COMPARING TOTAL HIP REPLACEMENT DRUG TREATMENTS FOR COST AND LENGTH OF STAY

A Thesis
Submitted to the Graduate Faculty
of the
North Dakota State University
of Agriculture and Applied Science

By

Blake James Huebner

In Partial Fulfillment of the Requirements
for the Degree of
MASTER OF SCIENCE

Major Department:
Statistics

May 2015

Fargo, North Dakota

North Dakota State University
Graduate School

Title

Comparing Total Hip Replacement Drug Treatments for Cost and Length of Stay

By

Blake James Huebner

The Supervisory Committee certifies that this ***disquisition*** complies with North Dakota State University's regulations and meets the accepted standards for the degree of

MASTER OF SCIENCE

SUPERVISORY COMMITTEE:

Dr. Rhonda Magel
Chair

Dr. Megan Orr

Dr. Craig Schnell

Approved:

5/13/2015
Date

Dr. Rhonda Magel
Department Chair

ABSTRACT

The objective of this study is to identify the potential effect anticoagulants, spinal blocks, and antifibrinolytics have on overall cost, length of stay, and re-admission rates for total hip replacement patients. We use ordinary least squares regression, multiple comparison testing, logistic regression, and chi square tests to fulfill this objective. The combination of warfarin and enoxaparin is associated with the highest cost and length of stay out of the anticoagulants studied. There is no clear combination of spinal blocks associated with the highest cost and length of stay. Tranexamic acid is associated with a reduction in length of stay and likelihood of receiving a blood transfusion, while not increasing overall cost. No drug combination in any category is associated with a change in re-admission rates.

ACKNOWLEDGMENTS

I would like to thank Dr. Rhonda Magel for advising me throughout the process of writing my thesis and my time here and North Dakota State University.

I would also like to thank the rest of my committee members, Dr. Megan Orr and Dr. Craig Schnell, for the time and input they contributed towards my thesis.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1. INTRODUCTION

In a time of rising medical costs, hospital administration look for any method to reduce overall costs to patients while maintaining the same level of care. In fact, after adjusting for inflation the average cost per stay from 1997 to 2010 increased by nearly 45% (Pfuntner, 2013). As a result of this rise in cost, there has been an increased interest in research on nurse to patient ratios, length of stay (LOS) flow models, and lists of methods to reduce overall cost. One research area that seems to be underwhelmed is like-type drug comparisons and how they affect overall cost and LOS. The objective of this thesis is to provide insight as to which particular drugs administered perioperatively to patients undergoing total hip replacement (THR) surgery within a Midwest hospital network contribute to a significant reduction to these two measurements.

Total Hip replacement surgery is considered one of the most successful surgeries in all of medicine (Foran, 2011). According to the Centers for Disease Control and Prevention, in 2010 more than 310,800 patients underwent this procedure in the United States (Wolford & Bercovitz, 2015). In fact, the number of hip replacements has more than doubled between 2000 and 2010, and projections indicate this surgery will continue to rise at staggering rates (Wolford, 2015). The surgery involves an orthopedic surgeon first removing the diseased or damaged cartilage and bone, and then fitting an implant to restore functionality of the hip (Foran, 2011). Candidates for the surgery include those with a damaged hip due to arthritis, a bone fracture, or other condition (Foran, 2011). There are numerous drugs administered to hip replacement patients throughout the surgical process. Within this study we will be concentrating our efforts of analysis on three types of drugs: anticoagulants, spinal blocks, and blood transfusion prevention.

First, we analyze the different combinations of anticoagulants administered to the patients. According to the American Academy of Orthopaedic Surgeons (AAOS, 2009), one of

the greatest risks of THR is the possibility of a complication called deep vein thrombosis (DVT). DVT is the formation of a blood clot within a deep vein, commonly in the lower extremities such as the thigh or calf. DVT can lead to impairment, or if the clot reaches the lungs, pulmonary embolism (PE) which can be fatal. Prevention of DVT is a three-pronged approach including: compression elastic stockings and medical devices, movement and rehabilitation, and anticoagulant therapy. Anticoagulants are typically administered the night before surgery and continue well into the postoperative care. The AAOS (2009) states, "Without this preventive treatment, as many as 80 percent of orthopaedic surgical patients would develop DVT, and 10 percent to 20 percent would develop PE."

Second, we analyze different spinal blocks administered to the patient. To understand the function of spinal blocks, it is important to know the different types of anesthesia. The following information was provided by the American Academy of Orthopaedic Surgeons (2014). There are two common types of anesthesia used intraoperatively which are general and regional. General anesthesia affects the whole body and temporarily renders the patient unconsious. Regional anesthesia blocks the nerves of a specific part of the body, but does not affect the brain or breathing. Spinal blocks are a type of regional anesthesia, and the only anesthesia we focus on for the duration of this study. When using a spinal block, the anesthesia is administered directly into the fluid surrounding the spinal cord, which creates a numbing effect for several hours (AAOS, 2014).

The last drug type we analyze is antifibrinolytics. In this study we focus on one drug of this type which is called tranexamic acid (TXA). Perioperative bleeding is a major concern for THR and is associated with not only higher risks, but also higher costs to the patients (Wera et al., 2013). The objective of TXA is to reduce bleeding and, therefore, reduce the risks associated

with blood loss which include receiving a blood transfusion (Wera, 2013). There has recently been an increase in the interest of using antifibrinolytics during orthopedic surgery, and the efficacy as well as possible side effects are still being studied, which will be discussed later.

Although the complications and efficacy of the drugs are discussed, the main goal of this study is to analyze drug combinations which may result in lower overall hospital cost and LOS while maintaining the same re-admission rate. We are provided with an existing data set of total hip replacement patients and compare costs and LOS of different anticoagulants administered. We then perform similar analyses on different spinal blocks, and a blood transfusion prevention drug. Afterwards, a recommendation is made as to which drugs tend to result in a minimal cost and LOS.

CHAPTER 2. LITERATURE REVIEW

Extensive research has been done on each drug within this study in terms of medical testing. Common traits studied include efficacy, possible side effects, and other medical interests. While less common, there has also been research done on a few of these drugs in relation to length of stay and costs to the patient. It is our intention to highlight important aspects and studies of these drugs in order to build a better understanding. It is important to note this research does not acknowledge or compare different dosages levels or drug delivery systems.

As mentioned previously, one of the major complications associated with hip replacement surgery is the risk of developing DVT which can lead to PE. To lower the risk, many patient are prescribed an anticoagulant as a preventative measure against blood clots. However, with blood thinners there is a possibility of increased bleeding. Three anticoagulants often prescribed include: warfarin, enoxaparin, and rivaroxaban. Warfarin is the most commonly used anticoagulant for THR (American Association of Hip and Knee Surgeons, 2009). It has been shown that warfarin is effective against thromboembolic complications while causing minimum bleeding complications (D'Ambrosia et al., 1975). Enoxaparin and rivaroxaban are also commonly used, in place of or in addition to warfarin. Clinical studies have shown that rivaroxaban provides a lower risk of symptomatic venous thromboembolism when compared to enoxaparin; however, the risk of major bleeding was higher when using rivaroxaban as opposed to enoxaparin (Eriksson et al., 2008; Gomez-Outes et al., 2012). Of the three, warfarin is associated with the least risk of bleeding complications (Eisenberg et al., 2012).

Several studies have found that using regional anesthesia compared with general anesthesia has a favorable outcome for the patient. Patients receiving regional anesthesia were less likely to develop DVT/PE, had decreased intraoperative blood loss, and were less likely to receive a blood transfusion (Mauermann et al., 2006; Rodgers & Walker, 2000; Thorburn et al.,

1980). Within the spinal block category we analyze three drugs: bupivacaine, lidocaine, and ropivacaine. Lidocaine began to be used as a spinal anesthetic in 1945 and has been widely used ever since (NYSORA, 2013). It is often chosen because of its rapid onset (3-5 minutes), dense blockage, and short duration of action (1-1.5 hours) (NYSORA, 2013; Zaric & Pace, 2008). Thus, it is recommended for short to intermediate length surgeries (NYSORA, 2013). The largest concern associated with lidocaine is the occurrence of transient neurologic symptoms (TNS) during postoperative care (NYSORA, 2013). TNS presents as pain in the lower back and lower extremities including the buttocks, thighs, and lower limbs after recovery from spinal anesthesia (NYSORA, 2013). As a result of this research into TNS, lowering the concentration of lidocaine is recommended, and other spinal anesthetics have risen in popularity. Bupivacaine is one alternative that has shown to have less incidence of TNS as compared with lidocaine (Hampl & Heinzmann-Wiedmer, 1998; Zaric et al., 2005; Zaric, 2008). However, it has been found that patients using bupivacaine have significantly longer times to ambulate and to void than when using lidocaine (Hampl, 1998). Bupivacaine is commonly used for intermediate to long surgeries because of its onset time of 8 minutes and duration of anaethesia lasting 210 to 240 minutes (NYSORA, 2013). Ropivacaine is the third spinal anesthetic and is relatively new compared to the others. Like bupivacaine, ropivacaine also shows a lower relative risk for developing TNS when compared with lidocaine (Zaric, 2008). When compared with bupivacaine, ropivacaine is shown to give patients more motor function, a faster postoperative recovery, and superior pain relief during the first 24 hours of recovery (Bertini et al., 2001; Mcnamee et al, 2002; Wulf & Biscoping, 1999).

Perioperative bleeding is a major concern with total hip replacement surgery as it is associated with additional risks and costs to the patient (Wera, 2013). As a result of major

bleeding, many patients require blood transfusions which can cause more complications and a longer LOS (Bower et al., 2010). Recently, tranexamic acid has been more commonly used in an attempt to reduce the overall blood loss. Several studies have concluded that TA effectively reduces blood loss and the need for transfusions while not increasing the risk of complications such as DVT (Poeran et al., 2014; Johansson et al., 2005; Gandhi et al., 2013). In addition, the administration of TA is also seen to reduce overall costs to the patient (Irisson et al., 2012; Panchmatia et al., 2012).

CHAPTER 3. METHODOLOGY

3.1. Data Description

Data on 1214 recent THR surgeries were provided by a hospital network with a total of five locations preforming the procedure. Other variables provided include: cost of hospital stay (in USD), length of stay (in days), age (in years), gender (M/F), blood transfusion (0/1), re-admittance (0/1), and indicator variables of drugs administered to the patient. Under blood transfusion, 0 indicates no transfusion whereas 1 indicates at least one transfusion. Under re-admittance (RA), 0 indicates no re-admittance and 1 indicates the patient needed to return due to complications within 30 days. The variable names for the indicator variables of anticoagulants and spinal blocks are called 'acombo' and scombo' respectively, and the coding key can be found in Tables 3.1 and 3.2. The blood transfusion prevention drug, tranexamic acid, is called 'b1' and is coded as 0/1; 0 indicates the drug was not administered and 1 indicates the drug was administered.

Table 3.1. Key for Anticoagulants

'acombo'	**Drug Combination**
0	No Anticoagulant
1	Warfarin
2	Enoxaparin
3	Rivaroxaban
12	Warfarin, Enoxaparin
13	Warfarin, Rivaroxaban
23	Enoxaparin, Rivaroxaban

Table 3.2. Key for Spinal Blocks

'scombo'	**Drug Combination**
0	No Spinal Block
1	Lidocaine
2	Bupivacaine
3	Ropivacaine
12	Lidocaine, Bupivacaine
13	Lidocaine, Ropivacaine
23	Bupivacaine, Ropivacaine
123	All Three Drugs

3.2. Analysis

An Ordinary Least Squares (OLS) Regression model is conducted to determine if a relationship between cost of hospital stay and drugs administered exists(Abraham & Ledolter, 2006). The first model will be formed with the dependent variable being cost, and the independent variables of the following: age, gender, and an indicator variable of which anticoagulant drugs were administered. If age and gender are insignificant they will be removed from the model. A similar example using backward regression techniques is given in Kleinbaum, Kupper, Muller, & Nizam (1998) to predict weight among children based on various other variables including race, gender, age, and height, among others (pages 403-422). Residual analysis will then be performed in order to check OLS assumptions. If the assumptions of equal variance or normality of residuals is violated a natural log transformation will be applied to the dependent variable. The natural log transformation is chosen due to ease of interpretation of coefficients. In addition, outliers will be located and removed based on influence. After these steps are completed the final model will be used to form conclusions on whether or not anticoagulants have a significant association with cost. If there is a difference in mean total cost

associated with the different anticoagulants, multiple comparison testing using Tukey's test and Dunnett's test will be done to determine which anticoagulants have significantly smaller/ larger mean total costs associated with them. A use of multiple comparison using Tukey's test and Dunnett's test may be found in Montgomery (2013) on pages 98-101.This same overall procedure will be used again by replacing anticoagulants with spinal blocks and again with blood transfusion prevention.

The same procedure will be followed again by replacing cost with LOS as the dependent variable. An OLS regression model will be formed followed by residual analysis, a natural log transformation, if necessary, and multiple comparison testing. Again, significant outliers may be removed based on influence. This procedure will be used separately for all three drug types.

A test will be conducted to determine if one or more of the anticoagulants had a significantly higher proportion of re-admittance. A chi square test will be used, and if chi square assumptions are not met, Fisher's exact test will be performed. A use of a chi square test comparing proportions may be found in Pagano and Gaureau (2000) comparing the proportion of head injuries between those individuals wearing a helmet versus those not wearing a helmet when a sample of 793 bicycle accidents is considered (pages 342- 347). An example of Fisher's exact test may be found in Daniel (1990), pages 120-122. A logistic regression model will be developed to test whether anticoagulants have an effect on RA while controlling for age and gender. A similar procedure will be followed as in the low birth weight study, the prostate cancer study, and the ICU study given in Hosmer and Lemeshow (2000)). This same overall procedure will be used again by replacing anticoagulants with spinal blocks and again with blood transfusion prevention. When analyzing the blood transfusion drug, a chi square test will be performed to see if the drug effectively reduces the probability of receiving a transfusion. A chi

square test will also be used to explore the relationship between blood transfusions and RA, as well as blood transfusions and gender.

If the drug combinations administered are confounded upon location, further analysis will be performed, so that results obtained will be controlled for location. A location with both large sample size and adequate variability of drugs administered will be chosen. A duplicate analysis, as previously described, will be performed on this chosen location.

CHAPTER 4. RESULTS

4.1. Dependent Variables

Before preforming the analysis, we will note summary statistics of each dependent variable. Recall, there were a total of 1214 THR surgeries performed. The average cost of a hospital stay for this sample was $10,975 with a standard deviation of $2,846. Figure 4.1 shows the histogram of cost; it appears to have a right skewed distribution with some large outliers.

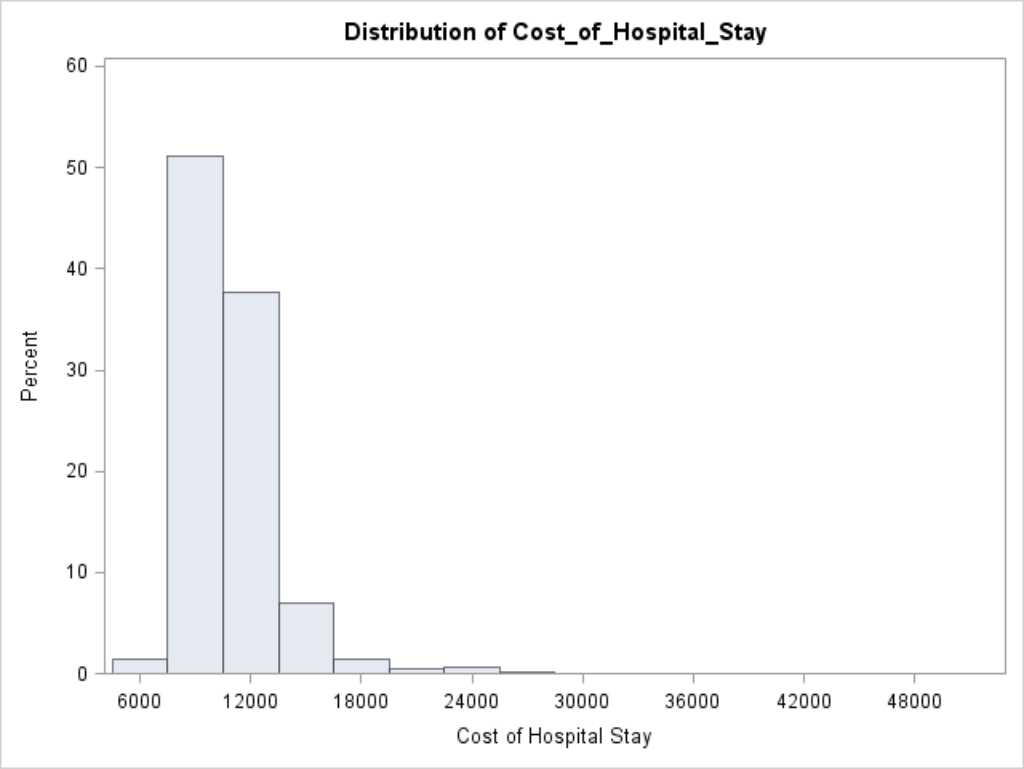

Figure 4.1. Histogram of Cost Distribution

LOS has a mean of 2.76 and a standard deviation of 1.31. This histogram is displayed in Figure 4.2; the distribution appears right skewed with large outliers on the top end.

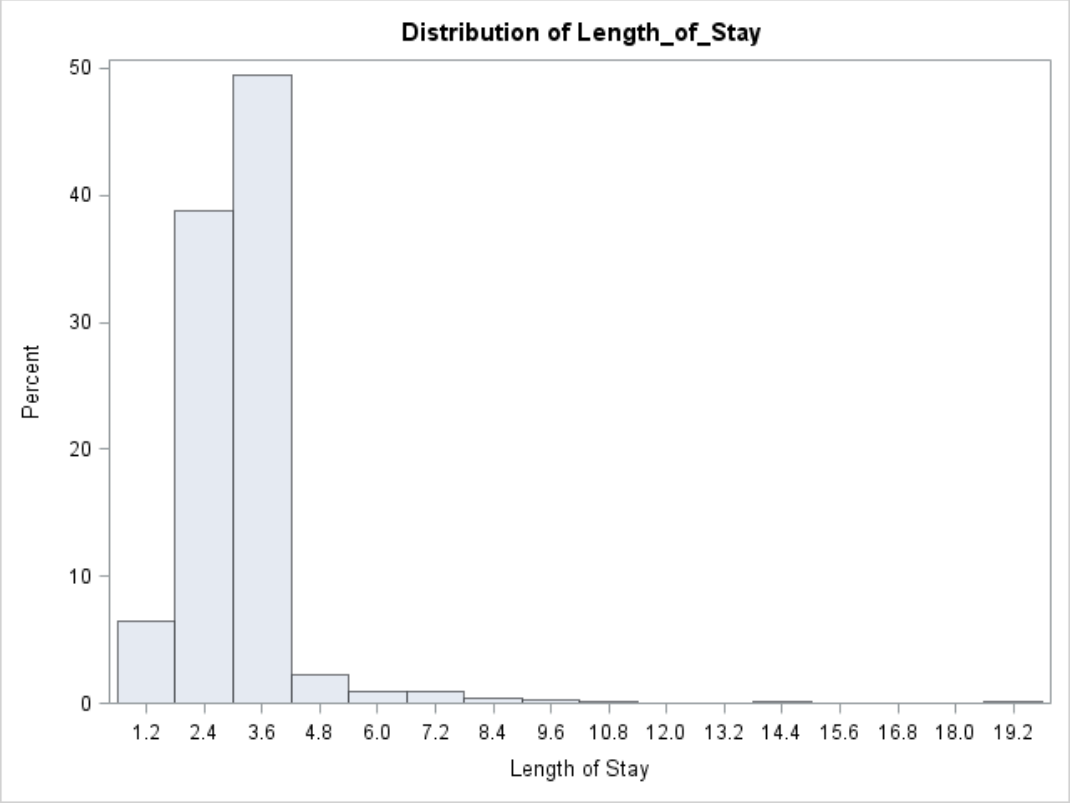

Figure 4.2. Histogram of LOS

Re-admittance is coded as 0 for no re-admittance, and 1 if a patient returned within 30 days due to complications. From this sample 2.72% of patients were re-admitted within 30 days and 97.28% were not re-admitted, as shown in the frequency table Table 4.1.

Table 4.1. Frequency Table of Adverse Effects

RA	Frequency	Percent	Cumulative Frequency	Cumulative Percent
0	1181	97.28	1181	97.28
1	33	2.72	1214	100.00

4.2. Anticoagulants

The first drug type we analyze is anticoagulants. The objective of this analysis is to minimize cost and LOS to the patients while not increasing RA. It is important to note how

often each anticoagulant or combination of anticoagulants is used in this sample; this is demonstrated in Table 4.2. It appears that administering a single anticoagulant is most common, followed by no anticoagulant, and least occurring is administering two anticoagulants.

Table 4.2. Anticoagulant Frequency Table

Acombo	Frequency	Percent	Cumulative Frequency	Cumulative Percent
0	137	11.29	137	11.29
1	463	38.14	600	49.42
2	258	21.25	858	70.68
3	265	21.83	1123	92.50
12	77	6.34	1200	98.85
13	3	0.25	1203	99.09
23	11	0.91	1214	100.00

Box plots for the hospital costs of patients receiving each type of anticoagulant are given in Figure 4.3. Table 4.3 gives the sample means and sample standard deviation of the hospital costs for patients receiving each type of anticoagulant.

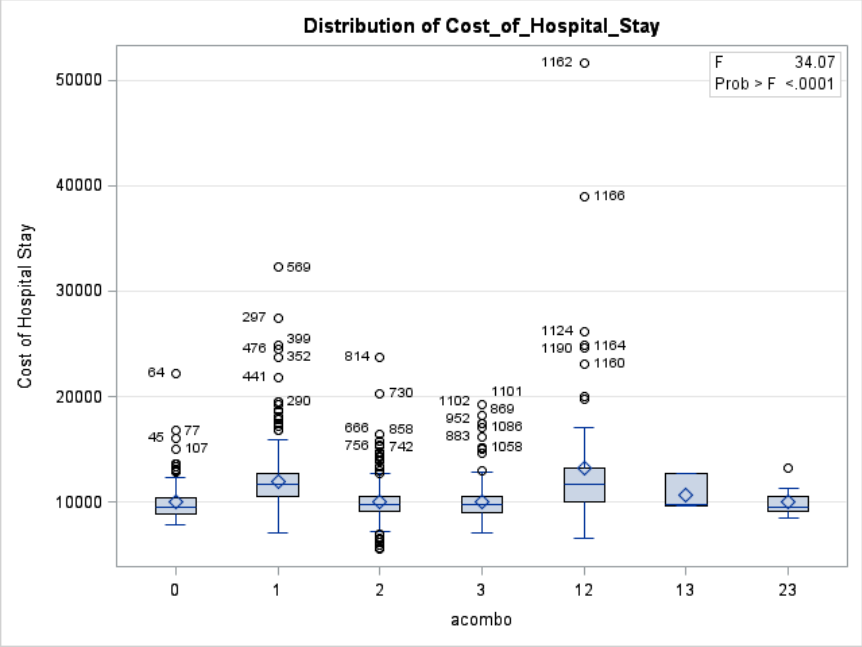

Figure 4.3. Distribution of Cost by Acombo

Table 4.3. Cost Summary Statistics by Acombo

Acombo	Mean	Standard Deviation
0	$10,027.06	$1,849.68
1	$11,956.46	$2,485.37
2	$10,068.67	$1,939.50
3	$10,023.33	$1,735.10
12	$13,230.43	$6,591.87
13	$10,687.45	$1,790.66
23	$9,985.25	$1,340.83
Overall	$10,975.00	$2,846.00

Note: Three outliers were removed before forming this table.

Three observations are removed from the sample before any model is attempted, because they are extremely large outliers. For the first regression modeling attempt, our dependent variable is cost and independent variables consist of the indicator variable for anticoagulants (acombo), gender and age. Gender and age are found to be insignificant, so they are removed from the model. Acombo groups 13 and 23 have small sample sizes of 3 and 11, respectively, so they are removed from the model. A residual analysis is conducted and it is determined that a natural log transformation should be performed on the variable cost in an attempt to fix the violated normality of residuals assumption. The ANOVA table for the final regression model can be found in Table 4.4. With an F value of 71.23, the overall model is highly significant. This result indicates that there is a significant difference in hospital cost associated with different anticoagulants. Figure 4.4 and Figure 4.5 show a histogram of the residuals from this model and residual plots, respectively. The assumption of normality appears valid. To check the homoscedasticity assumptions, refer to Figure 4.6 and Table 4.5. Figure 4.6 contains box plots of cost by each acombo. The outside bounds of the box represents the 25^{th} and 75^{th} percentiles. The inner line represents the median, and the diamond represents the mean. All outer dots

represent outliers. From the boxplots in Figure 4.6, the variances appear fairly similar. The sample standard deviations are given in Table 4.5; the largest standard deviation is 1.78 times larger than the smallest standard deviation. Moore and McCabe (2003) indicate that if the largest standard deviation is less than twice the size of the smallest standard deviation, it is reasonable to assume variances are approximately equal.

Table 4.4. Regression Model Output

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	4	8.6809	2.1702	71.23	<.0001
Error	1192	36.3154	0.0305		
Corrected Total	1196	44.9963			

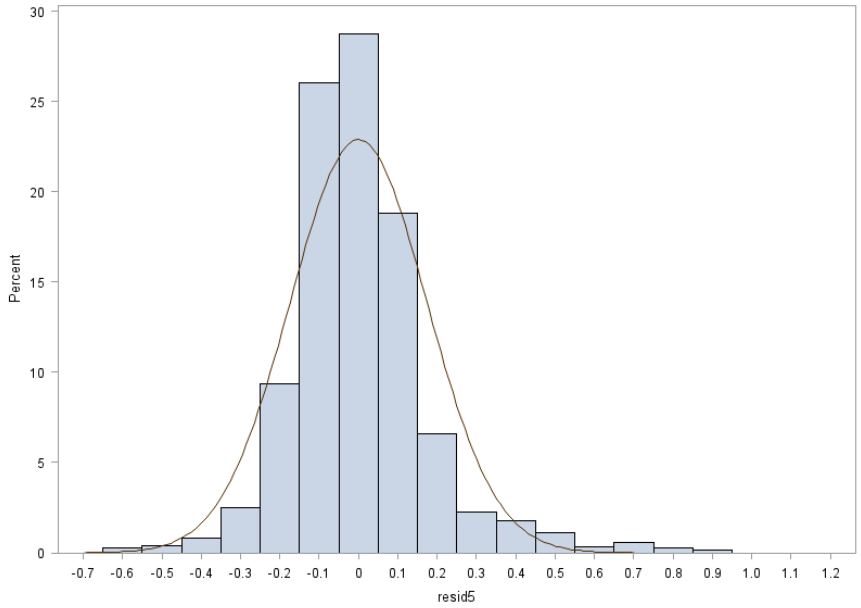

Figure 4.4. Histogram of Residuals

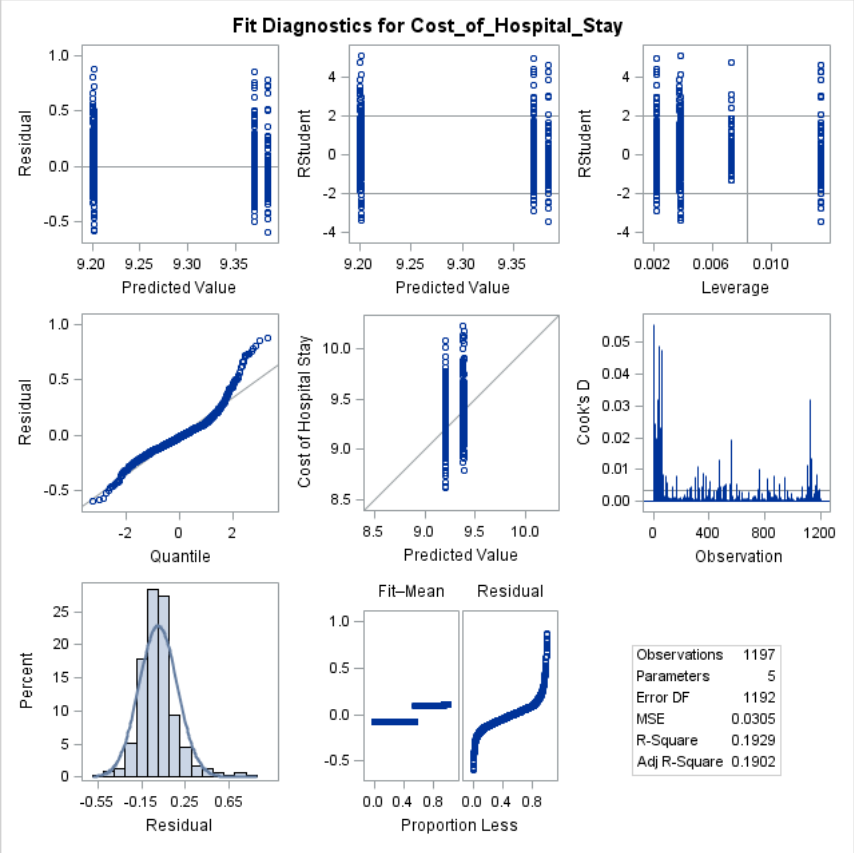

Figure 4.5. Residual Plots

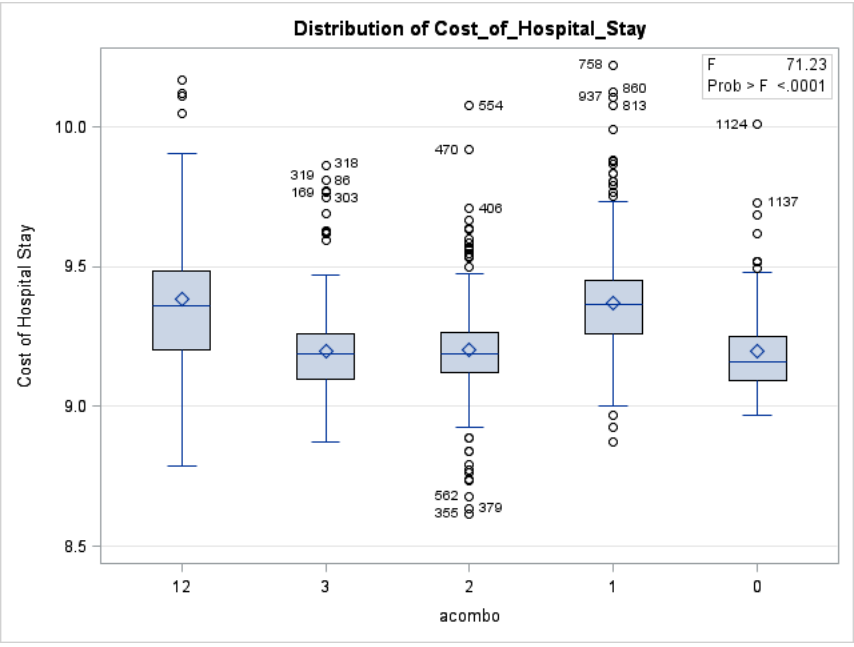

Figure 4.6. Distribution of Cost by Acombo

Table 4.5. Standard Deviation of Cost by Acombo

Acombo	Standard Dev
0	0.1541
1	0.1720
2	0.1753
3	0.1520
12	0.2712

Since there was a significant difference in hospital costs associated with the different anticoagulants, multiple comparison testing is performed. First, Dunnett's Test is used to compare each treatment against the control, which is the 0 group of no anticoagulant. Tukey's Studentized Range is used to compare all treatments against each other. The significant results of Dunnett's test and Tukey's test are shown in Tables 4.6 and 4.7, respectively. Only the significant pairwise comparisons are shown in the Tukey output. We have also provided a Tukey multiple comparison table for the untransformed hospital cost model in Table 4.8.

Table 4.6. Significant Cost Results from Dunnett - Transformed Model

Acombo Comparison	Percent Increase Estimate	95% Confidence Interval		.05 level significance
12 - 0	20.22%	13.16%	27.72%	***
1 - 0	18.50%	13.74%	23.46%	***
2 - 0	0.13%	-4.23%	4.69%	
3 - 0	0.03%	-4.30%	4.57%	

Table 4.7. Significant Cost Results from Tukey - Transformed Model

Acombo Comparison	Percent Increase Estimate	95% Confidence Interval		.05 level significance
12-2	20.06%	12.78%	27.81%	***
12-3	20.18%	12.91%	27.92%	***
12-0	20.22%	12.26%	28.74%	***
1-2	18.34%	14.04%	22.81%	***
1-3	18.46%	14.19%	22.89%	***
1-0	18.50%	13.13%	24.13%	***

Table 4.8. Significant Cost Results from Tukey - Untransformed Model

Acombo Comparison	Dollar Increase Estimate	95% Confidence Interval		.05 level significance
12-2	2,305.7	1,516.9	3,094.5	***
12-3	2,347.3	1,483.6	3,211.0	***
12-0	2,351.0	1,564.6	3,137.5	***
1-2	1,843.8	1,376.5	2,311.2	***
1-3	1,885.5	1,300.5	2,470.4	***
1-0	1,889.2	1,425.9	2,352.5	***

Because of the log transformation, results for Tables 4.6 and 4.7 are reported in percentages. An example of the interpretation is as such: by administering the anticoagulant group 12 as compared to group 2, the overall hospital cost is estimated to increase by 20.06%. From Table 4.7 we can make several statements about costs by acombo groups. Both groups 12 and 1 significantly increase cost when compared to groups 0, 2, and 3. There is no significant cost difference among groups 1 and 12; there is also no significant cost difference between groups 0, 2, and 3. A visual of this summary can be seen in Table 4.9. When looking at the untransformed hospital cost model, we see the significant pairwise comparisons are consistent between the two models.

Table 4.9. Rank of Acombo by Cost

Rank	Treatment
1 (highest)	12, 1
2 (lowest)	0, 2, 3

The next dependent variable considered is length of stay (LOS). Table 4.10 shows the summary statistics of LOS of patients receiving each of the various anticoagulants.

Table 4.10. LOS Summary Statistics by Acombo

Acombo	Mean	Std Dev
0	2.48	0.99
1	2.50	1.09
2	3.00	1.16
3	2.80	0.85
12	3.83	3.00
13	3.00	1.00
23	3.36	1.63
Overall	2.76	1.31

Note: Three outliers were removed before forming this table.

A similar regression procedure is conducted as with hospital cost, but with LOS as the dependent variable. The independent variables consist of the indicator variable for spinal blocks (scombo), gender, and age. Gender and age are significant so they will be left in the model. Acombo groups 13 and 23 are again removed due to small sample sizes, and three very large outliers are identified and removed. The natural log transformation is applied to the dependent variable of length of stay, so that the assumptions of equal variance and normality of residuals can be met. Output from the model can be seen in Tables 4.11, 4.12, and 4.13. It is noted that after controlling for gender and age, the type of acombo the patient received is still significant and associated with LOS. Refer to Figure 4.7; the histogram of the residuals and qq-plot suggest

the normality assumption is adequate. The standard deviation for each acombo is show in Table 4.14. The homoscedasticity assumption appears valid using the rule that the largest standard deviation is less than two times the smallest standard deviation.

Table 4.11. LOS Overall Regression Summary

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	6	30.9233	5.1539	41.98	<.0001
Error	1190	146.0791	0.1228		
Corrected Total	1196	177.0023			

Table 4.12. LOS Variable Regression Summary

Source	DF	Type III SS	Mean Square	F Value	Pr > F
acombo	4	11.6322	2.9080	23.69	<.0001
Gender	1	5.0124	5.0124	40.83	<.0001
Age	1	11.8244	11.8244	96.32	<.0001

Table 4.13. Coefficients of Age and Gender

Parameter	Estimate	Standard Error	t Value	Pr > |t|
Intercept	.4728	0.069	6.77	<.0001
Gender M	0.00	.	.	.
Gender F	.1307	.0204	6.39	<.0001
Age	0.0083	0.0008	9.69	<.0001

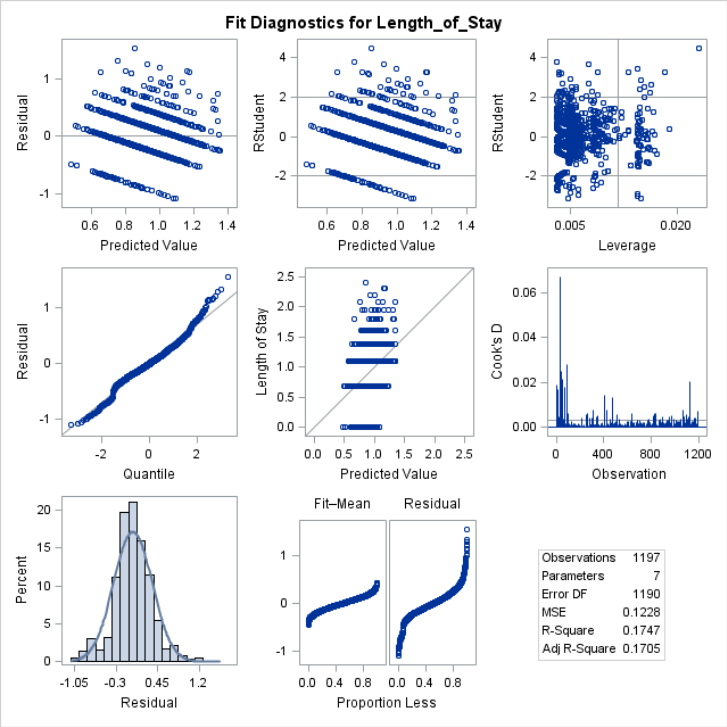

Figure 4.7. LOS Residual Plots

Table 4.14. LOS Standard Deviation by Acombo

Acombo	Standard Deviation
0	0.3724
1	0.4182
2	0.3180
3	0.3020
12	0.4609

Both Dunnett's test and Tukey's test are conducted for multiple comparisons. Since Dunnett's test produced very similar results, only the results from Tukey's test are provided. The significant results from Tukey's test can be found in Tables 4.15 and 4.16. In some multiple comparisons the significant pairings differ between the transformed and untransformed models; this is a result of the untransformed model assumptions possibly not being met.

Table 4.15. Significant LOS Results from Tukey - Transformed Model

Acombo Comparison	Percent Increase Estimate	95% Confidence Interval		.05 level significance
12-0	29.51%	12.81%	48.69%	***
12-1	30.80%	16.03%	47.45%	***
2-0	22.33%	10.55%	35.35%	***
2-1	23.54%	14.69%	33.08%	***
3-0	15.30%	4.25%	27.51%	***
3-1	16.44%	8.17%	25.35%	***

Table 4.16. Significant LOS Results from Tukey - Untransformed Model

Acombo Comparison	Days Increase Estimate	95% Confidence Interval		.05 level significance
12-3	0.5551	0.1758	0.9344	***
12-1	0.8481	0.4870	1.2093	***
12-0	0.8696	0.4534	1.2858	***
2-1	0.4968	0.2726	0.7209	***
2-0	0.5183	0.2133	0.8232	***
3-1	0.2923	0.0709	0.5152	***
3-0	0.3145	0.0109	0.6180	***

Again, we see the treatments have split into two clusters. Groups 12, 2, and 3 are all significantly higher than 0 and 1. There is no significant difference among the groups 12, 2, and 3; there is also no significant difference among the groups 0 and 1. A visual has been provided in Table 4.17.

Table 4.17. Rank of Acombo by LOS

Rank	Treatment
1 (highest)	12, 2, 3
2 (lowest)	0, 1

The last variable we are examining is re-admittance. To visually display the effect of acombo on the proportion of re-admittance, a frequency table is give in Table 4.18.

Table 4.18. Re-admittance x Acombo Frequency Table

	Acombo					
RA	0	1	2	3	12	Total
0	Freq 136 Col Pct 99.27	Freq 448 Col Pct 96.76	Freq 250 Col Pct 96.90	Freq 259 Col Pct 97.74	Freq 74 Col Pct 96.10	1167 97.25
1	Freq 1 Col Pct .73	Freq 15 Col Pct 3.24	Freq 8 Col Pct 3.10	Freq 6 Col Pct 2.26	Freq 3 Col Pct 3.90	33 2.75
Total	137	463	258	265	77	1200 100.0

A chi square test of independence is conducted and a p-value of .5191 is found. There is not enough evidence to suggest a relationship between RA and acombo. However, we should note the chi square assumption that each cell has an expected value greater than 5 was not met. In this case, we also conduct the Fisher's Exact Test which does not have this assumption. The p-value is .4762, so we can again conclude that acombo does not associated with RA. Further evidence is given by running a logistic regression in which RA (coded as 0 or 1) is the dependent variable and acombo is the independent variable. The logistic model concludes no difference in the likelihood of a re-admittance occurring among the different acombo treatments.

One possible complication with this analysis is the fact that acombo is confounded with location. Table 4.19 shows the frequency table of acombo and location. We can see that smaller hospitals such as hospital E only use one type of anticoagulant. Also, even the larger hospitals choose anticoagulants at different frequencies; hospital C uses acombo 2 and 3 quite frequently while hospital D uses acombo 1 the majority of the time. This may be an analytical problem for the analysis because the mean cost and LOS are quite different between locations. With this location and drug relationship, we cannot differentiate whether the location or anticoagulant is causing the differences in cost. Because of the insufficient sample size at some of the hospitals as well as confounding variables, we will conduct a separate analysis only using data from Hospital C. Hospital C was chosen because of its large sample size and relatively varied anticoagulant use. The summary tables for Hospital C data are presented in Tables 4.20 and 4.21. The same modeling process is followed as done previously. Only the results for Tukey's multiple comparison is provided. The significant multiple comparisons for cost are found in Tables 4.22 and 4.23. The significant multiple comparisons for LOS are found in Tables 4.24 and 4.25.

Table 4.19. Location x Acombo Frequency Table

	Acombo					
Location	**0**	**1**	**2**	**3**	**12**	**Total**
A	1	3	2	6	1	13
	7.69	23.08	15.38	46.15	7.69	1.08
	0.73	0.65	0.78	2.26	1.30	
B	0	102	0	0	7	109
	0.00	93.58	0.00	0.00	6.42	9.08
	0.00	22.03	0.00	0.00	9.09	
C	112	48	242	247	34	683
	16.40	7.03	35.43	36.16	4.98	56.92
	81.75	10.37	93.80	93.21	44.16	
D	24	310	5	12	35	386
	6.22	80.31	1.30	3.11	9.07	32.17
	17.52	66.95	1.94	4.53	45.45	
E	0	0	9	0	0	9
	0.00	0.00	100.00	0.00	0.00	0.75
	0.00	0.00	3.49	0.00	0.00	
Total	137	463	258	265	77	1200
	11.42	38.58	21.50	22.08	6.42	100.00

Note: The first number of each cell is the frequency, the second is the row percent, and the third is the column percent.

Table 4.20. Summary of Cost by Acombo Using Hospital C

Acombo	Mean	Std Dev
0	$9,602	$1,557
1	$9,944	$2,085
2	$10,104	$1,725
3	$9,827	$1,413
12	$11,499	$4,402
Overall	$9,980	$1,886

Table 4.21. Summary of LOS by Acombo Using Hospital C

Acombo	Mean	Std Dev
0	2.64	0.95
1	2.93	1.01
2	2.98	1.18
3	2.82	0.81
12	3.00	3.00
Overall	2.93	1.22

Table 4.22. Significant Cost Results from Tukey Using Hospital C - Transformed Model

Acombo Comparison	Percent Increase Estimate	95% Confidence Interval		.05 level significance
12-2	9.18%	1.18%	17.82%	***
12-1	11.60%	1.68%	22.50%	***
12-3	11.99%	3.79%	20.84%	***
12-0	14.61%	5.65%	24.33%	***
2-0	4.97%	0.10%	10.07%	***

Table 4.23. Significant Cost Results from Tukey Using Hospital C - Untransformed Model

Acombo Comparison	Dollar Increase Estimate	95% Confidence Interval		.05 level significance
12 - 2	1394.2	467.0	2321.3	***
12 - 1	1554.0	419.3	2688.8	***
12 - 3	1671.1	745.1	2597.1	***
12 - 0	1896.1	904.9	2887.3	***

Table 4.24. Significant LOS Results from Tukey Using Hospital C - Transformed Model

Acombo Comparison	Percent Increase Estimate	95% Confidence Interval		.05 level significance
12-2	32.81%	13.78%	55.02%	***
12-1	32.95%	10.02%	60.65%	***
12-3	37.18%	17.55%	60.10%	***
12-0	48.17%	25.59%	74.81%	***
2-0	11.57%	1.30%	22.87%	***

Table 4.25. Significant LOS Results from Tukey Using Hospital C - Untransformed Model

Acombo Comparison	Day Increase Estimate	95% Confidence Interval		.05 level significance
12 - 2	0.74	0.19	1.29	***
12 - 1	0.78	0.12	1.44	***
12 - 3	0.89	0.35	1.43	***
12 - 0	1.08	0.50	1.65	***
2- 0	0.34	0.01	0.67	***

There are differences between these tables and tables created with the overall data. There seems to be less disparity of costs between treatments, and more disparity of LOS; however, we see that acombo 12 is associated with the largest cost and LOS compared to all other treatments. Overall, it seems the 12 group of anticoagulants is least recommended in terms of cost and LOS.

The dataset from Hospital C was also used to test for a difference in RA among the treatments using a chi square test and Fisher's Exact test; the p-values are .0693 and .0676, respectively. Although the p-values are insignificant at α =.05, Table 4.26 is provided to visually compare the RA occurrences. From the table, it was observed that treatments 1 and 12 have a higher proportion of re-admittance than the others, but the overall relationship between acombo and RA is not significant.

Table 4.26. Re-admittance by Acombo using Hospital C

	Acombo					
RA	**0**	**1**	**2**	**3**	**12**	**Total**
0	111 99.11	44 6.44	235 34.41	242 35.43	32 4.69	664 97.22
1	1 0.15	4 0.59	7 1.02	5 0.73	2 0.29	19 2.78
Total	112	48	242	247	34	683

Note: The first number in each cell is the frequency; the second number is the column percent.

4.3. Spinal Blocks

The next drug category we analyze is spinal blocks. We investigate how the spinal blocks are associated with overall cost and LOS. We also test to see if the spinal blocks are associated with significantly different re-admittance rates. The aim is to identify the spinal block or blocks associated with the lowest hospital costs and shortest lengths of stay in which the re-admittance rates are not significantly higher. Table 4.27 shows the frequency table of spinal blocks. It appears that patients receiving scombo 2 or 12 is quite common, while scombo groups 3, 13, 23, and 123 are rare. Table 4.28 shows summary statistics of cost by scombo.

Table 4.27. Frequency Table of Scombo

scombo	Frequency	Percent	Cumulative Frequency	Cumulative Percent
0	82	6.75	82	6.75
1	78	6.43	160	13.18
2	525	43.25	685	56.43
3	2	0.16	687	56.59
12	519	42.75	1206	99.34
13	3	0.25	1209	99.59
23	2	0.16	1211	99.75
123	3	0.25	1214	100.00

Table 4.28. Cost Summary Statistics by Scombo

scombo	Mean	Standard Deviation
0	$10,718	$2,358
1	$12,719	$5,398
2	$10,060	$1,728
3	$14,790	$11,788
12	$11,682	$2,900
13	$10,445	$4,195
23	$6,213	$978
123	$11,485	$3,209

Note: Three outliers were removed before forming this table.

Refer to the regression procedure in 4.2; the modeling process will follow the same steps with the indicator variable for acombo replaced by the indicator variable for scombo. Gender and age are included in the first modeling attempt, but removed due to insignificance. Scombo groups 3, 13, 23, and 123 are removed due to small sample size along with the same 3 outliers removed from section 4.2. A natural log transformation is performed on the dependent variable cost in order to help the model meet regression assumptions. Output from the final regression model can be seen in Table 4.29. The overall F value is 60.16 and p-value is less than .0001

indicating the model is highly significant. Residual plots are given in Figure 4.8. The approximate normality of the error terms appears to be met. The standard deviations of the costs associated with patients given each of the different scombos are presented in Table 4.30. It appears that the equal variance assumption is satisfied since the largest sample standard deviation is less than twice the smallest sample standard devation.

Table 4.29. Regression Model Output

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	3	5.6520	1.8840	60.16	<.0001
Error	1197	37.4882	0.0313		
Corrected Total	1200	43.1402			

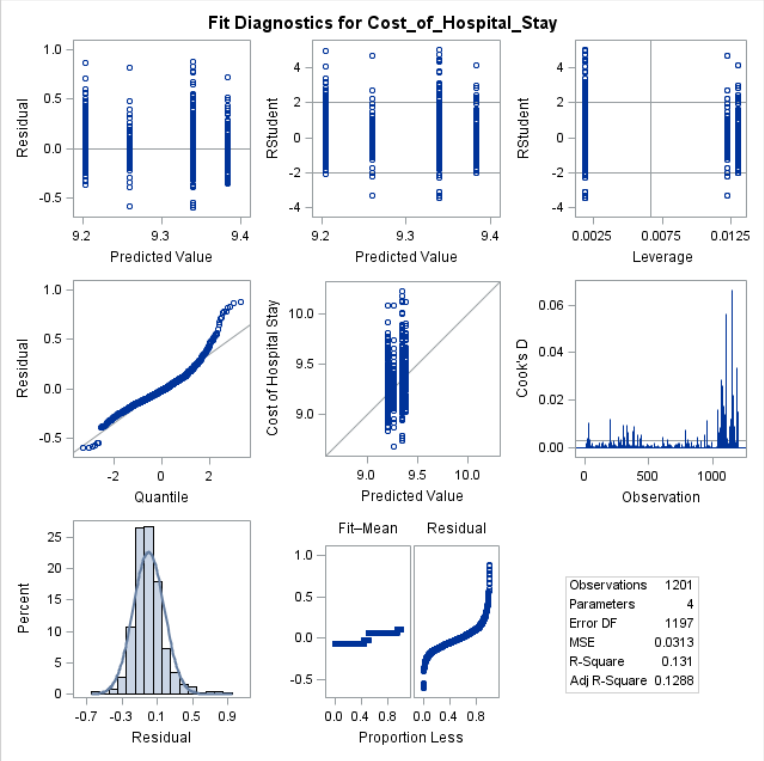

Figure 4.8. Residual Plots

Table 4.30. Cost Standard Deviation by Scombo

Scombo	Standard Deviation
0	.1957
1	.2268
2	.1506
12	.1898

Tukey's test is conducted to test each pairwise comparison. The significant results from Tukey's test are found in Table 4.31. We see that the treatments have split into three levels of cost. Scombo 1 and 12 are significantly higher than Scombo 0 and 2, and 0 is significantly higher than 2. A visual of this result can be seen in Table 4.32. In addition, Tukey's test results on the untransformed cost variable have been provided in Table 4.33. These results are intended to give the reader an easier context to interpret. Take note that the 0-2 pairwise comparison is no longer significant when using the untransformed model, but the underlying assumptions are not reasonably met in this model.

Table 4.31. Significant Cost Results from Tukey - Transformed Model

Scombo Comparison	Percent Increase Estimate	95% Confidence Interval		.05 level significance
1-0	13.18%	5.29%	21.66%	***
1-2	19.64%	13.17%	26.47%	***
12-0	8.23%	2.53%	14.25%	***
12-2	14.40%	11.22%	17.68%	***
0-2	5.70%	0.14%	11.58%	***

Table 4.32. Rank of Scombo by Cost

Rank	Treatment
1 (highest)	12, 1
2	0
3 (lowest)	2

Table 4.33. Significant Cost Results from Tukey - Untransformed Model

Scombo Comparison	Dollar Increase Estimate	95% Confidence Interval		.05 level significance
1-0	1,495.6	588.6	2,402.6	***
1-2	2,153.4	1,455.9	2,850.8	***
12-0	871.2	191.8	1,550.6	***
12-2	1,529.0	1,174.8	1,883.1	***
0-2	657.8	-20.9	1,336.4	

We will next consider how LOS is associated with each scombo. Table 4.34 shows the summary statistics of LOS by scombo.

Table 4.34. LOS Summary Statistics by Scombo

scombo	Mean	Standard Deviation
0	2.76	.95
1	3.22	2.15
2	2.89	1.05
3	7.50	4.95
12	2.55	1.35
13	3.00	1.00
23	3.50	.71
123	2.67	.58

Note: Three outliers were removed before forming this table.

The same regression procedure is followed, but with LOS as the dependent variable. Age and gender are included as dependent variables; both are significant, so they are left in the

model. Scombo 3, 13, 23, and 123 are removed due to small sample size, and the same three outliers removed during 4.2 are removed. A natural log transformation is performed on the dependent variable LOS. The output from the final model is provided in Tables 4.35, 4.36, and 4.37. The overall F value as well as each variable's F value are highly significant. The scombo used is significantly associated with length of stay after controlling for age and gender. Residual plots are given in Figure 4.9 and sample standard deviations of LOS associated with each scombo are given in Table 4.38. The underlying assumptions for the regression model appear to be reasonably met.

Table 4.35. Overall Regression Output for LOS

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	5	29.9767	5.9953	49.02	<.0001
Error	1195	146.1526	0.1223		
Corrected Total	1200	176.1294			

Table 4.36. Variable Regression Output for LOS

Source	DF	Type III SS	Mean Square	F Value	Pr > F
scombo	3	10.2527	3.4175	27.94	<.0001
Age	1	13.5886	13.5886	111.11	<.0001
Gender	1	4.1303	4.1303	33.77	<.0001

Table 4.37. Coefficients for Age and Gender

Parameter	Estimate	Standard Error	t Value	Pr > |t|
Intercept	0.1769	0.0575	3.07	0.0022
Age	0.0089	0.0008	10.54	<.0001
Gender F	0.1184	0.0203	5.81	<.0001
Gender M	0.0000	.	.	.

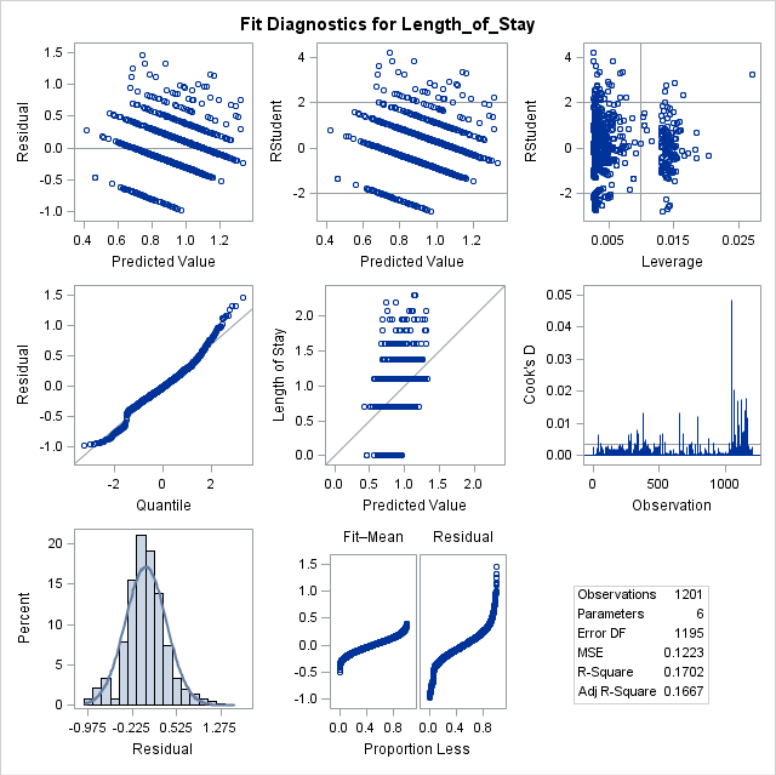

Figure 4.9. Residual Plots

Table 4.38. LOS Standard Deviation by Scombo

Scombo	Standard Deviation
0	.3224
1	.3761
2	.3098
12	.4328

Tukey's test is performed to compare all possible pairwise comparisons of length of stay associated with each scombo. The significant results of Tukey's test is provided in Tables 4.39 and 4.40. The only significant differences in this instance are between scombo 12 and all other treatments. It appears scombo 12 is associated with the shortest LOS, and there is no significant difference among the other treatments.

Table 4.39. Significant LOS Results from Tukey - Transformed Model

Scombo Comparison	Percent Increase Estimate	95% Confidence Interval		.05 level significance
1-12	23.34%	10.50%	37.67%	***
2-12	20.35%	13.83%	27.25%	***
0-12	14.70%	3.07%	27.65%	***

Table 4.40. Significant LOS Results from Tukey - Untransformed Model

Scombo Comparison	Day Increase Estimate	95% Confidence Interval		.05 level significance
1 - 12	0.51009	0.18173	0.83844	***
2 - 12	0.38662	0.22007	0.55317	***

We will now check for a difference in RA rate among the difference scombo treatments. The frequency table of RA with Scombo can be seen in Table 4.41. Looking at the table the percentage of RA seems approximately the same for each Scombo level.

Table 4.41. RA x Scombo Frequency Table

	Scombo				
RA	**0**	**1**	**2**	**12**	**Total**
0	80 97.56	76 97.44	511 97.33	505 97.30	1172 97.34
1	2 2.44	2 2.56	14 2.67	14 2.70	32 2.66
	82	78	525	519	1204

Note: The first number in each cell is the frequency; the second number is the column percent.

A chi square test of independence is conducted and a p-value of .9992 is reported. From the result we conclude there is not enough evidence to suggest a relationship between RA and Scombo. The assumption for chi square that each cell is greater or equal to 5 is not met for this test, so a Fisher's Exact test is performed. The p-value from Fisher's Exact test is approximately equal to 1. As a last test we form a logistic regression model with RA (coded as 0 or 1) as the dependent variable and scombo, age, and gender as independent variables. The logistic model concludes no difference in the likelihood of a re-admittance between the different scombo treatments.

As stated in section 4.2 scombo is confounded with location because certain hospitals favor certain drugs. Table 4.42 shows the frequency table of location and scombo. Certain hospitals favor certain drugs, so it appears we have a problem. For instance Hospital D seems to favor scombo 12. The lower LOS that we found from scombo 12 may be attributed to the drug, or it may be attributed to the hospital. Since Hospital C has a fairly large sample of patients and has used a variety of scombos with sample sizes of at least 30, regression modeling is done with the same process and previously described using only the sample from Hospital C. The sample means and standard deviations of cost by scombo using Hospital C data only are provided in Table 4.43. The sample mean and standard deviation of LOS by scombo using Hospital C data only are provided in Table 4.44. Significant results of Tukey's test are given in Tables 4.45 and 4.46 for cost differences. The only pairwise comparison found to be significant for cost is 1-2. Multiple comparisons for LOS found no significant pairwise comparisons at the .05 significance level.

Table 4.42. Location x Scombo Frequency Table

	Scombo				
Location	**0**	**1**	**2**	**12**	**Total**
A	0	9	0	3	12
	0.00	75.00	0.00	25.00	
	0.00	11.69	0.00	0.58	
B	38	16	43	12	109
	34.86	14.68	39.45	11.01	
	46.34	20.78	8.19	2.32	
C	42	31	472	149	694
	6.05	4.47	68.01	21.47	
	51.22	40.26	89.90	28.82	
D	1	21	9	350	381
	0.26	5.51	2.36	91.86	
	1.22	27.27	1.71	67.70	
E	1	0	1	3	5
	20.00	0.00	20.00	60.00	
	1.22	0.00	0.19	0.58	
Total	82	77	525	517	1201

Note: The first number of each cell is the frequency, the second is the row percent, and the third is the column percent.

Table 4.43. Cost Summary Statistics by Scombo for Hospital C

Scombo	Mean	Standard Deviation
0	$10,718	$2,358
1	$12,214	$3,054
2	$10,060	$1,728
12	$11,638	$2,813

Table 4.44. LOS Summary Statistics by Scombo for Hospital C

Scombo	Mean	Standard Deviation
0	2.756	0.950
1	3.013	1.164
2	2.900	1.046
12	2.503	1.154

Table 4.45. Significant Cost Results from Tukey - Transformed Model

Scombo Comparison	Percent Increase Estimate	95% Confidence Interval		.05 level significance
1-2	9.21%	1.70%	17.29%	***

Table 4.46. Significant Cost Results from Tukey - Untransformed Model

Scombo Comparison	Dollar Increase Estimate	95% Confidence Interval		.05 level significance
1 - 2	1084.8	226.3	1943.3	***

4.4. Blood Transfusion Prevention

The last category of drug we analyze is blood transfusion prevention. There is only one drug in this category, tranexamic acid, and, thus, the indicator variable b1 has 2 levels (0/1). 55% of patients are reported to have received the drug and 45% did not. First, we check the efficacy by looking at the frequency table of b1 and Blood Transfusion (BT) shown in Table 4.47. The table shows that 19.76% of patients who did not receive the drug needed a blood transfusion, while only 6.23% of patients who received the drug needed a transfusion. A chi square test is run and the p-value is less than .0001. The chi square test confirms there is a relationship between receiving b1 and receiving a blood transfusion. We then form a logistic regression model with a dependent variable BT (coded as 0 or 1) and independent variables b1,

age, and gender. The event being modeled is the probability of needing a blood transfusion. The odds ratio estimates from this model can be seen in Table 4.48. The reported odds ratio is four indicating the odds of needing a blood transfusion are four times the odd of patients who did not receive the drug as compared with those who did receive the drug.

Table 4.47. Frequency Table for b1 x Blood Transfusion

	Blood Transfusion		
b1	**0**	**1**	**Total**
0	536 80.24	132 19.76	668
1	512 93.77	34 6.23	546
Total	1048	166	1214

Note: The first number in each cell is the frequency; the second number is the row percent.

Table 4.48. Logistic Regression for BT=1

Effect	**Point Estimate**	**95% Wald Confidence Limits**	
b1 0 vs 1	4.000	2.668	5.996
Age	1.033	1.018	1.049
Gender F vs M	2.720	1.875	3.945

We now move into the cost analysis associated with b1. The summary statistics of cost by b1 can be seen in Table 4.49. The same regression procedure described in sections 4.2 and 4.3 will be followed, but with the independent variable b1 instead of the indicator variables associated with scombo or acombo. Age and gender are insignificant and, thus, removed from the model. Three extreme outliers are removed and a log transformation is performed on the dependent variable cost. The residual plots indicate the regression assumption are met for the

model. Output from the final regression model is seen in Table 4.50. The pairwise comparison is shown in Tables 4.51 and 4.52. We conclude that administering b1 significantly raises costs.

Table 4.49. Cost Summery Statistics by b1

b1	Mean	Standard Deviation
0	$10,479	$2,939
1	$11,582	$2,607

Note: Three outliers were removed before forming this table.

Table 4.50. Regression Model of Cost

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	1	3.4551	3.4551	88.75	<.0001
Error	1212	47.1814	0.0389		
Corrected Total	1213	50.6365			

Table 4.51. Pairwise Comparison of Cost – Transformed Model

b1 Comparison	Percent Increase Estimate	Simultaneous 95% Confidence Limits		.05 level significance
1 - 0	11.32%	8.86%	13.83%	***

Table 4.52. Pairwise Comparison of Cost – Untransformed Model

b1 Comparison	Dollar Increase Estimate	Simultaneous 95% Confidence Limits		.05 level significance
1 - 0	1076.5	811.8	1341.1	***

The same analysis is performed for LOS. Age and gender are included in the model due to significance. Three outliers are removed and the dependent variable LOS is transformed using a natural log transformation. The regression assumptions are met for the model. The summary

table is presented in Table 4.53. The model results can be seen in Tables 4.54 and 4.55. It is noted that using the drug b1 is significantly associated with LOS after controlling for age and gender. The pairwise comparison of LOS can be seen in Tables 4.56 and 4.57. There is evidence that administering b1 has a significant reduction on LOS. To check for a relationship between RA and b1, a chi square test is conducted. The frequency table for the chi square test is provided in Table 4.58. The p-value reported is .9553, so we conclude there is no difference in RA between administering and not administering b1.

Table 4.53. Summary LOS by B1

b1	Mean	Standard Deviation
0	2.97	1.20
1	2.43	0.96

Note: Three outliers were removed before forming this table.

Table 4.54. Regression Model of LOS

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	3	33.3354	11.1118	86.37	<.0001
Error	1210	155.6675	0.1286		
Corrected Total	1213	189.0030			

Table 4.55. Regression Model of LOS by Variable

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
b1	1	13.2162	13.2162	108.74	<.0001
Age	1	11.5175	11.5175	94.77	<.0001
Gender	1	5.2021	5.2021	42.80	<.0001

Table 4.56. Pairwise Comparison of LOS – Transformed Model

b1 Comparison	Percent Change Estimate	95% Confidence Limits		.05 level significance
1 - 0	-19.71%	-22.91%	-16.39%	***

Table 4.57. Pairwise Comparison of LOS – Untransformed Model

b1 Comparison	Day Change Estimate	95% Confidence Limits		.05 level significance
1 - 0	-0.59554	-0.73560	-0.45548	***

Table 4.58. Frequency Table of b1 x RA

	RA		
b1	**0**	**1**	**Total**
0	650 97.31	18 2.69	668
1	531 97.25	15 2.75	546
Total	1181	33	1214

Note: The first number in each cell is the frequency; the second number is the row percent.

The location problem discussed in Section 4.2 and 4.3 may also be relevant here. By looking at Table 4.59, it appears the use of b1 is confounded with location. Certain locations such as hospital E never administer the drug; however, the larger hospitals, Hospitals C and D, administer the drug to 23.82% and 93.52% of patients, respectively. With these vastly unequal proportions, we cannot conclude whether the cost and LOS differences are attributed to the drug or the hospital. To control for location we conduct a separate analysis on only the Hospital C

data. Hospital C has the largest sample size and the least unequal proportions in terms of administering b1. Summary tables of cost and LOS are presented in Table 4.60 and 4.61. Regression analysis was performed as previously described. The regression on cost yields a p-value of .6220. This result indicates there is no significant difference of cost between the two levels of b1 at Hospital C. Notice in the overall model we find a significant effect of b1 on cost; because we find a different result when controlling for location, that may indicate location is responsible for the difference in cost, rather than the drug b1. We then form a regression model to test whether b1 has a significant effect on LOS. The results for the pairwise comparison on LOS are given in Tables 4.62 and 4.63. The results indicate that administering b1 is associated with a reduction in LOS; this conclusion is consistent with the overall model.

Table 4.59. Location x b1 Frequency Table

Location	0	1	Total
A	11	2	13
	84.62	15.38	
	1.65	0.37	
B	92	17	109
	84.40	15.60	
	13.77	3.11	
C	531	166	697
	76.18	23.82	
	79.49	30.40	
D	25	361	386
	6.48	93.52	
	3.74	66.12	
E	9	0	9
	100.00	0.00	
	1.35	0.00	
Total	668	546	1214

Note: The first number of each cell is the frequency, the second is the row percent, and the third is the column percent.

Table 4.60. Summary Cost by B1 Using Hospital C

b1	Mean	Standard Deviation
0	$9,976	$1,909
1	$9,849	$1,010

Table 4.61. Summary LOS by B1 Using Hospital C

b1	Mean	Standard Deviation
0	2.96	1.16
1	2.73	0.74

Table 4.62. Pairwise Comparison of LOS Using Hospital C – Transformed Model

b1 Comparison	Percent Change Estimate	Simultaneous 95% Confidence Limits		.05 level significance
1 - 0	-6.52%	-11.26%	-1.53%	***

Table 4.63. Pairwise Comparison of LOS Using Hospital C – Untransformed Model

b1 Comparison	Day Change Estimate	Simultaneous 95% Confidence Limits		.05 level significance
1 - 0	-0.23895	-0.41976	-0.05813	***

CHAPTER 5. CONCLUSION

From the analysis, we find that different drugs administered are associated with overall cost and LOS. Although we cannot form conclusions based on side effects incurred by the patients, we can make general statements and speculations as to why some drugs have a higher or lower cost or LOS. It is our intention for hospitals to become aware of these disparities among perioperative drugs.

To view the rank of anticoagulants by category, we have created Table 5.1. It appears that the combination of warfarin and enoxaparin is the significantly highest drug combination in both the cost and LOS categories. We also see that not administering an anticoagulant yields the lowest overall cost and LOS. For the overall data it is recommended to administer no anticoagulant and not recommended to administer the combination of warfarin and enoxaparin. This does not however, take into account the occurrence of DVT, which may be higher among the patients who did not receive an anticoagulant. We also analyze acombo by location and get slightly different results. The combination of warfarin and enoxaparin is still significantly highest in terms of cost and LOS for Hospital C data, although not receiving an anticoagulant is now only significantly lower in terms of cost and LOS than receiving enoxaparin. Overall, we would advise against using the pairing of warfarin and enoxaparin in terms of cost and LOS. Future studies are advised to combine data on cost and LOS with data on DVT occurrence.

Table 5.1. Anticoagulant Ranks in Terms of Cost and LOS

Acombo	Cost Rank (1=highest)	LOS (1=highest)
Warfarin, Enoxaparin	1	1
Warfarin	1	2
Enoxaparin	2	1
Rivaroxaban	2	1
No Anticoagulant	2	2

The rank of scombo by each category can be found in Table 5.2. It appears that administering lidocaine results in the largest cost and LOS when compared to the other spinal block pairings. Our recommendation is to not administer lidocaine if lowering costs and LOS is important; this drug is also associated with the highest TNS occurrence. Besides that recommendation there is no clear cut overall best spinal block. It is up to the patient and doctor to decide whether a reduced cost or LOS is more important. When using only the Hospital C data, we found the only significant pairwise comparison to be between lidocaine and bupivacaine for cost, the largest and smallest cost categories, respectively. LOS yielded no significant pairwise comparisons. From this result we are not able to make specific drug recommendations, and conclude that the differences in cost and LOS from our full data may be attributed to the different locations, rather than the spinal blocks. This study does not analyze side effects associated with anesthesia, so future researchers are recommended to combine a cost/LOS analysis with side effect data.

Table 5.2. Spinal Block Ranks in Terms of Cost and LOS

Scombo	**Cost Rank (1=highest)**	**LOS (1=highest)**
Lidocaine	1	1
Lidocaine, Bupivacaine	1	2
No Spinal Block	2	1
Bupivacaine	3	1

When analyzing tranexamic acid, we found that administering the drug resulted in a significant increase in cost and reduction in LOS. However; when only using Hospital C data, we found no significant difference in cost; but there was a significant reduction in LOS. This means that the initial increase in cost that we witnessed may have been caused by the different

locations and not the drug. Overall, we recommend using tranexamic acid, as it reduces LOS and the need for transfusions while it may not increase cost.

REFERENCES

Abraham, Bovas, and Johannes Ledolter. Introduction to Regression Modeling. 1st ed. Belmont, CA: Thomson Brooks/Cole, 2006. Print.

American Academy of Orthopaedic Surgeons. "Anesthesia for Hip and Knee Surgery." AAOS. N.p., Mar. 2014. Web. 05 May 2015.

American Academy of Orthopaedic Surgeons. "Deep Vein Thrombosis." AAOS. N.p., Jan. 2009. Web. 05 May 2015.

Bertini, L., S. Mancini, P. Di Benedetto, A. Ciaschi, O. Martini, S. Nava, and V. Tagariello. "Postoperative Analgesia by Combined Continuous Infusion and Patient-controlled Epidural Analgesia (PCEA) following Hip Replacement: Ropivacaine versus Bupivacaine." Acta Anaesthesiologica Scandinavica 45.6 (2001): 782-85. Web.

Bower, Wendy F., Lawrence Jin, and Malcolm J. Underwood. "Peri-operative Blood Transfusion Increases Length of Hospital Stay and Number of Postoperative Complications in Non-cardiac Surgical Patients | HKMJ." Peri-operative Blood Transfusion Increases Length of Hospital Stay and Number of Postoperative Complications in Non-cardiac Surgical Patients | HKMJ. Hong Kong Med J, Apr. 2010. Web. 04 May 2015.

D'Ambrosia, R. D., P. R. Lipscomb, and E. J. McClain. "Prophylactic Anticoagulation in Total Hip Replacement." National Center for Biotechnology Information. U.S. National Library of Medicine, Apr. 1975. Web. 05 May 2015.

Daniel, Wayne W. Applied Nonparametric Statistics. Australia: Duxbury/Thomson Learning, 1990. Print.

Eisenberg, John M., Andrea Humphries, Ph.D, Amelia Williamson Smith, M.S., and Kim Farina, Ph.D. "Preventing Blood Clots After Hip or Knee Replacement Surgery or Surgery for a Broken Hip: A Review of the Research for Adults." AHRQ Effective Health Care Program. N.p., Mar. 2012. Web. 05 May 2015.

Eriksson, Bengt I., Lars C. Borris, Richard J. Friedman, Sylvia Haas, Menno V. Huisman, Ajay K. Kakkar, and Tiemo J. Bandel. "Rivaroxaban versus Enoxaparin for Thromboprophylaxis after Hip Arthroplasty." New England Journal of Medicine 358.26 (2008): 2765-775. Web.

Foran, Jared R.H., MD. "Total Hip Replacement." AAOS. N.p., Dec. 2011. Web. 05 May 2015.

Gandhi, Rajiv, Heather Mk Evans, Safiyyah R. Mahomed, and Nizar N. Mahomed. "Tranexamic Acid and the Reduction of Blood Loss in Total Knee and Hip Arthroplasty: A Meta-analysis." BMC Research Notes 6.1 (2013): 184. Web.

Gomez-Outes, A., A. I. Terleira-Fernandez, M. L. Suarez-Gea, and E. Vargas-Castrillon. "Dabigatran, Rivaroxaban, or Apixaban versus Enoxaparin for Thromboprophylaxis after Total Hip or Knee Replacement: Systematic Review, Meta-analysis, and Indirect Treatment Comparisons." Bmj 344.Jun14 1 (2012): E3675. Web.

Hampl, Karl F., and Sidonie Heinzmann-Wiedmer. "Transient Neurologic Symptoms after Spinal Anesthesia : A Lower Incidence with Prilocaine and Bupivacaine than with Lidocaine." Anesthesiology. Lippincott-Raven Publishers, Mar. 1998. Web.

Hosmer, David W., and Stanley Lemeshow. Applied Logistic Regression. 2nd ed. New York: Wiley, 1989. Print.

Irisson, E., Y. Hémon, V. Pauly, S. Parratte, J.-N. Argenson, and F. Kerbaul. "Tranexamic Acid Reduces Blood Loss and Financial Cost in Primary Total Hip and Knee Replacement Surgery." Orthopaedics & Traumatology: Surgery & Research 98.5 (2012): 477-83. Web.

Johansson, T., LG Pettersson, and B. Lisander. "Tranexamic Acid in Total Hip Arthroplasty Saves Blood and Money: A Randomized, Double-blind Study in 100 Patients." National Center for Biotechnology Information. U.S. National Library of Medicine, June 2005. Web. 04 May 2015.

Kleinbaum, David, Lawrence Kupper, Keith Muller, and Azhar Nizam. Applied Regression Analysis and Multivariable Methods. 3rd ed. New York, NY: Duxbury Press, 1998. Print.

Mauermann, William J., Ashley M. Shilling, and Zhiyi Zuo. "A Comparison of Neuraxial Block Versus General Anesthesia for Elective Total Hip Replacement: A Meta-Analysis." Anesthesia & Analgesia 103.4 (2006): 1018-025. Web.

Mcnamee, D. A., A. M. Mcclelland, S. Scott, K. R. Milligan, L. Westman, and U. Gustafsson. "Spinal Anaesthesia: Comparison of Plain Ropivacaine 5 Mg Ml-1 with Bupivacaine 5 Mg Ml-1 for Major Orthopaedic Surgery." British Journal of Anaesthesia 89.5 (2002): 702-06. Web.

Montgomery, Douglas C. Design and Analysis of Experiments. 8th ed. New York: John Wiley & Sons, 2013. Print.

Moore, David S., and George P. McCabe. *Introduction to the Practice of Statistics*. New York, NY: Freeman, (Wh) &, 2003. 755. Print.

NYSORA. "Spinal Anesthesia." NYSORA. The New York School of Regional Anesthesia, 10 Apr. 2013. Web. 03 May 2015.

Pagano, Marcello, and Kimberlee Gauvreau. Principles of Biostatistics. 2nd ed. Pacific Grove, CA: Duxbury, 2000. Print.

Panchmatia, Jaykar R., M.A., Soudeh Chegini, B.A., and Charlotte Lobban, M.B. "The Routine Use of Tranexamic Acid in Hip and Knee Replacements." National Center for Biotechnology Information. U.S. National Library of Medicine, 2012. Web. 05 May 2015.

Pfuntner, A, LM Wier, and C Steiner. Costs for Hospital Stays in the United States, 2010. HCUP Statistical Brief #146. Agency for Healthcare Research and Quality, Jan. 2013.

Poeran, Jashvant, Rehana Rasul, and Suzuko Suzuki. "Tranexamic Acid Use and Postoperative Outcomes in Patients Undergoing Total Hip or Knee Arthroplasty in the United States: Retrospective Analysis of Effectiveness and Safety." TheBmj. BMJ, 17 July 2014. Web. 04 May 2015.

Rodgers, Anthony, and Natalie Walker. "Reduction of Postoperative Mortality and Morbidity with Epidural or Spinal Anaesthesia: Results from Overview of Randomised Trials." TheBjm. BMJ 2000;321:1493, 16 Dec. 2000. Web.

Thorburn, J., J. R. Louden, and R. Vallance. "Spinal And General Anaesthesia In Total Hip Replacement: Frequency Of Deep Vein Thrombosis." BJA: British Journal of Anaesthesia 52.11 (1980): 1117-121. Web.

Wera, Glenn D., MD, Ryan M. Garcia, MD, and Victor M. Goldberg, MD. "Reducing Perioperative Bleeding with Antifibrinolytics." AAOS. N.p., Feb. 2013. Web. 05 May 2015.

Wolford, Monica L., M.A., and Anita Bercovitz, M.P.H. "Hospitalization for Total Hip Replacement Among Inpatients Aged 45 and Over: United States, 2000–2010." Centers for Disease Control and Prevention. Centers for Disease Control and Prevention, 12 Feb. 2015. Web. 05 May 2015.

Wulf, H., and J. Biscoping. "Ropivacaine Epidural Anesthesia and Analgesia Versus General... : Anesthesia & Analgesia." LWW. International Anesthesia Research Society, July 1999. Web. 03 May 2015.

Zaric, Dusanka, Christian Christiansen, Nathan L. Pace, and Yodying Punjasawadwong. "Transient Neurologic Symptoms After Spinal Anesthesia with Lidocaine Versus Other Local Anesthetics: A Systematic Review of Randomized, Controlled Trials." Anesthesia & Analgesia 100.6 (2005): 1811-816. Web.

Zaric, Dusanka, and Nathan L. Pace. "Transient Neurologic Symptoms (TNS) following Spinal Anaesthesia with Lidocaine versus Other Local Anaesthetics." The Cochrane Library. John Wiley & Sons, Ltd., 15 Apr. 2008. Web. 03 May 2015.