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The Transfusion Practices of Hospitalists and Their Response to an Educational Intervention:
An Exploratory Study

BY

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Degree to be awarded: MPH

Career MPH

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DTM&H, London School of Tropical Medicine and Hygiene, 2006

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A Special Studies Project submitted to the

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Abstract

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Purpose

Red blood cell transfusions are commonly ordered by hospitalists to treat anemic patients with little evidence of its impact on patient morbidity and mortality. The purpose of this study is to characterize the red blood cell transfusion practice patterns among this unstudied group, ascertain if transfusions are appropriate, and determine if an educational intervention changes hospitalist practice patterns.

Methods

This is a single center retrospective cohort study comparison of patients transfused by hospitalists before and after an educational intervention

Results

There was a 65.7 % drop in the total number of transfusions after the education intervention. A decline occurred in all individual categories of anemia, with statistical significance change in the categories chronic blood loss, hemolytic anemia, and AOCD.

Conclusions

The decrease in the number of transfusions performed after the educational intervention suggests that mistransfusions occur frequently in many types of anemia and education may be an effective way to promote appropriate use of red blood cells. Further studies are needed to validate our observations and corroborate their significance.

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Chapter I: Introduction

Introduction and Rationale

The modern history of human to human blood transfusion began with the London obstetrician James Blundell. In 1829 he successfully saved a woman dying of a postpartum hemorrhage with four ounces of blood taken from her husband.[1] Since that time the use of red blood cells has become commonplace, despite the fact that little evidence has been accumulated for its appropriate use. In 1942 anesthesiologists Dr. Adams and Dr. Lundy wrote an article stating that in their experience preoperative patients did better with a Hb >10 g/dL, [2] an opinion not supported by any animal or human studies. Today this is termed the 10/30 rule. It is an example of an unquestioned practice handed across generations of physicians principally based on the experience of those that have gone before.

In the 1980's blood product safety concerns were sparked by the discovery that the human immunodeficiency virus (HIV) could be acquired from a blood transfusion.[3] This stigmatizing and at the time untreatable illness served to stimulate research and heighten the debate over what is appropriate red blood cell transfusion practice. [4] The result is a growing body of literature unsupportive for an arbitrary transfusion trigger, the threshold hemoglobin that results in a clinician initiating a red blood cell transfusion.

In the United States (US) over 14 million units of blood were transfused in 2006.[5] The majority of these transfusions occur in the inpatient setting [5] and in medical patients. The French RECEPT group noted 53% of transfusion recipients were on medical wards and a study in the north of England reported 52% of red blood cell use was for medical indications.[6-8] Transfusions are especially common in patients over the age of 65.[6-8] The incidence of anemia in this age group is 11% for men and 10.2% for women.[9] An increase in red blood cell use is expected as the population of the US ages and lives longer. (Figure 1) If current transfusion practices continue small increases in this number of patients older than 65 will have a large impact on red blood cell demand.[6-8]

Despite knowing that red blood cell use is likely to increase it is difficult to predict how much blood will be needed in the coming years. Who receives red blood cells is variable and unstandardized. The reasons for this have been ascribed to patient's gender, age, [10-12] and provider's insufficient knowledge.[4] Differences in red blood utilization have also been attributed to variability in transfusion guidelines between institutions, [14-16] within institutions, [13-17] and to the poor adherence by individual providers to these institutional or departmental guidelines.[10-12, 18] Anesthesiologists,[17] intensivists,[13, 14] and obstetricians.[15, 16] are specific groups noted to have wide variability in their use of red blood cells. Such differences in utilization lead to the question, "When is it appropriate to give blood?"

It is estimated that up to 25% of the red blood cells transfused in the United States is inappropriate,[19-22] and in medical patients it may be as high as 35%.[21] Overuse is common because of the wide availability of red blood cells, a belief that complications are infrequent, and an unfounded fear that adverse outcomes will occur if a patient is not transfused.[4] These factors and the lack of conclusive research may lead many physicians to transfuse based on a predetermined hemoglobin value rather than on objective findings.[23]

This study will focus on the use of red blood cells by hospitalists, internal medicine physicians who devote the majority of their time to care for hospitalized patients. Medicare data show that since 2001 patients over the age of 65 are increasingly being cared for by hospitalists.[24] It is likely hospitalists will make a large percentage of the decisions to transfuse hospitalized patients and be asked to advise other specialties when to give red blood cells. A this time nothing is known about the rate of inappropriate blood transfusions, so called mistransfusions, which manifest as both over- and undertransfusions among hospitalists.

There are many favorable factors in place for the application of research within this group of physicians. First the organizational structure of the hospitalist specialty lends itself toward standardization of care, instead of each practitioner practicing as he or she sees fit medical conditions are treated similarly by groups of hospitalists. Secondly, the increase in the availability and governmental funding of electronic medical records and computer order entry makes it easier to track, monitor, and standardize the use of red blood cells. Third, hospitalists are increasingly involved in and are leading institutional quality improvement initiatives.[25] Hospitalists involvement in institutional practice policy is more likely to result in sustainable change. Fourth, the current socio political environment to reign in unnecessary health care costs makes it likely initiative to decrease inappropriate transfusions will have administrative support. Indeed, evidence already exists that elimination of mistransfusions will have economic benefit.[26] Finally, change is feasible. The initiation of transfusion guidelines in many clinical settings has already been proven effective in decreasing mistransfusion rates.[27, 28]

Purpose Statement

The purpose of this study is to characterize the red blood cell transfusion practice patterns among hospitalists at a single institution, ascertain if they are appropriate, and determine if an educational intervention changes red blood cell transfusion practice patterns.

The research questions answered by this study are:

1. What are the red blood cell transfusion practice patterns among hospitalists at Emory University Hospital Midtown (EUHM)?

2. Do hospitalists at EUHM follow evidence based red blood cell transfusion guidelines?

3. Will hospitalists use of red blood cells change after an educational intervention?

Significance Statement

The answers to these questions are needed to identify and describe patients who are being transfused by hospitalists. Documenting the practice patterns of hospitalists will add knowledge where none exists in the literature and help determine if transfusions are being done appropriately. Specific groups of patients inappropriately given red blood cells may be identified for further study.

Appropriate use of red blood cells is important because misuse has many adverse health, economic, and public health consequences. Red blood cell transfusions can induce significant adverse reactions that negatively impact patient health. These will be discussed in detail in the literature review. Societal and financial transfusion costs are high. A 1991 survey of 19 US teaching hospitals found the average cost to the patient for each unit of blood transfused was 219 dollars.[29] These costs of transfusion are only expected to increase as new blood safety measures are introduced.[26] Part of this increased cost is the inclusion of screening for emerging disease such West Nile Virus and Trypanosoma cruzi, in addition to the unintentional blood borne transmission of known disease such as HIV and hepatitis.[30-32] Conservatively estimating that 25% of the 14 million transfusions done in 2006 were unnecessary the cost savings in 1991 would be 766.5 million dollars. An example of the cost savings was demonstrated at a large tertiary care teaching hospital where over 1.6 million dollars was saved over a 3 year period after education and monitoring were instituted.[33] Finally, the demand for blood is growing faster than the rate of donation. Donation is problematic. 38% of the population is eligible to donate blood yet only 8 million people do so each year. Appropriate use of blood by the medical community is needed to make the best use of a scare resource.[34]

In summary, this exploratory study will describe the transfusion practices of a previously unstudied group positioned to influence and standardize the use of red blood cells, generate questions for future transfusion research, and demonstrate the efficacy of education as an intervention to decrease the inappropriate use of red blood cells.

Definition of Terms

Anemia – Hb <13 g/dL for adult males and < 12 g/dL for adult nonpregnant females [35]
Hospitalists - Internal medicine physicians who devote the majority of their time to care for hospitalized patients.[24]

Abbreviations:

ACS - Acute coronary syndrome
ACP - American College of Physician (ACP)
AOCD - Anemia of chronic disease (AOCD)
CI – Confidence Interval
CAD – Coronary Artery Disease
CABG - Coronary artery bypass graft
CHF – Congestive Heart Failure
EUHM - Emory University Hospital Midtown
Hb - Hemoglobin
HIV - Human immunodeficiency virus
ICU – Intensive care unit
IRB – Institutional Review Board
JCAHO (Joint Commission on Accreditation of Heath Care Organizations)
LVH – Left ventricular hypertrophy
NSTEMI - Non ST elevation myocardial infarction
OR – Odds ratio
RCT - Randomized Control Trials
SD – Standard Deviation
STEMI - ST elevation myocardial infarction
TRICC - Transfusion Requirements in Critical Care

Chapter II: Review of the Literature

Introduction

Published manuscripts were reviewed on the topic of red blood transfusion with a focus on those done in the inpatient setting. The literature review was unable to look at the transfusion practices of hospitalists directly because there are no studies. In order to look at how transfusion affects the inpatient adult population served by hospitalists several sections of the transfusion literature were reviewed.

The first section describes the effect of anemia and blood transfusions on the body. These studies delineate the lower limits to which animal and human tissue can tolerate anemia and the available evidence of red blood cells positive and negative effects on the body. Next, the review looked at the literature sought to define when to give blood to patients with cardiovascular disease. This subsegment of patients with cardiovascular disease merits special consideration by hospitalists. Patients with cardiovascular disease may require higher Hb concentrations than patients without cardiovascular disease because the myocardium has a higher oxygen consumption or oxygen extraction ratio compared to the rest of the body tissues making it more sensitive to anemia.[36 37] Both animal studies and human studies were reviewed on subjects with cardiovascular disease and those with active cardiovascular disease. The literature reviewed in this paper has been used by experts to develop guidelines. The pertinent transfusion guidelines applicable to our study population were reviewed as the starting point for the current and future transfusion guidelines used by hospitalists.

Effect of Anemia on the Body - Observational Studies

Studies of clinical signs and diagnostic tests are used by clinicians to determine which patients need red blood cells. Clinical signs used include tachycardia, low blood pressure, and low oxygen saturations. Clinical symptoms associated with anemia are fatigue, weakness, shortness of breath, lightheadedness, and palpitations. In healthy volunteers noticeable changes in cognition and fatigue occurred at Hb values < 7 g/dL and increased in proportion to falling Hb.[34-37] While helpful, clinical signs and symptoms are not diagnostic of symptomatic anemia and must be interpreted in the context of each patient's symptoms and comorbidities.

Currently there are no diagnostic tests that can definitively guide a hospitalist's decision to give blood, but some can be useful. Electrocardiographic changes are used to detect ischemia, or lack of oxygen to the heart, in animals and humans. Hemodilution studies in healthy animals noted myocardial ischemia was detectable on electrocardiography at Hb levels < 5 g/dL.[36, 38] Studies performed in healthy volunteers showed similar results albeit infrequently. A study using 55 healthy volunteers' electrocardiographic changes occurred only 5.7% of the time at Hb level between 5-7 g/dL.[39] The lack of specificity makes electrocardiography unreliable. Lactic acid levels have been postulated to detect tissue hypoxia, the physiologic reason to give red blood cells. When tested in clinical practice some patient with high lactic acid level need blood others do not making it an unreliable tool.[40]

What happens to patients with extremely low hemoglobin? Only observational literature is available and is restricted to the small subset of perioperative patients who refuse blood transfusions. The studies consistently demonstrate mortality rises when hemoglobin falls. A case control study of 125 patients undergoing surgery found a mortality rate of 7.1 % in patients with a preoperative Hb > 10 g/dL compared to 61.5% for patients with a preoperative Hb < 6 g/dL. [41] A retrospective cohort study of 1958 surgical patients who refused blood transfusion on religious ground noted a 33% mortality rate when preoperative hemoglobin levels were < 6.0 g/dL. Above preoperative hemoglobin levels > 7.0 g/dL there was no increased mortality.[42] When these studies were combined as a retrospective cohort study, there were 2083 consecutive surgical patients of which 300 had postoperative Hb levels < 8 g/dL. No patients with postoperative hemoglobin levels between 7.1-8.0 g/dL died, but there was a graded risk of death with worsening anemia. The study reported a 9% mortality if the Hb was between 5.1 – 7.0 g/dL, a 30% mortality if the Hb was between 3.1 – 5.0 g/dL 30%, and a 64% mortality if the Hb <3.0 g/dL.[50]

Severe anemia can be fatal, but can harm come from giving blood? The literature tells us that a transfusion is not a benign intervention. Although most transfusion reactions are minor they can occur in up to 20% of transfusions.[43] These reactions may be mild, moderate, or severe. A fever or purities due to an allergic reaction to components in the blood serum are examples of mild reactions. Acquisition of an infections disease could be mild if the patient does not suffer long-term consequences or severe if accidental transmission of viral hepatitis or HIV occurs despite pretransfusion testing.[35] Severe reactions are usually not, but may be fatal. These include; acute lung injury, marked by the abrupt onset of dyspnea due to pulmonary edema, hypotension, fever, and tachycardia; and accidental transfusion of a mismatched blood specimen which can lead to renal failure, disseminated intravascular coagulation, hypotension, and shock.[30, 44]

A growing body of evidence in the surgical, trauma and intensive care unit (ICU) literature strongly suggests that blood transfusion leads to an increase in the number of infections.[42-45] Higher rates of infection associated with transfusions occurred in patients with an acute traumatic injury, gastrointestinal cancer surgery, coronary bypass graft surgery, hip surgery, burns, the critically ill, and in patients requiring ventilation.[45, 46] In must be noted that these studies are confounded by the lack of clearly defined indications to give blood and problems controlling for the severity of illness. To overcome these limitations a meta-analysis was done that including 20 peer reviewed studies from 1986-2000 that contained both control and transfused groups. Using a stepwise multivariate logistic regression model the study demonstrated a relationship between allogenic transfusion and postoperative bacterial infection.[45] A larger comprehensive review of 272,596 surgical, trauma, and ICU patients in 45 observational studies corroborated this finding. In this large study in addition to infection it also considered the endpoints of mortality, multiorgan dysfunction syndrome, and acute respiratory distress syndrome. The authors noted that differences in study designs, heterogeneity and populations makes it difficult to draw concrete conclusion, but the fact that only one subgroup of one study demonstrated benefit from transfusion and there was a consistent direction of harm. This makes it likely that transfusion of red blood cells has little benefit and is likely associated with a higher risk of morbidity and mortality.[46] Red blood cell transfusion can be a life saving therapy, but is not without risk.

While the above observation studies are helpful they should be interpreted with the following considerations. First, there are many uncontrolled confounding variables that cannot be adjusted for in patients who receive blood. Second, treatment evaluated illness is assumed to be a marker for illness burden when this may not be true. Patients who receive blood may be, but are not necessarily more severely ill than others. What we can conclude from the observational studies is that in patients without cardiovascular disease the evidence supports the use of lower transfusion triggers

Randomized Control Trials (RCTs)

There are few well designed randomized control trials that attempt to determine if blood transfusions alter morbidity and mortality. The information that can be gleaned from them is limited due to several factors. The quality of the trials are poor with only 10 RCTs published with clearly defined transfusion triggers [47-56] The trials are summarized in Table 1. (All Tables and Figures are located in the Appendix starting on page 52). The 1780 patients represented in these trials are heterogeneous making it difficult to generalize any conclusions. Due to the small number of patients in each trail most of the RCTs are underpowered. Only three of the ten trials had more than 100 patients and only the largest trial had the power to evaluate outcomes Finally, the overlap of conservative and liberal transfusion triggers makes the trials difficult to compare.

The largest RCT trial was the Transfusion Requirements in Critical Care (TRICC) Trial. It valuated two transfusion triggers in 838 volume resuscitated patients admitted to the ICU. In the restrictive arm patients were randomized to a transfusion strategy in which blood was administered when the hemoglobin concentration fell below 7.0 g/dL. In the liberal transfusion group, patients were transfused to maintain hemoglobin concentration > 10.0 g/dL. For all patients the 30-day mortality was lower but not significantly lower in the restrictive transfusion group compared to the liberal group ($p = 0.11$, 95% CI -0.084 – 10.2). The findings were statistically significant in patients less than 55 years of age ($p = 0.02$, 95% CI 1.1-13.5%) and in less ill patients defined by having an Apache score less than 20 ($p=0.03$, 95% CI 1.1 – 13. %). In this group the overall mortality was less than patients randomized to the restrictive transfusion group, 22.2% compared to 28.1% ($p =0.5$, 95% CI -0.3 – 11.7%). Weaknesses of the study design were the lack of a control group and use of two arbitrarily fixed treatment points for what is usually a titrated therapy.

The TRICC trial and remained of the RCTs (Table 1) were included in a meta- analysis. The authors concluded the trails favored the restrictive use of red blood cells. Noting the limitations of the RCTs already mentioned and the preponderance (83%) of the evidence comes from the Transfusion Requirements in Critical Care (TRICC) trial[53] the evidence from RCT is not robust enough to provide evidence based guidelines to clinicians.

Cardiovascular Disease and Transfusion

Animals with experimentally induced coronary artery disease are less able to tolerate anemia. A 1978 study compared 10 normal canine hearts with 6 canine hearts with left ventricular hypertrophy (LVH). When 50 – 80% coronary stenosis was induced in the canine hearts with LVH myocardial ischemia was noted earlier and at a more pronounced rate than the normal hearts at Hb levels between 7-10 g/dL.[57] In a similar study arterial stenosis was induced in 20 mongrel dogs. Regional myocardial function declined when the hemoglobin was decreased to 15% of normal levels by isovolumentic exchange but was unimpaired when the stenosis was reversed.[38]

Analogous human studies were done in hospitalized patients with and without cardiovascular disease. Based on animal studies it would seem logical that patients with cardiovascular disease would benefit to transfusion at low Hb levels, but surprisingly the results were not clear.

A large cohort study of 1,958 adult surgical patients underwent a surgical procedure in an operating room. Logistic regression estimated the association between Hb concentration and mortality with adjustment for potential confounders. It found patients with cardiovascular disease had a higher relative risk of death as the hemoglobin concentration fell below 10 g/dL than in patients without cardiovascular disease. The study conclusions are not as impressive after noting a study design flaw. Only 55.2% of the patients had a postoperative Hb checked. The authors attempted to circumvent this flaw by running the analysis with an assumed 2 g/dL Hb drop and found their results were unchanged. Although not stated specifically this value was likely chosen because 2 g/dL was the mean Hb drop of the patients whose postoperative Hb was checked. Patients whose Hb dropped were older, sicker and more likely to have cardiovascular disease. [49] Using a lower assumed Hb drop may be more representative of the patient population and might significantly change the models outcome. A stepwise analysis would have been helpful. Another inconclusive study did a subgroup analysis of the ICU patients with cardiovascular disease in the randomized control TRICC trial mentioned above. The sub group analysis found that in contrast to overall trial results of decreased mortality in the restrictive group patients with cardiovascular disease may benefit from transfusion. The 327 patients with ischemic heart disease (defined as myocardial infarct, angina, congestive heart failure, and carcinogenic shock) in the liberal transfusion group had a small but non-significant improvement in primary and secondary outcomes. It was noted appropriately that the subgroup analysis ability to detect differences may be due to the small sample size.[58]

Although it may be possible that patients with heart disease benefit from red blood cells one observational study found no benefit to transfusion in patients with cardiovascular disease. In 8,787 patients undergoing hip fracture repair no statistically significant change was found in the short or longer term mortality between those given and not given blood down to postoperative Hb of 8 g/dL regardless of the presence or absence of cardiovascular disease. [59]

The high rate of comorbidities in the large population, long study duration, and the use of 20 facilities were particular strengths of the study.

The observational and outcome studies of patients with cardiovascular disease suggest a benefit to transfusion at low Hb levels, but are inconclusive.

Active Cardiovascular Disease and Transfusion

Based on the literature in patents with known cardiovascular disease, it would seem that anemic patients with active cardiovascular disease defined as a ST elevation myocardial infarction (STEMI), a non ST elevation myocardial infarction (NSTEMI), or those undergoing coronary artery bypass graft (CABG) surgery might clarify if transfusions are beneficial. Unfortunately, the evidence suggesting benefit is contradictory.

Studies showing Benefit

Some studies conclude transfusion is associated with poor outcomes. In 2,202 patients undergoing CABG the liberal transfusion group had a higher incidence of adverse outcomes than the conservative group. Patients enrolled where placed into three groups based on their initial hematocrit upon entering the ICU. The high (> or = 34%), medium (25% to 33%), and low (< or = 24%) group characteristics and incidence of myocardial infarction were compared. Logistical regression analysis found patients in the high group had an increased rate of myocardial infarction (8.3% vs. 5.5% vs. 3.6%; p < or = 0.03, high, medium vs. low) and mortality (8.6% vs. 4.5% vs. 3.2%; p < 0.001, high, medium vs. low) than those in the medium and low groups. The variable transfusions did not decrease myocardial infarction or mortality.[63] Another study used a prospective database of 1,410 patients of which 370 were anemic and had suspected acute coronary syndrome (ACS). Comparing baseline characteristics with chi-square for continuous variables and Student t test for continuous variables and testing the associations of the characteristics and outcomes with a univariate logistic regression model it found a higher rate of 30 day mortality and recurrent myocardial infarction in those who received a transfusion (odds ratio 3.05, 95% CI 1.8-5.17).[64]. Mortality was also associated with transfusion in an observational study of 24,111 patients with acute coronary syndrome that used data from three randomized control trials. Proportional hazard modeling found the risk of death to be 3.94 times higher in the 2401 patients who received blood. A stepwise multivariate logistical regression model adjusted for the influence of time, risk of bleeding, type of myocardial infarction, and procedures. Transfusions were not associated with improved survival when the nadir hematocrit values were in the range of 20-25% and were clearly associated with worse outcomes with values were >30%.[60] Study conclusions should be interpreted with caution as transfused patients were older, had more comorbidities, and required aggressive intervention measures associated with the use of antithrombotic drugs. A retrospective study of 85,111 with NSTEMI at 478 hospitals included 74, 271 patients who did not undergo CABG. 10.3% of these patients received a transfusion. As in the study just described transfused patients were more likely to be older and have comorbidities. After adjusting for difference patients who received a transfusion had a higher risk of death {adjusted risk odds ratio (OR) 1.67 (95% CI 1.48-1.88).[61]

Studies with adverse and beneficial outcomes

Some studies found adverse and beneficial outcomes depending on the degree of anemia. 4.6% of the patients with a STEMI and 2.7% of patient with a NSTEMI were transfused in a retrospective cohort study of 39,922 patients compiled from 16 acute coronary studies. Transfused patients with an STEMI and a Hb <12 g/dL had a lower risk of cardiovascular related death (adjusted OR 0.42, 95% CI 0.20 to 0.89). However, transfused patients with NSTEMI transfusion increased their mortality regardless of the Hb concentration (adjusted OR 1.42, 95% CI 1.14-2.09). The study concluded that anemia might be associated with mortality in patient with acute coronary syndrome (ACS) proportional to level of anemia. It should be noted that approximately 80% took place in setting of bleeding and mortality may be related to variables other than transfusion.[62] In a prospective study of 2,358, 8.1% of patients with ACS received a blood transfusion. Using a Cox regression model the study concluded there was an overall association between transfusion and 6 month mortality (28% vs. 11.7%, p <0.001). When subgroup analysis was done this held up for patients with a nadir Hb of > 8g/dL (adjusted hazard ratio 2.2, 95% CI 1.5-3.3, p<0.0001) but not for patients with a nadir Hb <8 g/dL where transfusion decreased mortality (adjusted hazard ratio 0.13, 95% CI .03-.65 p 0<013).[63] Similar findings were found in a retrospective study of 44,242 patients with ACS. Mortality increased when blood given to patients with nadir hematocrit >30% but transfusion decreases mortality in patient with nadir hematocrit < or equal to 24%.[64]

Study associated with improved outcome after transfusion

One study concluded transfusions were associated with better outcomes. A retrospective study based on Medicare claims data included 78,974 patients age >65 with a primary diagnosis of ACS where 3680 patients (4.7%) were transfused. A reduction in 30 day mortality was observed for patients who received a transfusion if their admission hemoglobin was <33%.[65] Interpretation of the study findings must take into account the following considerations. Although anemia was present in nearly half of the elderly patients the low rate of exposure to red blood cell limits statistical adjustment in the multivariate analysis. Furthermore the analysis was based on the admission hematocrit rather than the hematocrit associated with the transfusion. This lack of consideration for the time dependent use of red blood cells residual is a confounder that throws considerable doubt on the data validity. This study and many other transfusion studies performed in patients with cardiovascular disease relied heavily on logistic regression. The lack of specific information on the assumptions that were made limit the reader's ability to interpret the results. Additionally, the exclusion of variables in some models and the inclusion of extraneous variables in others could change the conclusions.

Summary

There are several alternative explanations for the contradictory findings in patients with active cardiovascular disease. They include the use of different patient populations, use of new anti-platelet agents in more recent studies, differing definitions of anemia, and small populations that result in underpowered studies. Additionally, despite the extensive statistical adjustment of the results, differences between patients who were and were not transfused may not be identified or were inadequately adjusted for.

Transfusion Guidelines

The evidence reviewed thus far is the basis for transfusion guidelines that may be used by hospitalists. Early use of guidelines as a quality control measure were pioneered by Virgil Slee in 1974 when he recommended single unit blood use if patients fell into specified groups of chronic anemia, trauma, and surgery.[66] In 1988 a consensus conference sponsored by the National Institutes of Health reported that there was insufficient evidence to support a single criterion for transfusion.[67] Since then there have been observational and RCT published with subsequent guidelines that also advise against a single transfusion threshold.   Universally they recommend giving blood for preoperative patients in the range of hemoglobin values been 6-10 g/dL depending on the presence of co morbidities. The majority of these guidelines address transfusion in the perioperative setting, the ICU, and in trauma patients.[40]   This leaves the American College of Physician (ACP) and the Canadian Medical Association Expert Working Group guidelines for the use of red blood cells outside these settings that are applicable to hospitalists They are listed below.

Canadian Medical Association Expert Working Group Guidelines:[68]

1. A physician prescribing transfusion of red blood cells or plasma should be familiar with the indications for and the benefits and risk from the use of these fractions.

   Level of evidence: N/A [1]

2. Documentation that supports the administration of the red blood cells or plasma should be found in the patient's chart.

   Level of evidence: N/A

3. Red blood cell transfusions should be administered primarily to prevent or alleviate symptoms, signs or morbidity due to inadequate tissue oxygen delivery (resulting from a low red blood cell mass).

   Level of evidence: II

1

Level of Evidence I – Evidence obtained from at least one properly randomized controlled trial
Level of Evidence II – Evidence obtained from well-designed controlled trials without randomization, cohort or case-control analytic studies, preferably from more than one center, or research or evidence obtained from comparisons between times or places with or without the intervention.
Level of Evidence III – Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees
Not Applicable – NA – opinions of the expert working group about issues that cannot be evaluated using accepted study designs.

4. There is no single value of hemoglobin concentration that justifies or requires transfusion; an evaluation of the patient's clinical situation should also be a factor in the decision.

   Level of evidence: II

5. In the setting of acute blood loss, red blood cell transfusion should not be used to expand vascular volume when oxygen carrying capacity is adequate.

   Level of evidence II

6. Anemia should not be treated with red blood cell transfusions if alternative therapies with fewer potential risks are available and appropriate.

   Level of evidence: II

American College of Physician (ACP) Guidelines [69]

1. Avoid an empiric, automatic transfusion threshold (for example, hemoglobin <10g/dL)

2. Regard elective transfusion with homologous blood as an outcome to be avoided.

3. Plan for the availability of autologous blood when acute blood loss can be predicted (before elective surgery).

4. Administer transfusion on a unit-by-unit basis, according to symptoms. Remember: one unit may be sufficient.

5. Consider erythropoietin therapy to treat the anemia associated with chronic disease.

6. Transfusions should be considered in the following situations:

- Acute anemia: to relieve symptoms related to blood loss when crystalloid infusions have failed to correct intravascular volume depletions
- Chronic anemia: to relieve symptoms related to decreased red blood cell volume when other therapeutic interventions such as iron replacement or erythropoietin treatment, or both, have been insufficient

7. Transfusions should not be used for the following reasons;

- To enhance the general sense of well being
- To promote wound healing
- Prophylactically (in the absence of symptoms)
- To expand vascular volume when oxygen-carrying capacity is adequate.

Education Effect

This research project evaluates the potential of education as an intervention to decrease the inappropriate use of red blood cells. It is documented that physicians who understand the risks and benefits of red blood cell use tend to transfuse less blood that those who know less.[4, 70] It is less clear if education provides a sustainable change in practice patterns. It been noted that private practitioners are less likely to follow transfusion guidelines than physicians in training.[21]

A hospital wide educational intervention utilizing an information sheet that listed appropriate criteria for transfusion had mixed results. Voluntary use of the transfusion sheets did not affect transfusion rates. Mandatory use of the transfusion sheets reduced use of RBC by 26%. The study noted no change in mortality and no change in the hospital population could account for the change.[27]

A systematic review of studies to reduce inappropriate transfusions found that overall, educational interventions are effective. However, in many of these studies, the methodologies used to assess appropriateness of transfusion differed and lacked evidence-based criteria as part of their design. It concluded that well designed studies are needed to determine which behavioral interventions are most effective.[70]

Summary of Current Problem and Study Relevance

Anemia is a common problem of hospitalized patients that is routinely treated with red blood cell transfusions. Overuse of this scare resource may be widespread and can cause unintended adverse health, fiscal, and public health consequences. To date the literature suggests red blood cell transfusion increases morbidity and mortality across heterogeneous patient groups without cardiovascular disease with sparse evidence that its use in non bleeding patients with a Hb >7 g/dL leads to improved outcomes. Its use in patients with cardiovascular disease remains unclear with some studies showing a benefit at a yet undefined threshold.

The lack of definitive data to guide the generation of Level 1 evidence based guidelines limits their use for hospitalists. The utility of available guidelines is further limited because studies are based on surgical, ICU, and trauma literature that may not be generalized to medical inpatients and do not differentiate between patients with and without cardiovascular disease.

Hospitalists are poised to care for increasing numbers of anemic patients. Exploratory research is needed to understand if hospitalists are using red blood cells appropriately. Characterizing patients taken care of by hospitalists could facilitate the application of existing literature to these patients and discover if particular groups of anemic patients are being inappropriately given red blood cells. The results of this research is not expected to be useful in isolation for decisions making, but may provide significant insights into why, how, and when transfusions occur in medical inpatients. This information could guide future research initiatives.

Education has been shown to be an effective intervention in changing transfusion practice. This exploratory study of an education initiative among hospitalists at a mixed academic/community hospital sought to document its efficacy and potential to improve compliance with a recognized transfusion guideline. If effective, it may provide a template for larger studies in various institutional settings.

Chapter III: Methodology

Introduction

The study was conducted in a 511 bed community-based tertiary care teaching hospital affiliated with the Emory University.

Population and Sample

The hospitalists in this study consisted of a group of 22 internal medicine trained physicians employed by EUHM between 9/1/2006 and 06/30/2007. All physicians in the study had completed residency training. Research data was drawn from two databases; the hospital ICD-9 billing data base and the hospital pathology database.

ICD-9 Database:

The ICD-9 database is used by the billing department after a patient has been discharged from the hospital. Trained coders review physician notes and assign an ICD-9 code to every medical diagnoses documented and procedure that occurred during the patients hospital stay. The patients were pulled from this hospital data base by a trained information technology technician. The search criteria specified the hospitalists by name and included patients who were admitted, discharged, or consulted on by these hospitalist from 11/1/2006 – 1/31/2007 and 4/01/2007 to 06/30/207. Demographic data obtained included the patient's age and sex. Demographic data and ICD-9 codes for each patient was placed in an excel spreadsheet and given to the primary investigator.

Pathology Database:

The transfused patient study population was drawn from patients ≥18 years old who had an order for a red blood cell transfusion written by a hospitalist and were discharged in the time periods from 11/1/2006 – 1/31/2007 and 4/01/2007 to 06/30/2007. The 3 month time periods where chosen because they included a sufficient patient population to document the populations characteristics and note differences after implementation of the educational intervention. The patients were identified from a continuously updated pathology database that captures when and who enters an order for a red blood cell transfusion on all hospitalized patients.

Exclusion Criteria

Patients were excluded from the study if they met the following criteria; were admitted expressly for red blood cell transfusion from a medical or specialty clinic; or the patient was on dialysis. These exclusion criteria were used to assure that study participants were transfused based on the clinical assessment of a hospitalist.

Research Design

The research design is a single center retrospective cohort study which was approved by the Emory Institutional Review Board (IRB). A conceptual model of the study was created (Figure 2).

The retrospective cohort study design is applicable as the exposure (anemia) is followed shortly by the outcome (transfusion) and the potential for discovery of a wide variety of information to direct future study. Weaknesses of the study design are the potential that valuable patient and provider characteristics will not be recorded. The lack of control subjects and blinding of the investigator could result in the generation of further research questions and preliminary conclusions that are erroneous, possibly due to confounding variables or presence of data deemed important when it is merely associative.

Data Collection:

The study timeline included three phases of data collection: a 3-month pre education period to establish the baseline transfusion practices of hospitalists; a 2 month educational intervention phase; and a 3 month post education phase. Patient data was collected during the first and last stages of the study (Figure 3). Study patients were identified using the pathology database. For patients who received more than one transfusion only the initial blood transfusion was included in this study. Red blood cell transfusion was defined as the administration of a unit of red blood cell following a documented order by a hospitalist.

Data collected from the hospital chart included patient demographic data and laboratory data. Demographic data included age, sex, the primary cause of anemia, if the primary reason for admission was anemia, history of a stroke, hypertension, arrhythmias, and the presence of cardiac disease. Laboratory data collected included the discharge creatinine, admission Hb, discharge Hb and the trigger hemoglobin, defined as the hemoglobin value that immediately preceded the first red blood cell transfusion. Noting the importance of the underlying etiology in determining a provider's threshold to transfuse, the reason for initial transfusion was categorized into one of 5 categories: acute blood loss, chronic blood loss, and hemolytic anemia, anemia of chronic disease, B12 / folate deficiency, or unknown. When not specified in the medical record the etiology of the bleeding was inferred from the physician notes and discharge summaries. Acute blood loss was defined as documented or suspected active blood loss from any site Chronic blood loss was defined as a hypochromic microcytic anemia due to deficient iron intake, poor absorption of iron, or excessive blood loss. Hemolytic anemia was defined as anemia resulting from the destruction of red blood cells caused by genetic disorders, infection, or toxic chemicals. Anemia of chronic disease (AOCD) was defined as anemia attributable to a chronic medical condition that alters the production and lifespan of red blood cells. These chronic medical conditions include chronic infectious, inflammatory disorders or neoplastic disorders that are not due to marrow replacement by tumor, bleeding, or hemolysis. It is further defined by hypoferremia in the presence of adequate iron stores [76, 77]and by the history of "AOCD" recorded in the chart. B12 deficiency was defined as a low B12 level (<180 pg/ml) on laboratory testing or the history B12 deficiency noted in the chart. Folate deficiency was defined as a low folate level (<5.2 ng/ml) on laboratory testing or the history "folate deficiency" noted in the chart. Unknown was defined as any cases not meeting the above class criteria.

Noting that patients with anemia are transfused for different reasons each patients was coded as having received a transfusion for low hemoglobin/anemia, symptomatic anemia, hemoglobin drop of unclear etiology, or not given. Low hemoglobin/anemia is defined as the notation of low hemoglobin, low hematocrit, or anemia in the medical records at the time of the transfusion. .Symptomatic anemia is defined as the presence of anemia and the terms symptomatic anemia, dizziness, weakness, tachycardia, palpitations or shortness of breath as recorded in the chart in the days preceding the transfusion. Hemoglobin drop of unclear etiology is defined as a drop in the hemoglobin as compared to the admission hemoglobin without the documentation or suspicion of active bleeding, acute blood loss from a surgical procedure or noted in the medical record as hemoglobin drop of unknown etiology. Not given is defined when no reason for the transfusion was documented nor any reason could be inferred from the physician's notes or discharge summary.

Noting that patients are admitted with anemia or become anemic in the hospital it was determined if the primary reason for admission as anemia or other. Anemia was defined as the primary reason for being admitted when the physician notes or discharge summary indicated admission was needed to diagnose and treat low or expected low hemoglobin.

Because of an apriori hypothesis that hospitalists are more likely to transfuse patients with cardiovascular disease we defined a "cardiovascular disease" variable. We defined cardiovascular disease as the presence of angina pectoris, acute myocardial infarction, congestive heart failure, or arthrosclerosis as recorded in the chart. Angina pectoris was defined as a history of chest pain induced by exertion or emotion or ameliorated by rest or nitroglycerin, or history of angina in the chart. Congestive heart failure was defined by the history of "congestive heart failure" recorded in the chart. Acute myocardial infarction was defined as heart muscle damage noted by electrographic changes or the presence of elevated cardiac enzymes with an eventual decline toward normal values. Arthrosclerosis was defined as a history of angina pectoris defined above, myocardial infarction, or peripheral vascular disease.

The primary investigator and a trained research staff assistant abstracted charts with the use of an excel spread sheet that included the variables defined above.   A random sample of patients abstracted by the trained staff on the standardized form was reviewed by the primary investigator for quality assurance.

Noting that unaccounted for differences in the types and characteristics of patients seen in the pre and post education periods might explain any differences seen in the use of red blood cell discharge billing data was used to characterize the pre education and post education populations. Demographic and discharge ICD-9 billing codes were obtained from the hospital billing department for each study period. The ICD-9 codes were placed into the following categories by the primary investigator: acute blood loss, chronic blood loss, AOCD, hemolytic anemia, B12/Folate deficiency, anemia, and cardiovascular disease for the pre education and post education groups. A list of the ICD codes placed in each category are listed in Table 2. The patients identified in the pathology databases as being transfused by a hospitalist were cross referenced with the ICD-9 code data base to determine if all study patients were present in both databases.

Inappropriate transfusion for patients without documented cardiovascular disease was defined as administration of red blood cells in an asymptomatic, not actively bleeding patient for a Hb >7.0 g/dL. Inappropriate transfusion in patients with cardiovascular disease was defined as administration of red blood cells in an asymptomatic, non bleeding patient for a Hb > 9 g/dL.

Outcome of Interest

The primary outcome of interest was the number of times an initial red blood cell transfusion was given to a hospitalized patient cared for by a hospitalist.

Education of Staff

Beginning 2/1/07 and concluding on 3/31/07 an education initiative was performed. The primary investigator developed the educational material. It consisted of a hospital grand rounds presentation, review of the current literature at a journal club, and personal communication with individual hospitalists unable to attend the formal educational sessions. The following points were emphasized. Red blood cells are indicated for the improvement of tissue oxygenation, there is limited research to support its use, the research that is available supports a conservative, restrictive use of red blood cells, and there are hazards associated with the use of red blood cell use. Hospitalists were introduced to a transfusion guideline, [67, 71] (Figure 4) but during the study there was no standardized protocol for transfusions.

Instruments

A standardized excel spreadsheet was used to collect the data. Each patient was entered using their medical record number as the unique patient identifier and the information collected from the hospital chart was collated into the database.

Data Analysis

We used SPSS (SPSS Statistics version 17.0) for statistical analysis. The data in the excel database was converted into SPSS and the analysis of the results performed using the units within each variable category. The characteristics of the patients of the pre and post education periods for the ICD-9 and pathology databases were reported with means and SD for continuous variables and percentages for categorical variables. The distributions of these variables were compared with chi-square tests for categorical variables. The chi square test was chosen because the categorical variables are dichotomous and this test can demonstrate that our results are not due to chance alone. An unpaired T test was used to compare the transfusion triggers of the pre-education and the post-education groups. The unpaired T test was chosen because these groups are unpaired and the population was normally distributed and the sample size was large.

Data from the ICD-9 database and pathology database were combined for statistical analysis. The ICD-9 database included all the patients seen by hospitalists during the study periods and therefore this data was felt to be a valid denominator for statistical analysis of the pathology database.

Limitations

This study has several limitations. The validity of the ICD-9 and chart review data is dependent on the quality of physician documentation. We found that explicit documentation of red blood cell transfusion and the rationale to transfusion was often lacking. Our experience seems representative with prior studies noting the quality of medical record documentation is historically poor and may not be reliable.[72] The lack of reliable data could have resulted in subjective assignment to a data category when insufficient information was present. A potential confounder was a larger number of patients with renal insufficiency in the pre education period. Renal insufficiency is associated with a higher incidence of anemia (60-80%) [73, 74] and may have resulted in a greater incidence of anemia in the pre education period. Because we collected data retrospectively and combined two different databases to generate some of the conclusions there is a chance that data does not accurately represent the studied population.

There were limitations to the study design. The single center study design is limiting because it is known that red blood cell use varies between institutions[75, 76] and the finding may not be representative of other institutions. We assumed education was the only variable that changed the hospitalists' transfusion practices, however there may be unmeasured variable(s) that were also responsible for a change in red blood cell use. One possible variable was the presence of the primary investigator as part of the study group which could have influenced practice patterns due to a Hawthorne effect. The use of an academic hospitalists who may have a heightened sense of ethics or adherence to the education may have enhanced the result. Physicians who are more accustomed to changing quickly when presented with scientific research may be more likely to alter their behavior. The use of discharge ICD-9 billing data as the denominator for statistical analysis is flawed. Patients with multiple causes of anemia were used more than once resulting in inexact calculations.

The use of a transfusion guideline (Figure 4) instead of the ACP and Canadian Medical Association Expert Working Group transfusion guidelines could hamper the use of our conclusions. Using the transfusion guideline in isolation to identify mistransfusions in patients without cardiovascular disease may overestimate mistransfusions as there may be clinical variables other than the Hb level that precipitated use of red blood cells. Similarly the use of a Hb >9g/dL to identify mistransfusion in patient with cardiovascular disease may overestimate the number of mistransfusions.

Chapter IV: Results

Introduction

The following section will describe and compare the characteristics of the population taken care of by hospitalists and the patients who received a red blood transfusion in the pre and post education study periods.

Hospitalist ordering characteristics

Twenty-two different hospitalists wrote orders for 248 red blood cell transfusions given during the two study periods. The mean number of transfusions per hospitalists was 10.78 with a SD of 5.97. The maximum number of transfusions ordered by one hospitalist was 25, which was 10.1% of the total. The least number of transfusions ordered by two hospitalists was 1 which was 0.4% of the total. A histogram of the percentage of transfusions ordered by each hospitalists shows the distribution of the number of transfusions ordered by the hospitalists (Figure 5). Comparison of the number of transfusions between the pre and post education periods show that orders to transfusions were spread over many hospitalists (Figure 6) and distribution of transfusion triggers was similar between hospitalists (Figure 7). Figure 8 notes the variability in the overall red blood cell use and Figure 9 the variability in the use of red blood cells in the causes of anemia. Standard deviation (SD) of the mean trigger Hb declined overall and within each category between the pre and post educational periods except in the categories AOCD and unknown etiology.

Database Population Characteristics

ICD-9 Database

There were no statistically significant differences in the characteristics of the population taken care of by hospitalists during the pre education period and post education period except for the condition HTN which was more prevalent in the post education period ($p < 0.001$) and chronic obstructive pulmonary disease (COPD) which was more prevalent in the pre education period ($p < 0.013$) (Table 3).

Pathology Database

A total of 273 patients were identified in the pathology database as being transfused by a hospitalist. 25 of these patients were excluded because they were on dialysis or admitted from a clinic at the request of another physician for a blood transfusion. All patients identified in the pathology database were cross-referenced and found to be in the ICD-9 database. The 248 patients included in the analysis are described in Table 4 and Table 5.. There were no significant differences in the proportion of male and female patients, ages, trigger Hb, presence of cardiovascular disease, primary reason for admission, or reason for transfusion in the pre and post education groups. (Table 4).

Primary Reason for Anemia

The proportions of patients receiving blood for the different categories of anemia were similar in the pre and post education periods (Table 4). In both periods AOCD was the most common reason for transfusion followed by acute and chronic blood loss.

Some categories did not contain many patients. Hemolytic anemia was noted as the primary reason for anemia in 12 patients in the pre education period, but in only 2 patients in the post education period. There were only 5 patients in both the pre and post education periods for the categories B12/folate deficiency and unknown etiology.

Reason for Admission

The majority of patients (60.9%) in the study were admitted for the reasons other than anemia or active bleeding. The proportion of patients admitted with a primary diagnosis of anemia was similar in the pre and post education periods (Table 6).

Primary Reason for Transfusion

There were no statistically significant changes in the proportion of the primary reason for transfusion given by a hospitalist in the pre and post education periods. The most common reason for transfusion was "Low Hb" used >77% of the time in both the pre and post educational periods. Patients transfused were documented in the medical record as being symptomatic more often in the post education period compared to the pre education period (12.5% vs. 10.9%) The largest change occurred in the "not given" category. Of the 11 patients identified in this category in the pre education period, 10 patients had AOCD and 1 patient had no diagnosis of anemia. In the post education period the single patient in this category was documented to have AOCD (Table 7).

Hospitalist Adherence to a Transfusion Guideline

Comparison of an accepted transfusion guideline (Figure 4) shown to the hospitalists in the education phase of the study to actual practice patterns provides an estimate of the number of inappropriate transfusion. This guideline recommends that patients without cardiovascular disease who were not actively bleeding administration of red blood cells not receive blood unless the Hb was <7 g/dL. Using this criterion, 75% of patients in the pre education period were mistransfused compared to 68% in the post education period (Table 8). The majority of mistransfusions was given to patients whose primary reason for anemia was AOCD.

In patients with cardiovascular disease who were not actively bleeding the mistransfusion was defined by this study as administration of red blood cells for a Hb >9 g/dL. Using this criterion, mistransfusions were rare. Three patients were mistransfused in the pre education period compared to only one in the post education period (Table 9).

Combined Database Analysis

Effect of Education:

There was a 65.7 % decrease in the total number of transfusions after the education intervention. When the individual categories of anemia were examined individually a chi square test demonstrated a statistical significant decrease (p value <.05) for the categories hemolytic anemia, and AOCD (Table 10).

While the total number of transfusions decreased and the overall mean hemoglobin declined after the educational intervention, the difference was not statistically significant (p = 0.76). When the mean trigger Hb and discharge Hb of individual etiologies of anemia were compared in the pre and post education period no statistically significant differences was found. The category B12/Folate did not have enough patients for statistical testing (Table 11 and Table 12).

Realizing that the mean Hb may be affected by outliers a stepwise analysis was performed to exclude this possibility. When outlier Hb were eliminated using trigger Hb values >5 g/dL and trigger Hb values >6 g/dL unpaired t tests demonstrated no difference in the overall mean Hb or the mean Hb for the different etiology of anemia, except when all categories of anemia were combined for a trigger Hb > 6 g/dL ($p = .04546$) (Table 13 and Table 14).

Cardiovascular Disease

After the educational intervention the overall number of transfusions in patients with and without cardiovascular disease declined significantly ($p < 0.0001$) (Table 15).

When all patients with cardiovascular disease were examined as a group in was noted they were transfused at a higher mean trigger Hb in the pre education period compared to the post education period. When individual etiologies of anemia were examined only the AOCD patients had a lower mean trigger Hb in the post education period. Insufficient data was available for calculation of mean trigger Hb in the categories hemolytic anemia and B12/Folate deficiency. There was an increase in the mean trigger Hb in the categories acute blood loss and chronic blood loss (Table 17).

Sex

Both men and women were transfused significantly less ($p < 0.0001$) after the educational intervention (Table 18). When men and women were examined separately the only etiology of anemia where both sexes had statistically significant decline in the mean trigger hemoglobin was AOCD (Table 19 and Table 20).

Age

Red cell use dropped in all age groups with statistically significant reduction found in patients aged 26-85. Patients over the age of 65 have been documented to be the largest consumers of red blood cells. [6-8] In this study 43.1 % of the transfusions were given to patients over the age of 65. The ICD-9 database included 1323 patients over the age of 65. When both study period data sets were combined for analysis we noted 8.09% of patients over the age of 65 were transfused. Viewed separately, in the pre education period 10.3% of patients were over the age of 65 were transfused compared to 5.89% of patients in the post education period. The decrease of 42.76% was statistically significant (P = 0.0092) (Table 21).

Chapter V: Conclusions, Implications, and Recommendations

Introduction

The results of this study characterize the patient population receiving transfusions and the red blood cell transfusion practice patterns of hospitalists, a previously unstudied group of physicians. Specifically, it suggests that red blood cells are being overused and that education may be a starting point to standardize the use of red blood cells.

The results of the preceding statistical analysis of the ICD-9 and Pathology Databases are summarized below in the order of the research questions.

Conclusions.

<u>*Research Question 1*</u>. *What are the red blood cell transfusion practice patterns among hospitalists at Emory University Hospital Midtown (EUHM)?*

Hospitalists were noted to encounter patients and initiate transfusions for a wide variety of causes of anemia. It is notable that the majority of transfusion occurred in patients admitted for reasons other than anemia or active bleeding (60.9%). Documentation of the reason of anemia was nonspecific, most often written as "low Hb or anemia."

While there was no gender differences in the rates of transfusion between the study periods, several clinical characteristics may have affected transfusion rates. There was a trend to transfuse at higher Hb values if patients had cardiovascular disease in the pre and post education periods in patients with AOCD. Advanced age, defined as age >65, was associated with a high rate of transfusion as was the range of Hb values between 7 and 9 g/dL

Practice patterns were variable between hospitalists and among the categories of anemia without any discernable pattern.

<u>Research Question 2</u>. *Do hospitalists at EUHM follow evidence based red blood cell transfusion guidelines?*

Hospitalists may be more likely to follow evidence based guidelines for patients with cardiovascular disease than for those without cardiovascular disease.

Mistransfusions occurred infrequently in asymptomatic patients with cardiovascular disease in both study periods. Smaller numbers of patients in this subgroup makes it difficult to conclude if hospitalists followed the guidelines or the study did not include enough patients to determine true practice patterns.

The overall decrease in the number of patients transfused suggests that mistransfusions declined significantly. Because it occurred in all categories of anemia it is possible that mistransfusions are not limited to a specific type of anemia. This study's mistransfusion rate asymptomatic patients without cardiovascular disease (pre-education 75%, post-education 68%) is higher than other studies. A study of patients with chronic pernicious anemia found 51% of patients received blood when they could have been treated without a transfusion.[77] A study of 263 patients with iron deficiency anemia found 24% of transfusions were not justified.[78] Our high rate of mistransfusion may be due to a faulted study design, a stricter definition of mistransfusion, and that physicians were not given adequate information to make an informed decision when to give blood.

Research Question 3. *Will hospitalists use of red blood cells change after an educational intervention?*

Decreased transfusion trigger variability and the statistically significant decline in transfusions after the educational intervention suggest that hospitalists are not aware of appropriate red blood cell use. Red blood cell decline in use was found in all age groups except the very old and very young which may be due to the small numbers of patients in these groups. Although there was a trend toward reduced blood use in all categories of anemia it was statistically significant only in patients with AOCD and hemolytic anemia. This may be because knowledge is most lacking in the treatment of these anemias. Although possible, an alternate explanation that a few physicians were responsible for the mistransfusion in the post education period and education did not affect their practice patterns was not supported by the variability in practice data.

It was expected that the mean hemoglobin would also decrease as a result of the educational initiative. It did for most categories of anemia, however the changes were not statistically significant. Small sample size may have limited the power of the study and a larger study might show a statistically significant drop. A drop in the overall number of transfusions without a significant change in the mean could also suggest that there are other variables hospitalists consider when making a decision to transfuse. Possible undocumented variables could be patient preference or the influence of sub specialists.

The reason "Low Hb" given for >77% of transfusions in the pre and post educational periods could be because hospitalists were unaffected by the education given the guidelines provided to them recommended not to transfuse unless the Hb was < 7g/dL. It could also represent an ingrained or default documentation of anemia. Evidence of improved knowledge in appropriate transfusion practice was suggested by the increase in symptomatic anemia documentation in the post education period compared to the pre education period (12.5% vs. 10.9%). Additional evidence of improved knowledge was the decreased numbers of cases were "no reason" for transfusion was given in the post education period.

Implications

<u>Research Question 1</u>. *What are the red blood cell transfusion practice patterns among hospitalists at Emory University Hospital Midtown (EUHM)?*

Practice pattern of hospitalists were variable. Red blood cells may be overused in hospitalized patients with any diagnosis of anemia, and in many age groups. This study could not ascribe any one variable that significantly influenced the use of red blood cells by hospitalists. Cardiovascular disease is one variable that appears to influence hospitalists to transfuse at a higher Hb than patients without cardiovascular disease, but the small number of patients make it difficult to draw meaningful conclusions from this study.

<u>Research Question 2</u>. *Do hospitalists at EUHM follow evidence based red blood cell transfusion guidelines?*

The lack of adherence to an accepted transfusion guideline before and after the educational initiate implies that knowledge of the guideline may not be enough to change practice patterns. There may be unmeasured or unknown variable that influence hospitalists to give red blood cells. It is also possible that particular combinations of variables may increase the use of red blood cells.

Research Question 3. Will hospitalists' use of red blood cells change after an educational intervention?

The decrease in the number of transfusions across types of anemia and age groups after the educational initiative implies that hospitalists are unfamiliar with appropriate transfusion practices and that educational initiatives could reduce the misuse of this scarce resource.

Recommendations

Research Question 1. What are the red blood cell transfusion practice patterns among hospitalists at Emory University Hospital Midtown (EUHM)?

This study is a small snapshot of one hospitalist groups transfusion practices. Further research is needed to fully characterize the population taken care of, and the practice patterns of hospitalists. The following studies are recommended.

1. A multicenter study of academic and community hospitals to characterize the patients being transfused by hospitalists. The study objective would be to determine if mistransfusions are occurring and if so the extent of the problem.

2. A qualitative study of hospitalists to determine the factors that influence the use of red blood cells followed by a case control study to determine if the factors elucidated in the qualitative study are valid.

3. A prospective randomized control trial comparing patients transfused in the non ICU setting with chronic blood loss, AOCD, B12/folate deficiency and hemolytic anemia

compared to placebo, the use of iron supplementation and erythropoeitin to determine which treatment alters morbidity and mortality. The ideal study would be powered to include enough patients with cardiovascular disease to do a subgroup analysis.

4. Targeted study of the different etiologies of anemia to determine optimal management and appropriate circumstances to initiate a transfusion.

Research Question 2. *Do hospitalists at EUHM follow evidence based red blood cell transfusion guidelines?*

Qualitative and quantitative research is needed to determine if other variables, or combinations of variables influence transfusions

Transfusion guidelines could be implemented as a hospital policy. We know that clinical practice guidelines have improved compliance with evidence based treatment of CHF and septic shock.[79, 80] Similar results have been found with transfusions. A transfusion policy change in patients undergoing CABG, hip replacement, colectomies and transuretral prostatectomies without education reduced the use of transfusions.[81] Based on current knowledge there is a lack of evidence to support strict enforcement of transfusion guidelines strict enforcement.. That said, transfusion guidelines could be very effective if the following steps are followed.

1. Obtain institutional support. Policies supported by institutions are an evidenced based strategy to reduce unnecessary transfusions.[82]
2. Improve documentation. Physicians are required to document if therapeutic procedure or drug is appropriate by JCAHO (joint commission on accreditation of

heath care organizations) [83] Documentation that justifies a transfusion will be needed to know the effectiveness of the transfusion guideline.

3. Consider individualized feedback to physicians through the use of chart audits in a timely manner to improve transfusion practice.[84]
4. Update transfusion guidelines to reflect evidenced based practice when new research is published

<u>Research Question 3</u>. *Will hospitalist's use of red blood cells change after an educational intervention?*

This study found education may be helpful in reducing inappropriate transfusions by hospitalists. Further research is needed to determine the type and extent of education needed. The following studies are recommended.

1. Similar education initiatives in other hospitalist groups and facilities to determine effect of a single initiative on the short and long term transfusion rate.

2. Comparative study of a one time educational initiative and educational sheet presented to hospitalists at the point of order entry on the short and long term transfusion rate.

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Appendix

Table 1- Summary of Randomized Control Trials

Author	Clinical Setting	Subjects – Eligibility	Mean Age of Patients(SD)		Sex of Patients		Restrictive/ Liberal	Outcomes of Interest	Transfusion Threshold – low	Transfusion Threshold High	Conclusion
			Restrictive	Liberal	Restrictive Ratio	Liberal Ratio					
Blair et al 1986[48]	Acute severe upper gastrointestinal hemorrhage N = 50	Acute severe upper gastrointestinal hemorrhage	64 (17.6)	60 (17.8)	M:F 2:1	M:F 2:1	5/26 24/24	Impedance Clotting time, rebleeding episodes, surgery, final outcome, blood transfusion requirements	Given blood if Hb <8 g/dl or shock persisted after initial colloid resuscitation in first 24 hours after admission	Given at least 2 units of blood on admission to the hospital	Transfusion requirements reduced, need for surgical operation fell, morality reduced 3.5% for bleeding peptic ulcer Conclude hypercoagulable response to hemorrhage that may be reversed by blood transfusion.
Fortune et al 1987[53]	Trauma/acute hemorrhage N = 25	Class III or Class IV Acute hemorrhage with clinical signs of shock	46.9	46.5	Not given	Not given	12 / 13	Heart rate, vascular pressures, cardiac output, Hct, arterial and mixed venous oxygen content	All given crystalloid then Hct was maintained close to 30% with RBC transfusions	All given crystalloid then Hct was maintained close to 40% with RBC transfusions	In trauma patient no benefit in tissue oxygenation to raising the Hct > 30 %
Bracey 1999[49]	Cardiac Surgery N=428	First time elective coronary revascularization	61 (11)	62 (11)	M/F 174/38	M/F 179/37	74/212 104/216	Transfusion incidence, duration of mechanical ventilation, length of stay in the ICU, length of postoperative stay in the hospital, morbidity, mortality, patient self assessment of fatigue and anemia (postoperative day 3 and 5)	Transfused for Hb <8.0 g/dL unless >750 ml blood loss since prior transfusion, hypovolemia with hypotension, excessive acute blood loss, acute respiratory failure, inadequate cardiac output, inadequate oxygenation, need for vasopressors	Transfused at the discretion of individual physicians considering the clinical situation and that the institutional guidelines suggest transfusion for a postoperative Hb < 9.0 g/dL	Lower Hb 8.0 g/dL did not affect patients need for mechanical ventilation, length of hospital stay, mortality, morbidity, or self assessment for patients with Hb >8 g/dL

Bush 1997[50]	Vascular Surgery N=99	Elective aortic and intrarenal arterial reconstruction	66 (10)	49 (11)	M/F 32/18	M/F 41/8	40/50 43/49	Primary Outcomes: Myocardial ischemia, myocardial infarction, death Secondary outcomes: length of ICU stay, hospital stay, graft patency	Transfused if Hb< 9.0 g/dL	Transfused if Hb <10.0 g/dL	Hb 9.3-9.8 g/dL were well tolerated. No increase in morality, cardiac morbidity or length of hospital stay with a Hb trigger of 9.0 g/dL. Decreased need for banked blood and reduced patient exposure and expense.
Carson 1998[51]	Orthopedic Surgery N=94	Hip fracture undergoing surgical repair with Hb <10.0 g/dL	83.3 (10.8)	81.3 (8.1)	M/F 11/31	M/F 9/33	19/42 41/42	Primary Outcomes: death, ability to walk 10 ft without assistance 60 days after surgery Secondary Outcomes: 30 and 60 day mortality, place of residence at 60 days, functional status in 60 days, in-hospital myocardial infarction, thromboembolism, stroke, pneumonia	Transfusion if symptomatic anemia or if Hb <8.0 g/dL	Transfused 1 unit when randomized and to keep Hb >10 g/dL	Symptomatic anemia use as a transfusion trigger decreased the use of RBCs no differences in rates of cardiovascular events, length of hospital stay, exercise tolerance
Hebert 1995[55]	Critical Care N=69	Critically ill admitted to 1 of 5 tertiary care ICU with normovolemia after initial care with Hb <9 g/dL in first 72 hours	58.6 (15)	59 (21)	M/F 14/19	M/F 19/17	18/33 35/36	Outcomes – 30 Day all-cause mortality, ICU mortality, hospital mortality, survival times. Assessment of organ dysfunction; number of organ failures, rates of multiple organ system failure. Length of ICU and hospital stay.	Transfused if Hb was ≤7.0- 7.5 g/dL; Hb maintained at 7.0-9.0 g/dL	Transfused if Hb ≤ 10.0 – 10.5 g/dL ; Hb maintained at 10.0 – 12.0 g/dL	Restrictive use of red blood cell in critically ill patients seems to be a safe practice without differences in morbidity and mortality from liberally transfused patients.
Hebert 1999[54]	Critical Care N=838	Critical ill admitted to 1 of 22 tertiary care and 3 community ICUs with normovolemia after initial care with Hb <9 g/dL in first 72 hours	57.1 (18.1)	58.1 (18.3)	M/F 269/149	M/F 255/165	280/416 420/420	All cause mortality, 30 and 60 day all cause mortality, organ failure score, organ dysfunction score, (APACHE score), length of stay	Transfused to maintain Hb between 7.0-9.0 g/dL	Transfused to maintain Hb between 10.0 – 12.0 g/dL	All cause mortality lower in restrictive group. 30 day mortality lower in patients age, 55 yrs with APACHE score <20 in restrictive group.
Johnson 1992[56]	Cardiac Surgery N=38	Elective coronary revascularization who donated 3 units of red blood cells preoperatively	58.2 (7.5)	60.5 (6.9)	M/F 20/0	M/F 16:2	15/20 18/18	Length of postoperative ventilatory support, type and amount of pharmacological support, volume of crystalloid given, alveolar-arterial oxygen gradients, heart	Given blood to keep Hct 32% if autologous blood was available	Received autologous blood if Hct <25%	No significant differences in exercise tests between two groups, post operative hemodynamics

								rate, rhythm, cardiac output, central venous pressure, pulmonary capillary wedge pressure, systemic arterial pressure, postoperative mediastinal blood loss, use of blood products, Hct, complications, length of stay in the ICU and hospital, exercise duration.			
Lotke 1999[57]	Orthopedic Surgery N= 127	Total knee arthoplasty who donated 2 units of autologous red blood preoperatively	68.7	69.7	M/F 20/42	M/F 19/46	16/62 65/65	Hemoglobin, Length of stay Surgical complications Nonsurgical complications, use of pain medicines, patients sense of well being, examiners sense of patients well being, physical therapy progress	Transfused if Hb <9.0 g/dL	Transfused 2 units of blood postoperatively	Higher number of nonsurgical complications in restrictive group. Higher physical therapy score in first 3 days, no difference in groups on postoperative day 4
Topley 1956[86]	Trauma N=22	> 1 Liter of blood loss. No risk of raising Hb >100% of normal or <30% of normal	Not given	Not given	Not given	Not given	8/12 10/10	Laboratory – Hb, red cell count, transfused red cell count, reticulocyte count (daily X 2 weeks then less freq over 3 months)	Maintain RBC volume 70-80% of normal	Maintain RBC volume >100% of normal	"Anemia of trauma is largely preventable by adequate blood transfusion in the majority of civilian Injuries
Total							475/875 760/880				

Abbreviations M, male; F, female; RBC, red blood cells; Hct, hematocrit; Hb, hemoglobin

Table 2 - Categories of Anemia and Cardiovascular Disease linked with ICD-9 codes

Acute blood loss	ACPOSTHEMORRHAG ANEMIA 786.3 HEMOPTYSIS 786.3 EPISTAXIS 784.7 HEMATURIA 599.7 GASTROINTEST HEMORR NOS 578.9 BLOOD IN STOOL 578.1 HEMATEMESIS 578.0 RECTAL & ANAL HEMORRHAGE 569.3 CHR DUODEN ULCER W HEM 532.40 ESOPHAGEAL HEMORRHAGE 530.82	ULCER ESOPHAGUS W BLEED 530.21 MALLORY-WEISS SYNDROME 530.7 HEMORRHAGE NOS 459.0 HEMOPERITONEUM 568.81 DIVRTICULIT-COLON/HEMOR 562.13 DIVRTICULOS-COLON/HEMOR 562.12 GASTRODUODENIT NOS&HEMOR 535.51 GASTRITIS NEC & HEMORRAG 535.41 ALCOHL GASTRIT & HEMORRG 535.31 CHR PEPTIC ULCER W HEM 533.40
Chronic blood loss	APLASTIC ANEMIAS NEC 284.8 PANCYTOPENIA 284.1 DEFICIENCY ANEMIA NOS 281.9	PERNICIOUS ANEMIA IRON DEFIC ANEMIA NOS CHR BLOOD LOSS ANEMIA
AOCD	ANEMIA-OTHER CHRONIC DIS 285.29 ANEMIA IN NEOPLASTIC DIS 285.22	ANEMIA IN CHR KIDNEY DIS 285.21
Hemolytic anemia	ACQ HEMOLYTIC ANEMIA NOS 283.9 OTH NONAUTO HEM ANEMIA 283.19 AUTOIMMUN HEMOLYTIC ANEM 283.0 HERED HEMOLYTIC ANEM NOS 282.9 HB-S/HB-C DIS W CRISIS 282.64 HB-SS DISEASE W CRISIS 282.62	SICKLE CELL DISEASE NOS 282.60 THALASSEMIA NEC 282.49 THLASSEMIA HB-S W CRISIS 282.42 THLASEMA HB-S W/O CRISIS 282.41 GLUTATHIONE DIS ANEMIA HEMOGLOBINOPATHIES NEC
b/12 folate	FOLATE-DEFICIENCY ANEMIA 281.2	B12 DEFIC ANEMIA NEC 281.1
Anemia	ANEMIA NOS 285.9	ANEMIA NEC 285.8
Cardiovascular disease	VENOUS INSUFFICIENCY NOS 459.81 PERIPH VASCULAR DIS NOS 443.9 ATHEROSCLEROSIS NEC ATH EXT NTV ART GNGRENE 440.24 ATH EXT NTV AT W CLAUDCT ATH EXT NTV ART GNGRENE 440.24 ATH EXT NTV ART ULCRTION 440.23 ATH EXT NTV AT W RST PN 440.22 ATH EXT NTV AT W CLAUDCT 440.21 ATHSCL EXTRM NTV ART NOS 440.20 RENAL ARTERY ATHEROSCLER 440.1 AORTIC ATHEROSCLEROSIS 440.0 LATE EFFECT CV DIS NOS 438.9 LATE EFFECT CV DIS NEC 438.89 HEART DISEASE NOS 429.9 ILL-DEFINED HRT DIS NEC 429.89 CHR ISCHEMIC HRT DIS NEC 414.8	COR ATH BYPASS GRAFT NOS 414.05 CRN ATH ATLG VN BPS GRFT 414.02 CRNRY ATHRSCL NATVE VSSL 414.01 COR ATH UNSP VSL NTV/GRF 414.00 ANGINA PECTORIS NEC/NOS 413.9 OLD MYOCARDIAL INFARCT 412 AC ISCHEMIC HRT DIS NEC 411.89 ACUTE COR OCCLSN W/O MI 411.81 INTERMED CORONARY SYND 411.1 AMI NOS-SUBSEQUENT EPISD 410.92 AMI NOS-INITIAL EPISODE 410.91 AMI NEC-INITIAL EPISODE 410.81 SUBENDO INFRC-LATR EPISD 410.72 SUBENDO INFRC-INIT EPISD 410.71 INFER AMI NEC-INIT EPISD 410.41 INFEROPOS AMI-INIT EPISD 410.31 ANTER AMI NEC-INIT EPISD 410.11

Table 3 - Characteristics of Patients in the Pre education and Post education groups

Characteristics		Pre Education		Post Education			
		Count	Column N %	Count	Column N %	Chi Square	P value
SEX	Male	851	47.6%	796	43.9%	1.837	0.175
	Female	937	52.4%	1017	56.1%	3.275	0.070
AGE	16-25	44	2.5%	65	3.6%	11.188	0.191
	26-35	147	8.2%	135	7.4%		
	36-45	268	15.0%	236	13.0%		
	46-55	334	18.7%	361	19.9%		
	56-65	334	18.7%	354	19.5%		
	66-75	289	13.4%	263	14.5%		
	76-85	240	13.5%	257	14.2%		
	86-95	115	6.4%	129	7.1%		
	96-105	17	1.0%	13	0.7%		
ICU		162	7.0%	141	7.3%	0.164	0.686
Anemia		274	15.3%	251	13.8%	1.583	0.208
Aplastic Anemia or Pancytopenia		25	1.4%	36	2.0%	1.866	0.173
Hemolytic Anemia		42	2.3%	33	1.8%	1.234	0.267
AOCD		108	6.0%	99	5.5%	0.558	0.455
B12folate		14	0.8%	11	0.6%	0.406	0.524
Chronic Blood Loss / Iron Deficiency		123	6.9%	118	6.5%	0.198	0,656
Acute Blood Loss		126	7.0%	120	6.6%	0.259	0.611
HTN		721	40.3	899	49.6%	31.203	**<.0001**
CHF		395	22.1%	428	23.6%	1.173	0.279
Arrhythmia		306	17.1%	299	16.5%	0.249	0.618
Cardiovascular disease		446	24.9%	479	26.4%	1.028	0.311
HIV		123	6.9%	112	6.2%	0.726	0.394
ESRD		29	1.6%	35	1.9%	0.491	0.483
CRI		321	18.0%	289	15.9%	2.592	0.107

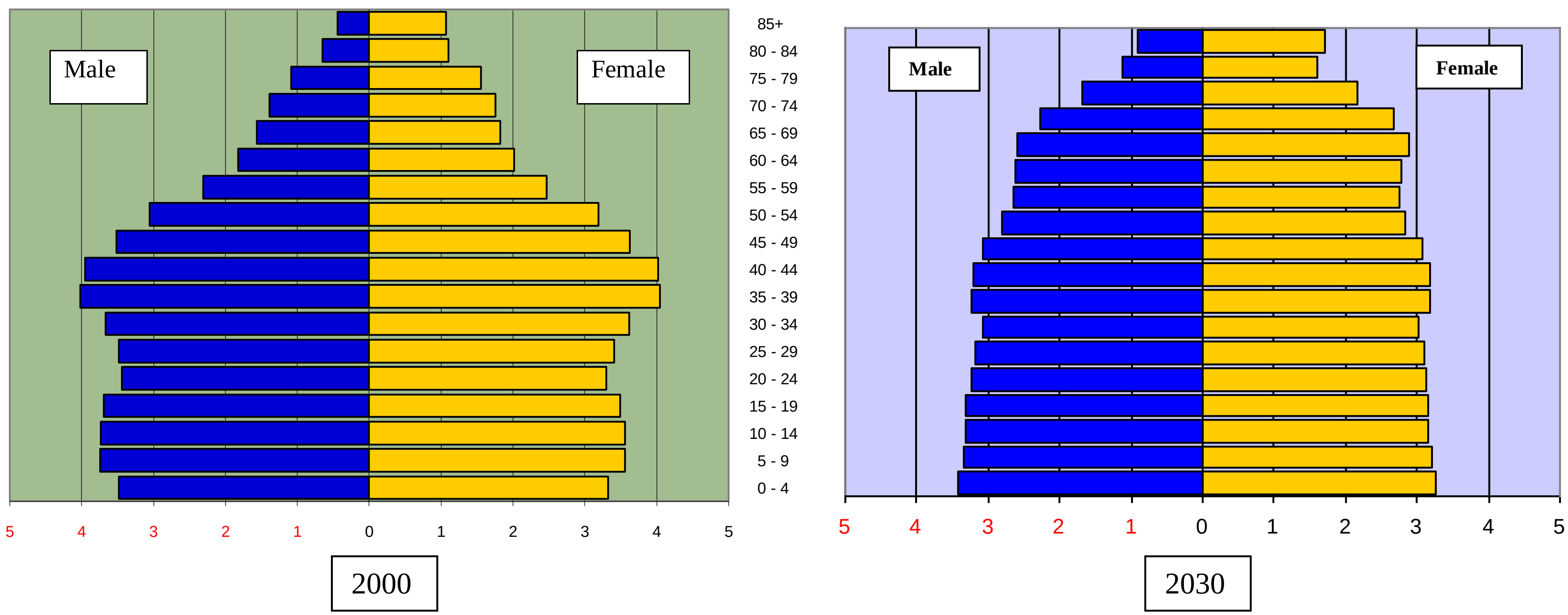
Table 4- Characteristics of Patients identified in the Pathology Databases and transfused by a hospitalist

Characteristic		Study Period						Chi Square	P Value
		pre education			post education				
		Count	Column N %	Mean	Count	Column N %	Mean		
Age	All Ages	184	100%	58.72	64	100%	61.55	8.213	0.413
	Age 14-25	5	2.7%	22.80	3	4.7%	23.33		
	Age 26-35	15	8.2%	31.13	2	3.1%	28.00		
	Age 36-45	37	20.1%	41.08	6	9.4%	42.17		
	Age 46-55	28	15.2%	51.43	14	21.9%	50.36		
	Age 56-65	31	16.8%	60.35	15	23.4%	61.13		
	Age 66-74	22	12.0%	69.09	7	10.9%	70.86		
	Age 76-85	31	16.8%	80.94	11	17.2%	81.73		
	Age 86-95	11	6.0%	88.64	5	7.8%	89.00		
	Age 96-105	4	2.2%	97.00	1	1.6%	98.00		
Trigger group Hb	Hb 3-3.9	2	1.1%		0	0.0%	NA	0.000	0.984
	Hb 4-4.9	4	2.2%		1	1.6%	NA	0.087	0.769
	Hb 5-5.9	8	4.3%		3	4.7%	NA	0.012	0.914
	Hb 6-6.9	31	16.8%		12	18.8%	NA	0.010	0.919
	Hb 7-7.9	78	42.4%		27	42.2%	NA	0.000	0.986
	Hb 8-8.9	50	27.2%		18	28.1%	NA	0.012	0.912
	Hb 9-9.9	8	4.3%		3	4.7%	NA	0.012	0.914
	Hb 10-10.9	3	1.6%		0	0.0%	NA	0.125	-
	Hb 11-11+	0	0.0%		0	0.0%	NA	-	-
Cardiovascular Disease		51	27.7%		17	26.6%	NA	0.032	0.858
Arrhythmia		15	8.2%		11	17.2%	NA	4.131	**0.042**
CVA		19	10.3%		6	9.4%	NA	0.047	0.828
HTN		50	27.3%		37	57.8%	NA	19.320	**.>0.0001**
AOCD		100	54.3%		38	59.4%	NA	0.486	0.486
Hemolytic Anemia		15	8.2%		2	3.1%	NA	1.879	0.170
Chronic Blood Loss		46	25.0%		15	23.4%	NA	0.063	0.803
Acute Blood Loss		48	26.1%		21	32.8%	NA	1.070	0.301
B12 or Folate Deficiency		8	4.3%		2	3.1%	NA	0.183	0.668

Table 5 - Comparison of the Creatinine and Hb levels of the pre and post education periods

Characteristic	Study Period		Independent T test p value	95% CI
	pre education	post education		
	Mean	Mean		
Discharge Creatinine	1.33	1.44	0.538	-0.3690 – 0.1929
Admit Hb	8.93	9.18	0.408	-0.8609 – 0.3506
Trigger Hb	7.54	7.49	0.766	-0.2712 – 0.3679
Discharge Hb	9.90	9.83	0.673	-0.2690 – 0.4161

Figure 1 - Population Pyramids of the United States, Percent of Total Population



Source: U.S. Census Bureau, Population Division, Interim State Population Projections, 2007

Figure 2 - Conceptual Model

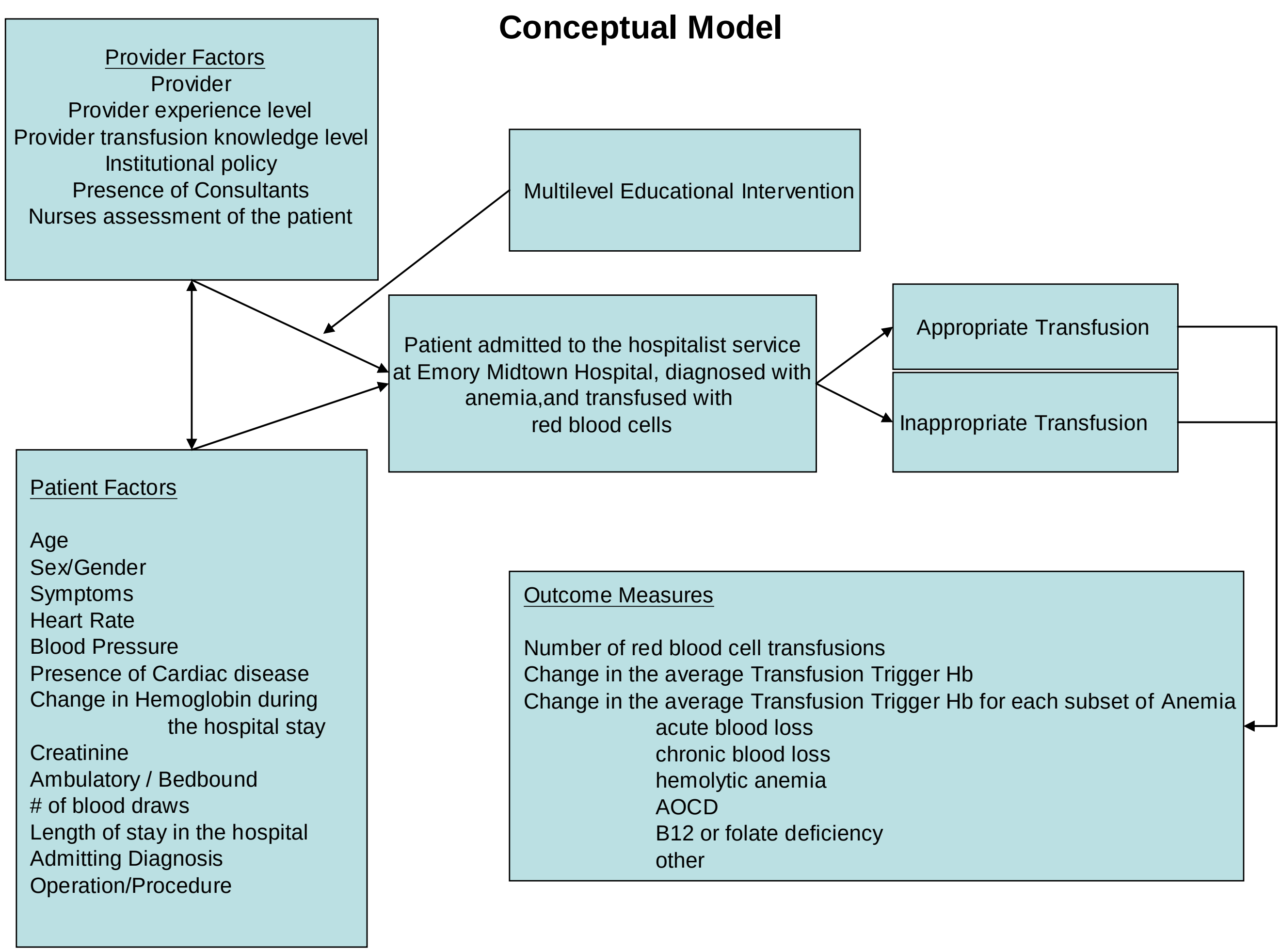


Figure 3 - Study Design

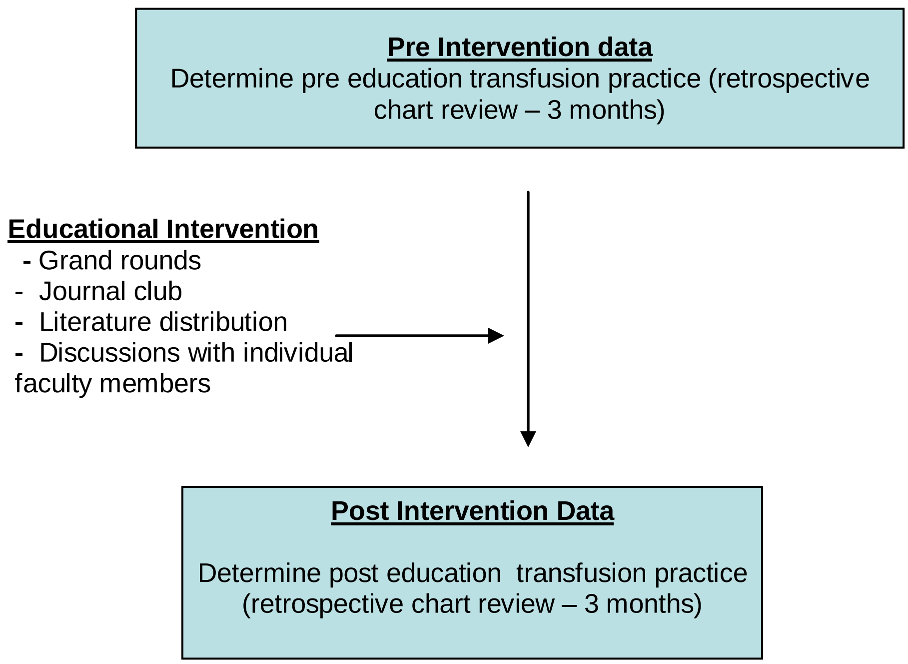


Figure 4 - Transfusion Guideline

- Hemoglobin (Hgb) <7 g/dL: RBC transfusion indicated.
  - To avoid increase in cardiac output
  - To increase the body's oxygen carrying capacity
- Hgb 7 to 10 g/dL: Correct strategy is unclear
- Hgb >10 g/dL: RBC transfusion not indicated

Adapted from Murphy, MF, et al. British Committee for Standards in Haematology, Blood Transfusion Task Force. Br J Haematol 2001; 113:24.

Figure 5 - Number of transfusions ordered by each hospitalist

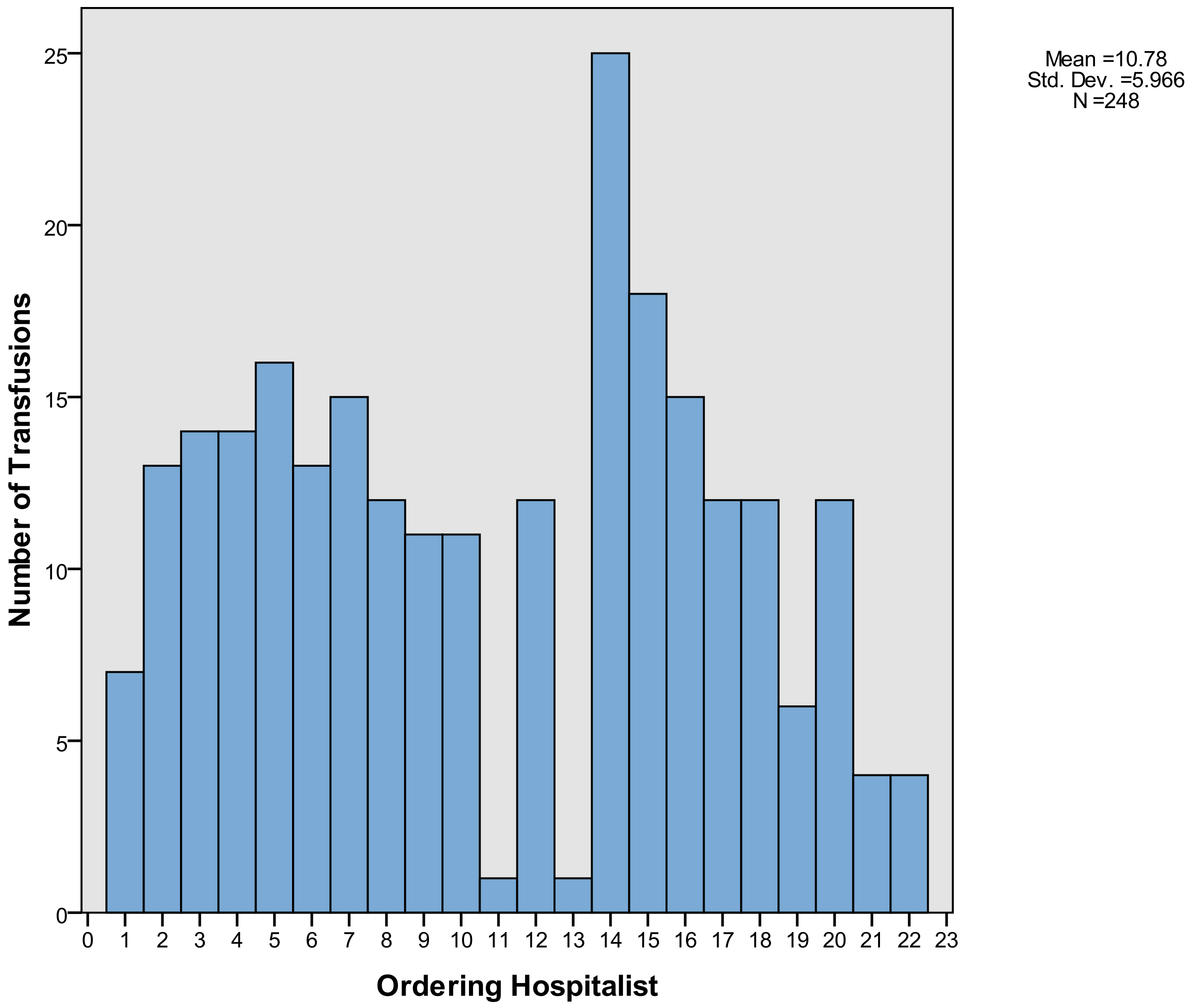


Figure 6 - Comparison of trigger Hb for each hospitalist in the pre and post education periods

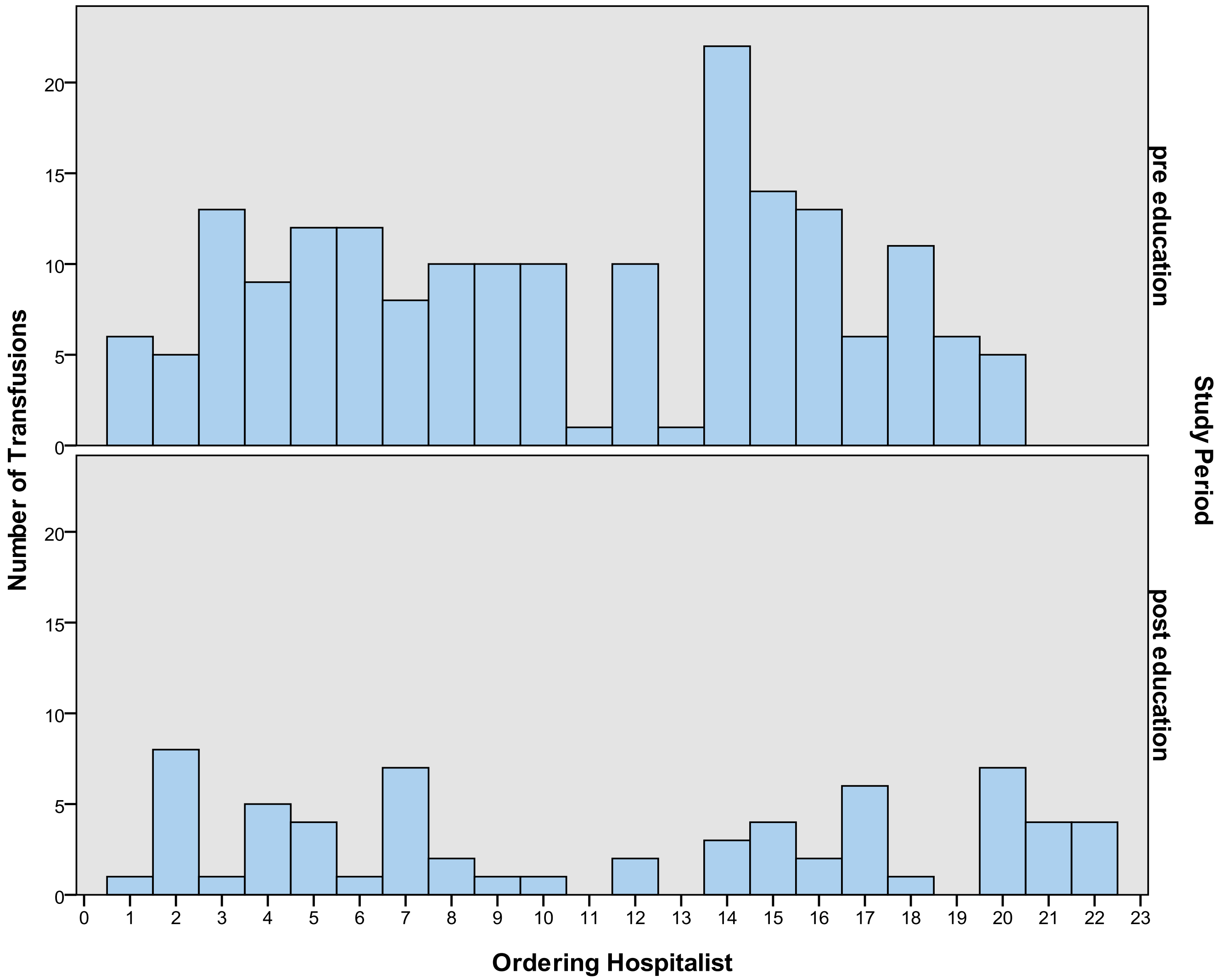


Figure 7 - Comparison of the trigger Hb ordered in the pre and post educational period by each hospitalist, excluding patients with acute blood loss

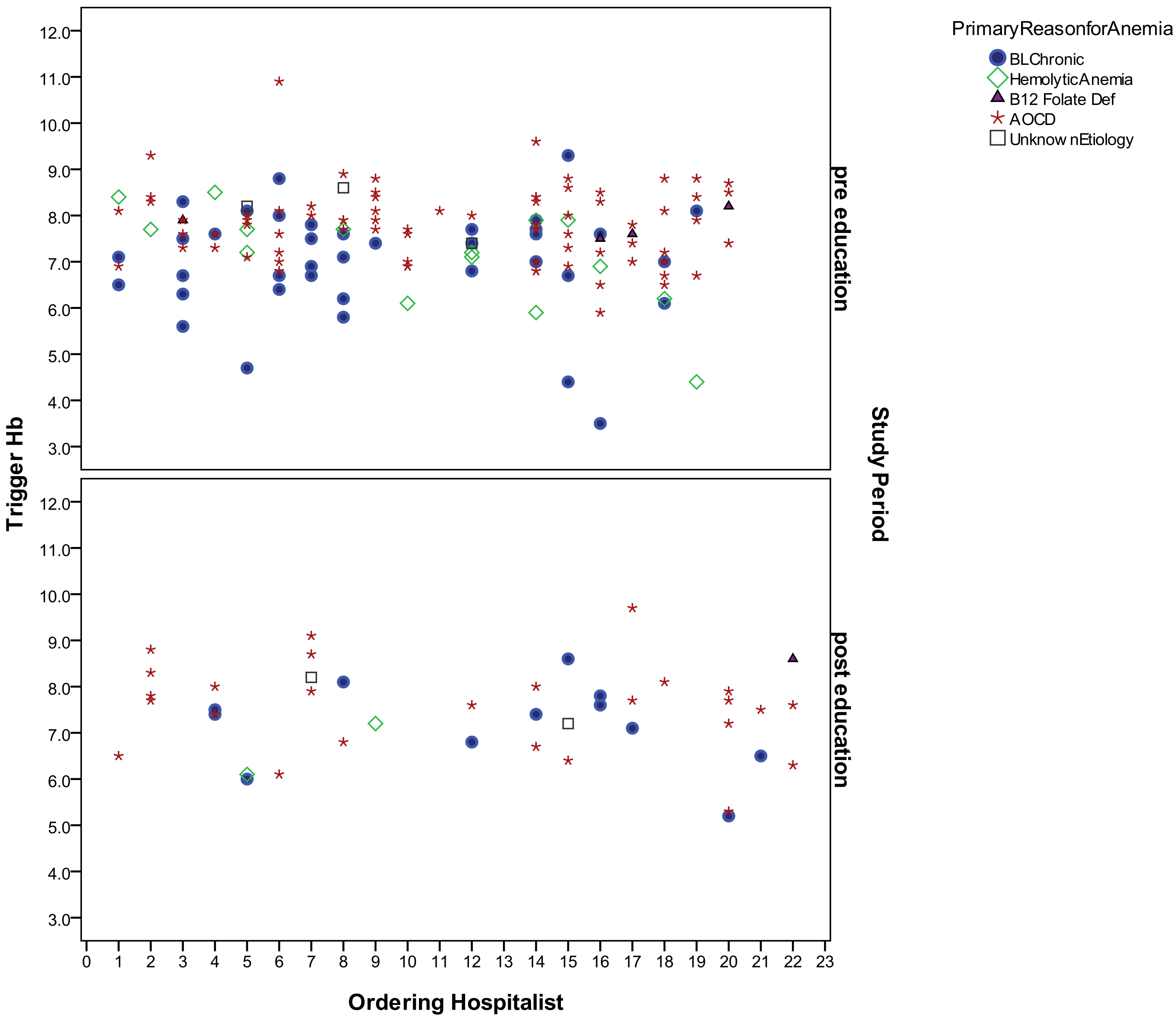


Figure 8 - Variability of red blood cell use in the pre and post educational period

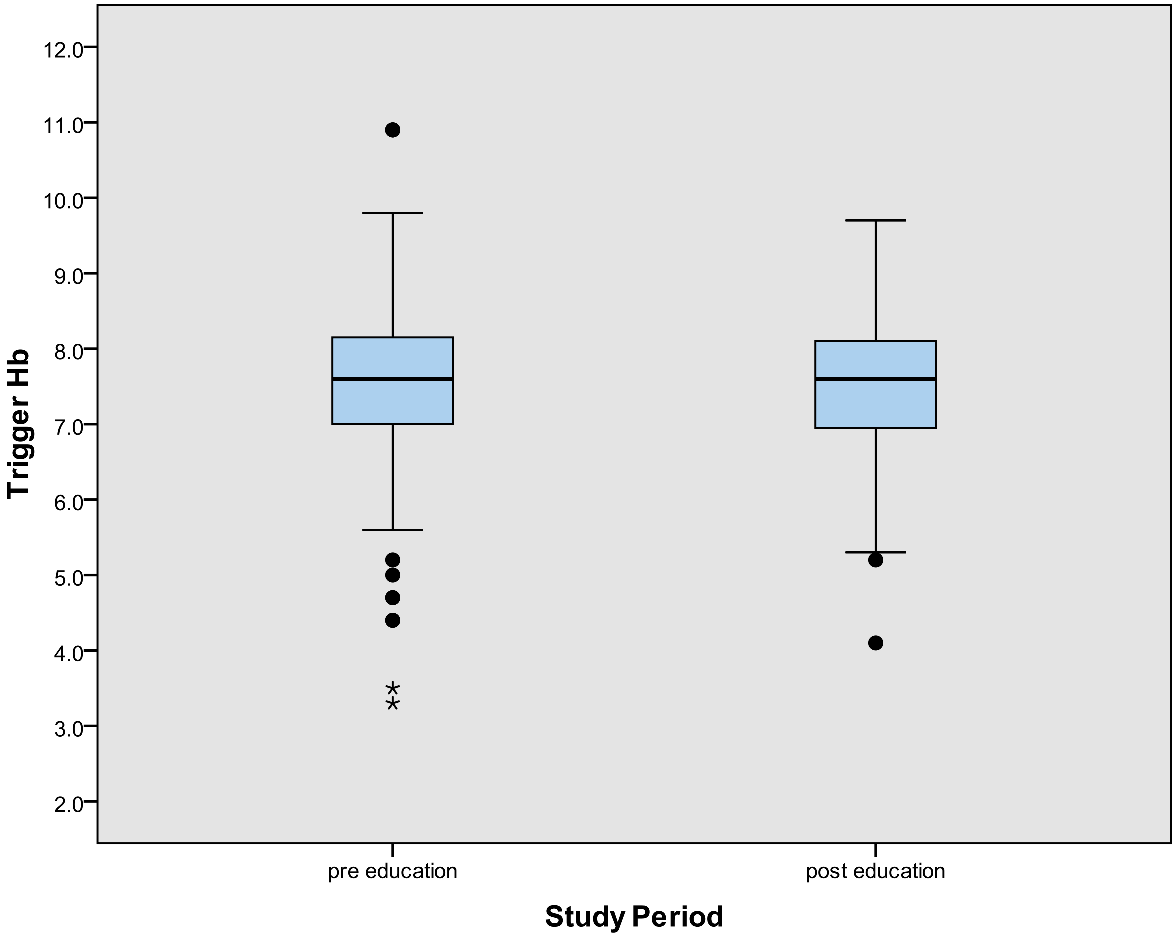


Figure 9 - Variability in the distribution of trigger Hb for the causes of anemia

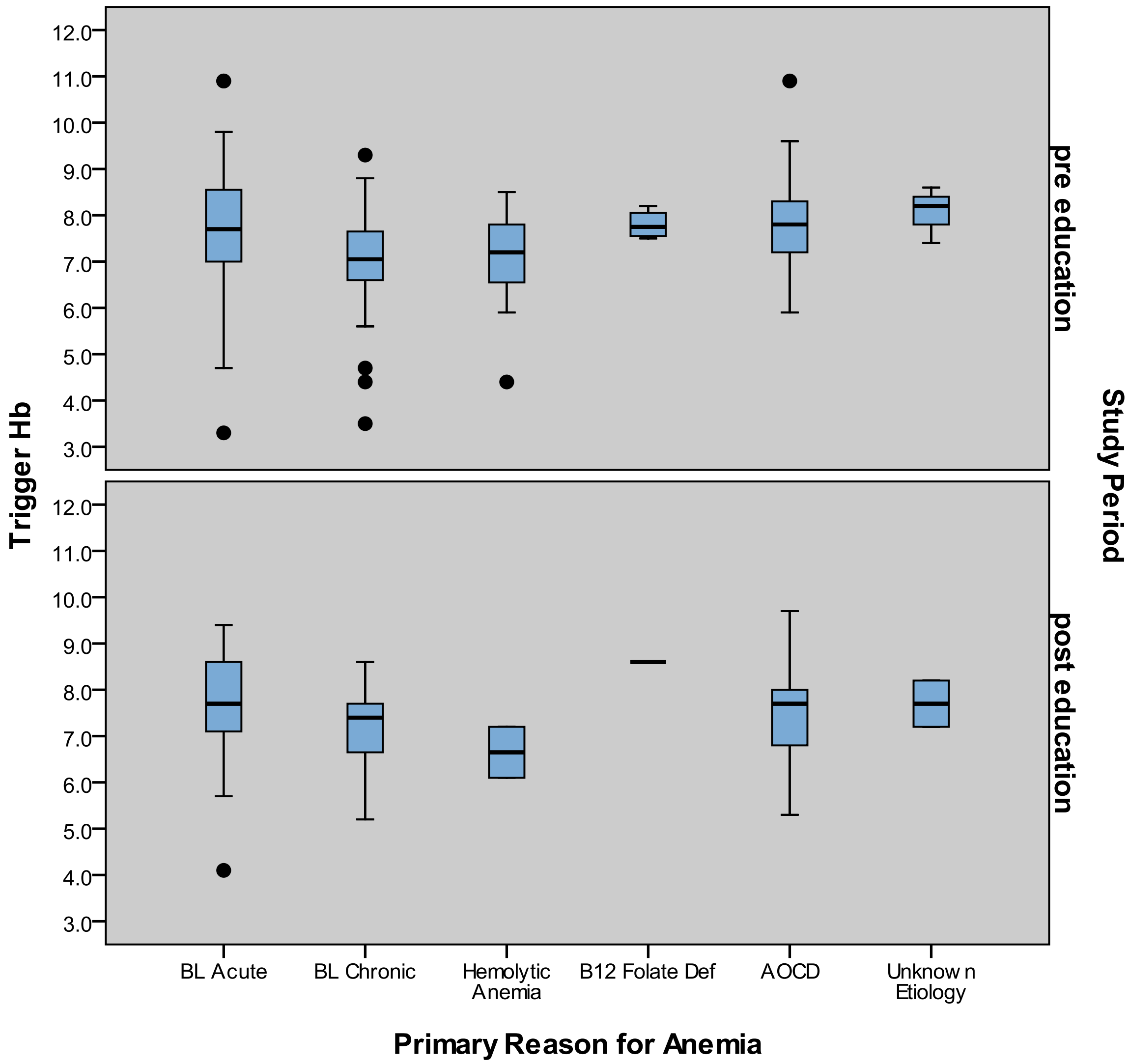


Table 6 - Comparison of the Reasons for Admission in the pre and post education periods

			Study Period				
			Pre education	Post education	Total	Chi square	P value
Reason for Admit	Other	Count	110	41	151	0.208	0.6486
		% within Study Period	59.8%	64.1%	60.9%		
	Anemia	Count	74	23	97		
		% within Study Period	40.2%	35.9%	39.1%		

Table 7 - Comparison of the reasons for transfusion in the pre and post education periods

Reason for Transfusion		Study Period		Total	Chi square	P value
		Pre education	Post education			
Low Hb/Anemia	Count	142	50	192	0.025	0.854
	% within Study Period	77.2%	78.1%	77.4%		
Symptomatic Anemia	Count	20	8	28	0.016	0.899
	% within Study Period	10.9%	12.5%	11.3%		
Hb drop of unclear etiology	Count	11	5	16	0.048	0.8265
	% within Study Period	6.0%	7.8%	6.5%		
Not Given	Count	11	1	12	1.166	**.0280**
	% within Study Period	6.0%	1.6%	4.8%		
Total	Count	184	64	248		
	% within Study Period	100.0%	100.0%	100.0%		

Figure 10 - Number of transfusions for each reason for anemia within each primary reason for anemia

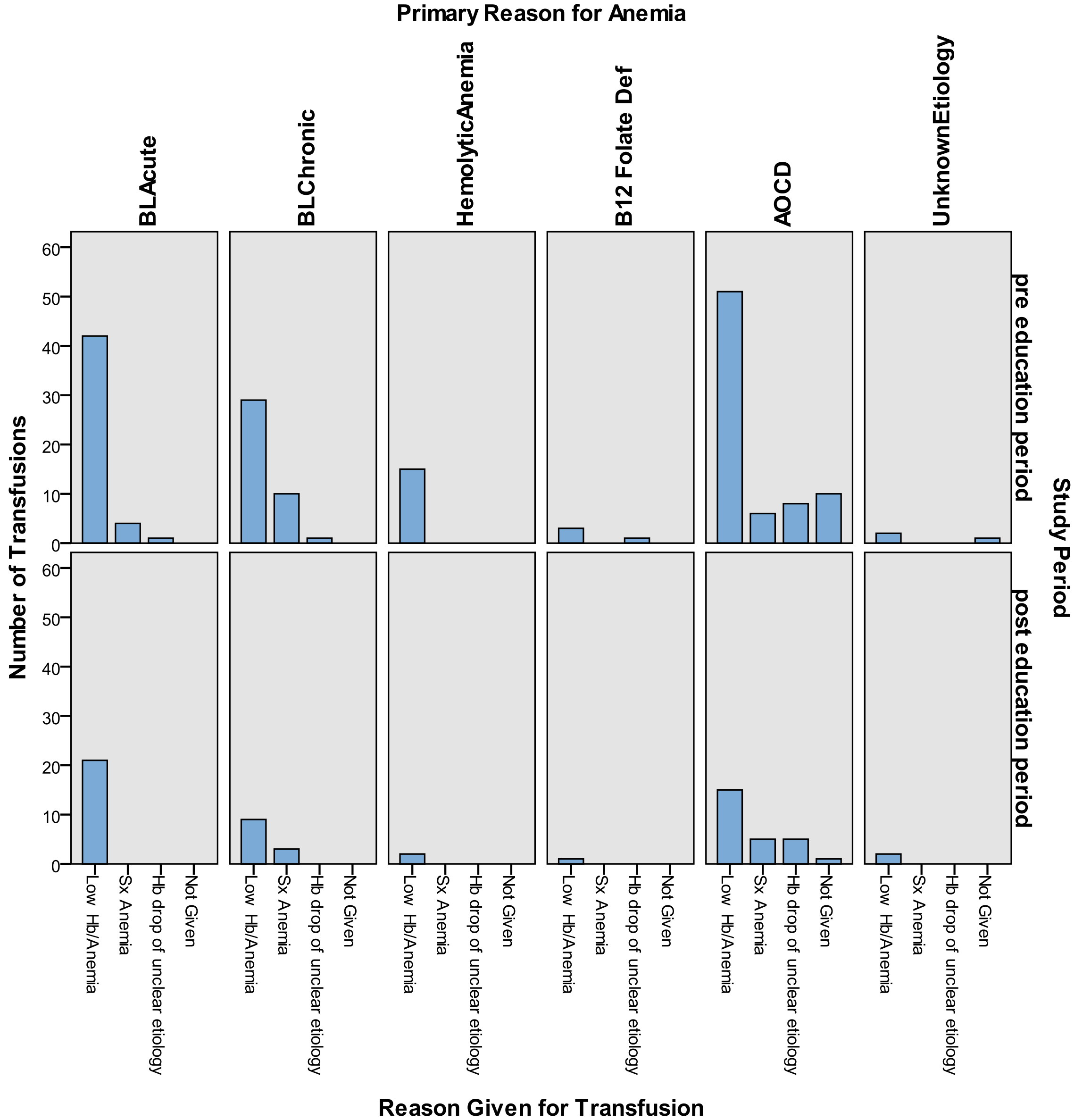


Table 8 - Number of asymptomatic patients without acute blood loss and without CAD/CHF given blood for Hb >7g/dL

	Study Period	
Type of Anemia	Pre education	Post education
BL Chronic	19	6
Hemolytic Anemia	10	1
B12/folate	3	1
AOCD	42	9
Unknown Etiology	0	2
TOTAL	74	19
Number of asymptomatic patients without CAD/CHF	99	28
% Inappropriate Transfusions	74 / 99 = 74.74%	19 / 28 = 67.86%

Table 9 - Number of asymptomatic patients without acute blood loss with CAD/CHF given blood for Hb >9g/dL

	Study Period	
Type of Anemia	Pre education	Post education
BL Chronic	1	0
Hemolytic Anemia	0	0
B12/folate	0	0
AOCD	2	1
Unknown Etiology	0	0
TOTAL	3	1
Number of asymptomatic patients with CAD/CHF	38	15
% Inappropriate Transfusions	3/ 38 = 7.89%	1/ 15 = 6.67%

Table 10 - Comparison of the transfusion rates for type of anemia in the pre and post education periods

Type of Anemia	Pre transfusion total number of patients in ICD-9 database	Post transfusion total number of patients in ICD-9 database	Pre transfusion number of patients given blood	Post transfusion number of patients given blood	Chi square with Yates correction	P value
All patients	1788	1813	184	64	63.115	**<0.0001**
Acute Blood Loss	126	120	47	21	0.351	0.5536
Chronic Blood Loss	123	118	40	12	3.027	0.0819
Hemolytic Anemia	42	33	15	2	7.656	**0.0057**
B12FolateDef	14	11	4	1	0.497	0.4808
AOCD	108	99	75	26	36.839	**<0.0001**
Anemia	274	251	NA	NA		
Other	Unknown	Unknown	3	2	Cant calculate	Can't calculate

Table 11 - Comparison of mean hemoglobin for individual etiologies of anemia in the pre and post education periods

Primary Reason for Anemia	Study Period	Count	Mean	Standard Deviation	Unpaired T test P-Value	95% CI
Acute Blood Loss	pre education	47	7.7	1.5	0.8367	-0.666 – 0.820
	post education	21	7.6	1.2		
Chronic Blood Loss	pre education	40	7.0	1.1	0.802	-.088 – 0.550
	post education	12	7.2	0.9		
Hemolytic Anemia	pre education	15	7.1	1.1	0.5686	-1.249 – 2.188
	post education	2	6.7	0.8		
B12 Folate Def	pre education	4	7.8	0.3	NA	NA
	post education	1	8.6	.		
AOCD	pre education	75	7.8	0.8	0.2486	-0.160 – 0.612
	post education	26	7.6	1.0		
Unknown Etiology	pre education	3	8.1	0.6	0.5771	-1.506 – 2.240
	post education	2	7.7	0.7		

Table 12 - Comparison of the discharge Hb for the primary reason for anemia in the pre and post education period

		Discharge Hb				
Primary Reason for Anemia	Study Period	Count	Mean	Standard Deviation	95% CI	Independent T test P value
Acute Blood Loss	pre education	47	10.1	0.9	-.2514 – 0.7943	0.304
	post education	21	9.8	1.1		
Chronic Blood Loss	pre education	40	9.7	1.3	-7985 - .9035	0.902
	post education	12	9.7	1.1		
Hemolytic Anemia	pre education	15	9.0	1.1	-1.5205 – 2.0205	0.768
	post education	2	8.8	1.5		
B12 or Folate Deficiency	pre education	4	10.9	1.9	NA	NA
	post education	1	11.3	.		
AOCD	pre education	75	10.0	1.1	-.4710 – 0.6364	0.768
	post education	26	9.9	1.5		
Unknown Etiology	pre education	3	10.3	1.0	-2.2603 – 2.5603	0.856
	post education	2	10.2	0.5		

Table 13 - Comparison of mean hemoglobin for individual etiologies of anemia in the pre and post education periods for trigger Hb ≥ 5g/dL

Primary Reason for Anemia	Study Period	Mean	N	Std. Deviation	Unpaired T test P-Value	95% CI
Acute Blood Loss	pre education	7.816	45	1.3040	0.8388	-0.580 – 0.712
	post education	7.750	20	0.9254		
Chronic Blood Loss	pre education	7.230	37	0.7951	0.8201	-0.491 – 0.617
	post education	7.167	12	0.9316		
Hemolytic Anemia	pre education	7.314	14	0.8170	0.2989	-0.656 – 1.984
	post education	6.650	2	0.7778		
B12 or Folate Deficiency	pre education	7.800	4	0.3162	NA	NA
	post education	8.600	1	.		
AOCD	pre education	7.795	75	0.8082	0.2486	-0.160 – 0.612
	post education	7.569	26	0.9826		
Unknown Etiology	pre education	8.067	3	0.6110	0.5771	-1.506 – 2.240
	post education	7.700	2	0.7071		
Total	pre education	7.649	178	0.9718	0.447	-0.171 – 0.387
	post education	7.541	63	0.9537		
	total	7.621	241	0.9663		

Table 14 - Comparison of mean hemoglobin for individual etiologies of anemia in the pre and post education periods for trigger Hb ≥ 6g/dL

Primary Reason for Anemia	Study Period	Mean	N	Std. Deviation	Unpaired T test P-Value	95% CI
Acute Blood Loss	pre education	8.051	41	1.1048	0.4992	-.375 – 0.761
	post education	7.858	19	0.8113		
Chronic Blood Loss	pre education	7.317	35	0.7233	0.9115	-.0532 – 0.477
	post education	7.345	11	0.7299		
Hemolytic Anemia	pre education	7.423	13	0.7373	0.1926	-.0442- 1.99
	post education	6.650	2	0.7778		
B12 or Folate Deficiency	pre education	7.800	4	0.3162	NA	-
	post education	8.600	1	.		
AOCD	pre education	7.820	74	0.7825	0.3947	-0.211 – 0.541
	post education	7.660	25	0.8846		
Unknown Etiology	pre education	8.067	3	0.6110	0.5771	-1.506 – 2.240
	post education	7.700	2	0.7071		
Total	pre education	7.746	170	0.8812	**0.04546**	-0.160- 0.356
	post education	7.648	60	0.8418		
	Total	7.720	230	0.8703		

Table 15 - Comparison of patient with and without cardiovascular disease transfused in the pre and post education periods

	Pre education	Post education	Chi Square	P value
w CV disease not transfused	446 – 51 = 395	479–17 = 462	19.946	**<0.0001**
w CV transfused	51	17		
w/out CV disease not transfused	1342 – 133 = 1209	1385 – 47 =1338	45.905	**<0.0001**
w/out CV disease transfused	133	47		

Table 16 - Comparison of the mean trigger Hb in patients without cardiovascular disease in the pre and post education periods

Primary Reason for Anemia	Study Period	N	Mean	Std. Deviation	Independent T test P value
Acute Blood Loss	pre education	34	7.574	1.4623	0.471
	post education	19	7.442	1.1730	
Chronic Blood Loss	pre education	31	6.948	1.1489	0.681
	post education	10	7.000	0.8919	
Hemolytic Anemia	pre education	12	7.183	1.1946	0.491
	post education	2	6.650	0.7778	
Folate Def	pre education	3	7.867	0.3512	-
	post education	1	8.600	.	
AOCD	pre education	52	7.675	0.7501	0.527
	post education	13	7.523	0.9918	
Unknown Etiology	pre education	1	7.400	.	-
	post education	2	7.700	0.7071	

Table 17 - Comparison of the mean trigger Hb in patients with cardiovascular disease in the pre and post education periods

Primary Reason for Anemia	Study Period	N	Mean	Std. Deviation	Independent T test P value
Acute Blood Loss	pre education	13	7.862	1.6414	0.3060
	post education	2	8.850	0.7778	
Chronic Blood Loss	pre education	9	7.189	1.0612	0.701
	post education	2	8.000	0.8485	
Hemolytic Anemia	pre education	3	6.867	0.5774	-
	post education	0[a]	.	.	
Folate Def	pre education	1	7.600	.	-
	post education	0[a]	.	.	
AOCD	pre education	23	8.065	0.8845	0.520
	post education	13	7.615	1.0115	
Unknown Etiology	pre education	2	8.400	0.2828	-
	post education	0[a]	.	.	

Table 18 - Comparison of male and female transfusions in the pre and post education period

	number of patients not transfused	number of patients transfused	Chi square with Yates correction	P value
Male pre education	851	80	26.567	**<0.0001**
Male post education	796	22		
Female pre education	937	104	28.528	**<0.0001**
Female post education	1017	42		

Table 19 - Comparison of the mean trigger Hb for primary reasons of anemia in men in the pre and post education periods

Primary Reason For Anemia	Study Period	N	Mean	Std. Deviation	Independent t test p value
Acute Blood Loss	pre education	24	7.500	1.7273	0.907
	post education	12	7.567	1.3103	
Chronic Blood Loss	pre education	12	7.083	1.0616	0.849
	post education	2	6.900	2.4042	
Hemolytic Anemia	pre education	6	7.083	0.8864	0.908
	post education	1	7.200	.	
AOCD	pre education	36	7.481	0.7574	**0.046**
	post education	7	8.186	1.1739	
Unknown Etiology	pre education	2	8.400	0.2828	-
	post education	0[a]	.	.	

a. t cannot be computed because at least one of the groups is empty.

Table 20 - Comparison of the mean trigger Hb for primary reasons of anemia in women in the pre and post education periods

Primary Reason For Anemia	Study Period	N	Mean	Std. Deviation	Independent t test P value
Acute Blood Loss	pre education	23	7.813	1.2414	0.641
	post education	9	7.589	1.1219	
Chronic Blood Loss	pre education	28	6.968	1.1627	0.521
	post education	10	7.220	0.6321	
Hemolytic Anemia	pre education	9	7.144	1.2581	0.454
	post education	1	6.100	.	
B12 or Folate Deficiency	pre education	4	7.800	0.3162	0.109
	post education	1	8.600	.	
AOCD	pre education	39	8.085	0.7510	**<0.001**
	post education	19	7.342	0.8242	
Unknown Etiology	pre education	1	7.400	.	0.788
	post education	2	7.700	0.7071	

Table 21 - Comparison of transfusions in pre and post education periods by age category

Age	Total pt in ICD-9 database – pre education / # transfusions = % of pt transfused	Total pt in ICD-9 database – post education = % of patients transfused	Chi square	P value
16-25	44/5 = 8.77	65/3 = 4.29	0.654	0.4186
26-35	147/15 = 7.98	135/2 = 1.41	7.029	**0.0080**
36-45	268/37 = 10.66	236/6 = 2.37	16.048	**<0.0001**
46-55	334/28 = 6.64	361/14 = 3.73	4.769	**0.0290**
56-65	334/31 = 7.03	354/15 = 3.98	5.394	**0.0202**
66-74	289/22 = 5.88	263/7 = 2.53	5.212	**0.0224**
76-85	240/31 = 9.97	257/11 = 4.00	9.094	**0.0026**
86-95	115/11 = 7.53	129/5 = 3.68	2.011	0.1562
96-105	17/4 = 20.00	13/1 = 7.14	0.243	0.6220
Age >65	661 /68 = 10.29	662/39 = 5.89	6.781	**0.0092**