Project Presentation: MultiModal Analgesia

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3/14/2018

Overview

CU Denver's Anesthesiology Department is interested in the impact that a new practice (use of multimodal analgesia and rescue blocks) may have on recovery times after ACL-related surgeries as opposed to the conventional method of administering analgesia pre-operatively.

Primary question:
What is the impact of the new practice on recovery times?

Secondary questions:
1. How often do we need to perform rescue blocks postoperatively?
2. Are there predictive factors for those we do rescue blocks on post-operatively?
3. How often is the practice adhering to multimodal analgesia pre-op/post-op?

Analgesia Dataset

With over 54 variables, the first steps involved getting familiar with all the variables, then renaming the CSV file headers with shorter names.

Exploratory Data Analysis (EDA)

Before meeting with the client, I tried to get familiar with the data on my own. The main question revolves around whether the new practice (multimodal analgesia) improves recovery time over the old practice (pre-operative blocks).

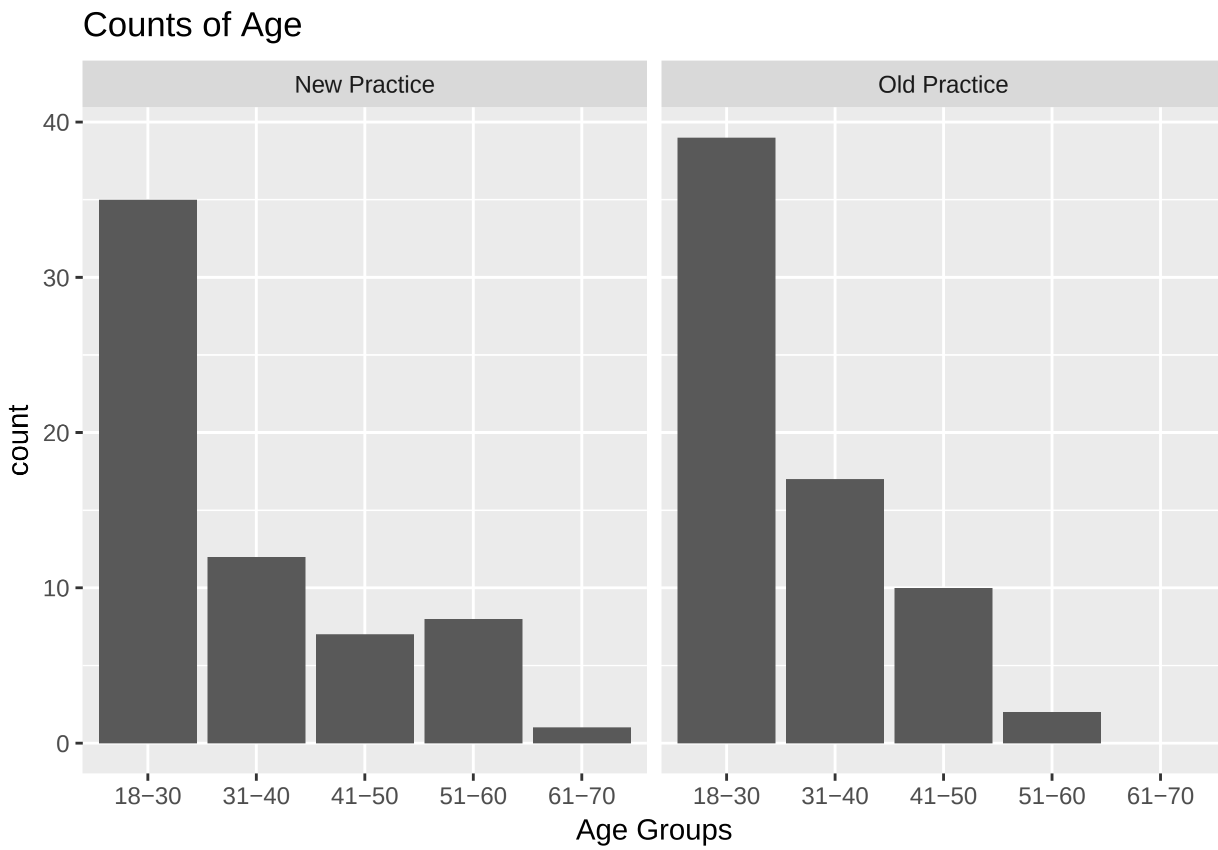
Old Practice	New Practice	Total Observations
63	68	131

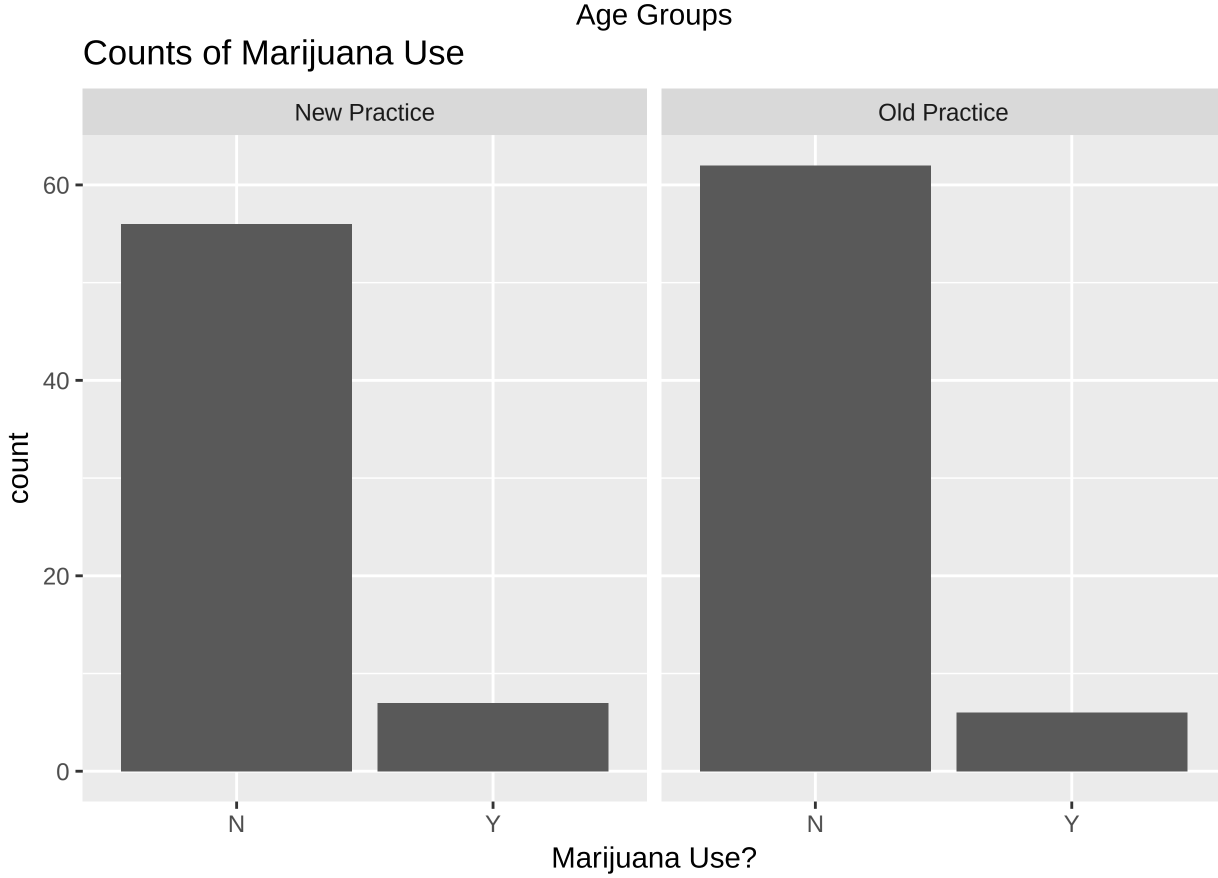
Response and Explanatory Variables

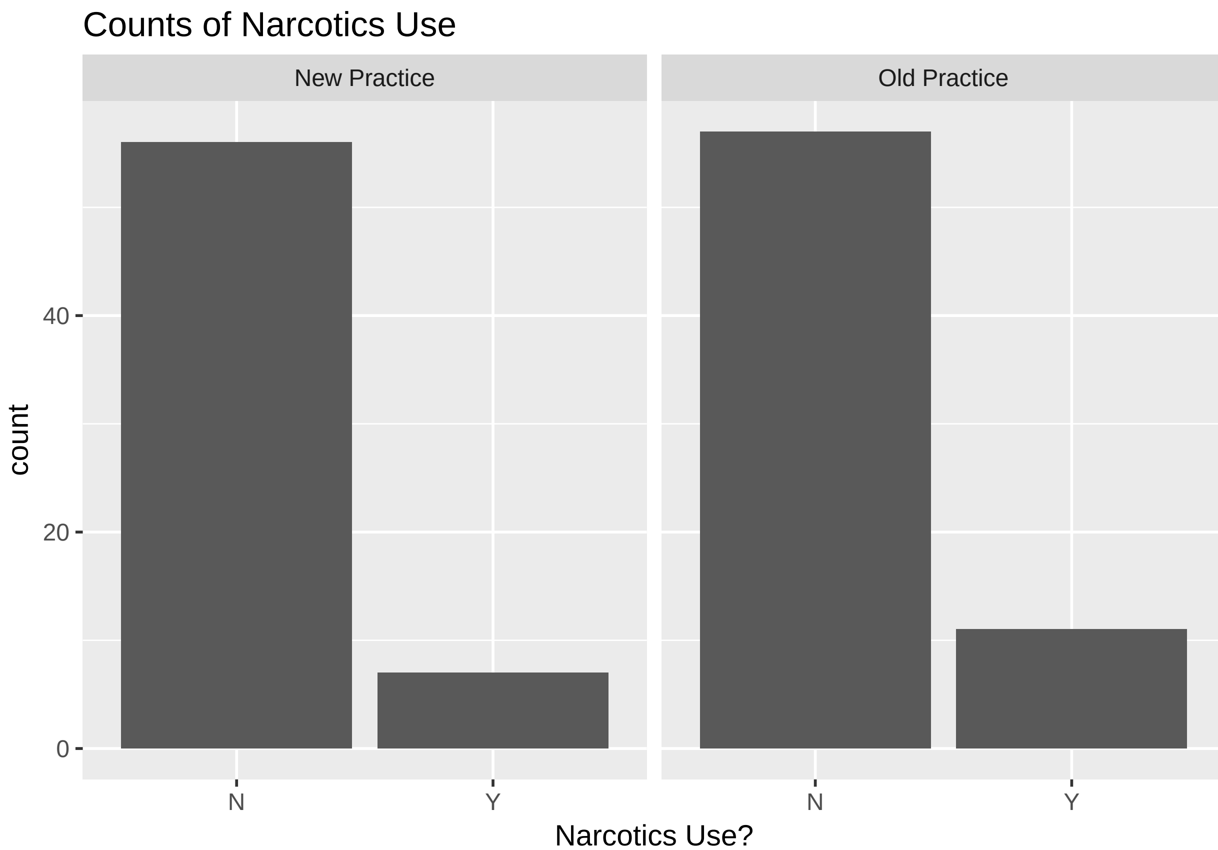
The primary response variable (the variable we wish to explain) is recovery time (total_PACU). The remaining variables are considered potential explanatory variables.

Confounders

The following bar graphs provide comparisons of age groups, users of marijuana, and users of narcotics to see if the counts of these cases might be significantly different between the "old" and "new" practice observations. If the counts for age, users of marijuana, or users of narcotics is significantly different between our two groups of interest ("old" practice and "new" practice), such variables may introduce confounding effects, or biased association between our explanatory variables of interest and our response variable.


Counts of Age
New Practice
Old Practice
count
0
10
20
30
40
18−30
31−40
41−50
51−60
61−70
Age Groups

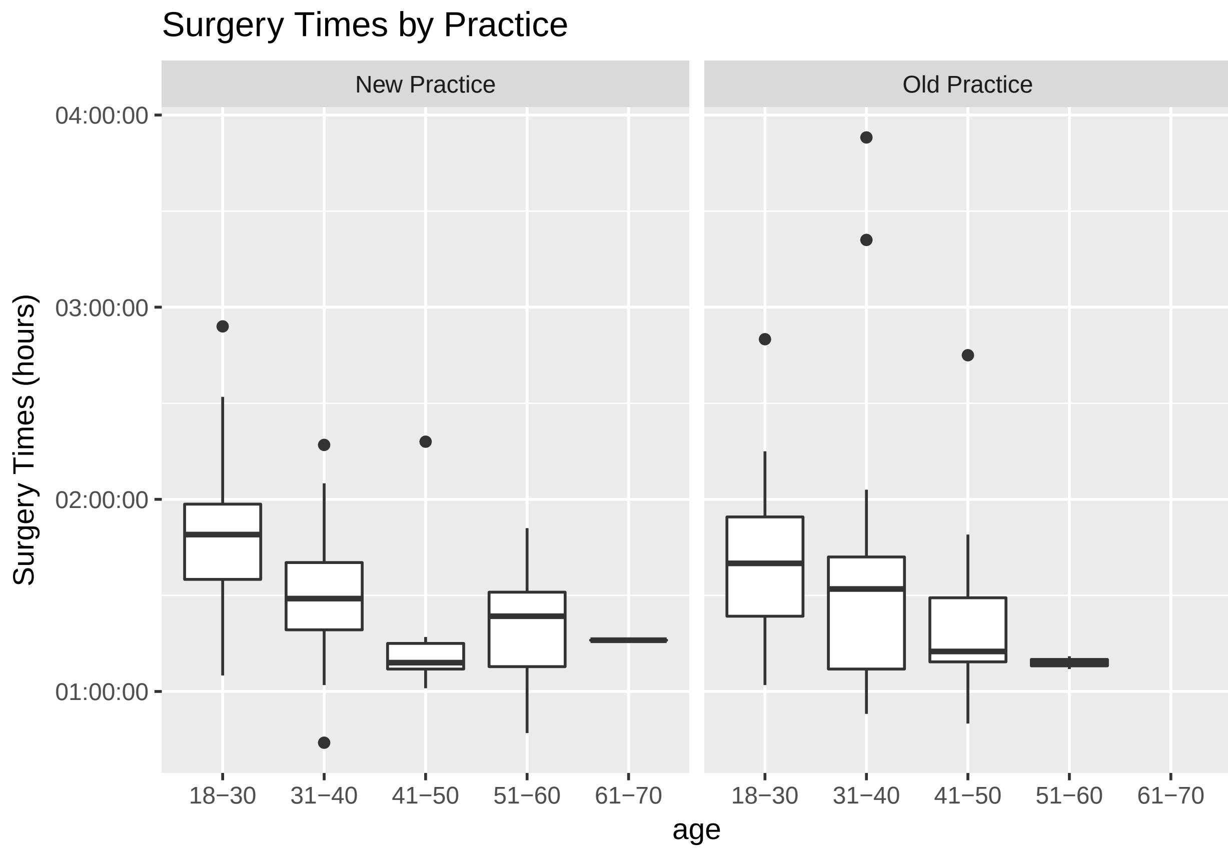

Counts of Marijuana Use
New Practice
Old Practice
count
0
20
40
60
N
Y
Marijuana Use?

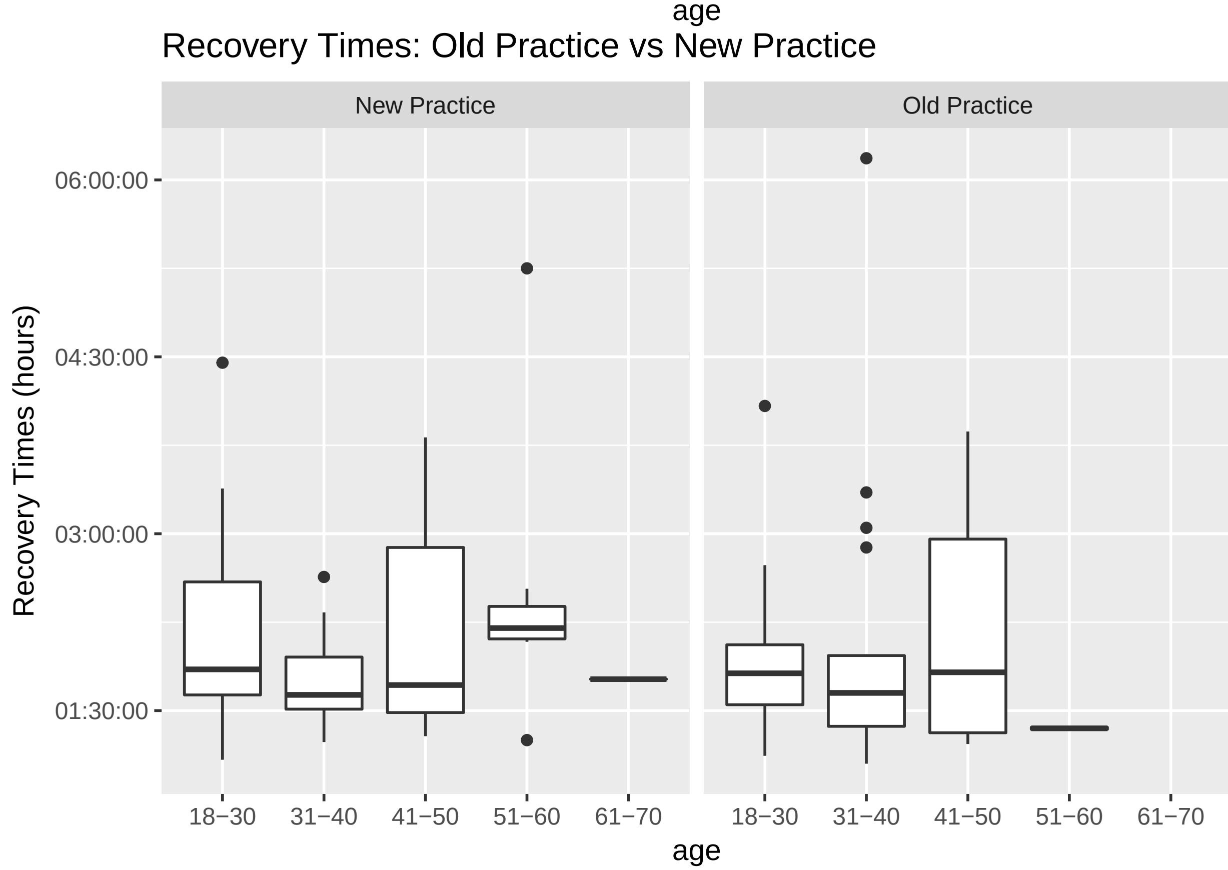


We can see that the counts for age groups, marijuana use, and narcotics use are fairly equal between the New and Old practice observations so we can rule out these variables contributing to / directly affecting the Recovery Time.

Boxplots

Boxplots are a standard EDA tool that help look for outliers. I checked the surgery times and recovery times to evaluate central tendencies for both values, comparing the New Practice values to the Old Practice values.



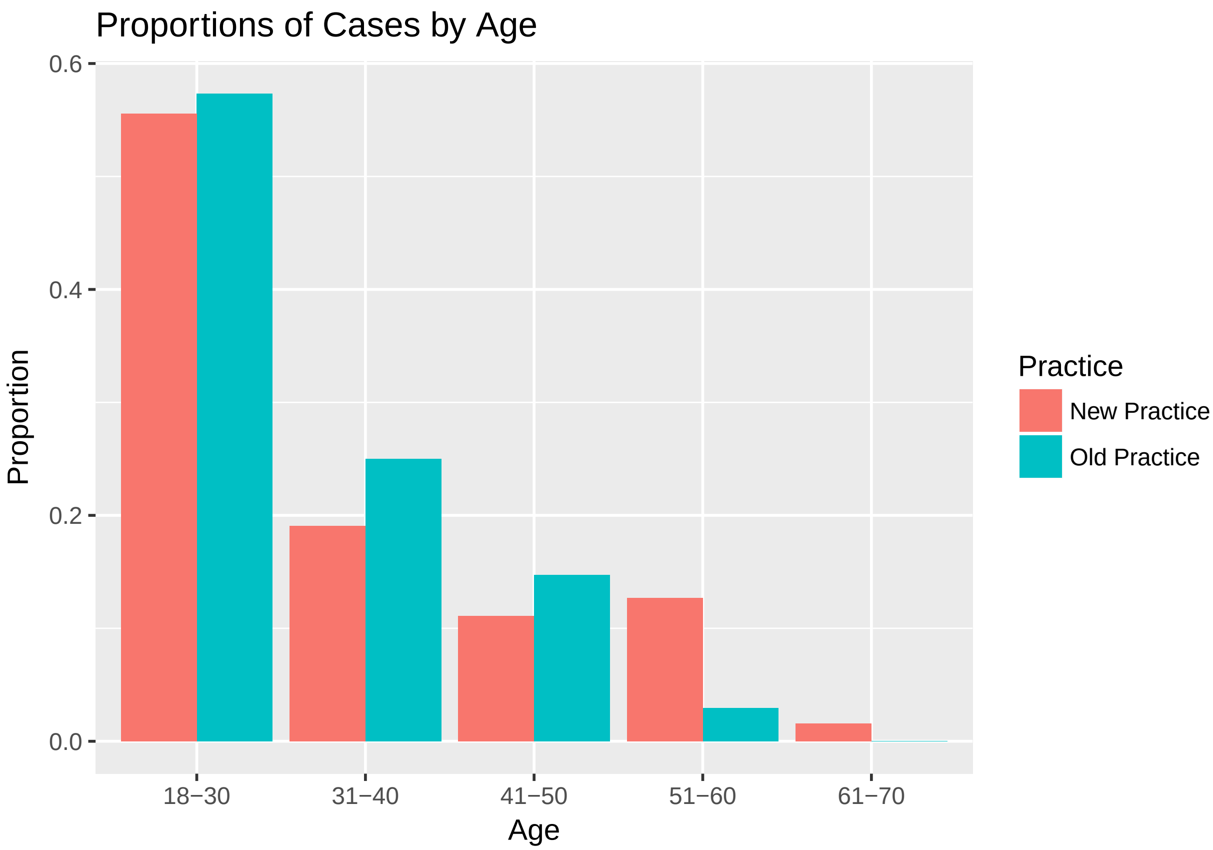


At this time, I will not remove any outliers; further below in the analysis, we eliminate cases by surgery type.

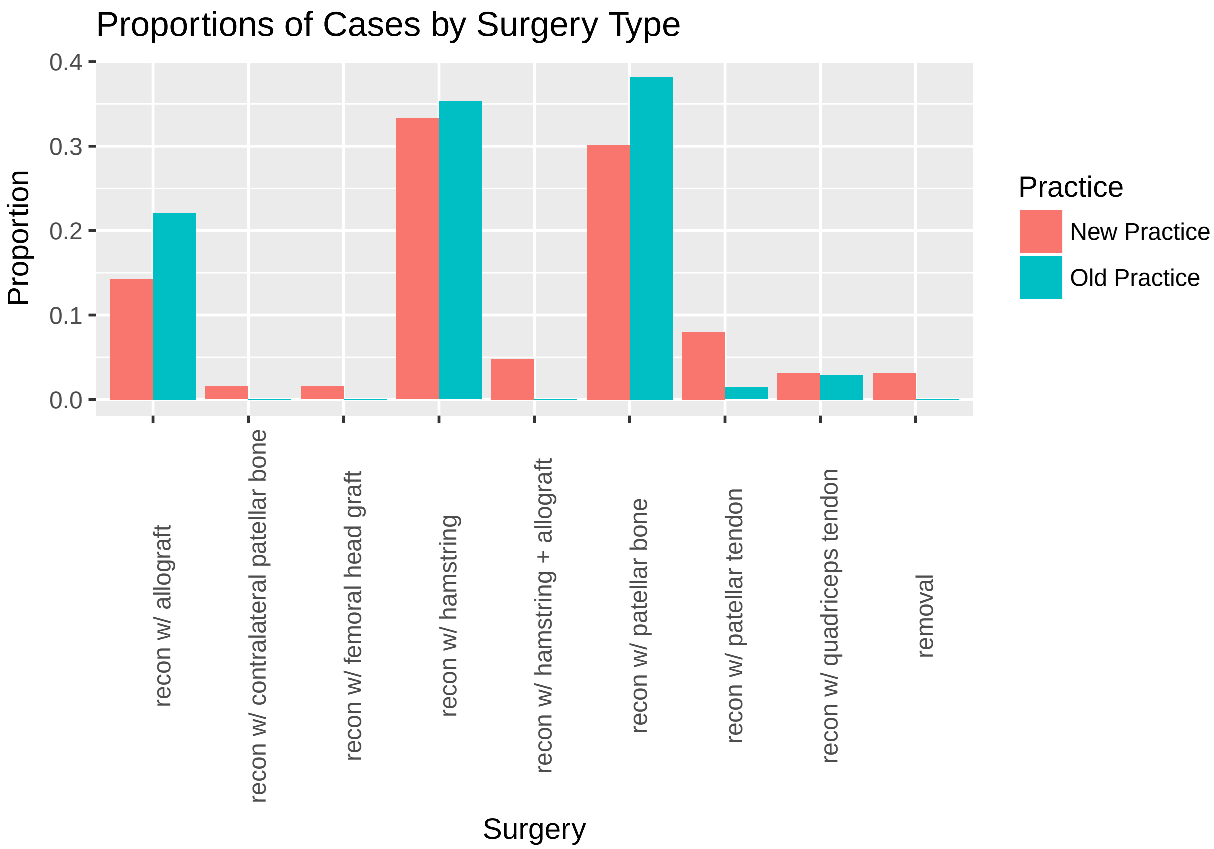
After that data subsetting, we can reconsider removing outliers.

First Presentation to Client: January 22, 2018

Proportion of cases for each age-group, comparing numbers for old practice versus new practice:



Compare numbers for surgery type:

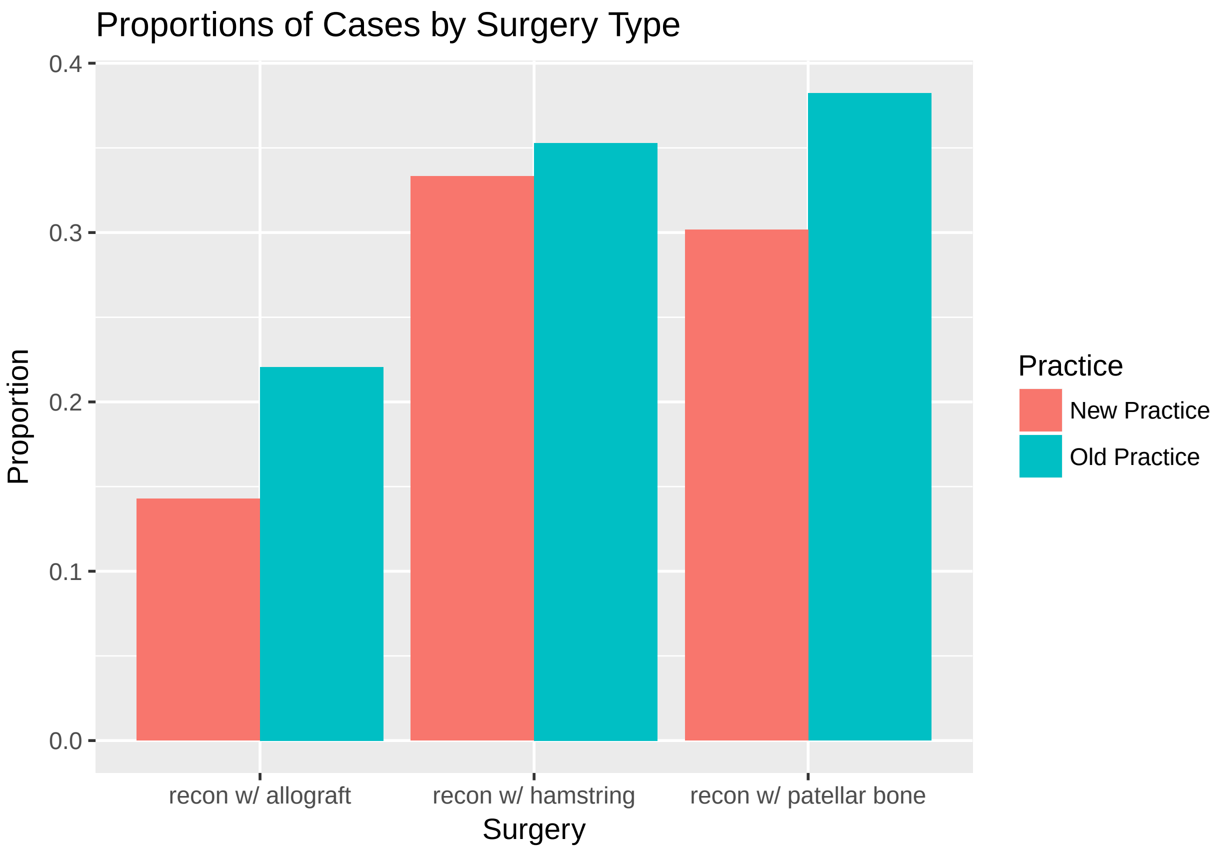


From this graph, it was agreed that we would limit the data analysis to the observations related to the three surgery types with the most observations.

Reducing the Dataset

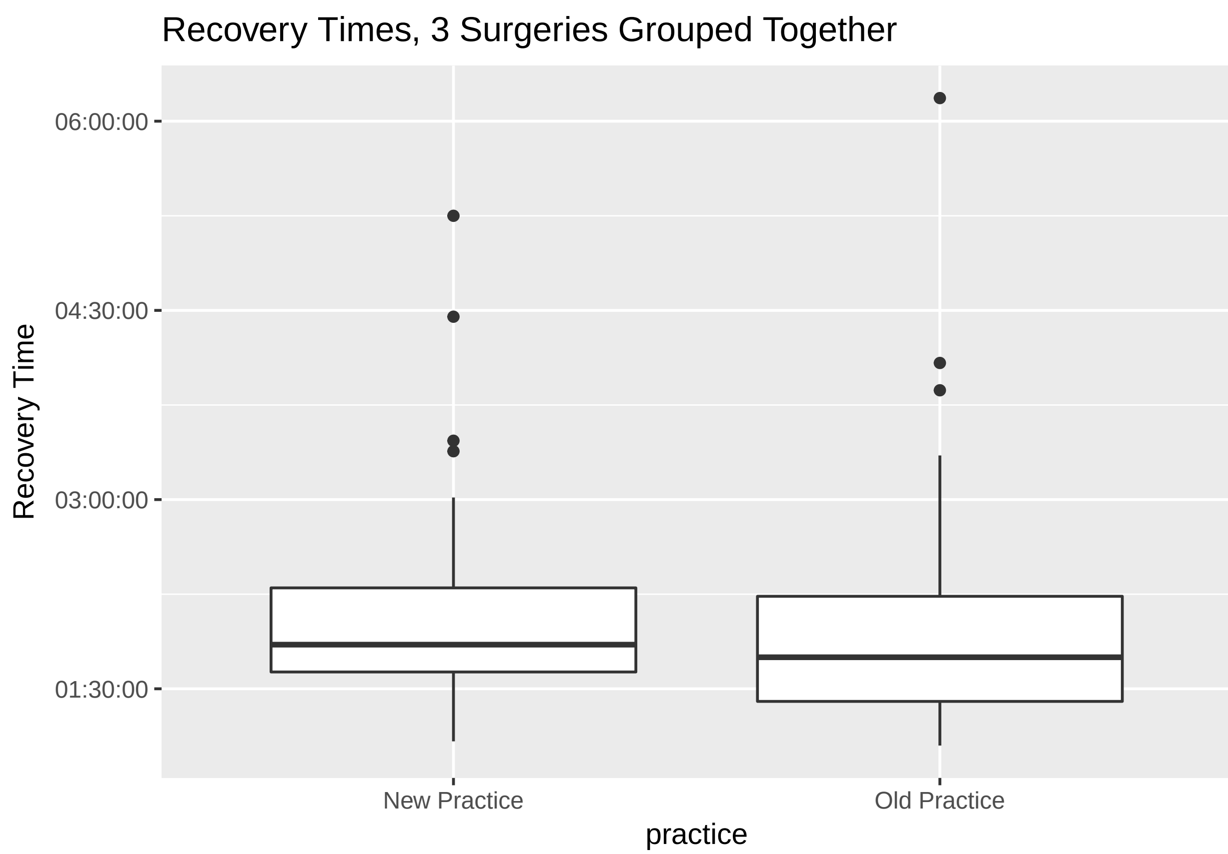
Data was kept for the following surgery types: “Knee arthroscopy & ACL recon w/ allograft”, “Knee arthroscopy & ACL recon w/ hamstring”, “Knee arthroscopy & ACL recon w/ patellar bone”

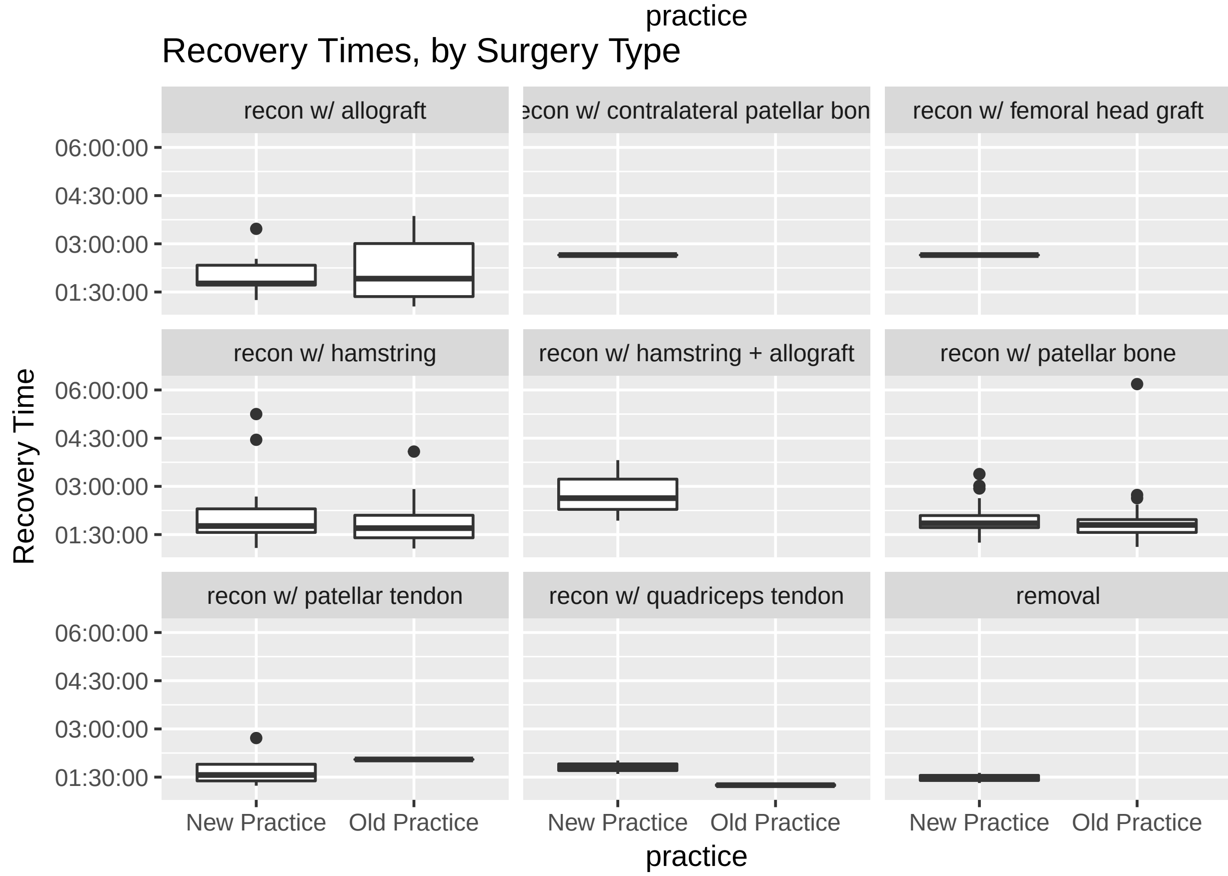
Let’s run the comparison again for cases by surgery:




```
##
##                              N  Y
##   recon w/ allograft         9 15
##   recon w/ hamstring        21 24
##   recon w/ patellar bone 19 26
```

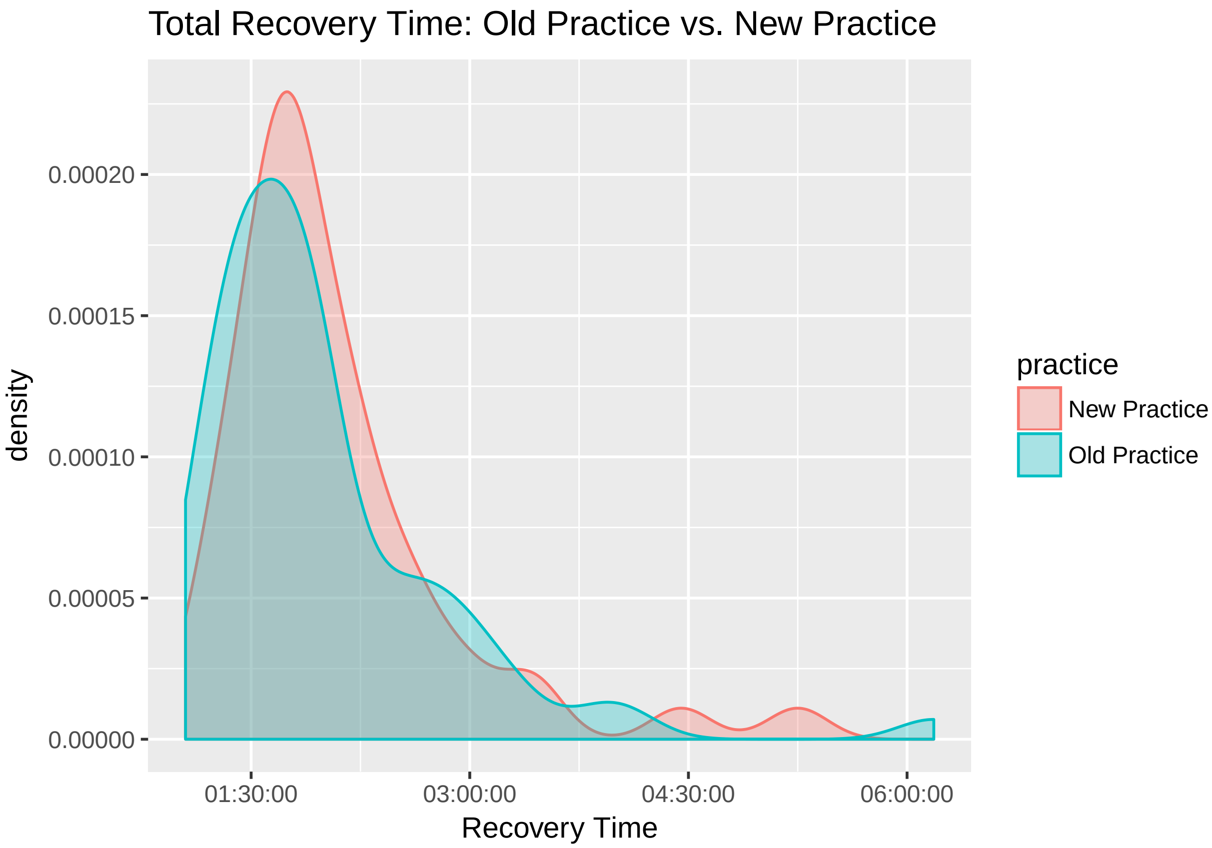
Because recovery time is important, I decided to look at boxplots of recovery times, subsetting the data (1): Old Practice vs New Practice; (2) By Surgery Type.





The comparison of recovery time by surgery type was not always useful, especially when there weren't cases/observations for both Old Practice and New Practice, but they were worth a look. In trying to search for any cases where the new practice resulted in better recovery times, there was only one surgery type (recon with patellar tendon) where new practice cases exhibited a better recovery time.

Let's have a look at the density plots of recovery time for Old Practice vs. New Practice:



The central tendency values for the OLD practice cases (in seconds):

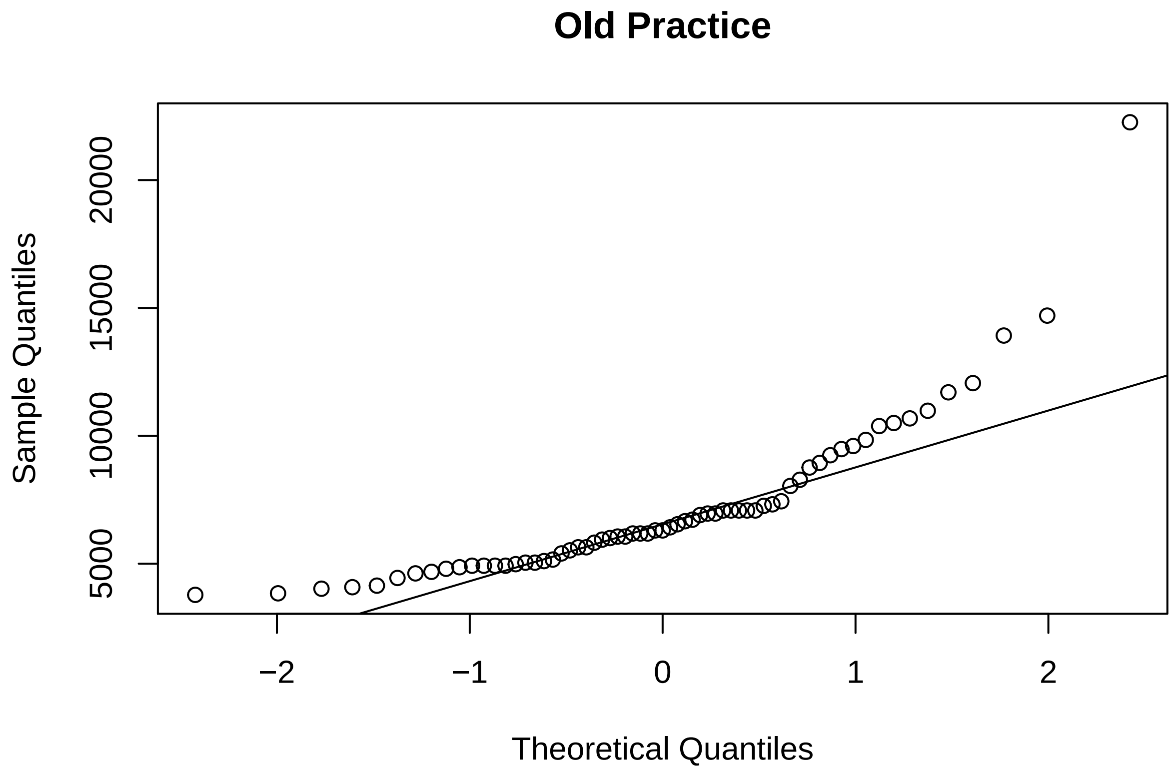
```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    3780    5040    6300    7160    8040   22260
```

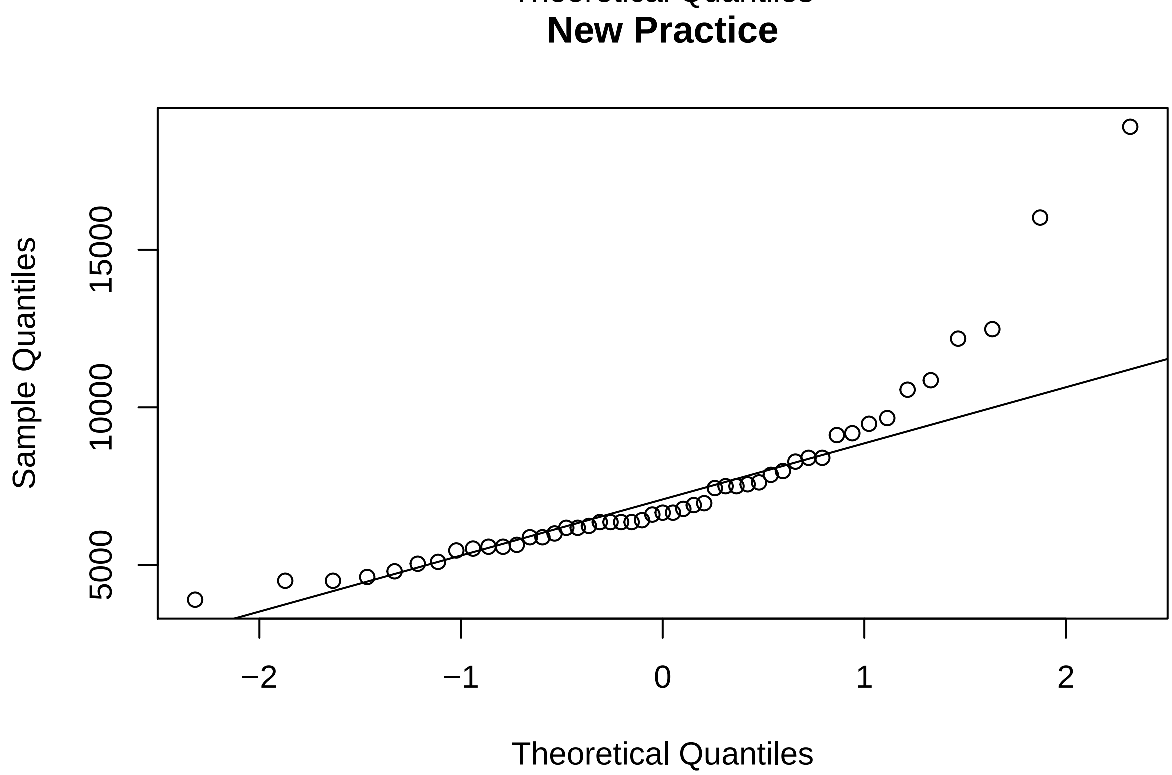
The central tendency values for the NEW practice cases (in seconds):

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    3900    5880    6660    7469    8280   18900
```

Statistical Analyses

Let's take a look a the normality of the recovery times to determine what type of two-sample statistical test we should perform.





The Q-Q plot shows that we need to compare two means with non-normal errors. Therefore, we will use the Wilcoxon Signed Rank test:

```
##
##  Wilcoxon rank sum test with continuity correction
##
```

```
## data:  as.numeric(newDF$total_pacu[newDF$pre_op == "Y"]) and as.numeric(newDF$total_pacu[newDF$pre_op
## W = 1403, p-value = 0.2792
## alternative hypothesis: true location shift is not equal to 0
```

If we repeat the analysis with the original dataset set (all surgery types), we find the p-value is even worse:

```
##
##  Wilcoxon rank sum test with continuity correction
##
## data:  as.numeric(clean$total_pacu[newDF$pre_op == "Y"]) and as.numeric(clean$total_pacu[newDF$pre_op
## W = 1999.5, p-value = 0.9658
## alternative hypothesis: true location shift is not equal to 0
```

Fit a Linear Model

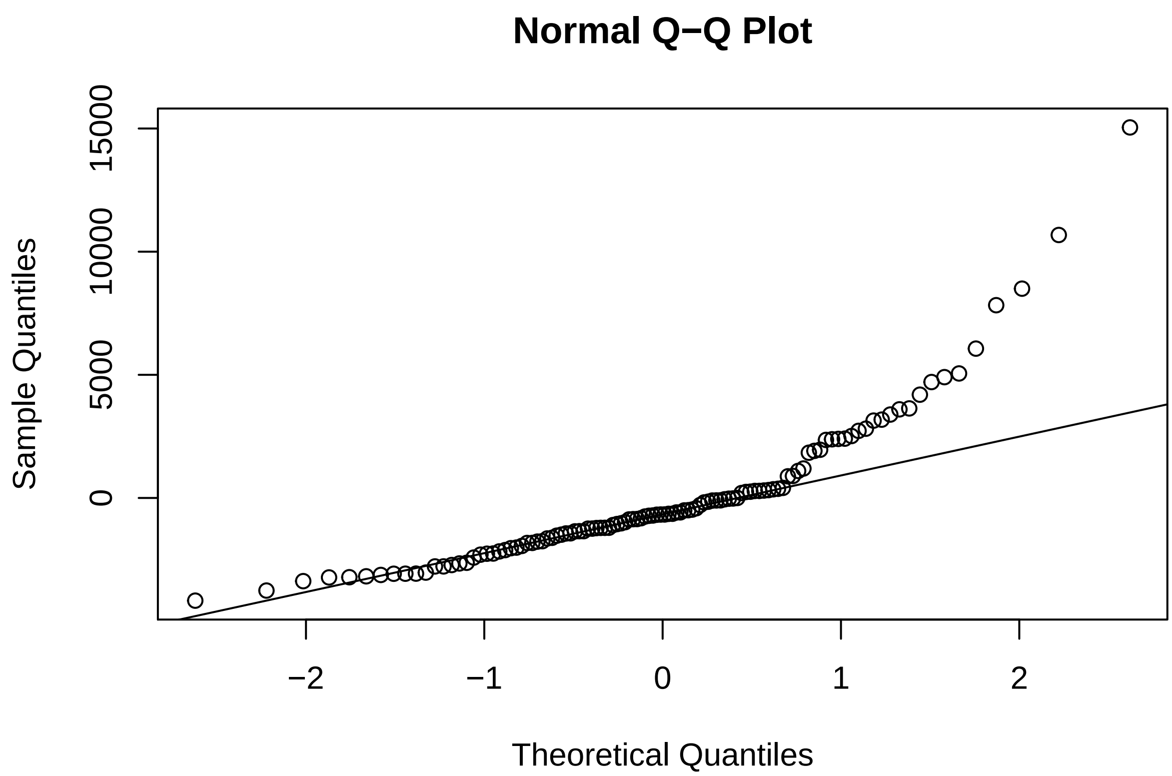
Though the two-sample tests don't show a statistically significant difference, some of the variability in recovery times may be due to systematic differences among the cases. Controlling for these may give better power to distinguish the recovery times.

Let's try fitting a linear model, considering practice (new/old), surgery times (surg_tot), and age as potential explanatory variables:

```r
m <- lm(as.numeric(total_pacu) ~pre_op+age+as.numeric(surg_tot), data=newDF)
summary(m)
```

```
##
## Call:
## lm(formula = as.numeric(total_pacu) ~ pre_op + age + as.numeric(surg_tot),
##     data = newDF)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -4168.2 -1727.1  -671.7   400.6 15043.4
##
## Coefficients:
##                       Estimate Std. Error t value Pr(>|t|)
## (Intercept)          6603.3656  1315.8188   5.018 2.09e-06 ***
## pre_opY              -207.0249   595.9094  -0.347    0.729
## age31-40              203.8861   760.0367   0.268    0.789
## age41-50              801.5767   913.3746   0.878    0.382
## age51-60             1124.2928  1087.7643   1.034    0.304
## age61-70             -702.6097  3074.6521  -0.229    0.820
## as.numeric(surg_tot)    0.1007     0.1943   0.518    0.605
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 3015 on 107 degrees of freedom
## Multiple R-squared:  0.0179, Adjusted R-squared:  -0.03717
## F-statistic: 0.325 on 6 and 107 DF,  p-value: 0.9226
```

```r
qqnorm(m$residuals)
qqline(m$residuals)
```




```r
m_robust<-lm(as.numeric(total_pacu) ~pre_op+age+as.numeric(surg_tot), data=newDF)
summary(m_robust)
```

```
##
## Call:
## lm(formula = as.numeric(total_pacu) ~ pre_op + age + as.numeric(surg_tot),
##     data = newDF)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -4168.2 -1727.1  -671.7   400.6 15043.4
##
## Coefficients:
##                       Estimate Std. Error t value Pr(>|t|)
## (Intercept)          6603.3656  1315.8188   5.018 2.09e-06 ***
## pre_opY              -207.0249   595.9094  -0.347    0.729
## age31-40              203.8861   760.0367   0.268    0.789
## age41-50              801.5767   913.3746   0.878    0.382
## age51-60             1124.2928  1087.7643   1.034    0.304
## age61-70             -702.6097  3074.6521  -0.229    0.820
## as.numeric(surg_tot)    0.1007     0.1943   0.518    0.605
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 3015 on 107 degrees of freedom
## Multiple R-squared:  0.0179, Adjusted R-squared:  -0.03717
## F-statistic: 0.325 on 6 and 107 DF,  p-value: 0.9226
```

Results of Preliminary Analysis

we cannot reject the null hypothesis that there is no difference in recovery times between the old practice (pre-operative blocks) and the new practice (multimodal analgesia).

Second Phase: Analysis of Rescue Blocks

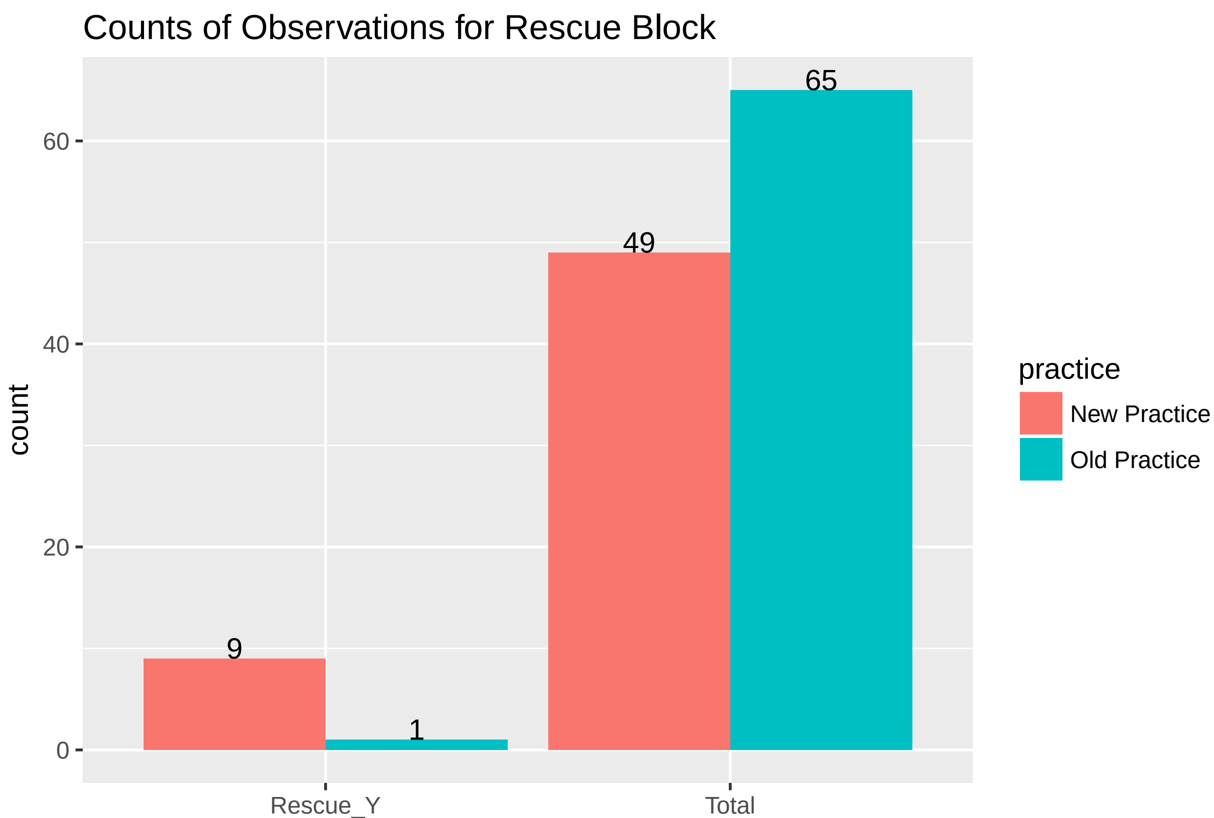
Having found no statistical significance in changes to recovery time (total_pacu) due to the new practice of administering multimodal analgesia (rather than pre-operative blocks), the next step is to move on and try to answer as many of the other questions that the client sent over with the data:

Primary question:
What is the impact of the new practice on recovery times?

Secondary questions:
1. How often do we need to perform rescue blocks postoperatively?
2. Are there predictive factors for those we do rescue blocks on post-operatively?
3. How often is the practice adhering to multimodal analgesia pre-op/post-op?

Rescue Block Cases: Surgery and Recovery Times

Looking into candidates for predictive factors on who receives rescue blocks post-operatively, let's evaluate surgery time and recovery times for patterns.



Since there is only one case of a Rescue Block with the Old Practice, let's eliminate the Old Practice observations and just focus on the New Practice Rescue Blocks to see if we can answer the client's remaining questions.

Rescue Block Question 2: Frequency of Rescue Blocks

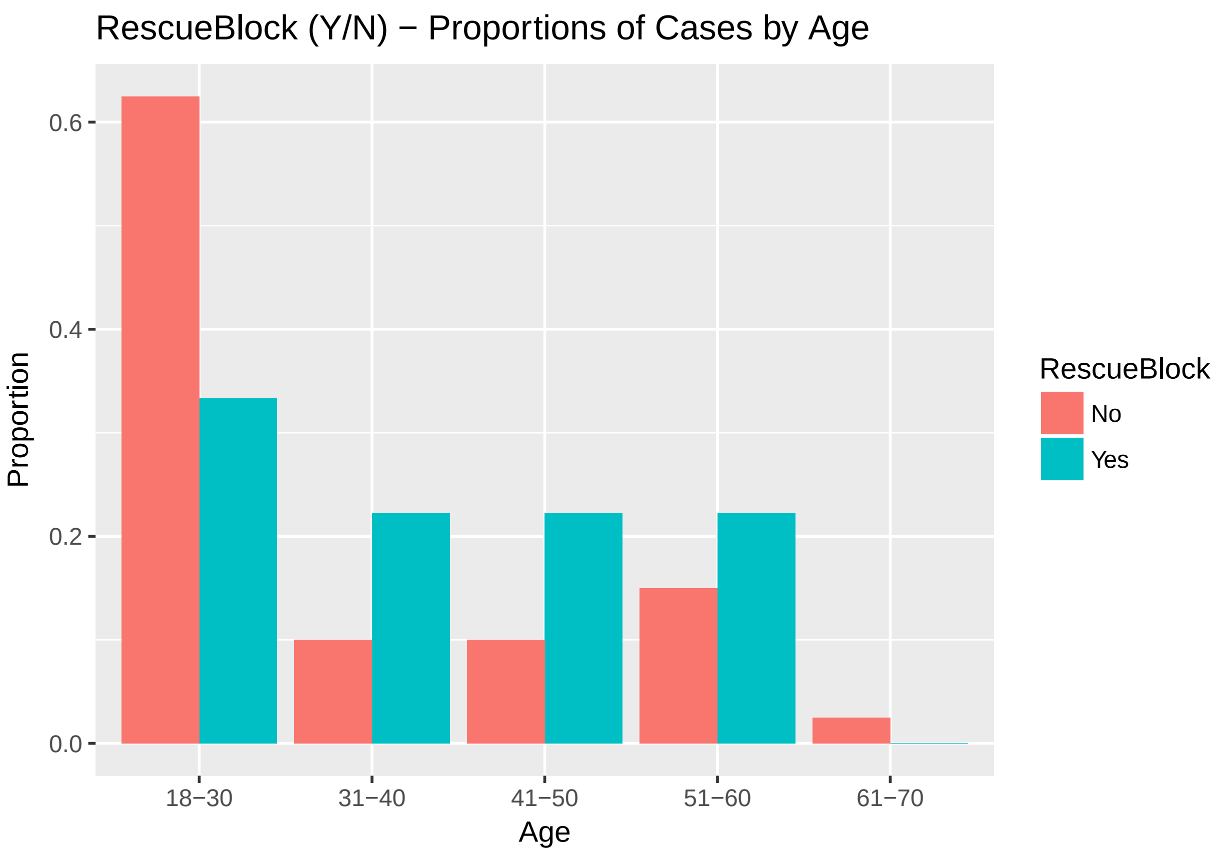
9 of the 49 new practice observations resulted in a post-operative rescue block. That's about 20% of the cases.

Rescue Block Question 3: Predictive Factors

Let's see if we can find some predictive factors on why 20% of the new practices require a post-operative block by looking into the 9 of the 49 cases that required rescue blocks.

Age

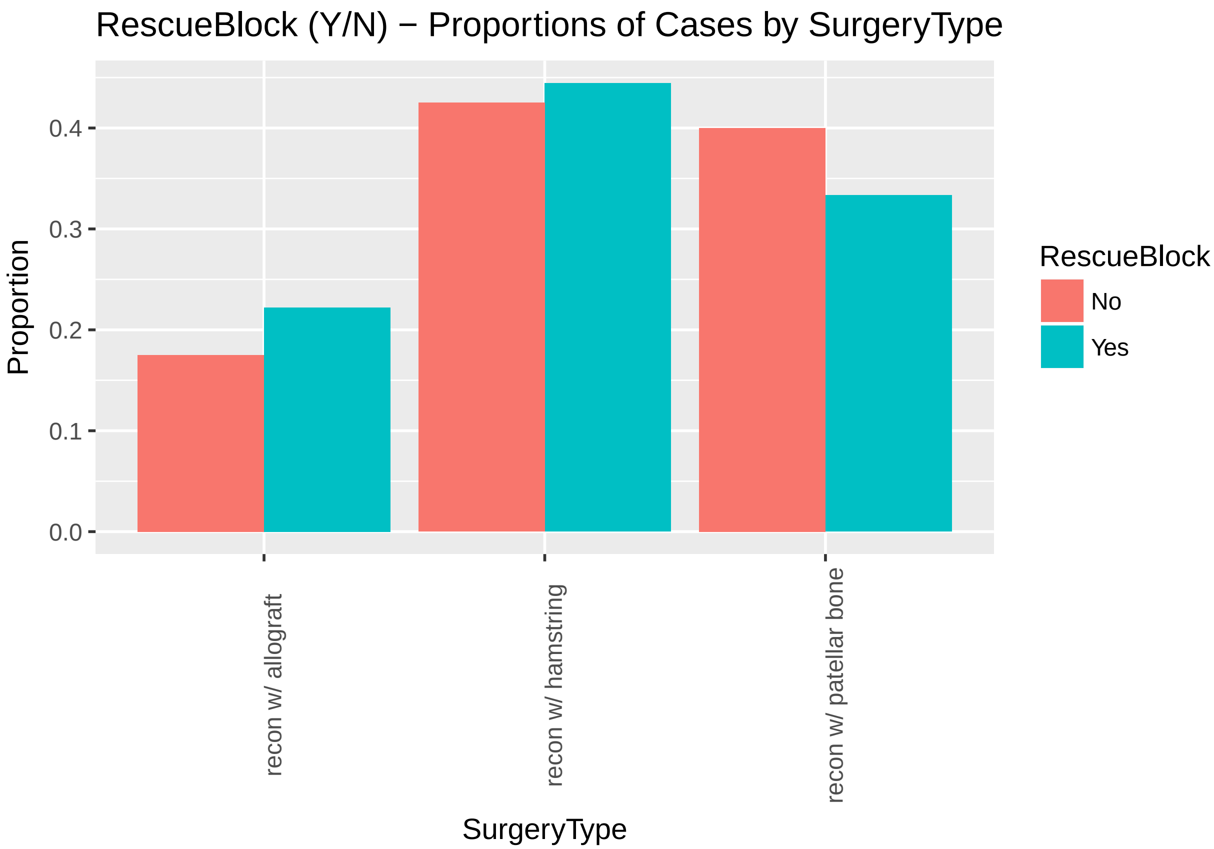
To evaluate if age might have to do something with whether one might need a rescue block or not, let's look at the distribution of Rescue Block cases (Y/N) across our age groups. Of the 9 cases requiring Rescue Blocks, was there a larger proportion of those cases in a given age group?



It appears that age might play into whether or not one requires a rescue block; more than 60% of those cases that did not require a rescue block were in the 18-30 age group, while the distribution of cases across age group for those requiring a rescue block was more evenly distributed.

Type of ACL Surgery

As we did with ages, let's see if a certain type of surgery might be cause for getting a rescue block:



Of the three surgery types kept in the analysis, reconstruction with hamstring represented more than half of the cases requiring rescue blocks, but the same is true for those not requiring rescue blocks, so I don't believe

Fisher's Exact Count Test to check for association

Since the Rescue Block question is binomial (either you needed a rescue block or you didn't), the appropirate test would be a chi-square (for large samples) or a Fisher's test (counts less than 5). Fisher's test seemed appropriate.

The null hypothesis of Fisher's Exact Test is that the treatment (new practice versus old practice) have no affect on outcome (recovery time). I ran the Fisher's test on a contingency table of age versus recovery time and a separate contingency table of surgery type versus recovery time.

```
(age_ct <- table(rescue_dat$age, rescue_dat$RescueBlock))
```

```
##
##         No Yes
##   18-30 25   3
##   31-40  4   2
##   41-50  4   2
##   51-60  6   2
##   61-70  1   0
```

```
fisher.test(age_ct)
```

```
##
##  Fisher's Exact Test for Count Data
##
```

```
## data:  age_ct
## p-value = 0.3917
## alternative hypothesis: two.sided
```

```r
(surg_ct <- table(rescue_dat$surgery, rescue_dat$RescueBlock))
```

```
##
##                           No Yes
##   recon w/ allograft       7   2
##   recon w/ hamstring      17   4
##   recon w/ patellar bone 16   3
```

```r
fisher.test(surg_ct)
```

```
##
##  Fisher's Exact Test for Count Data
##
## data:  surg_ct
## p-value = 1
## alternative hypothesis: two.sided
```

In both cases, the p-value does not allow us to reject the null hypothesis. Age and type of surgery are not associated with whether one needs a Rescue Block or not.

Proportions of Pre-Op Meds

Here I performed a test of proportions: did the proportion of the average amounts of pre-op used associate with those cases requiring rescue bocks versus those not requiring rescue blocks.

Note: Marnie to validate whether this is the right statistical test or not. Results not included in PowerPoint slide.

```
##              Sums for Rescue=Y Sums for Rescue=N
## preop_pregab               375              2100
## preop_cele                2200             11400
## preop_aceta               5000             30500
```

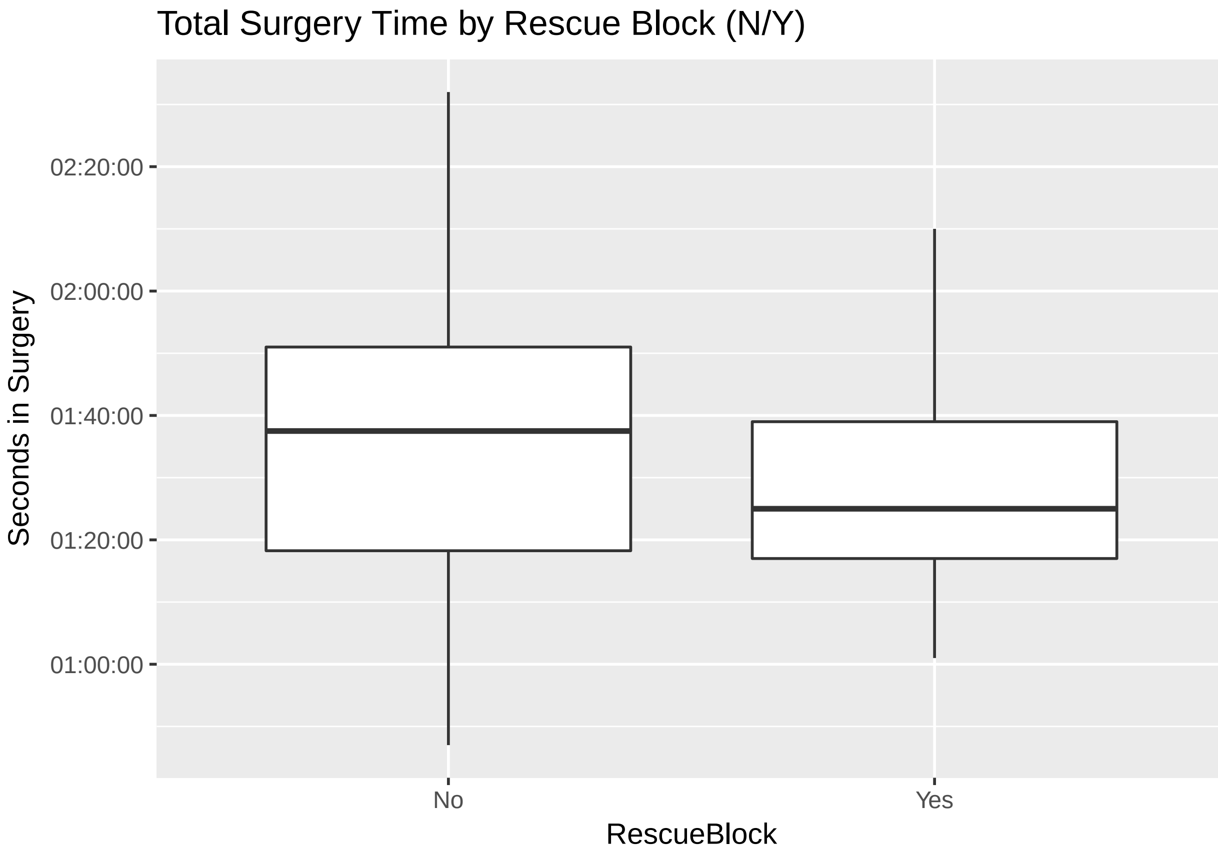
```
##
##  Pearson's Chi-squared test
##
## data:  pre_op_sums
## X-squared = 34.79, df = 2, p-value = 2.789e-08
```

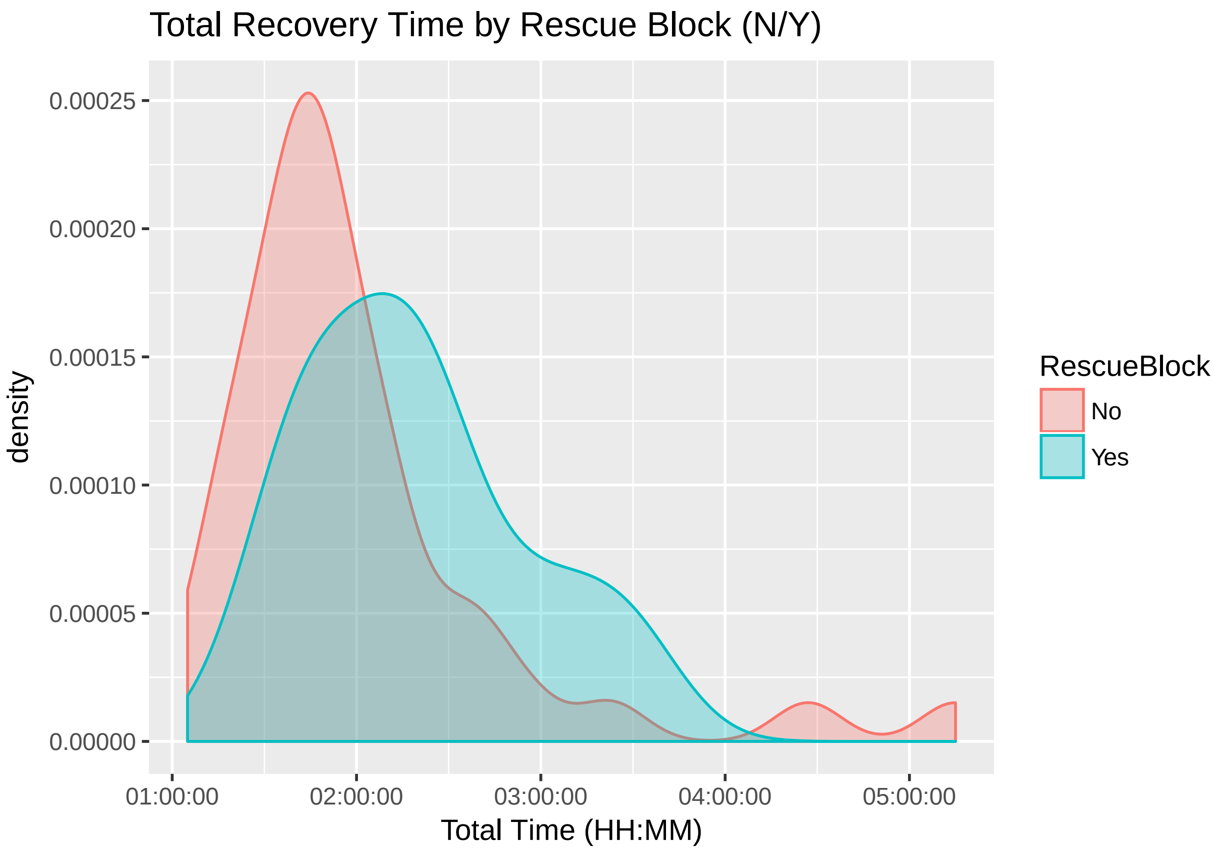
```
##              Avg Qty for Rescue=Y Avg Qty for Rescue=N
## preop_pregab             41.66667                 52.5
## preop_cele              244.44444                285.0
## preop_aceta             555.55556                762.5
```

```
##
##  Pearson's Chi-squared test
##
## data:  pre_op_avg
## X-squared = 2.5187, df = 2, p-value = 0.2838
```

Rescue Block Cases: Recovery Times

Focusing only on the 49 new practice observations (9 with rescue blocks, 40 without rescue blocks), we can look at recovery times:





Surgery Time Central Tendencies + Recovery Time Central Tendencies

The central tendency values for recovery times (in seconds) for cases WITH rescue block:

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    3660    4620    5100    5367    5940    7800
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    5580    6660    8280    8340    9120   12480
```

The central tendency values for recovery times (in seconds) for cases WITH rescue block:

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    2820    4695    5850    5770    6660    9120
```

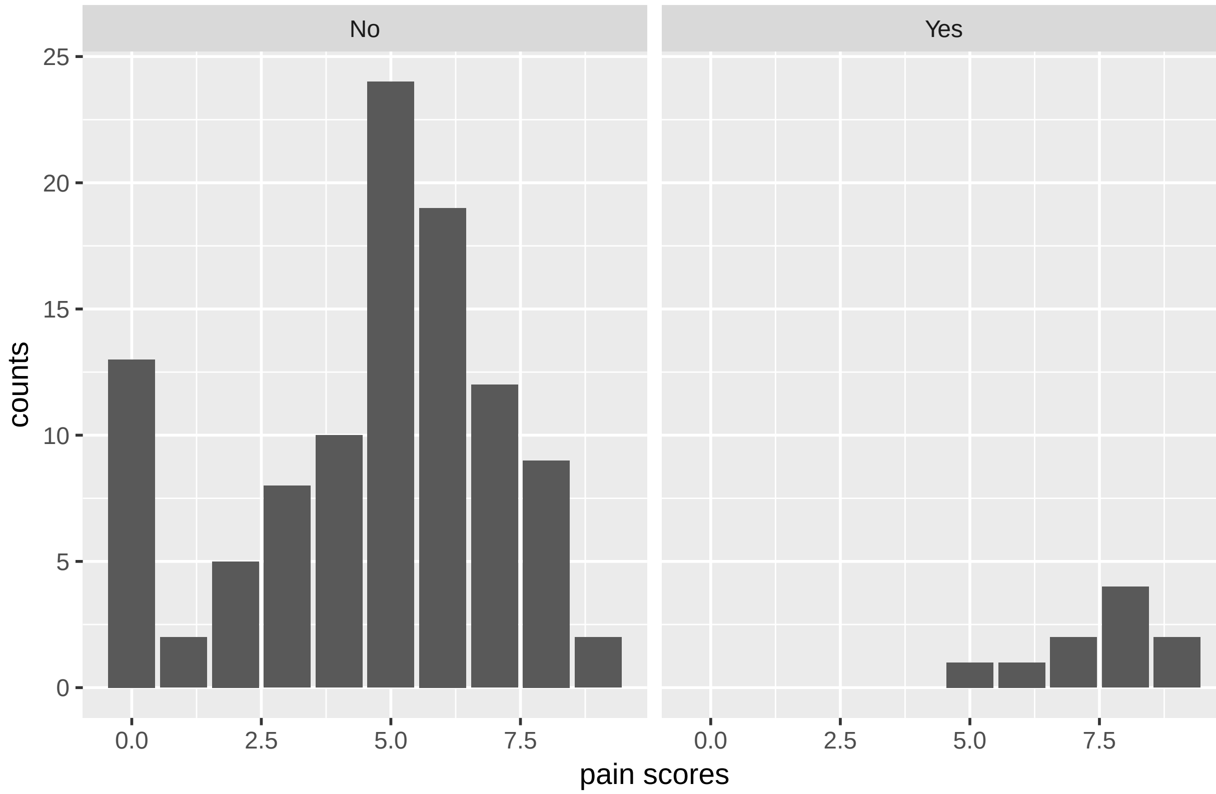
```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    3900    5625    6390    7274    7680   18900
```

Rescue Block Cases: Pain Scores

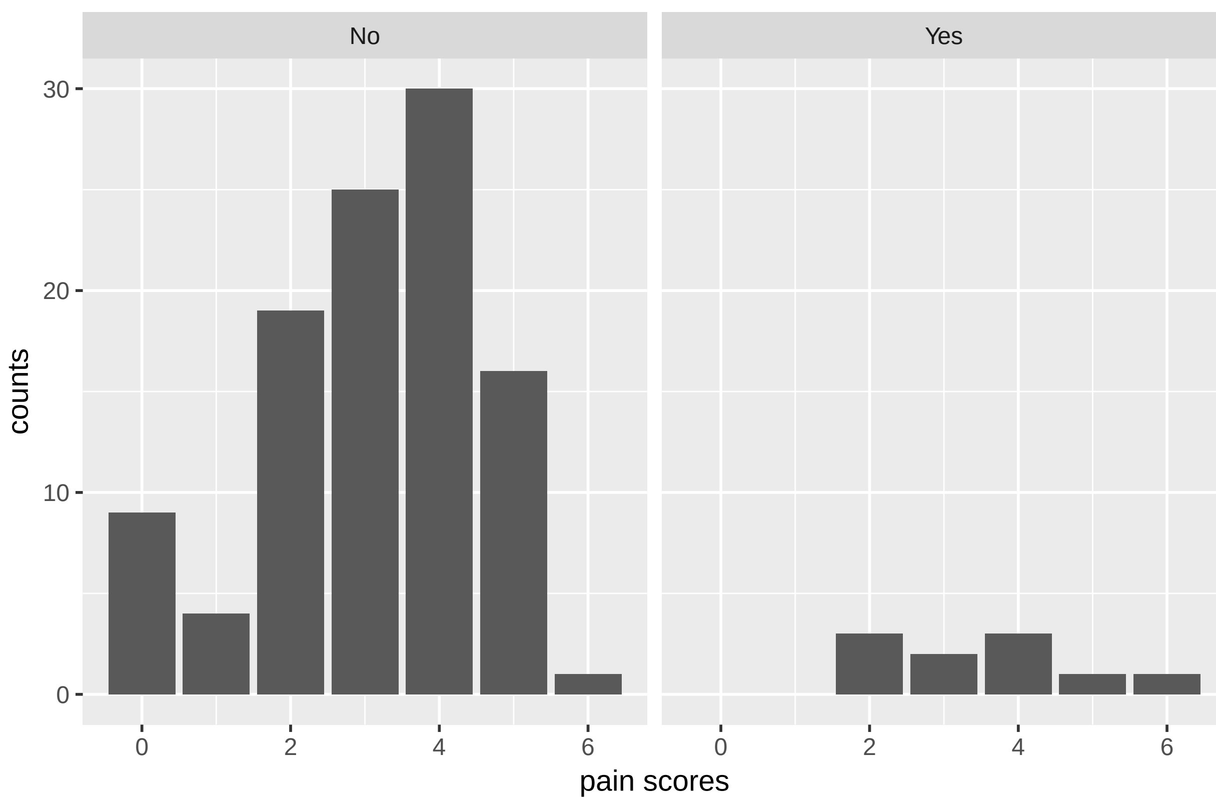
Looking into candidates for predictive factors on who receives rescue blocks post-operatively, evaluate pain scores, which are available at the following intervals: arrival, 15 minutes in, peak, and discharge.

Pain scores ranked from 0 (no pain) to 10 (unbearable pain).

Pain Score: Arrival, by Rescue Block(N/Y)



Pain Score: Discharge, by Rescue Block(N/Y)



Conclusion

At this interim period (end of Winter Term), this completes my current analysis of the analgesia data. There is further investigation that needs to be done on evaluating possible predictors of what may contribute to those cases that require a Rescue Block.

In summary, I have established the following:
1. There is no improvement in recovery time (PACU) when moving from the old practice (pre-operative blocks) to the new practice (multi-modal analgesia).
2. Attempting a linear model also proved that there is no relation between the practice method and the recovery time.
3. There may be predictors to when a rescue block is required, but at this time, I have ruled out: age, surgery type, and possibly the quantities of pre-operative meds given to the patient.
4. There are several more variables to consider: intra-operative meds, post-operative meds, and time spent in surgery.