction. Of the patients included in the study, 3,551 developed moderate to severe HAA (25.14%). Patients who developed moderate to severe HAA had an average daily blood loss of 24.4 mL / day. Assuming for the current study's cohort of patients that all patients with average daily blood loss greater than 24.4 mL / day developed moderate to severe HAA, an estimated 151 patients (34.87%) would develop HAA without the proposed medical device and 5 patients would develop HAA with the proposed medical device. This proportion of patients who develop HAA can be used to calculate the OR for developing HAA which results in an OR of 45.84, meaning patients are 45.84 times more likely to develop HAA without the use of the proposed medical device. This vastly exceeds the adjusted OR calculated using Bodley's [12] number for risk of developing HAA per 5 mL increases in daily phlebotomy, which had a maximum odds

ratio of 7.568. The origin of this large discrepancy is unclear. While the current study ignores clearing volumes, this would increase the average daily volume of phlebotomy drawn using current practices and result in an even larger OR for risk of developing HAA. The discrepancy may be due to an underestimation of test volumes required by the local hospital system compared to the systems studied in Salisbury et al [16]. Further studies should use rates of HAA in the patient population to examine the widespread applicability of the odds ratios reported in Bodley [12] for increased risks per 5 mL increases in average daily phlebotomy to other patient populations.

Estimations of average daily phlebotomy using the proposed medical device show that the proposed device could have significant, positive impacts on patient outcomes including reducing the number of transfusions and patients diagnosed with HAA. Comparing average daily phlebotomy for the current practices and using the proposed medical device, there is a statistically reduction in average daily phlebotomy even with minimum tube draw volumes considered up to 2.5 mL. This shows that the proposed device would still provide significant reductions in adverse patient outcomes even if more conservative volumes were requested by test labs.

Further studies on the potential benefits of blood saving devices in healthcare should be conducted to determine the true benefits of the technology. Future studies should investigate the interaction between reducing testing frequency and the implementation of blood saving devices as well as evaluate the accuracy of the odds ratios reported in Bodley [12] by collecting rates of HAA, transfusion, and patient mortality as well as accurate blood draw volumes. Future studies could look more in depth at the benefits of blood saving technology by patient demographics such as location and age. Prototypes should be developed for blood saving devices to determine more accurately their capabilities and the potential benefits of the devices in reducing average daily phlebotomy, including by defining savings due to the capture and return of clearing volumes.

Study Limitations

This study is limited by the information available in the blood draw orders obtained from the local hospital system. No information was included on patient conditions or demographics. This includes whether or not patients required a transfusion, died in hospital care, or developed HAA. This also means that clearing volumes had to be omitted from analysis as there was no differentiation between patients who had and did not have an in-line device used.

This study heavily relies on the odds ratios reported in Bodley [12] for changes in patient risk per increases of 5 mL in average daily phlebotomy. As stated previously, comparison of the model developed using odds ratios reported in Bodley [12] differ from those reported in the literature and further study is required to determine the generalizability of the results of Bodley [12].

The results of this study are relegated to only theoretical impacts and no practical data is available regarding the performance of the proposed medical device. It is assumed that the proposed medical device can be feasibly designed and implemented for use with all patients to achieve the demonstrated blood savings. Accuracy of the model's results also rely on the assumption that hospital staff correctly follow manufacturer instructions for use of medical devices.

Conclusion

Diagnostic blood draws are a significant contributor to poorer patient outcomes such as the development of HAA, requiring a transfusion, and in-hospital mortality. A theoretical medical device was proposed and its effects on patients' average daily phlebotomy and risk of negative outcomes were modeled. The model showed that the proposed device can significantly reduce average daily phlebotomy even when considering minimum per tube draw volumes up to 2.5 mL. The proposed device is estimated to save up to 13 mL of blood per patient per day in the ICU. The proposed device is also estimated to reduce the costs of transfusions by a maximum of $346 per patient. While small volume tubes do show an improvement in risk compared to current practices, the proposed device shows an even greater reduction in risk. Future studies should investigate the accuracy of this model and explore designs for the theoretical medical device.

References

1. Bush VJ, Leonard L, Szamosi DI. Advancements in blood collection devices. Laboratory Medicine. 1998; 29(10): 616-622.
2. Villani R, Romano AD, Rinaldi R, Sangineto M, Santoliquido M, Cassano T, Serviddio G. Prevalence and risk factors for hospital-acquired anemia in internal medicine patients: Learning from the "less is more" perspective. Intern Emerg Med. 2023; 18(1): 177-183. https://doi.org/10.1007/s11739-022-03147-x PMID: 36346557.
3. Wu DW, Li YM, Wang F. How long can we store blood samples: A systematic review and meta-analysis. eBioMedicine. 2017; 24: 277-285. PMID: 28965875.
4. Lalthanthuami HT, Kumari MJ, Venkateswaran R, Lakshmi PR, Ramamoorthy L. Performance of 3 mL versus 5 mL discarded volume for blood sampling from central venous access device. J Lab Physicians. 2021; 13(2): 112-117. https://doi.org/10.1055/s-0041-1726669 PMID: 34483554.
5. Baron DM, Hochrieser H, Posch M, Metnitz B, Rhodes A, Moreno RP, Pearse RM, Metnitz P. Preoperative anaemia is associated with poor clinical outcome in non-cardiac surgery patients. British Journal of Anaesthesia. 2014; 113(3): 416-423. https://doi.org/10.1093/bja/aeu098.
6. Turner J, Parsi M, Badireddy M. Anemia. In StatPearls. StatPearls Publishing. [accessed November 2023]. www.ncbi.nlm.nih.gov/books/NBK499994/ PMID: 29763170.
7. Nguyen WB, Wyse JM, Drollinger SM, Cheng K. Anemia screening in naval aviation: Is hemoglobin a better indicator than hematocrit as the primary index? Military Medicine. 2020; 185(3-4): 461-467. https://doi.org/10.1093/milmed/usz243.
8. Badireddy M, Baradhi KM. Chronic anemia. In StatPearls. StatPearls Publishing. [accessed November 2023]. pubmed.ncbi.nlm.nih.gov/30521224 PMID: 30521224.
9. Salisbury AC, Reid KJ, Alexander KP, Masoudi FA, Lai SM, Chan PS, Bach RG, Wang TY, Spertus JA, Kosiborod M. Diagnostic blood loss from phlebotomy and hospital-acquired anemia during acute myocardial infarction. Arch Intern Med. 2011; 171(18): 1646-1653. https://doi.org/ 10.1001/archinternmed.2011.361.

10. Briggs EN, Hawkins DJ, Hodges AM, Monk AM. Small volume vacuum phlebotomy tubes: A controlled before-and-after study of a patient blood management initiative in an Australian adult intensive care unit. Crit Care Resusc. 2019; 21(4): 251-257. PMID: 31778631.

11. Siegal DM, Belley-Côté EP, Lee SG, Hill S, D'Aragon F, Zarychanski R, Rochwerg Bram, et al.. Small-volume blood collection tubes to reduce transfusions in intensive care. JAMA. 2023. https://doi.org/10.1001/jama.2023.20820.

12. Bodley T, Chan M, Levi O, Clarfield L, Yip D, Smith O, Friedrich JO, Hicks LK. Patient harm associated with serial phlebotomy and blood waste in the intensive care unit: A retrospective cohort study. PLoS One. 2021; 16(1): e0243782. https://doi.org/10.1371/journal.pone.0243782.

13. Szumilas M. Explaining Odds Ratios. J Can Acad Child Adolesc Psychiatry. 2010; 19(3): 227-229. PMID: 20842279.

14. Chornenki N, James T, Barty R, Liu Y, Rochwerg B, Heddle N, Siegal D. Blood loss from laboratory testing, anemia, and red blood cell transfusion in the intensive care unit: a retrospective study. Transfusion. 2020; 60(2): 256-261. https://doi.org/10.1111/trf.15649.

15. Garcia J, Xian J, Pedroza C, Salahuddin M, Mak G, Keene A, Cherian S, Young A, Vijhani P, Doshi P. Pediatric size phlebotomy tubes and transfusions in adult critically ill patients: a pilot randomized controlled trial. Pilot and Feasibility Studies. 2020; 6: 112. https://doi.org/10.1186/s40814-020-00657-3.

16. Salisbury AC, Reid KJ, Alexander KP, Masoudi FA, Lai SM, Chan PS, Bach RG, Wang TY, Spertus JA, Kosiborod M. Diagnostic blood loss from phlebotomy and hospital-acquired anemia during acute myocardial infarction. Arch Intern Med. 2011; 171(18): 1646-1653. https://doi.org/ 10.1001/archinternmed.2011.361.

Figure Captions

Figure 1. Distribution of blood draw orders across 30 ordering departments of a local hospital system for 433 patients.

Figure 2. Average daily phlebotomy per patient using current and controlled conditions. Current practice is assumed to draw a volume of blood equivalent to the capacity of the tube.

Figure 3. Average daily phlebotomy using the proposed device with minimum draw conditions. Minimum draw conditions imposed on a per-tube basis and average daily phlebotomy was calculated with the new tube volumes for each minimum draw condition.

Figure 4. Average adjusted odds ratios with standard error for a proposed blood drawing device with and without minimum draw conditions.

Figure 5. Average cost reductions of transfusions per patient for eight draw regimes. Cost reductions reported in USD per patient.

Figure 6. Average daily phlebotomy using the proposed medical device and pediatric sized tubes. Pediatric blood diagnostic tube sizes were assigned according to the type of tests that were performed: 0.5 mL for hematology, 0.6 mL for chemistries, 2.5 mL for coagulation tests, 1 mL for arterial blood gases, and 10 mL for blood cultures.

Tables

Table 1. Example of calculation for blood required for testing based on physician order.

Test	Test Volume (mL)	Add-Up Volume (mL)	System Calculation	Running Total (mL)
T1	10	2	System uses test volume	10
T2	4	0	RT* > Test Vol., add RT and add-up volume	10 + 0 = 10 10 > 4, keep 10
T3	3	2	RT > Test Vol., add RT and add-up volume	10 + 2 = 12 12 > 3, keep 12
T4	5	1	RT > Test Vol., add RT and add-up volume	12 + 1 = 13 13 > 5, keep 13

*RT – Running Total

Table 2. Summary of BDPD and average daily phlebotomy using current methods and with the proposed medical device.

	Current Practices	Proposed Device
Average (mL/day/patient)	22.88	9.96
Maximum (mL/day)	91.49	30.35
Minimum (mL/day)	1.10	0.48
Standard Deviation (mL/day)	11.54	4.60

Table 3. Summary of average daily phlebotomy using a proposed medical device with minimum draw conditions.

	0.5 mL Minimum	1 mL Minimum	1.5 mL Minimum	2 mL Minimum	2.5 mL Minimum	3 mL Minimum
Average (mL/day/patient)	10.62	11.69	13.99	16.49	18.95	21.71
Maximum (mL/day)	33.75	38.98	49.86	62.23	72.65	82.69
Minimum (mL/day)	0.58	0.68	0.78	0.80	0.95	1.10
Standard Deviation (mL/day)	5.00	5.58	6.75	8.07	9.33	10.65

Table 4. Average surplus in daily phlebotomy between current practices and controlled draw regimes with proposed medical device.

	Current Practice	0.5 mL Minimum	1 mL Minimum	1.5 mL Minimum	2 mL Minimum	2.5 mL Minimum	3 mL Minimum
Average (mL/day/patient)	12.93	0.66	1.73	4.03	6.54	8.99	11.76
Maximum (mL/day)	61.14	3.93	9.34	19.51	31.89	42.30	52.34
Minimum (mL/day)	0.62	0.00	0.00	0.30	0.32	0.47	0.62
Standard Deviation (mL/day)	7.47	0.57	1.38	2.69	4.13	5.37	6.55

Table 5. Dunn's test comparisons between average daily phlebotomy using current practices and the proposed medical device with minimum draw conditions.

	Z Score	Adjusted P-value	Significance ($p < 0.05$)
Proposed Device	20.298	3.773 x 10-90	Significant
0.5 mL Minimum	19.491	1.825 x 10-83	Significant
1.0 mL Minimum	17.756	1.076 x 10-69	Significant
1.5 mL Minimum	13.549	2.492 x 10-41	Significant
2.0 mL Minimum	8.951	7.039 x 10-19	Significant
2.5 mL Minimum	5.319	1.462 x 10-7	Significant
3.0 mL Minimum	1.821	7.382 x 10-2	Non- Significant

Table 6. Adjusted odds ratio for risk of developing HAA using current practices and the proposed medical device.

	Proposed Device	0.5 mL Minimum	1 mL Minimum	1.5 mL Minimum	2 mL Minimum	2.5 mL Minimum	3 mL Minimum
Average	1.593	1.550	1.486	1.363	1.245	1.143	1.040
Maximum	7.568	6.763	5.687	3.967	2.679	1.915	1.388
Minimum	1.021	1.017	1.014	1.011	1.010	1.005	1.000
Standard Deviation	0.585	0.514	0.422	0.282	0.171	0.098	0.046

Table 7. Adjusted odds ratio for risk of requiring a transfusion using current practices and the proposed medical device.

	Proposed Device	0.5 mL Minimum	1 mL Minimum	1.5 mL Minimum	2 mL Minimum	2.5 mL Minimum	3 mL Minimum
Average	1.552	1.513	1.454	1.340	1.231	1.135	1.038
Maximum	6.820	6.130	5.201	3.696	2.547	1.852	1.365
Minimum	1.020	1.017	1.013	1.010	1.009	1.005	1.000
Standard Deviation	0.526	0.464	0.383	0.259	0.159	0.092	0.043

Table 8. Adjusted odds ratio for risk of patient mortality using current practices and the proposed medical device.

	Proposed Device	0.5 mL Minimum	1 mL Minimum	1.5 mL Minimum	2 mL Minimum	2.5 mL Minimum	3 mL Minimum
Average	1.294	1.276	1.248	1.190	1.132	1.079	1.023
Maximum	3.207	3.006	2.721	2.211	1.764	1.454	1.208
Minimum	1.012	1.010	1.008	1.006	1.006	1.003	1.000
Standard Deviation	0.224	0.203	0.174	0.127	0.083	0.051	0.025

Table 9. Probability of requiring a transfusion based on adjusted odds ratios and estimated cost of transfusions per patient treated.

Draw Regime	Current Practices	Proposed Device	0.5 mL Minimum	1 mL Minimum	1.5 mL Minimum	2 mL Minimum	2.5 mL Minimum	3 mL Minimum
Average Probability of Transfusion	0.475	0.360	0.363	0.370	0.387	0.408	0.427	0.448
Estimated Cost for 3 units of PRBC per Patient Treated (USD/patient)	666,387	1,193	1,213	1,243	1,306	1,373	1,437	1,509
Average Cost Reduction per Patient (USD/patient)	--	346	326	296	233	166	102	30
Estimated Device Price (USD)	--	115	109	99	78	55	34	10

Table 10. Adjusted odds ratios for decreases in average daily phlebotomy between small volume tubes and current practices.

	OR HAA	OR Transfusion	OR Mortality
Average	1.30	1.28	1.16
Max	3.65	3.41	2.11
Min	1.02	1.02	1.01
Standard Deviation	0.23	0.21	0.11

Table 11. Calculated odds ratios for probability of events occurring in Garcia et al [15].

Condition	Number of Patients Using Pediatric Tubes (n=100)	Number of Patients Using Adult Tubes (n=100)	Odds Ratio
Transfusion (Hb < 7g/dL)	6	11	1.94
Mortality	9	10	1.12

Figures

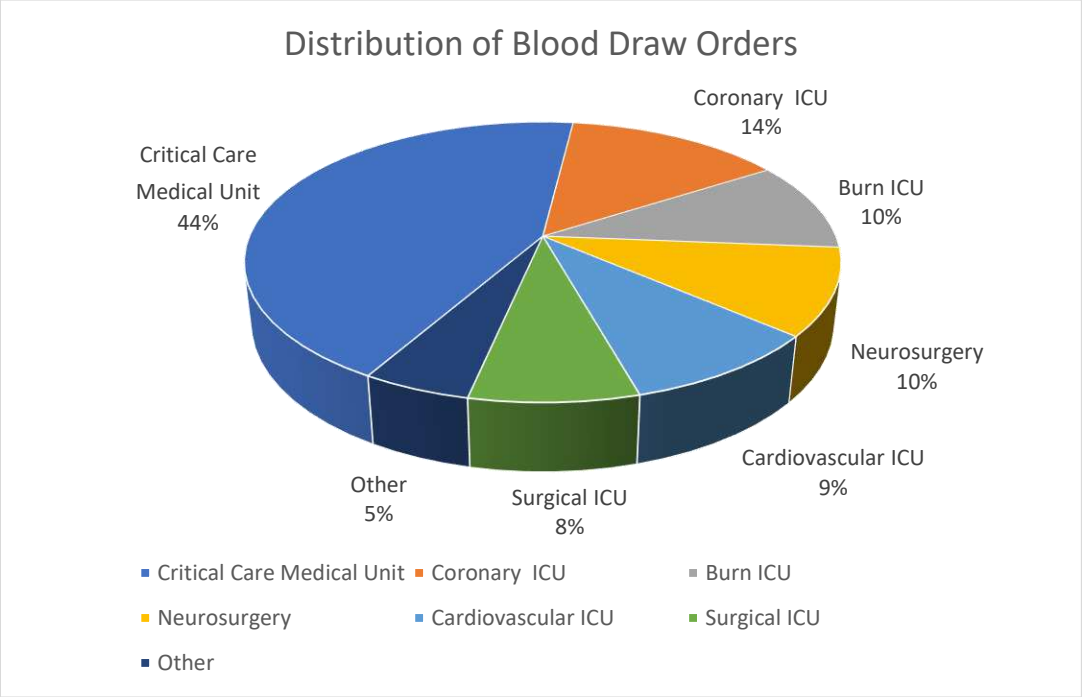

Figure 1. Distribution of blood draw orders across ordering departments of local hospital system for 433 patients.

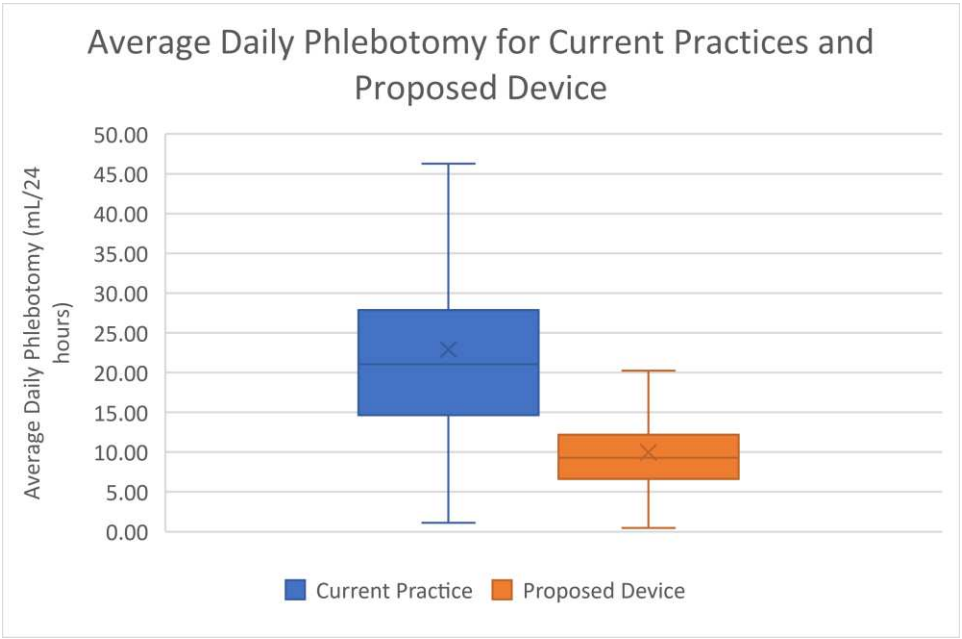

Figure 2. Average volume of blood drawn per patient per day using current and controlled conditions.

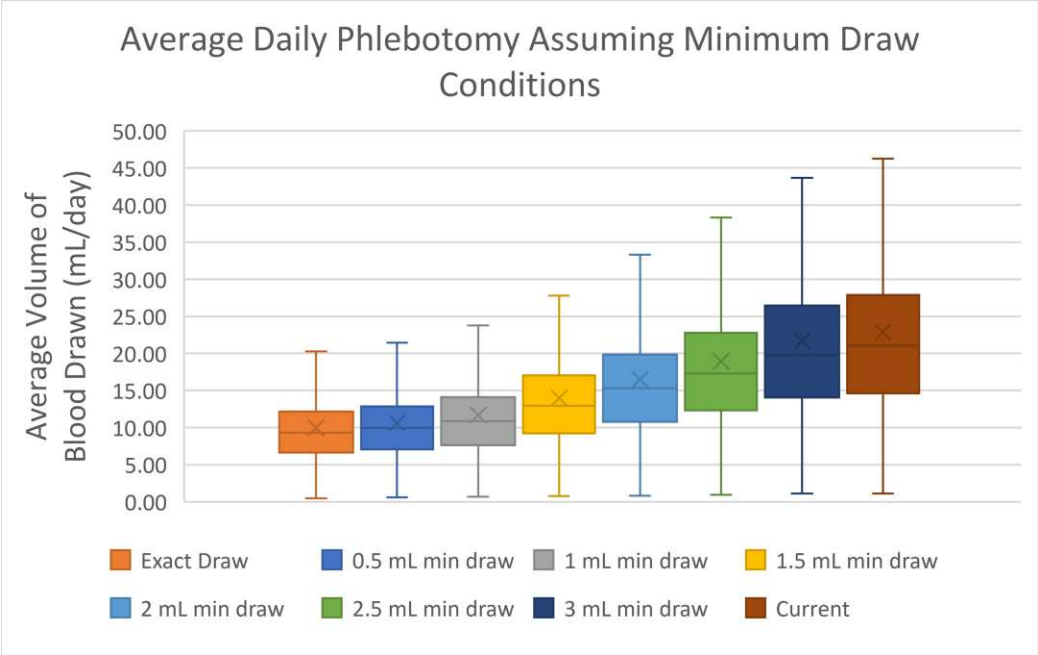

Figure 3. Average daily phlebotomy using the proposed device with minimum draw conditions.

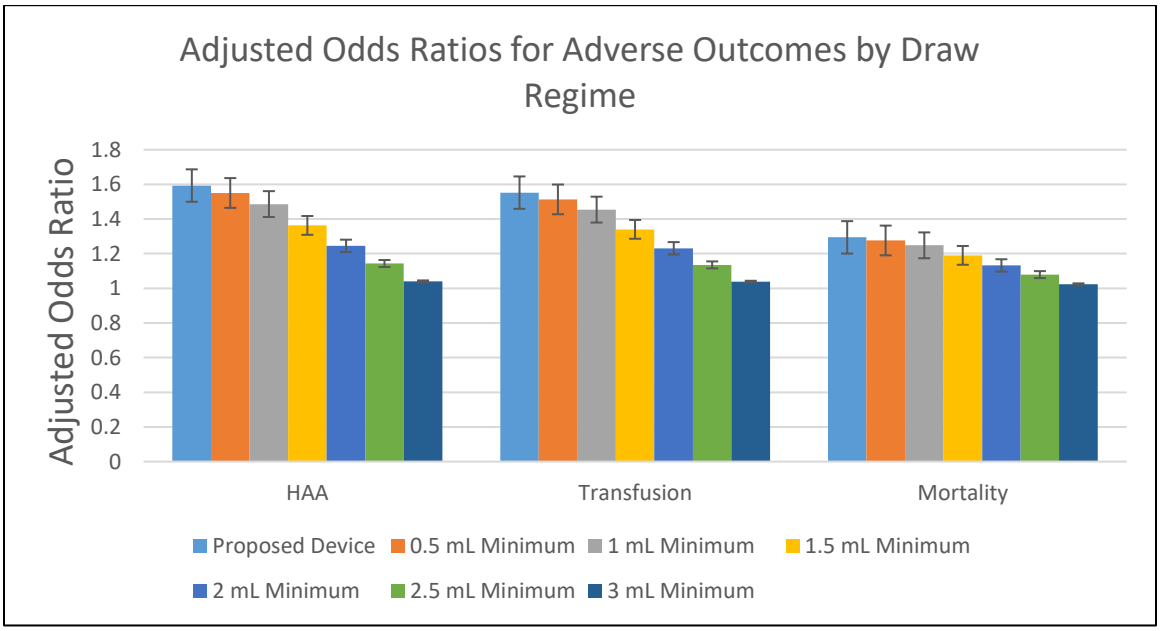

Figure 4. Average adjusted odds ratios with standard error for a proposed blood drawing device with and without minimum draw conditions.

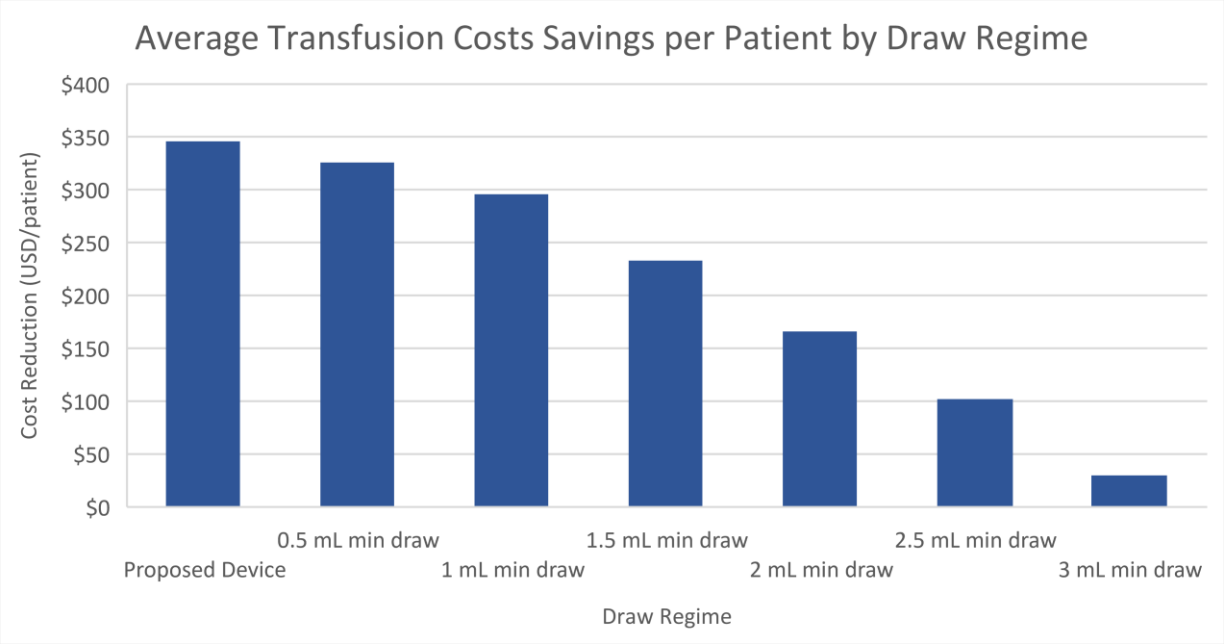

Figure 5. Average cost reductions of transfusions per patient for eight draw regimes.

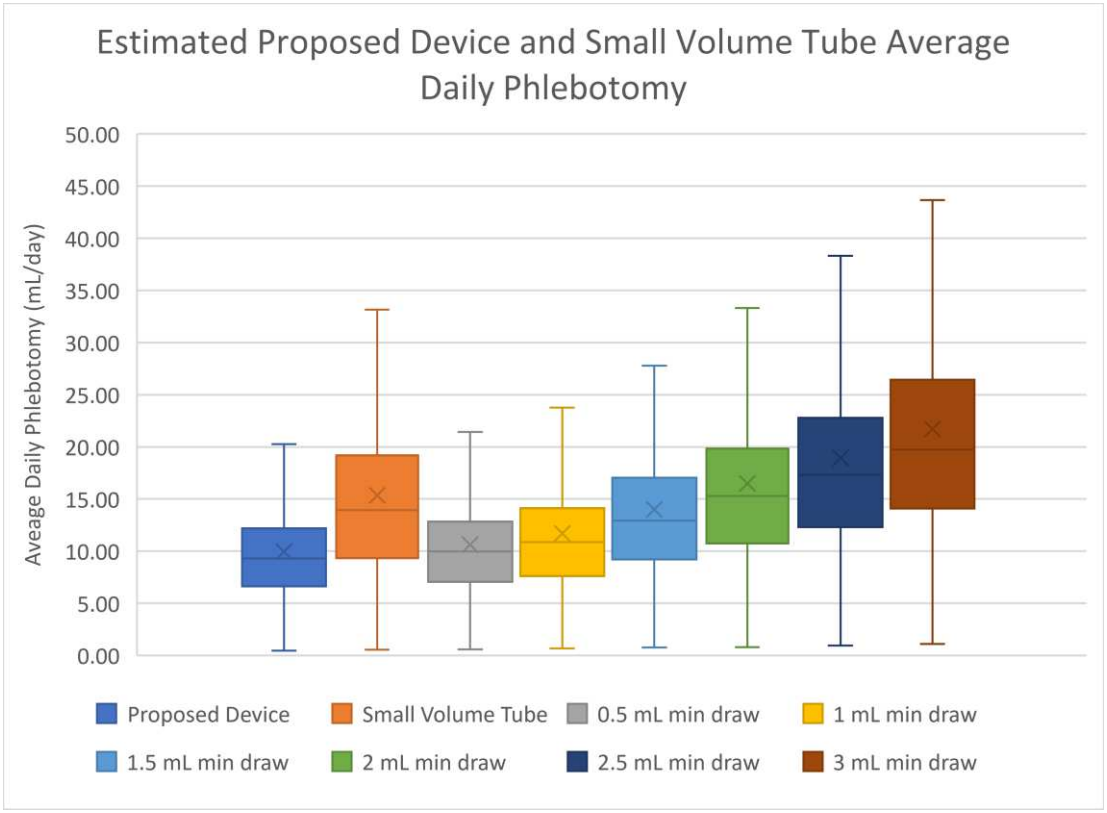

Figure 6. Average daily phlebotomy using the proposed medical device and pediatric sized tubes.

Chapter 3: Extended Review of Literature and Extended Methodology

Extended Review of Literature

A major contributor to high volumes of blood waste and development of HAA is the excessive drawing of blood for diagnostic testing. The available literature on iatrogenic anemia and blood drawn during hospital stays is inconsistent due to differences in hospital procedure, patient populations, and laboratory technician preferences. It has been reported that patients in the ICU lose on average between 25 to 70 mL of blood per patient per day through phlebotomy, with one study reporting a maximum of 377 mL drawn per day [16, 17, 18]. This volume of blood drawn can be excessive especially when considering that a healthy adult produces only 500 mL of blood per week and a critically ill patient less than that [17]. It is estimated that the volume of blood drawn for testing is between 8.5 and 12 times the volume required by analytic equipment for testing [5]. Frequent tests contribute to the large volume of blood wasted. On average, 2 mL of blood is discarded for every draw [5]. While frequency of testing varies between hospital and ordering physician, one study reported average draw rates of 4.1 daily blood draws for patients who received an RBC transfusion and 3.0 for patients who did not [18].

The excessive drawing of blood can have drastic consequences on patient outcomes including the development of anemia. Anemia disproportionately affects women and the elderly as well as infants and neonates. Generally, symptoms of anemia include fatigue, weakness, headaches, chest pains, palpitations, and pallor or jaundice [19]. Anemia reduces the oxygen carrying capacity of blood and can lead to tissue hypoxia if left untreated [7]. Patients who develop anemia prior to undergoing a surgical operation have higher in-hospital mortality rates than patients with normal preoperative Hb concentrations [9]. Anemia has also been linked to increased hospital length of stay and higher hospital resource consumption per patient. Patients who undergo surgery are even more at risk of developing HAA post-operation as many patients have depressed bone marrow, and RBC production, following an operation [9]. In pregnant women, premature labor and increased blood loss can occur as well as birth defects such as low birth weight or anemia in the baby [6].

To avoid the complications of anemia, patients require transfusions of PRBC. Standard practice in hospitals dictates that patients whose hemoglobin (Hb) concentration drops below 8.3 g/dL ± 1.3 g/dL receive a transfusion of PRBC, but this varies between hospitals and geographic regions [20]. A study of 7,273 patients found that upon admission to the ICU, patients had a median Hb of 9.7 g/dL and that 67% of patients had reductions in Hb concentration to 9.0 g/dL or less during their stay in the ICU [21]. Of the admitted patients, 47.5% received a median transfusion of 3 units of PRBC and a median of 8.4 g/dL concentration of Hb was observed upon discharge for all patients. It has also been reported that up to 85% of patients with an ICU stay longer than 7 days receive at least one unit of PRBC [17]. Blood transfusions can pose significant risks to patients. The most serious risks include administrative error such as the transfusion of incompatible blood types and subsequent allergic reaction, acute lung injury, bacterial contamination, and infection [22]. Transfusions also represent a significant financial burden to hospitals, patients, and insurance companies. Transfusions require up to six personnel to carry out the procedure including nurses, perfusionists, clinician doctors, co-doctors, and porters [23]. A 2010 study estimated cost of transfusions based on an activity-based costing model to cost hospitals on average $761 ± $294 per unit of red blood cells, approximately $1,080 ± $417 when adjusted for inflation using the Bureau of Labor Statistic's Consumer Price Index [24]. Transfusions can further strain a hospital's resources by increasing length of patient stay, postoperative complications, and the need for patient operations within 30-days of transfusion. It is estimated that each unit of PRBCs raises Hb concentration by 1 g/dL [25]. Depending on the severity of a patient's anemia, the cost of transfusion can vary greatly. Transfusions administered to resolve HAA are typically referred to as unnecessary transfusions. Blood used in transfusions is also an extremely valuable resource. Because hospitals rely on donors for collecting blood, scarcity of transfusable blood is a common issue.

Identifying rates of HAA is extremely difficult due to the variance in standard of care between healthcare systems. Independent studies have reported that HAA occurs in 20 to 67% of all ICU admissions [5, 16, 26]. All studies of HAA are retroactive and vary considerably in sample size making it difficult to accurately determine rates of HAA. Additionally, rates of HAA depends on the blood drawing practices of the hospital system

or the ordering physician leading to high variance both between hospitals and within hospital departments. Most studies identified do consistently use the World Health Organization's (WHO) definition of amenia as an Hb concentration less than 13 g/dL in men and 12 g/dL in women [27]. A more consistent way to report HAA rates is to look at individual patient risk based on the volume of blood drawn. A study which reviewed admission of 428 ICU admissions identified that for every 5 mL increase in average daily blood drawn, the odds ratio for Hb concentrations below 8.0 g/dL was 1.18, the odds ratio for needing an RBC transfusion was 1.17, and the odds ratio for mortality was 1.10 [17].

Much of the literature investigating reducing the volume of blood drawn has focused on implementation of administrative programs. Several studies have looked at the implementation of different systems to limit blood drawing including educating physicians, technicians, and phlebotomists, creating audit and feedback systems, implementing computerized order entry system changes, and restricting functions [28]. Professional organizations have also been focused on administrative controls. The Canadian Society of Internal Medicine, the Canadian Association of Pathologists, and Resident Doctors of Canada publicly support avoiding repeat testing when patients demonstrate clinical or laboratory stability [28]. The American Board of Internal Medicine also supports these recommendations. For the most part, there has been little innovation in the development of new medical devices to reduce the volume of blood drawn.

Few studies exist investigating the impact of medical devices on blood drawn. Those that have been conducted suffer from heterogeneity and bias which makes comparison of results difficult [29, 30]. The Safedraw [Merit Medical] and VAMP [Edwards Lifescience] are examples of the latest innovations in this area. Both devices are designed to reduce the volume of blood discarded at the bed side and provide a closed system for phlebotomy to reduce risk of air embolism and contamination. While these devices have shown benefit in eliminating blood discarded due to clearing volumes, they do not directly address the overdrawing of blood for testing without greatly complicating the blood draw process, which limits their use and overall impact on reducing excess blood drawn with evacuated tubes.

Researchers have begun to investigate evacuated Small Volume Tubes (SVT) and soft draw tubes to reduce the volume of blood drawn from ICU patients. SVTs are

evacuated tubes with smaller container volumes. Typically, SVTs are simply pediatric sized tubes used on adult patients. Soft draw tubes are evacuated tubes with reduced pressure vacuums designed to draw smaller volumes of blood without requiring different sized containers. One study reported that using small volume tubes reduced overall patient blood loss from phlebotomy per patient by 73% without interfering with testing [31]. Another study found that in a cohort of 318 patients, SVTs decreased fall in Hb concentration during short admissions without increasing error in sample analysis [32]. SVTs may be promising solutions to reducing daily blood phlebotomy; however, the use of SVTs may not be feasible for some hospitals where smaller tubes are not compatible with the available analytical equipment [33]. SVTs also do not address the blood waste resulting from discarding clearing volumes which may explain why some studies have found no significant improvements in PRBC transfusion rates or long term Hb concentrations [32, 34]. Soft draw tubes are similar to SVTs such that they fail to address clearing volume waste. Soft draw tubes do have the benefit over SVTs of being standard adult sized tubes that interface with modern lab equipment. The lower vacuum used in soft draw tubes also has the additional benefit of reducing hemolysis in collected samples [35].

Extended Methodology

Data was obtained from a local hospital system for 433 patients for analysis. The data includes a de-identified list of patients, physician-initiated blood draw orders for each patient, size of tube used for each blood draw, a list of unique identifiers for each tube, a list of tests run on each tube, the volume of blood required by the testing lab for a given test, and how many days each patient was in the hospital when a blood draw order was given. From this data, the average blood drawn per patient per day (BDPD) was calculated based on the ordering system used by the local hospital system assuming that full tube volumes are drawn.

The BDPD was evaluated as if a product was in use that allowed caregivers to draw an exact volume of blood. The average daily phlebotomy for each patient was calculated assuming a minimum required draw volume ranging from 0 mL per tube up to a minimum of 3 mL at 0.5 mL increments. Testing labs can be hesitant to order the minimal amount of blood for testing out of fear that an insufficient volume will be drawn for testing, requiring

phlebotomists to draw from patients again. By simulating varying minimum draw volumes, the impact of the proposed medical device can be evaluated if a buffer volume is included in the draw volume. Using published odds ratios for increased risk of developing HAA and requiring blood transfusions for increased volumes of blood drawn, the increases in risk to patient outcomes between the controlled and uncontrolled daily average phlebotomy volumes were compared. Using the average daily phlebotomy volumes calculated with and without the control device, the volume of unnecessary blood drawn for each patient was determined. Excess volumes of blood drawn was quantified and compared to results in Garcia et al [36] to determine similarity between the study's results and reported reductions in average daily phlebotomy due to the use of small volume tubes.

The local hospital system utilizes SoftLab, a laboratory information systems suite developed by SCC, for its blood sample ordering and analysis. SoftLab takes a physician's request for blood tests and calculates the volume of blood required for testing. Lab technicians assign two values to each blood test in the system; a test volume and an add-up volume. When an order for a set of blood tests for a patient is received, SoftLab considers the first test in the list for a given tube type and set this as the initial draw volume. SoftLab then compares the test volume to the next test with the same tube type. If the next test volume is greater than the initial volume, it is then set as the new calculated volume. If the next test has a test volume less than the initial volume, its add-up volume is added and the calculated volume is the running total for the draw order. The running total is then compared to all subsequent tests for the same tube type in a similar manner.

In the example shown in Table 1, a physician has ordered four tests to be completed, T1 – T4, all using the same tube type. The first test has a test volume of 10 mL which is set as the initial volume. The initial volume is added to the add up volume of T2 prior to comparing to the test volume. T2's test volume of 4 mL is less than the current running total of 10 mL meaning its test volume is not taken as the new running total. Adding the add up volume for T3 and comparing the running total to T3's test volume, 12 mL is greater than 3 mL, so the test volume is not taken as the new running total. The add up volume for T4 is now added to the running total and compared to T4's test volume. Again, the running total of 13 mL is greater than the test volume of 5 mL and the test volume is not taken as

the new running total. This means that a final volume of 13 mL is required to complete the suite of tests in this example.

Table 1. Example of calculation for blood required for testing based on physician order.

Test	Test Volume (mL)	Add-Up Volume (mL)	System Calculation	Running Total (mL)
T1	10	2	System uses test volume	10
T2	4	0	RT* > Test Vol., add RT and add-up volume	10 + 0 = 10 10 > 4, keep 10
T3	3	2	RT > Test Vol., add RT and add-up volume	10 + 2 = 12 12 > 3, keep 12
T4	5	1	RT > Test Vol., add RT and add-up volume	12 + 1 = 13 13 > 5, keep 13

*RT – Running Total

From the calculation of the running total blood required for an order, the minimum required blood volume for each tube can be calculated. It was assumed that the minimum required volume is the actual volume drawn. Once the minimum required blood volume for each tube is determined, the average volume drawn per day for a given patient can be determined by dividing the drawn volume by the number of days spent in the hospital. This can then be expanded to determine the average daily draw per patient by dividing the average volume of blood drawn per day for each patient by the total number of patients in the dataset as shown in Equation 1.

$$BDPD = \frac{\sum_{i=1}^{n} V_{Daily,i}}{n} \quad (1)$$

Where $BDPD$ is the average daily blood draw per patient, $V_{Daily,i}$ is the average daily draw volume for a given patient i, and n is the number of patients.

Increases in odds ratios (OR) for developing HAA, mortality, and requiring blood transfusions based on increased volumes of blood draw are discussed in the literature [18]. An odds ratio is a measure of association between the odds of an event occurring in a group that is and a group that is not exposed to a treatment or event [37]. The odds ratio is related

to logistic regression. For a single, continuous predictor variable, the logit for the probability of an event occurring is given in Equation 2.

$$\log\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 x \tag{2}$$

Where p is the probability of an event occurring for a given predictor variable x, β_0 is the model intercept, and β_1 is the difference in the log odds per unit of x. The odds ratio equation is given in Equation 3.

$$\mathrm{OR} = \frac{Odds_R}{Odds_T} \tag{3}$$

Where OR is the odds ratio between the odds of an event occurring in a reference group, $Odds_R$, and treatment group, $Odds_T$. Taking the natural log of both sides of Equation 3 gives

$$\log(\mathrm{OR}) = \log\left(\frac{Odds_R}{Odds_T}\right)$$

According to the properties of the natural log, it is known that this is equivalent to,

$$\log(\mathrm{OR}) = \log(Odds_R) - \log(Odds_T)$$

Using the definition that β_1 is the difference in the log odds per unit of x,

$$\log(\mathrm{OR}) = \beta_1$$

This means that for an increase in the predictor variable x, the adjusted odds ratio is given in Equation 4.

$$\mathrm{OR_{adj}} = e^{\beta_1 x} = e^{\log(\mathrm{OR})x} = \mathrm{OR}^{\mathrm{x}} \tag{4}$$

Where $\mathrm{OR_{adj}}$ is the increase in odds of an event occurring between a reference and treatment group for an increase in the predictor variable x. Using estimates of the OR for the occurrence of HAA, PRBC transfusion, and mortality from the literature per 5 mL of daily average phlebotomy, the increase in odds of a patient developing HAA, requiring a transfusion, or mortality while in the hospital can be estimated.

Equation 4 was compared to odds ratios calculations available in the literature. Bodley [18] reports that the odds ratio for nadir Hb < 8.0 g/dL per 1 mL increase in daily average phlebotomy is 1.033. For an increased average daily phlebotomy of 5 mL, the adjusted odds ratio is calculated as:

$$\mathrm{OR_{adj}} = 1.033^5 = 1.18$$

Bodley [18] reports the odds ratio for increased daily phlebotomy of 5 mL as 1.18. This example shows that Equation 4 for calculations of adjusted odds ratios for increased daily phlebotomy are in agreement with methods found in the literature.

The odds of an event occurring can be defined as shown in Equation 5.

$$Odds_n = \frac{p}{1-p} \tag{5}$$

where p is the probability of an event occurring in some group n. The odds equation in Equation 5 can be considered with the ratio of odds as shown in Equation 3. When comparing the odds of an event occurring in a reference and a treatment group, the probability of the event occurring in the treatment group can be defined as shown in Equation 6:

$$p_{Treatment} = \frac{p_R}{\mathrm{OR}(1-p_R)+p_R} \tag{6}$$

where $p_{Treatment}$ is the probability of an event occurring in a treatment group, $p_{Reference}$ is the probability of an event occurring in the reference group with no controls, and OR is the ratio between the two groups' odds of the event occurring. Using the expanded relationship between odds, the odds ratio, and probability shown in Equation 6 and the known probability of patients requiring transfusions without interventions, the likelihood of patients requiring a transfusion when medical devices are introduced into the phlebotomy process was determined.

Appendix A: Code Used for Data Analysis

A1. Program to Calculate Average Daily Phlebotomy, MATLAB Code

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
% Title: Data Extraction and Analysis, Blood Draw Orders
% Filename: thesis_code.m
% Author: Sam Menzie
% Date: 12/22/2023
% Description:
% This sketch takes patient blood draw order data from an Excel file,
% identifies the number of patients and individual tubes used, assigns
% indexes, and calculates the volume of blood drawn from patients. The
% sketch then applies conditions that would be present if a proposed
% medical device were used to limit the blood drawn to only what is
% required for the specific tests run on the blood sample.
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

clear all; close all;

%% Loading Patient Data

patient_data = readtable('UM_BLOOD_DRAW_500_ICU','Range','A1:S750325');
%
n = height(patient_data(:,1));
%
patient_id = table2array(patient_data(:,1));
%visit_id = table2array(patient_data(:,2));
%order_id = table2array(patient_data(:,3));
draw_days = table2array(patient_data(:,4));
%tube_barcode = table2array(patient_data(:,5));
tube_id = table2array(patient_data(:,6));
tube_type = table2array(patient_data(:,7));
tube_cap = table2array(patient_data(:,8)) ./ 100; % Tube volume in mL
%min_tube_vol = table2array(patient_data(:,9)) ./ 100;
%group_test_id = table2array(patient_data(:,12));
test_id = table2array(patient_data(:,14));
%test_name = table2array(patient_data(:,15));
draw_vol = table2array(patient_data(:,16)) ./ 100;
%cell_draw_vol = array2table(table2array(patient_data(:,16)) ./ 100);
add_vol = table2array(patient_data(:,17)) ./ 100;
%cell_add_vol = array2table(table2array(patient_data(:,17)) ./ 100);
%min_test_vol = array2table(table2array(patient_data(:,18)) ./ 100);

% Identify List of Unique Patients and Create Patient Structure
[~,y_patid] = unique(patient_id(:,1));
J = patient_id(y_patid,1);
JL = length(J);

clear y_patid;

patients(JL) = struct();

for i=1:JL

   patients(i).name = string(J(i,1));

end

testvect = zeros(JL,15345);
sparsevect = zeros(1, 15345);
```

```
k = 1;

for z = 1:1:JL
    for i = 1:1:n

        if patient_id{i,1} == patients(z).name

            testvect(z,k) = i+1;

            k = k + 1;
        end
    end

k = 1;
end

for z = 1:1:JL
    sparsevect = sparse(testvect(z,:));
    patients(z).index = nonzeros(sparsevect);

    clear sparsevect;
end

clear testvect;

%% Determine Patient Length of Stay

for i = 1:1:JL

    temp_day = 0;

    for k = 1:1:length(patients(i).index)
        if (draw_days(patients(i).index(k)-1,1)+1) > temp_day

            temp_day = draw_days(patients(i).index(k),1)+1;

        end
    end

    patients(i).max_day = temp_day;

end

% Identify List of Unique Tubes
[~,x_idx] = unique(tube_id(:,1));
M = tube_id(x_idx,1);
L = length(M);

clear i_dx;

tubes(L) = struct();


%% Assign Tubes Structure and Calculate Tube Volumes

for i=1:1:L

   tubes(i).name = string(M(i,1));

end
```

```
tubevect = zeros(L,96);
sparsevect = zeros(1, 96);
k = 1;

for z = 1:1:L
    for i = 1:1:n

        if string(tube_id(i,1)) == tubes(z).name

            tubevect(z,k) = i+1;

            k = k + 1;
        end
    end

    k = 1;

end

for z = 1:1:L

    sparsevect = sparse(tubevect(z,:));
    tubes(z).index = nonzeros(sparsevect);
    clear sparsevect;
end

clear tubevect;

where_max = zeros(L,1);

for i = 1:1:L   % Calculate the current practice test vol

        tubes(i).current_volume = tube_cap(tubes(i).index(1)-1,1);

end

for i = 1:1:L   % Calculate the initial test volume

    temp_vol = 0;
    temp_add = 0;

    for k = 1:1:length(tubes(i).index)
        if draw_vol(tubes(i).index(k)-1,1) > temp_vol

            where_max(i,1) = k;
            temp_vol = draw_vol(tubes(i).index(k)-1,1);
            temp_add = add_vol(tubes(i).index(k)-1);

        end

        if draw_vol(tubes(i).index(k)-1,1) == temp_vol & add_vol(tubes(i).index(k)-1) >
temp_add % Adjusts max volume test so that the test with the largest add up volume and
draw vol is initial value

            where_max(i,1) = k;
            temp_vol = draw_vol(tubes(i).index(k)-1,1);
            temp_add = add_vol(tubes(i).index(k)-1);

        end

    end
```

```
    tubes(i).initial_volume = temp_vol;
end

for i = 1:1:L   % Calculate the total test volume for exact draw NO MIN


    addup_vol = 0;

    for k = 1:1:length(tubes(i).index)
        if k ~= where_max(i,1)

            addup_vol = add_vol(tubes(i).index(k)-1) + addup_vol;

        end
    end

    tubes(i).exactdraw_vol = tubes(i).initial_volume + addup_vol;

end


%% Compare to minimum draw requirements

for i = 1:1:L   % Calculate the total test volume for 0.5 mL min

    if tubes(i).exactdraw_vol < 0.5

        tubes(i).exactdraw_05min = 0.5;

    else

        tubes(i).exactdraw_05min = tubes(i).exactdraw_vol;

    end
  % Calculate the total test volume for 1 mL min

    if tubes(i).exactdraw_vol < 1

        tubes(i).exactdraw_1min = 1;

    else

        tubes(i).exactdraw_1min = tubes(i).exactdraw_vol;

    end

  % Calculate the total test volume for 1.5 mL min

    if tubes(i).exactdraw_vol < 1.5

        tubes(i).exactdraw_15min = 1.5;

    else

        tubes(i).exactdraw_15min = tubes(i).exactdraw_vol;

    end

  % Calculate the total test volume for 2 mL min
```

```
    if tubes(i).exactdraw_vol < 2 & tubes(i).current_volume >= 2

        tubes(i).exactdraw_2min = 2;

    else

        tubes(i).exactdraw_2min = tubes(i).exactdraw_vol;

    end

    if tubes(i).exactdraw_vol < 2 & tubes(i).current_volume < 2

        tubes(i).exactdraw_2min = tubes(i).current_volume;

    end

  % Calculate the total test volume for 2.5 mL min

    if tubes(i).exactdraw_vol < 2.5 & tubes(i).current_volume >= 2.5

        tubes(i).exactdraw_25min = 2.5;

    else

        tubes(i).exactdraw_25min = tubes(i).exactdraw_vol;

    end

    if tubes(i).exactdraw_vol < 2.5 & tubes(i).current_volume < 2.5

        tubes(i).exactdraw_25min = tubes(i).current_volume;


    end

   % Calculate the total test volume for 3 mL min

    if tubes(i).exactdraw_vol < 3 & tubes(i).current_volume >= 3

        tubes(i).exactdraw_3min = 3;

    else

        tubes(i).exactdraw_3min = tubes(i).exactdraw_vol;

    end

    if tubes(i).exactdraw_vol < 3 & tubes(i).current_volume < 3

        tubes(i).exactdraw_3min = tubes(i).current_volume;

    end
end

for i = 1:1:L   % Remove out of scope containers & containers with test volumes >
container volume

    if tube_cap(tubes(i).index(1)-1,1) >= 10

        tubes(i).exactdraw_vol = 0;
        tubes(i).current_volume = 0;
```

```
        tubes(i).exactdraw_3min = 0;
        tubes(i).exactdraw_25min =0;
        tubes(i).exactdraw_2min =0;
        tubes(i).exactdraw_15min =0;
        tubes(i).exactdraw_1min =0;
        tubes(i).exactdraw_05min =0;

    end

    if tubes(i).exactdraw_vol > tube_cap(tubes(i).index(1)-1,1)

        tubes(i).exactdraw_vol = 0;
        tubes(i).current_volume = 0;
        tubes(i).exactdraw_3min = 0;
        tubes(i).exactdraw_25min =0;
        tubes(i).exactdraw_2min =0;
        tubes(i).exactdraw_15min =0;
        tubes(i).exactdraw_1min =0;
        tubes(i).exactdraw_05min =0;

    end

end

%% Calculate Average Patient Draw per Day

for i = 1:1:JL

    patients(i).tubes_used = string(unique(tube_id(patients(i).index-1, 1)));

end

temp_total = zeros(8,JL);

for i = 1:1:JL

    initial_total = zeros(8,JL);

    for k = 1:1:L
        for z = 1:1:length(patients(i).tubes_used)
            if patients(i).tubes_used(z) == tubes(k).name

                initial_total(1,i) = tubes(k).current_volume + initial_total(1,i);
                initial_total(2,i) = tubes(k).exactdraw_vol + initial_total(2,i);
                initial_total(3,i) = tubes(k).exactdraw_05min + initial_total(3,i);
                initial_total(4,i) = tubes(k).exactdraw_1min + initial_total(4,i);
                initial_total(5,i) = tubes(k).exactdraw_15min + initial_total(5,i);
                initial_total(6,i) = tubes(k).exactdraw_2min + initial_total(6,i);
                initial_total(7,i) = tubes(k).exactdraw_25min + initial_total(7,i);
                initial_total(8,i) = tubes(k).exactdraw_3min + initial_total(8,i);

            end
        end
    end

                temp_total(1,i) = initial_total(1,i);
                temp_total(2,i) = initial_total(2,i);
                temp_total(3,i) = initial_total(3,i);
                temp_total(4,i) = initial_total(4,i);
                temp_total(5,i) = initial_total(5,i);
                temp_total(6,i) = initial_total(6,i);
```

```
                temp_total(7,i) = initial_total(7,i);
                temp_total(8,i) = initial_total(8,i);
end

for i = 1:1:JL

    patients(i).current_ave_pd = temp_total(1,i) / patients(i).max_day;

    patients(i).exdr_ave_pd = temp_total(2,i) / patients(i).max_day;

    patients(i).exdr_05min_ave_pd = temp_total(3,i) / patients(i).max_day;

    patients(i).exdr_1min_ave_pd = temp_total(4,i) / patients(i).max_day;

    patients(i).exdr_15min_ave_pd = temp_total(5,i) / patients(i).max_day;

    patients(i).exdr_2min_ave_pd = temp_total(6,i) / patients(i).max_day;

    patients(i).exdr_25min_ave_pd = temp_total(7,i) / patients(i).max_day;

    patients(i).exdr_3min_ave_pd = temp_total(8,i) / patients(i).max_day;

end
```

A2. Program to Categorize Blood Tests and Calculate Average Daily Phlebotomy for Small Volume Tube Simulation, MATLAB Code

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
% Title: Small Volume Tubes and Study Comparison, Blood Draw Orders
% Filename: thesis_code.m
% Author: Sam Menzie
% Date: 2/1/2024
% Description: This sketch takes blood draw data sorted in another sketch
% and applies volumes of blood per tube for typically drawn volumes
% reported in the literature.
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

clear all; close all;

%% Loading Patient Data

patient_data = readtable('UM_BLOOD_DRAW_500_ICU','Range','A1:S750325');

n = height(patient_data(:,1));

patient_id = table2array(patient_data(:,1));
%visit_id = table2array(patient_data(:,2));
%order_id = table2array(patient_data(:,3));
%draw_days = table2array(patient_data(:,4));
%tube_barcode = table2array(patient_data(:,5));
tube_id = table2array(patient_data(:,6));
tube_type = table2array(patient_data(:,7));
tube_cap = table2array(patient_data(:,8)) ./ 100; % Tube volume in mL
%min_tube_vol = table2array(patient_data(:,9)) ./ 100;
%group_test_id = table2array(patient_data(:,12));
group_test_name = table2array(patient_data(:,13));
%test_id = table2array(patient_data(:,14));
test_name = table2array(patient_data(:,15));
%draw_vol = table2array(patient_data(:,16)) ./ 100;
%cell_draw_vol = array2table(table2array(patient_data(:,16)) ./ 100);
%add_vol = table2array(patient_data(:,17)) ./ 100;
%cell_add_vol = array2table(table2array(patient_data(:,17)) ./ 100);
%min_test_vol = array2table(table2array(patient_data(:,18)) ./ 100);

% Identify List of Unique Patients and Create Patient Structure
[~,y_patid] = unique(patient_id(:,1));
J = patient_id(y_patid,1);
JL = length(J);

clear y_patid;

% Identify List of Unique Tubes
[~,x_idx] = unique(tube_id(:,1));
M = tube_id(x_idx,1);
L = length(M);

clear i_dx;

load("patient_struct8.mat");
load("tubes_struct9.mat");


for k = 1:1:L   % Calculate the current practice test vol for categorized tests
    for i = 1:1:n
```

```
      if string(tube_id(i,1)) == tubes(k).name % if the given tube appears in this row
of data

            % ABG
            if strcmp(group_test_name(i,1), 'Blood Gas, Mott, Arterial') || ...
               strcmp(group_test_name(i,1), 'Blood Gas, Mott, Venous') || ...
               strcmp(group_test_name(i,1), 'Blood Gas, UH, Arterial') || ...
               strcmp(group_test_name(i,1), 'Blood Gas, UH, Venous') || ...
               strcmp(group_test_name(i,1), 'Core Lab,Gas Venous BG') || ...
               strcmp(group_test_name(i,1), 'CRRT Circut Ionized Ca, UH') || ...
               strcmp(group_test_name(i,1), 'ER Gas Lytes, Arterial BG') || ...
               strcmp(group_test_name(i,1), 'ER Gas Lytes, Venous BG') || ...
               strcmp(group_test_name(i,1), 'ER Oximetry, Venous') || ...
               strcmp(group_test_name(i,1), 'O2 Monitor Calibration, Venous, UH')

               tubes(k).category_volume = 2;
               tubes(k).SVT = 1;

            % Blood Cultures
            if strcmp(group_test_name(i,1), 'Type and Screen') || ...
                  strcmp(group_test_name(i,1), 'Type and Screen.')

               tubes(k).category_volume = 0;
               tubes(k).SVT = 0;

            % Chemistry / Misc
            elseif strcmp(group_test_name(i,1), '11-Deoxycortisol, Serum') || ...
                  strcmp(group_test_name(i,1), 'Acute Hepatitis Panel') || ...
                  strcmp(group_test_name(i,1), 'Adenovirus PCR') || ...
                  strcmp(group_test_name(i,1), 'Adenovirus qPCR, Plasma') || ...
                  strcmp(group_test_name(i,1), 'Alpha-1-Antitrypsin-CRP') || ...
                  strcmp(group_test_name(i,1), 'ANA Screening Algorithm') || ...
                  strcmp(group_test_name(i,1), 'ANCA (Neutrophil Cytoplasmic Ab) Panel
Incl AntiMPO and PR3') || ...
                  strcmp(group_test_name(i,1), 'Aspergillus Ag, S') || ...
                  strcmp(group_test_name(i,1), 'Aspergillus Galactomannan, BAL') ||
...
                  strcmp(group_test_name(i,1), 'Bartonella PCR, B') || ...
                  strcmp(group_test_name(i,1), 'Basic Metabolic Panel') || ...
                  strcmp(group_test_name(i,1), 'Beta-2 Glycoprotein 1') || ...
                  strcmp(group_test_name(i,1), 'Bilirubin, Fractions') || ...
                  strcmp(group_test_name(i,1), 'Body Fluid Count and Differential') ||
...
                  strcmp(group_test_name(i,1), 'Borrelia Scr (Lyme)') || ...
                  strcmp(group_test_name(i,1), 'Broad-Range PCR') || ...
                  strcmp(group_test_name(i,1), 'Cardiolipin Antibody') || ...
                  strcmp(group_test_name(i,1), 'Celiac Disease Dx Algorithm') || ...
                  strcmp(group_test_name(i,1), 'Celiac Dx, IgA') || ...
                  strcmp(group_test_name(i,1), 'Cerebrospinal Fluid Count and
Differential') || ...
                  strcmp(group_test_name(i,1), 'Cholesterol, Fluid') || ...
                  strcmp(group_test_name(i,1), 'CMV qPCR, CSF') || ...
                  strcmp(group_test_name(i,1), 'Comp. Metabolic Panel') || ...
                  strcmp(group_test_name(i,1), 'Copeptin proAVP, Plasma') || ...
                  strcmp(group_test_name(i,1), 'Coxiella burnetii (Q fever) PCR, B')
|| ...
                  strcmp(group_test_name(i,1), 'Cryoglobulin Evaluation') || ...
                  strcmp(group_test_name(i,1), 'Cytomegalovirus (CMV) IgG, Qual') ||
...
                  strcmp(group_test_name(i,1), 'Cytomegalovirus (CMV) IgM, Qual') ||
...
```

```
                    strcmp(group_test_name(i,1), 'D. Assoc OTHER (DIS)') || ...
                    strcmp(group_test_name(i,1), 'DAT Monospecific') || ...
                    strcmp(group_test_name(i,1), 'Diphtheria/Tetanus Ab Panel, S') ||
...
                    strcmp(group_test_name(i,1), 'Drug Screen, Serum') || ...
                    strcmp(group_test_name(i,1), 'EBV Panel') || ...
                    strcmp(group_test_name(i,1), 'EBV qPCR (Whole blood)') || ...
                    strcmp(group_test_name(i,1), 'ENA 10 Antibody Panel') || ...
                    strcmp(group_test_name(i,1), 'Enceph, Autoimm/Paraneo, CSF') || ...
                    strcmp(group_test_name(i,1), 'Estimated Glomerular Filtration Rate')
|| ...
                    strcmp(group_test_name(i,1), 'Fluids Cytology') || ...
                    strcmp(group_test_name(i,1), 'Free Light Chains, Serum') || ...
                    strcmp(group_test_name(i,1), 'Fungitell with Reflex to Titer (BAL)')
|| ...
                    strcmp(group_test_name(i,1), 'Fungitell with Reflex to Titer
(serum)') || ...
                    strcmp(group_test_name(i,1), 'Glucose, Fluid') || ...
                    strcmp(group_test_name(i,1), 'H. pylori C Urea Breath Test') || ...
                    strcmp(group_test_name(i,1), 'Hantavirus Antibody (IgG, IgM)') ||
...
                    strcmp(group_test_name(i,1), 'Helicobacter pylori IgG, Qualitative')
|| ...
                    strcmp(group_test_name(i,1), 'Hemoglobin Electrophoresis') || ...
                    strcmp(group_test_name(i,1), 'Hep A Ab (IgG + IgM)') || ...
                    strcmp(group_test_name(i,1), 'Hep B Core Ab (IgG + IgM)') || ...
                    strcmp(group_test_name(i,1), 'Hepatic Function Panel') || ...
                    strcmp(group_test_name(i,1), 'Hepatitis A IgM Ab') || ...
                    strcmp(group_test_name(i,1), 'Hepatitis B Core IgM Ab') || ...
                    strcmp(group_test_name(i,1), 'Hepatitis B Surface Ab') || ...
                    strcmp(group_test_name(i,1), 'Hepatitis B Surface Ag') || ...
                    strcmp(group_test_name(i,1), 'Hepatitis C Antibody') || ...
                    strcmp(group_test_name(i,1), 'HHV8 qPCR (CSF) 8000') || ...
                    strcmp(group_test_name(i,1), 'HHV8 qPCR (whole blood) 8000') || ...
                    strcmp(group_test_name(i,1), 'HIV Antigen Antibody') || ...
                    strcmp(group_test_name(i,1), 'HSV 1 and 2 IgG Antibodies') || ...
                    strcmp(group_test_name(i,1), 'HSV 1 and 2 qPCR, Plasma') || ...
                    strcmp(group_test_name(i,1), 'IgG / IgM Titer') || ...
                    strcmp(group_test_name(i,1), 'Immunoglobulins IGG/A/M') || ...
                    strcmp(group_test_name(i,1), 'Lacosamide, S') || ...
                    strcmp(group_test_name(i,1), 'LDH, Fluid') || ...
                    strcmp(group_test_name(i,1), 'Leptin Level') || ...
                    strcmp(group_test_name(i,1), 'Leptospira, IgM, Serum') || ...
                    strcmp(group_test_name(i,1), 'Lipase, Fluid') || ...
                    strcmp(group_test_name(i,1), 'Lipid Panel') || ...
                    strcmp(group_test_name(i,1), 'Manganese, Serum') || ...
                    strcmp(group_test_name(i,1), 'Miscellaneous Mayo, Genetics') || ...
                    strcmp(group_test_name(i,1), 'Monoclonal Gammopathy') || ...
                    strcmp(group_test_name(i,1), 'Mumps IgG Antibody') || ...
                    strcmp(group_test_name(i,1), 'MUMPS PCR') || ...
                    strcmp(group_test_name(i,1), 'MVista Blastomyces Ag, Serum') || ...
                    strcmp(group_test_name(i,1), 'MVista Coccidioides Ag, U') || ...
                    strcmp(group_test_name(i,1), 'MVista Histoplasma Ag, S') || ...
                    strcmp(group_test_name(i,1), 'Myeloperoxidase Antibody') || ...
                    strcmp(group_test_name(i,1), 'NAB Titer/Pattern') || ...
                    strcmp(group_test_name(i,1), 'NK Function') || ...
                    strcmp(group_test_name(i,1), 'NT-ProBNP, Fluid') || ...
                    strcmp(group_test_name(i,1), 'Oligoclonal Banding') || ...
                    strcmp(group_test_name(i,1), 'Parathyroid Hormone, Intact') || ...
                    strcmp(group_test_name(i,1), 'Phospholipid Ab IgA, S') || ...
                    strcmp(group_test_name(i,1), 'PNH, PI-Linked AG, Blood') || ...
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                    strcmp(group_test_name(i,1), 'Posaconazole Level') || ...
                    strcmp(group_test_name(i,1), 'Protein Electrophor., Ser') || ...
                    strcmp(group_test_name(i,1), 'Protein, Fluid') || ...
                    strcmp(group_test_name(i,1), 'Proteinase 3 Ab, Serum') || ...
                    strcmp(group_test_name(i,1), 'Quantiferon TB') || ...
                    strcmp(group_test_name(i,1), 'Renal Panel') || ...
                    strcmp(group_test_name(i,1), 'Rubella IgG Antibody') || ...
                    strcmp(group_test_name(i,1), 'Sendout, Generic') || ...
                    strcmp(group_test_name(i,1), 'Serotonin Release Assay, UFH, MS, S')
|| ...
                    strcmp(group_test_name(i,1), 'Sodium, Fluid') || ...
                    strcmp(group_test_name(i,1), 'Soluble IL-2R') || ...
                    strcmp(group_test_name(i,1), 'Soluble Transferrin Receptor (STR)')
|| ...
                    strcmp(group_test_name(i,1), 'Thiamin (Vitamin B1), WB') || ...
                    strcmp(group_test_name(i,1), 'Tick-Borne DNA Panel, B') || ...
                    strcmp(group_test_name(i,1), 'Total Iron Binding Panel') || ...
                    strcmp(group_test_name(i,1), 'Toxoplasma IgG, Qual') || ...
                    strcmp(group_test_name(i,1), 'Toxoplasma IgM Ab, Qual') || ...
                    strcmp(group_test_name(i,1), 'Toxoplasma qPCR, CSF') || ...
                    strcmp(group_test_name(i,1), 'Toxoplasma qPCR, Whole Blood') || ...
                    strcmp(group_test_name(i,1), 'Triglyceride, Fluid') || ...
                    strcmp(group_test_name(i,1), 'Tropheryma whipplei PCR') || ...
                    strcmp(group_test_name(i,1), 'TSH with Reflex to Free T4 and FT3 as
Indicated') || ...
                    strcmp(group_test_name(i,1), 'Varicella Zoster (VZV) IgG Ab, Qual')
|| ...
                    strcmp(group_test_name(i,1), 'Varicella zoster virus DNA; PCR') ||
...
                    strcmp(group_test_name(i,1), 'Vitamin A and Vitamin E, Serum') ||
...
                    strcmp(group_test_name(i,1), 'Volatile Alcohol Screen') || ...
                    strcmp(group_test_name(i,1), 'Voriconazole Level') || ...
                    strcmp(group_test_name(i,1), 'VWF Multimer Interpretation') || ...
                    strcmp(group_test_name(i,1), 'VZV Antibody IgG CSF') || ...
                    strcmp(group_test_name(i,1), 'VZV qPCR, Plasma')||...
                    strcmp(group_test_name(i,1), 'Factor V Leiden Mutation') || ...
                    strcmp(group_test_name(i,1), 'FNA Cytology') || ...
                    strcmp(group_test_name(i,1), 'HLA Antibody Screen Mixed (HLASM)') ||
...
                    strcmp(group_test_name(i,1), 'HLA Antibody Spec. ClassI (HLAC1)') ||
...
                    strcmp(group_test_name(i,1), 'HLA Antibody Specificity (HLAS)') ||
...
                    strcmp(group_test_name(i,1), 'HLA ClassI Low Res. Typing (HLC1L)')
|| ...
                    strcmp(group_test_name(i,1), 'JAK2 V617F Mutation Detection') || ...
                    strcmp(group_test_name(i,1), 'Legionella DNA (PCR)') || ...
                    strcmp(group_test_name(i,1), 'Leukemia/Lymphoma, non-blood') || ...
                    strcmp(group_test_name(i,1), 'Methylmalonic Acid, Serum') || ...
                    strcmp(group_test_name(i,1), 'Pulmonary Cytology') || ...
                    strcmp(group_test_name(i,1), 'Solid Organ Txp Monthly PRA (PRAMO)')

                tubes(k).category_volume = 5;
                tubes(k).SVT = 0.6;

            % Coagulation
            elseif strcmp(group_test_name(i,1), 'DIC Panel') || ...
                    strcmp(group_test_name(i,1), 'Lupus Anticoagulant Assays') || ...
                    strcmp(group_test_name(i,1), 'MIXING STUDY GROUP TEST') || ...
                    strcmp(group_test_name(i,1), 'PT and  INR') || ...
```

```
                strcmp(group_test_name(i,1), 'ROTEM Testing, Initial Run') || ...
                strcmp(group_test_name(i,1), 'vonWillebrand''s Panel')

            tubes(k).category_volume = 4.5;
            tubes(k).SVT = 2.5;

        % Hematology
        elseif strcmp(group_test_name(i,1), 'CBC and DIFF') || ...
                strcmp(group_test_name(i,1), 'CBC With Platelet No Differential') ||
...
                strcmp(group_test_name(i,1), 'CBC, OR') || ...
                strcmp(group_test_name(i,1), 'CD3 count/Transplantation Profile
(CD3, CD19)') || ...
                strcmp(group_test_name(i,1), 'CD4 count/T-cell Subset Quantitation
(CD3, 4, 8)') || ...
                strcmp(group_test_name(i,1), 'POST Phase 1') || ...
                strcmp(group_test_name(i,1), 'RBC Morphology') || ...
                strcmp(group_test_name(i,1), 'Reticulocyte Count') || ...
                strcmp(group_test_name(i,1), 'WBC Morphology') || ...
                strcmp(group_test_name(i,1), 'White Blood Cell Differential')

            tubes(k).category_volume = 5;
            tubes(k).SVT = 0.5;

        % Out of Scope Tests
        elseif strcmp(group_test_name(i,1), 'Albumin, Fluid') || ...
                strcmp(group_test_name(i,1), 'Amylase, Fluid') || ...
                strcmp(group_test_name(i,1), 'Arbovirus Ab Panel IgG and IgM, CSF')
|| ...
                strcmp(group_test_name(i,1), 'BAL Fluid Count/Diff with Reflex to
Respiratory Culture') || ...
                strcmp(group_test_name(i,1), 'Bence Jones Quantitation') || ...
                strcmp(group_test_name(i,1), 'BKV qPCR, Urine') || ...
                strcmp(group_test_name(i,1), 'Body Fluid Crystal Exam') || ...
                strcmp(group_test_name(i,1), 'Calcium, 24hr Urine') || ...
                strcmp(group_test_name(i,1), 'Chlamydia trachomatis-Neisseria
gonorrhoeae RNA') || ...
                strcmp(group_test_name(i,1), 'Creatinine, 24hr Urine') || ...
                strcmp(group_test_name(i,1), 'Creatinine, Fluid') || ...
                strcmp(group_test_name(i,1), 'D-Lactate, U') || ...
                strcmp(group_test_name(i,1), 'Drug Screen, Urine IA') || ...
                strcmp(group_test_name(i,1), 'Epilepsy-Autoimmune Evaluation, CSF')
|| ...
                strcmp(group_test_name(i,1), 'ER Respiratory Panel + SAR- CoV-2 ;
PCR') || ...
                strcmp(group_test_name(i,1), 'ER SARS-CoV-2 (COVID-19) by PCR') ||
...
                strcmp(group_test_name(i,1), 'Ethyl Glucuronide') || ...
                strcmp(group_test_name(i,1), 'Herpes Simplex virus 1,2 DNA') || ...
                strcmp(group_test_name(i,1), 'Influenza (A, B), RSV; PCR') || ...
                strcmp(group_test_name(i,1), 'Metanephrines, Urine') || ...
                strcmp(group_test_name(i,1), 'Microalbumin, Urine') || ...
                strcmp(group_test_name(i,1), 'Mira Vista Blastomyces Ag, Urine') ||
...
                strcmp(group_test_name(i,1), 'MiraVista Histoplasma Antigen, Urine')
|| ...
                strcmp(group_test_name(i,1), 'Miscellaneous Invitae Test') || ...
                strcmp(group_test_name(i,1), 'MVista Blastomyces Ag, Urine') || ...
                strcmp(group_test_name(i,1), 'NC Rapid Novel Coronavirus(COVID-
19)PCR') || ...
```

```
                    strcmp(group_test_name(i,1), 'Novel Coronavirus (COVID-19), PCR') ||
...
                    strcmp(group_test_name(i,1), 'Other Cytology') || ...
                    strcmp(group_test_name(i,1), 'Pneumocystis jiroveci DNA; PCR') ||
...
                    strcmp(group_test_name(i,1), 'POC Glucose, whole blood') || ...
                    strcmp(group_test_name(i,1), 'Preg Screen, Urine POC') || ...
                    strcmp(group_test_name(i,1), 'Protein, Urine') || ...
                    strcmp(group_test_name(i,1), 'Rapid Novel Coronavirus (COVID-19),
PCR') || ...
                    strcmp(group_test_name(i,1), 'Respiratory Pathogen Panel + SAR- CoV-
2 ; PCR') || ...
                    strcmp(group_test_name(i,1), 'Respiratory Pathogen Panel; PCR') ||
...
                    strcmp(group_test_name(i,1), 'SARS-CoV2 (COVID-19), STAT PCR') ||
...
                    strcmp(group_test_name(i,1), 'SARS-CoV-2 Total Antibody,
Nucleocapsid, Qualitative') || ...
                    strcmp(group_test_name(i,1), 'SARS-CoV-2 Total Antibody, Spike
(RBD), Qualitative') || ...
                    strcmp(group_test_name(i,1), 'STAT Respiratory Pathogen Panel; PCR')
|| ...
                    strcmp(group_test_name(i,1), 'STI Panel RNA, Urine') || ...
                    strcmp(group_test_name(i,1), 'Surgical Pathology Request') || ...
                    strcmp(group_test_name(i,1), 'Susceptibility, Anaerobic, MIC') ||
...
                    strcmp(group_test_name(i,1), 'Total Bilirubin, Fluid') || ...
                    strcmp(group_test_name(i,1), 'Urea Nitrogen, 24hr Urine') || ...
                    strcmp(group_test_name(i,1), 'Urea Nitrogen, Fluid') || ...
                    strcmp(group_test_name(i,1), 'Urinalysis, Automated with
Microscopy') || ...
                    strcmp(group_test_name(i,1), 'Urinalysis, Automated with URCC reflex
and Microscopy') || ...
                    strcmp(group_test_name(i,1), 'Urine Macroscopic') || ...
                    strcmp(group_test_name(i,1), 'Urine Microscopic') || ...
                    strcmp(group_test_name(i,1), 'Urine Organic Acids')

                tubes(k).category_volume = 0;
                tubes(k).SVT = 0;

            elseif strcmp(group_test_name(i,1), '')

                Blood Cultures
                if strcmp(test_name(i,1), 'Antibody ID INT') || ...
                   strcmp(test_name(i,1), 'Blood Type.') || ...
                   strcmp(test_name(i,1), 'DAT') || ...
                   strcmp(test_name(i,1), 'One Label for Blood Bank')

                    tubes(k).category_volume = 0;
                    tubes(k).SVT = 0;

                % Chemistry / Misc
                elseif strcmp(test_name(i,1), 'Acetaminophen Level') || ...
                       strcmp(test_name(i,1), 'Adrenocorticotropic Hormone (ACTH)') ||
...
                       strcmp(test_name(i,1), 'Albumin Level') || ...
                       strcmp(test_name(i,1), 'Aldolase, Serum') || ...
                       strcmp(test_name(i,1), 'Aldosterone, Serum') || ...
                       strcmp(test_name(i,1), 'Alkaline Phosphatase') || ...
                       strcmp(test_name(i,1), 'Alpha-Fetoprotein, CSF') || ...
                       strcmp(test_name(i,1), 'Alpha-Fetoprotein, Tumor Marker') || ...
```

```
                    strcmp(test_name(i,1), 'ALT') || ...
                    strcmp(test_name(i,1), 'Amikacin Level, Peak') || ...
                    strcmp(test_name(i,1), 'Amikacin Level, Random') || ...
                    strcmp(test_name(i,1), 'Amikacin Level, Trough') || ...
                    strcmp(test_name(i,1), 'Ammonia Level') || ...
                    strcmp(test_name(i,1), 'Amylase') || ...
                    strcmp(test_name(i,1), 'ANA Scr with IFA') || ...
                    strcmp(test_name(i,1), 'ANA, HEp-2000 Cells') || ...
                    strcmp(test_name(i,1), 'ANCA (Neutrophil Cytoplasmic Ab), Reflex
to AntiMPO and PR3') || ...
                    strcmp(test_name(i,1), 'Anti-GBM Ab') || ...
                    strcmp(test_name(i,1), 'Anti-Nuclear Ab Screen') || ...
                    strcmp(test_name(i,1), 'Anti-Scleroderma Ab,70 Ag') || ...
                    strcmp(test_name(i,1), 'Anti-Thyroid Peroxidase') || ...
                    strcmp(test_name(i,1), 'Arbovirus IgM Antibody Panel') || ...
                    strcmp(test_name(i,1), 'AST') || ...
                    strcmp(test_name(i,1), 'B2-Microglobulin') || ...
                    strcmp(test_name(i,1), 'Beta Hydroxybutyrate') || ...
                    strcmp(test_name(i,1), 'Bilirubin, Total') || ...
                    strcmp(test_name(i,1), 'B-type Natriuretic Peptide') || ...
                    strcmp(test_name(i,1), 'CA 125') || ...
                    strcmp(test_name(i,1), 'Calcium Level') || ...
                    strcmp(test_name(i,1), 'Calcium Level, PTHI') || ...
                    strcmp(test_name(i,1), 'Calcium, Ionized') || ...
                    strcmp(test_name(i,1), 'Calprotectin, Feces') || ...
                    strcmp(test_name(i,1), 'Carbamazepine Level') || ...
                    strcmp(test_name(i,1), 'Carcinoembryonic Antigen') || ...
                    strcmp(test_name(i,1), 'Ceruloplasmin') || ...
                    strcmp(test_name(i,1), 'Charge HGBE Interpretation') || ...
                    strcmp(test_name(i,1), 'Cholesterol, Total') || ...
                    strcmp(test_name(i,1), 'CK MB Isoenzyme') || ...
                    strcmp(test_name(i,1), 'CKMB %') || ...
                    strcmp(test_name(i,1), 'Complement C3') || ...
                    strcmp(test_name(i,1), 'Complement C4') || ...
                    strcmp(test_name(i,1), 'Confirmatory Blood Type') || ...
                    strcmp(test_name(i,1), 'Confirmatory Blood Type.') || ...
                    strcmp(test_name(i,1), 'Copper') || ...
                    strcmp(test_name(i,1), 'Cortisol Level') || ...
                    strcmp(test_name(i,1), 'C-Peptide') || ...
                    strcmp(test_name(i,1), 'C-Reactive Protein') || ...
                    strcmp(test_name(i,1), 'Creatine Phosphokinase') || ...
                    strcmp(test_name(i,1), 'Creatinine') || ...
                    strcmp(test_name(i,1), 'Cyc. Citrullinated Pep AB') || ...
                    strcmp(test_name(i,1), 'Cyclosporine') || ...
                    strcmp(test_name(i,1), 'Cystatin C') || ...
                    strcmp(test_name(i,1), 'Digoxin Level') || ...
                    strcmp(test_name(i,1), 'Dilantin Level') || ...
                    strcmp(test_name(i,1), 'Dilantin, Free') || ...
                    strcmp(test_name(i,1), 'Drug Screen, Ur Mass Spec') || ...
                    strcmp(test_name(i,1), 'ds-DNA Antibody') || ...
                    strcmp(test_name(i,1), 'eGFR Cystatin') || ...
                    strcmp(test_name(i,1), 'Erythropoietin (EPO)') || ...
                    strcmp(test_name(i,1), 'Estimated GFR, Creatinine-based formula
(CKD-EPI 2021)') || ...
                    strcmp(test_name(i,1), 'Ethanol Label') || ...
                    strcmp(test_name(i,1), 'Ethanol Level') || ...
                    strcmp(test_name(i,1), 'Everolimus') || ...
                    strcmp(test_name(i,1), 'Ferritin') || ...
                    strcmp(test_name(i,1), 'Folic Acid Level') || ...
                    strcmp(test_name(i,1), 'Free Carbamazepine') || ...
                    strcmp(test_name(i,1), 'Fructosamine') || ...
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```
                    strcmp(test_name(i,1), 'Fungal Serology Panel, Serum') || ...
                    strcmp(test_name(i,1), 'Fungitell Titer (serum)') || ...
                    strcmp(test_name(i,1), 'Gastrin') || ...
                    strcmp(test_name(i,1), 'Gentamicin Level, Trough') || ...
                    strcmp(test_name(i,1), 'G-Glutamyl Transpeptidase') || ...
                    strcmp(test_name(i,1), 'Haptoglobin') || ...
                    strcmp(test_name(i,1), 'hCG, Beta CSF') || ...
                    strcmp(test_name(i,1), 'hCG, Beta Subunit') || ...
                    strcmp(test_name(i,1), 'Hemoglobin A1C') || ...
                    strcmp(test_name(i,1), 'Hemoglobin, Serum') || ...
                    strcmp(test_name(i,1), 'Hepatitis Be Antigen') || ...
                    strcmp(test_name(i,1), 'Herpes Simplex virus DNA, PCR, CSF') ||
...
                    strcmp(test_name(i,1), 'High Sensitive Trop T, 2 Hour') || ...
                    strcmp(test_name(i,1), 'High Sensitive Troponin T') || ...
                    strcmp(test_name(i,1), 'Hydroxycarbazepine, HPLC') || ...
                    strcmp(test_name(i,1), 'Immunofixation') || ...
                    strcmp(test_name(i,1), 'Immunoglobulin E, Total') || ...
                    strcmp(test_name(i,1), 'Immunoglobulin IGA') || ...
                    strcmp(test_name(i,1), 'Immunoglobulin IGA, Electrophoresis') ||
...
                    strcmp(test_name(i,1), 'Immunoglobulin IGG') || ...
                    strcmp(test_name(i,1), 'Immunoglobulin IGG, Electrophoresis') ||
...
                    strcmp(test_name(i,1), 'Immunoglobulin IGM') || ...
                    strcmp(test_name(i,1), 'Immunoglobulin IGM, Electrophoresis') ||
...
                    strcmp(test_name(i,1), 'Lactate Dehydrogenase') || ...
                    strcmp(test_name(i,1), 'Lactic Acid') || ...
                    strcmp(test_name(i,1), 'Lactic Acid, CSF') || ...
                    strcmp(test_name(i,1), 'Lamotrigine') || ...
                    strcmp(test_name(i,1), 'LDH, CSF') || ...
                    strcmp(test_name(i,1), 'LDL Cholesterol, Direct') || ...
                    strcmp(test_name(i,1), 'Lidocaine Level') || ...
                    strcmp(test_name(i,1), 'Lipase') || ...
                    strcmp(test_name(i,1), 'Lithium') || ...
                    strcmp(test_name(i,1), 'LiverKidney Microsomal Antibody') || ...
                    strcmp(test_name(i,1), 'Magnesium Level') || ...
                    strcmp(test_name(i,1), 'Magnesium, Obstetrical') || ...
                    strcmp(test_name(i,1), 'National Prion 14-3-3 Testing') || ...
                    strcmp(test_name(i,1), 'Neutrophil Gelatinase-associated
Lipocalin') || ...
                    strcmp(test_name(i,1), 'NT-ProBNP') || ...
                    strcmp(test_name(i,1), 'Osmolality, Serum') || ...
                    strcmp(test_name(i,1), 'pH, Pleural Fluid') || ...
                    strcmp(test_name(i,1), 'Phenobarbital Level') || ...
                    strcmp(test_name(i,1), 'Phosphatidylethanol (PEth), whole
blood') || ...
                    strcmp(test_name(i,1), 'Phosphorus Level') || ...
                    strcmp(test_name(i,1), 'Potassium Level') || ...
                    strcmp(test_name(i,1), 'Prealbumin Level') || ...
                    strcmp(test_name(i,1), 'Pregnancy Screen, Serum') || ...
                    strcmp(test_name(i,1), 'Procalcitonin') || ...
                    strcmp(test_name(i,1), 'Prolactin') || ...
                    strcmp(test_name(i,1), 'Prostate Specific Antigen') || ...
                    strcmp(test_name(i,1), 'Protein Level') || ...
                    strcmp(test_name(i,1), 'Protein Level, CSF') || ...
                    strcmp(test_name(i,1), 'Rapid Plasma Reagin-RPR') || ...
                    strcmp(test_name(i,1), 'Renin, Plasma Mass') || ...
                    strcmp(test_name(i,1), 'Rheumatoid Factor') || ...
                    strcmp(test_name(i,1), 'Salicylate Level') || ...
```

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                    strcmp(test_name(i,1), 'Serotonin Releasing Assay') || ...
                    strcmp(test_name(i,1), 'Sirolimus (Rapamycin)') || ...
                    strcmp(test_name(i,1), 'Smooth Muscle Antibody') || ...
                    strcmp(test_name(i,1), 'Sodium Level') || ...
                    strcmp(test_name(i,1), 'Tacrolimus') || ...
                    strcmp(test_name(i,1), 'Theophylline Level') || ...
                    strcmp(test_name(i,1), 'Thiocyanate Level') || ...
                    strcmp(test_name(i,1), 'Thyroid Stimulating Immunoglobulin,
Serum') || ...
                    strcmp(test_name(i,1), 'Thyroxine (T4), Free') || ...
                    strcmp(test_name(i,1), 'Thyroxine (T4), Total') || ...
                    strcmp(test_name(i,1), 'Tobramycin Level, Peak') || ...
                    strcmp(test_name(i,1), 'Tobramycin Level, Random') || ...
                    strcmp(test_name(i,1), 'Tobramycin Level, Trough') || ...
                    strcmp(test_name(i,1), 'Total Hemolytic Complement') || ...
                    strcmp(test_name(i,1), 'Transferrin Level') || ...
                    strcmp(test_name(i,1), 'Triglycerides') || ...
                    strcmp(test_name(i,1), 'Triiodothyronine(T3), Tot') || ...
                    strcmp(test_name(i,1), 'Triiodothyronine, Free') || ...
                    strcmp(test_name(i,1), 'Troponin-I') || ...
                    strcmp(test_name(i,1), 'Tryptase') || ...
                    strcmp(test_name(i,1), 'TSH, 3rd Generation') || ...
                    strcmp(test_name(i,1), 'Urea Nitrogen') || ...
                    strcmp(test_name(i,1), 'Uric Acid') || ...
                    strcmp(test_name(i,1), 'Valproic Acid Level') || ...
                    strcmp(test_name(i,1), 'Valproic Acid, Free') || ...
                    strcmp(test_name(i,1), 'Vancomycin Level, Peak') || ...
                    strcmp(test_name(i,1), 'Vancomycin Level, Random') || ...
                    strcmp(test_name(i,1), 'Vancomycin Level, Trough') || ...
                    strcmp(test_name(i,1), 'Vitamin A (Retinol), Serum') || ...
                    strcmp(test_name(i,1), 'Vitamin B12') || ...
                    strcmp(test_name(i,1), 'Vitamin D, 25-Hydroxy') || ...
                    strcmp(test_name(i,1), 'Vitamin D, Dihydroxy 1,25') || ...
                    strcmp(test_name(i,1), 'Vitamin E (A-Tocopherol), Serum') || ...
                    strcmp(test_name(i,1), 'VZV DNA CSF, PCR') || ...
                    strcmp(test_name(i,1), 'Zinc')

                tubes(k).category_volume = 5;
                tubes(k).SVT = 0.6;

                % Coagulation
                elseif strcmp(test_name(i,1), 'ADAMTS 13 Activity') || ...
                       strcmp(test_name(i,1), 'ADAMTS 13 Inhibitor') || ...
                       strcmp(test_name(i,1), 'Anti 2A Unfractionated Heparin') ||
...
                       strcmp(test_name(i,1), 'Antithrombin Activity') || ...
                       strcmp(test_name(i,1), 'Anti-Xa LMW Heparin') || ...
                       strcmp(test_name(i,1), 'Anti-Xa Unfractionated Heparin') ||
...
                       strcmp(test_name(i,1), 'Apixaban Level') || ...
                       strcmp(test_name(i,1), 'Argatroban Level') || ...
                       strcmp(test_name(i,1), 'Aspirin Platelet Function Test') ||
...
                       strcmp(test_name(i,1), 'Chromogenic Factor 10') || ...
                       strcmp(test_name(i,1), 'D-Dimer') || ...
                       strcmp(test_name(i,1), 'F8/VWAGN Ratio') || ...
                       strcmp(test_name(i,1), 'Factor 10 Assay') || ...
                       strcmp(test_name(i,1), 'Factor 11 Assay') || ...
                       strcmp(test_name(i,1), 'Factor 13 Assay') || ...
                       strcmp(test_name(i,1), 'Factor 2 Assay') || ...
                       strcmp(test_name(i,1), 'Factor 5 Assay') || ...
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                        strcmp(test_name(i,1), 'Factor 7 Assay') || ...
                        strcmp(test_name(i,1), 'Factor 8 Assay') || ...
                        strcmp(test_name(i,1), 'Factor 8 Inhibitor Assay') || ...
                        strcmp(test_name(i,1), 'Factor 9 Assay') || ...
                        strcmp(test_name(i,1), 'Factor 9 Inhibitor Assay') || ...
                        strcmp(test_name(i,1), 'Fibrinogen - Clottable') || ...
                        strcmp(test_name(i,1), 'Heparin Antibody Assay') || ...
                        strcmp(test_name(i,1), 'Hexagonal Phospholipid
Neutralization') || ...
                        strcmp(test_name(i,1), 'Medical Director Coagulation
Interpretation') || ...
                        strcmp(test_name(i,1), 'P2Y12 Platelet Function Test') ||
...
                        strcmp(test_name(i,1), 'Partial Thromboplastin Time') || ...
                        strcmp(test_name(i,1), 'Protein C Activity') || ...
                        strcmp(test_name(i,1), 'Protein S Antigen Free') || ...
                        strcmp(test_name(i,1), 'Rivaroxaban Level') || ...
                        strcmp(test_name(i,1), 'Thrombin Time') || ...
                        strcmp(test_name(i,1), 'vonWillebrand Activity') || ...
                        strcmp(test_name(i,1), 'vonWillebrand Antigen') || ...
                        strcmp(test_name(i,1), 'VWF / VWAGN Ratio')

                    tubes(k).category_volume = 4.5;
                    tubes(k).SVT = 2.5;

                % Hematology
                elseif strcmp(test_name(i,1), 'Body Fluid Hematocrit') || ...
                        strcmp(test_name(i,1), 'Body Fluid Specific Gravity') || ...
                        strcmp(test_name(i,1), 'Erythrocyte Sedimentation Rate;
Westergren') || ...
                        strcmp(test_name(i,1), 'G6PD, QUALITATIVE') || ...
                        strcmp(test_name(i,1), 'Hematocrit') || ...
                        strcmp(test_name(i,1), 'Immature Platelet Fraction') || ...
                        strcmp(test_name(i,1), 'Pathologist Review of Peripheral
Blood') || ...
                        strcmp(test_name(i,1), 'Platelet Count') || ...
                        strcmp(test_name(i,1), 'RBC Morphology Phantom') || ...
                        strcmp(test_name(i,1), 'RED CELLS LR') || ...
                        strcmp(test_name(i,1), 'Sickle Cell Screening Test')

                    tubes(k).category_volume = 5;
                    tubes(k).SVT = 0.5;

                % Out of Scope Tests
                elseif strcmp(test_name(i,1), 'Acid Fast Bacillus Culture') || ...
                        strcmp(test_name(i,1), 'AFB Blood Culture') || ...
                        strcmp(test_name(i,1), 'Anaerobic Culture') || ...
                        strcmp(test_name(i,1), 'Bence Jones Screen, Urine') || ...
                        strcmp(test_name(i,1), 'Billing for PRVD') || ...
                        strcmp(test_name(i,1), 'BK Virus DNA, Quantitative, Plasma')
|| ...
                        strcmp(test_name(i,1), 'Blood Culture') || ...
                        strcmp(test_name(i,1), 'Body Fluid Culture/Smear') || ...
                        strcmp(test_name(i,1), 'Body Fluid PH') || ...
                        strcmp(test_name(i,1), 'Body Fluid red cells side 3') || ...
                        strcmp(test_name(i,1), 'Bordetella pertussis-parapertussis
DNA, PCR') || ...
                        strcmp(test_name(i,1), 'Candida auris, PCR') || ...
                        strcmp(test_name(i,1), 'Catheter Tip, Aerobic Culture') ||
...
                        strcmp(test_name(i,1), 'Chloride, Urine') || ...
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                        strcmp(test_name(i,1), 'Clostridium difficile Antigen and
Toxin') || ...
                        strcmp(test_name(i,1), 'Clostridium Difficile Toxin B DNA')
|| ...
                        strcmp(test_name(i,1), 'Cotinine, Urine Screen') || ...
                        strcmp(test_name(i,1), 'Creatinine, Urine') || ...
                        strcmp(test_name(i,1), 'Cryptococcus Antigen') || ...
                        strcmp(test_name(i,1), 'CSF Culture/Smear') || ...
                        strcmp(test_name(i,1), 'Culture, Fungal Blood') || ...
                        strcmp(test_name(i,1), 'Cytomegalovirus, Quantitative,
Plasma') || ...
                        strcmp(test_name(i,1), 'Deep Tissue Culture') || ...
                        strcmp(test_name(i,1), 'Deep Tissue Culture/Smear') || ...
                        strcmp(test_name(i,1), 'Epstein Barr Virus DNA,
Quantitative, Plasma') || ...
                        strcmp(test_name(i,1), 'Five Labels for Requisition') || ...
                        strcmp(test_name(i,1), 'Foreign Body Culture') || ...
                        strcmp(test_name(i,1), 'Fungal Serology Panel, CSF') || ...
                        strcmp(test_name(i,1), 'Fungitell Titer (BAL)') || ...
                        strcmp(test_name(i,1), 'Fungus Calcofluor Stain') || ...
                        strcmp(test_name(i,1), 'Gastrointestinal panel PCR') || ...
                        strcmp(test_name(i,1), 'Glucose Level, CSF') || ...
                        strcmp(test_name(i,1), 'Glucose, Urine') || ...
                        strcmp(test_name(i,1), 'Gram Stain') || ...
                        strcmp(test_name(i,1), 'Gram Stain Only') || ...
                        strcmp(test_name(i,1), 'Gram Stain, Respiratory') || ...
                        strcmp(test_name(i,1), 'Heater-Cooler AFB Blood Culture') ||
...
                        strcmp(test_name(i,1), 'Helicobacter Pylori Stool Antigen')
|| ...
                        strcmp(test_name(i,1), 'Hem Path Review Phantom') || ...
                        strcmp(test_name(i,1), 'HEM save for department use') || ...
                        strcmp(test_name(i,1), 'Hepatitis B Virus, Quantitative,
Serum') || ...
                        strcmp(test_name(i,1), 'Hepatitis C Virus, Quantitative,
Serum') || ...
                        strcmp(test_name(i,1), 'Human Immunodeficiency Virus,
Quantitative, Plasma') || ...
                        strcmp(test_name(i,1), 'Legionella Pneumophila Antigen') ||
...
                        strcmp(test_name(i,1), 'Meningitis Encephalitis panel') ||
...
                        strcmp(test_name(i,1), 'Methicillin Resistant Staphylococci
Culture') || ...
                        strcmp(test_name(i,1), 'Microbiology Extra Specimen') || ...
                        strcmp(test_name(i,1), 'Microbiology Problem Culture') ||
...
                        strcmp(test_name(i,1), 'Myoglobin, Urine') || ...
                        strcmp(test_name(i,1), 'One Label for Requisition') || ...
                        strcmp(test_name(i,1), 'Order Hgbe Confirmation') || ...
                        strcmp(test_name(i,1), 'Organism Identification Only') ||
...
                        strcmp(test_name(i,1), 'Osmolality, Urine') || ...
                        strcmp(test_name(i,1), 'Pathologist Review - PB MD Request')
|| ...
                        strcmp(test_name(i,1), 'Pathologist Review of Fluid') || ...
                        strcmp(test_name(i,1), 'Peritoneal Dialysate Culture') ||
...
                        strcmp(test_name(i,1), 'Phencyclidine (PCP)') || ...
                        strcmp(test_name(i,1), 'Pink Top') || ...
                        strcmp(test_name(i,1), 'Potassium, Urine') || ...
```

```
                        strcmp(test_name(i,1), 'Protein, Urine (for calculation)')
|| ...
                        strcmp(test_name(i,1), 'Quantitative Biopsy Culture') || ...
                        strcmp(test_name(i,1), 'Quantitative Deep Tissue - Bone
Culture') || ...
                        strcmp(test_name(i,1), 'Quantitative Respiratory Cult/Smr')
|| ...
                        strcmp(test_name(i,1), 'Research - Two Tubes') || ...
                        strcmp(test_name(i,1), 'Respiratory Culture Phantom') || ...
                        strcmp(test_name(i,1), 'Respiratory Culture, Non-Sputum') ||
...
                        strcmp(test_name(i,1), 'Seven Labels for Requisition') ||
...
                        strcmp(test_name(i,1), 'Slide for MD request') || ...
                        strcmp(test_name(i,1), 'Sodium, Urine') || ...
                        strcmp(test_name(i,1), 'Specimen Processing Problem') || ...
                        strcmp(test_name(i,1), 'Sputum Culture') || ...
                        strcmp(test_name(i,1), 'Stain, Acid Fast') || ...
                        strcmp(test_name(i,1), 'Staphylococcus Culture') || ...
                        strcmp(test_name(i,1), 'Sterile Body Fluid Culture/Smear')
|| ...
                        strcmp(test_name(i,1), 'Stool Occult Blood Test') || ...
                        strcmp(test_name(i,1), 'Streptococcus Pneumoniae Antigen')
|| ...
                        strcmp(test_name(i,1), 'Three Labels for Requisition') ||
...
                        strcmp(test_name(i,1), 'Too Old? Phantom Test') || ...
                        strcmp(test_name(i,1), 'T-Subsets,CD3,4,8 (BAL)') || ...
                        strcmp(test_name(i,1), 'Two Labels for Requisition') || ...
                        strcmp(test_name(i,1), 'Urea Nitrogen, Urine') || ...
                        strcmp(test_name(i,1), 'Urine Alert for Abn UPRO and Hi PH')
|| ...
                        strcmp(test_name(i,1), 'Urine Culture') || ...
                        strcmp(test_name(i,1), 'Urine Culture Phantom') || ...
                        strcmp(test_name(i,1), 'Urine Eosinophil Cytoprep') || ...
                        strcmp(test_name(i,1), 'Urine Pregnancy, Qual') || ...
                        strcmp(test_name(i,1), 'Urine Prot. Electrophor.') || ...
                        strcmp(test_name(i,1), 'Urogenital Culture') || ...
                        strcmp(test_name(i,1), 'Vancomycin Resistant Enterococci
Culture') || ...
                        strcmp(test_name(i,1), 'Wound Culture/Smear') || ...
                        strcmp(test_name(i,1), 'XHLD - Aptio Output Module') || ...
                        strcmp(test_name(i,1), 'Yeast Culture')

                    tubes(k).category_volume = 0;
                    tubes(k).SVT = 0;

            end
        end
    end

        if strcmp(tube_type(i,1), 'SYR') || strcmp(tube_type(i,1), 'XBC') || ...
        strcmp(tube_type(i,1), 'XBS') || strcmp(tube_type(i,1), 'URINE') || ...
        strcmp(tube_type(i,1), 'UCP') || strcmp(tube_type(i,1), 'TISSUE') || ...
        strcmp(tube_type(i,1), 'URINE2') || strcmp(tube_type(i,1), 'USP') || ...
        strcmp(tube_type(i,1), 'XAT') || strcmp(tube_type(i,1), 'XBDS') || ...
        strcmp(tube_type(i,1), 'XBDU') || strcmp(tube_type(i,1), 'XFU') || ...
        strcmp(tube_type(i,1), 'XM4') || strcmp(tube_type(i,1), 'XXM4') || ...
        strcmp(tube_type(i,1), 'XOC') || strcmp(tube_type(i,1), 'XSC') || ...
        strcmp(tube_type(i,1), 'XST') || strcmp(tube_type(i,1), 'ZEUS') || ...
        strcmp(tube_type(i,1), 'STERILE')
```

```
                        tubes(k).category_volume = 0;
                        tubes(k).SVT = 0;

            end
        end
    end
end


% Add SVTs until minimum test volume is satisfied

for i = 1:1:L

    tubes(i).number_small_tubes = 1;

    if tubes(i).SVT~= 0
        while (tubes(i).SVT * tubes(i).number_small_tubes) < tubes(i).exactdraw_vol

            tubes(i).number_small_tubes = tubes(i).number_small_tubes + 1;

        end
    end

    tubes(i).SVT_total = tubes(i).SVT * tubes(i).number_small_tubes;

end

for i = 1:1:L

    if isempty(tubes(i).SVT_total)
        tubes(i).SVT_total = 0;
    end

end

%% Calculate Average Patient Draw per Day

temp_total = zeros(2,JL);

for i = 1:1:JL

    initial_total = zeros(2,JL);

    for k = 1:1:L
        for z = 1:1:length(patients(i).tubes_used)
            if patients(i).tubes_used(z) == tubes(k).name

                initial_total(1,i) = tubes(k).category_volume + initial_total(1,i);
                initial_total(2,i) = tubes(k).SVT_total + initial_total(2,i);

            end
        end
    end


                temp_total(1,i) = initial_total(1,i);
                temp_total(2,i) = initial_total(2,i);
end

for i = 1:1:JL
```

```
    patients(i).with_cats_ave_pd = temp_total(1,i) / patients(i).max_day;
    patients(i).SVT_ave_pd = temp_total(2,i) / patients(i).max_day;

end

save("tubes_struct9",'tubes');
save("patient_struct9",'patients');
```

A3. Program to Conduct Non-Parametric Hypothesis Tests, R Code

````
---
title: "Blood Draw Orders Statistical Analysis"
author: "Sam Menzie"
date: "2024-01-30"
output: word_document
---
```{r setup, include=FALSE}
knitr::opts_chunk$set(echo = TRUE)

library(FSA);
library(car);
library(corrplot);
library(lmtest, pos = 4);

```
```{r, echo = FALSE}

patient_data = read.table("patient_data.csv", header = TRUE, sep = ","); # Number of tubes per patient and surplus blood drawn. Average daily phlebotomy to compare for statistical significance

# NON PARAMETRIC EVALUATION

dfdailyphlebotomy <- data.frame(patient_data$draw_conditions, patient_data$daily_ave_phlebotomy);

dfdailyphlebotomy$rank <- rank(dfdailyphlebotomy$patient_data.daily_ave_phlebotomy);
kruskal.test(rank~patient_data.draw_conditions, data = dfdailyphlebotomy);

dunnTest(patient_data$daily_ave_phlebotomy, patient_data$draw_conditions, method = "bh");

```
````

Bibliography

1. Bush VJ, Leonard L, Szamosi DI. Advancements in blood collection devices. Laboratory Medicine. 1998; 29(10): 616-622.
2. Becton Dickinson – BD vacutainer blood collection tubes. [accessed November 2023]. www.bd.com/en-us/products-and-solutions/products/product-families/bd-vacutainer-blood-collection-tubes#overview.
3. LabCE – Blood collection tubes. [accessed November 2023]. www.labce.com/spg263741_blood_collection_tubes.aspx.
4. Wu DW, Li YM, Wang F. How long can we store blood samples: A systematic review and meta-analysis. eBioMedicine. 2017; 24: 277-285. PMID: 28965875.
5. Villani R, Romano AD, Rinaldi R, Sangineto M, Santoliquido M, Cassano T, Serviddio G. Prevalence and risk factors for hospital-acquired anemia in internal medicine patients: Learning from the "less is more" perspective. Intern Emerg Med. 2023; 18(1): 177-183. https://doi.org/10.1007/s11739-022-03147-x PMID: 36346557.
6. Turner J, Parsi M, Badireddy M. Anemia. In *StatPearls*. StatPearls Publishing. [accessed November 2023]. www.ncbi.nlm.nih.gov/books/NBK499994/ PMID: 29763170.
7. Badireddy M, Baradhi KM. Chronic anemia. In *StatPearls*. StatPearls Publishing. [accessed November 2023]. pubmed.ncbi.nlm.nih.gov/30521224 PMID: 30521224.
8. Nguyen WB, Wyse JM, Drollinger SM, Cheng K. Anemia screening in naval aviation: Is hemoglobin a better indicator than hematocrit as the primary index? Military Medicine. 2020; 185(3-4): 461-467. https://doi.org/10.1093/milmed/usz243.
9. Baron DM, Hochrieser H, Posch M, Metnitz B, Rhodes A, Moreno RP, Pearse RM, Metnitz P. Preoperative anaemia is associated with poor clinical outcome in non-cardiac surgery patients. British Journal of Anaesthesia. 2014; 113(3): 416-423. https://doi.org/10.1093/bja/aeu098.
10. World Health Organization – WHO guidelines on drawing blood: Best practices in phlebotomy 2010. [accessed November 2023]. www.ncbi.nlm.nih.gov/books/NBK138665/.
11. Face Med Store – What is the most common method for drawing venous blood: Syringe, vacuum tube, or butterfly needle? [accessed November 2023].

facemedstore.com/blogs/blog/what-is-the-most-common-method-for-drawing-venous-blood-syringe-vacuum-tube-or-butterfly-needle.

12. Agency for Clinical Innovation – Central venous access devices. [accessed February 2024]. www.aci.health.nsw.gov.au/__data/assets/pdf_file/0010/239626/ACI-CVAD-clinical-practice-guide.pdf.
13. TPNCare – PICC line blood draw. [accessed November 2023]. www.youtube.com/watch?app=desktop&v=qleKCmrFcs4.
14. Lalthanthuami HT, Kumari MJ, Venkateswaran R, Lakshmi PR, Ramamoorthy L. Performance of 3 mL versus 5 mL discarded volume for blood sampling from central venous access device. J Lab Physicians. 2021; 13(2): 112-117. https://doi.org/10.1055/s-0041-1726669 PMID: 34483554.
15. Cole M, Price L, Parry A, Picton S, Waters F, Marshall S, Goran C, Parnham A, Wastell H, Reid MM, Pearson ADJ, Boddy AV, Veal GJ. A study to determine the minimum volume of blood necessary to be discarded from a central venous catheter before a valid sample is obtained in children with cancer. Pediatr Blood Cancer. 2007; 48(7): 687-95. https://doi.org/ 10.1002/pbc.20873 PMID: 16676305.
16. Shander A, Corwin HL. A narrative review on hospital-acquired anemia: Keeping blood where it belongs. Transfusion Medicine Reviews. 2020; 34(3): 195-199. https://doi.org/10.1016/j.tmrv.2020.03.003.
17. Helmer P, Hottenrott S, Steinisch A, Röder D, Shubert J, Steigerwald U, Choorapoikayil S, Meybohm P. Avoidable blood loss in critical care and patient blood management: Scoping review of diagnostic blood loss. J Clin Med. 2022; 11(2): 320. https://doi.org/10.3390/jcm11020320 PMID: 35054014.
18. Bodley T, Chan M, Levi O, Clarfield L, Yip D, Smith O, Friedrich JO, Hicks LK. Patient harm associated with serial phlebotomy and blood waste in the intensive care unit: A retrospective cohort study. PLoS One. 2021; 16(1): e0243782. https://doi.org/10.1371/journal.pone.0243782.
19. Freeman AM, Rai M, Morando DW. Anemia screening. In *StatPearls*. StatPearls Publishing. [accessed November 2023]. https://pubmed.ncbi.nlm.nih.gov/29763080 PMID: 29763080.

20. Beverina I, Borotto E, Novelli C, Radrizzani D, Brando B. Iatrogenic anemia and transfusion thresholds in ICU patients with COVID-19 disease at a tertiary care hospital. Transfus Apher Sci. 2021; 60(2): 103069. https://doi.org/10.1016/j.transci.2021.103068 PMID: 33612448.

21. Chornenki N, James T, Barty R, Liu Y, Rochwerg B, Heddle N, Siegal D. Blood loss from laboratory testing, anemia, and red blood cell transfusion in the intensive care unit: a retrospective study. Transfusion. 2020; 60(2): 256-261. https://doi.org/10.1111/trf.15649.

22. Goodnough LT. Risks of blood transfusion. Anesthesiology Clinics of North America. 2005; 23(2): 241-252. https://doi.org/10.1016/j.atc.2004.07.004.

23. Indelen C, Kizmaz YU, Kar A, Shander A, Kirali K. The cost of one unit blood transfusion components and cost-effectiveness analysis results of transfusion improvement program. Turk Gogus Kalp Damar Cerrahisi Derg. 2021; 29(2): 150-157. https://doi.org/10.5606/tgkdc.dergisi.2021.20886 PMID: 34104508.

24. Shander A, Hofmann A, Ozawa S, Theusinger OM, Gombotz H, Spahn DR. Activity-based costs of blood transfusions in surgical patients at four hospitals. Transfusion. 2010; 50(4): 753-765. https://doi.org/10.1111/j.1537-2995.2009.02518.x PMID: 20003061.

25. Naidech AM, Kahn MJ, Soong W, Green D, Batjer HH, Bleck TP. Packed red blood cell transfusion causes greater hemoglobin rise at a lower starting hemoglobin in patients with subarachnoid hemorrhage. Neurocrit Care. 2008; 9(2): 198-203. https://doi.org/10.1007/s12028-008-9113-8 PMID: 18542851.

26. Juárez-Vela R, Andrés-Esteban EM, Gea-Caballero V, Sánchez-González JL, Marcos-Neira P, Serrano-Lázaro A, Tirado-Anglés G, Ruiz-Rodríguez JC, Durante A, Santolalla-Arnedo I, Garcia-Erce JA, Quintana-Diaz M. Related factors of anemia in critically ill patients: A prospective multicenter study. J Clin Med. 2022; 11(4): 1031. https://doi.org/10.3390/jcm11041031 PMID: 35207301.

27. Capellini MD, Motta I. Anemia in clinical practice-definition and classification: Does hemoglobin change with aging? Semin Hematol. 2015; 52(4): 261-269. https://doi.org/ 10.1053/j.seminhematol.2015.07.006 PMID: 26404438.

28. Jalbert R, Gob A, Chin-Yee I. Decreasing daily blood work in hospitals: What works and what doesn't. Int J Lab Hematol. 2019: 41(Suppl 1): 151-161. https://doi.org/10.1111/ijlh.13015 PMID: 31069984.

29. Page C, Retter A, Wyncoll D. Blood conservation devices in critical care: A narrative review. Ann Intensive Care. 2013; 3: 14. https://doi.org/10.1186/2110-5820-3-14 PMID: 23714376.

30. Siegal DM, Manning N, Chornenki NLJ, Hillis CM, Heddle NM. Devices to reduce the volume of blood taken for laboratory testing in ICU patients: A systematic review. J Intensive Care Med. 2020; 35(10): 1074-1079. https://doi.org/10.1177/0885066618810374 PMID: 30482081.

31. Sanchez-Giron F, Alvarez-Mora F. Reduction of blood loss from laboratory testing in hospitalized adult patients using small-volume (pediatric) tubes. Arch Pathol Lab Med. 2008; 132(12): 1916-1919. https://doi.org/10.5858/132.12.1916 PMID: 19061290.

32. Briggs EN, Hawkins DJ, Hodges AM, Monk AM. Small volume vacuum phlebotomy tubes: A controlled before-and-after study of a patient blood management initiative in an Australian adult intensive care unit. Crit Care Resusc. 2019; 21(4): 251-257. PMID: 31778631.

33. Salisbury AC, Reid KJ, Alexander KP, Masoudi FA, Lai SM, Chan PS, Bach RG, Wang TY, Spertus JA, Kosiborod M. Diagnostic blood loss from phlebotomy and hospital-acquired anemia during acute myocardial infarction. Arch Intern Med. 2011; 171(18): 1646-1653. https://doi.org/ 10.1001/archinternmed.2011.361.

34. Siegal DM, Belley-Côté EP, Lee SG, Hill S, D'Aragon F, Zarychanski R, Rochwerg Bram, et al.. Small-volume blood collection tubes to reduce transfusions in intensive care. JAMA. 2023. https://doi.org/10.1001/jama.2023.20820.

35. Phelan MP, Reineks EZ, Berriochoa JP, Schold JD, Hustey FM, Chamberlin J, Kovach A. Impact of use of smaller volume, smaller vacuum blood collection tubes on hemolysis in emergency department blood samples. American Journal of Clinical Pathology. 2017; 148(4): 330-335. https://doi.org/10.1093/ajcp/aqx082

36. Garcia J, Xian J, Pedroza C, Salahuddin M, Mak G, Keene A, Cherian S, Young A, Vijhani P, Doshi P. Pediatric size phlebotomy tubes and transfusions in adult

critically ill patients: a pilot randomized controlled trial. Pilot and Feasibility Studies. 2020; 6: 112. https://doi.org/10.1186/s40814-020-00657-3.

37. Szumilas M. Explaining Odds Ratios. J Can Acad Child Adolesc Psychiatry. 2010; 19(3): 227-229. PMID: 20842279.