**Introduction**

Toradol is an anti-inflammatory drug used to relieve moderate to severe short-term pain in adults. According to drugs.com, it works by reducing the hormones that cause pain and inflammation in the body. Several sites recommend it to be taken no more than 4 times a day every 4-6 hours by injection or by tablet. Additionally, it should not be taken for more than 5 days consecutively. As such, clinical uses for the drug include pain management before and after surgeries (as demonstrated by this study), as well as athletes needing pain relief for a game or any situation in which the pain isn’t recurring or long-term. In the specific context of the study done on this sample 174 women underwent elective abdominal hysterectomies for cervical or uterine cancer on the gynecologic oncology service at the University of Wisconsin. Ultimately the study included 147 women and track 15 variables. The variables are: the year the surgery was done, the patient’s age at the time of their surgery, the duration of the surgery, their diagnosis, the invasiveness of their cancer, the days until they returned to their normal diet, if they experienced pain greater than a 4/10, if they stayed longer than five days, if they had a radical hysterectomy, number of ovaries removed, lymph node sampling, if Toradol was used, if additional surgeries were completed, if the patient had complications, and the amount of morphine they used. Obviously, the use of morphine may conflict with the use of Toradol and lessen the need for it. The policies of HMOs to limit stays means that the surgery year might impact the length of stay. Additionally, diet is a factor in hospital stay which could impact the long stay variable. Variables like stage, diagnosis, age may cause greater pain or additional reasons to increase the length of time spent in the hospital. In this analysis, the effect of Toradol is being assessed to determine its effectiveness in pain management and hospital stay. Two models will be built where the response will be if the patient experience pain greater than 4/10 or not and if their stay was shorter or longer than five days. Toradol and the other variables will be used as predictors in an additive model which will then be improved using different techniques to build the best model to predict the two response variables. After the models are built, the impact of Toradol will be assessed to discuss its clinical effectiveness on this sample.

Chart, histogram

Description automatically generatedGraphical user interface

Description automatically generated**Initial Data Analysis**

Chart, histogram

Description automatically generatedIn the histograms of all the variables in the data, we can observe a few interesting trends. Firstly, years was changed to be a categorical variable from 1-3 by year. This was to make the modeling process easier in the future. Age appears to be most concentrated between 30-70 with no distinct outliers. The duration of the surgery was most commonly 2-3 hours but being longer wasn’t uncommon. Most patients returned to their normal diet within 3 days, and all returned within 7. The vast majority of patients were in the same stage, making it not useful as a predictor. The use of Toradol wasn’t even, more used it than didn’t. The number of surgeries per year was fairly close, which could allow for stratification if necessary. Most patients had both ovaries removed, didn’t receive an additional procedure, and didn’t experience complications.

The scatter plots of the variables revealed some trends but nothing that was immediately noticeable. Age generally increased the likelihood of pain and long stay. Morphine use also was positively correlated with these two factors. The amount of days until returning to a normal diet was strongly positively correlated with stay because it usually is a factor on getting discharged. People also tend to eat more normally when their in less pain, but that relationship wasn’t as strong.

**Methods**

To start with the model building, each response was modeled with all the other predictors in an additive logit model. The response that wasn’t used was left out as a predictor so as not to confound the data and allow for a better analysis of Toradol. From there a backwards AIC variable selection was used to refine the model to explain more of the variance in the sample. After these two initial models were built, there were analyzed for fit using deviance of the residuals and compared using a Chi-squared ANOVA test. This test compared the refined against the full model to choose the better version. This process was then repeated for a complementary log log link and a probit link. This gave three models that were then compared using their AIC values to pick the best model. This model was then analyzed for outliers and high leverage points to further access the effectiveness of the model.

**Results**

Graphical user interface

Description automatically generatedThe model that best predicted the probability of bad pain was the logit function with the predictors age, additional procedure, complications, and morphine. This function had the lowest AIC value and the highest deviance of the residuals. Additionally, the graphs show the least number of high leverage points for this model. Although the outliers were greater than the cloglog.

The model that best predicted the probability of a stay longer than five days was the complementary log log function with the predictors surgery year, amount of time to resume diet, and morphine. This function had the lowest AIC value and the highest deviance of the residuals. Additionally, the graphs show the least number of high leverage points for this model and the least number of outliers.

Chart

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**Summary**

The use of Toradol was not a significant predictor in any of the models that were created. This could be due to confounding factors in the sample, but further research should be done on whether these factors are better for pain management than Toradol. The use of Toridol did not increase the likelihood of not experiencing bad pain when viewing it strictly as the sole predictor. It was better for long stay, however the year the surgery was done most likely affected those results due to the HMO policies.

**Appendix**

## Introductory Data Summaries

### Histograms of the variables

```{r}

par(mfrow = c(2,3))

hist(ketorolac$DOS.yr)

hist(ketorolac$Age)

hist(ketorolac$duration)

hist(ketorolac$Diagnosis)

hist(ketorolac$Stage)

hist(ketorolac$General.diet)

hist(ketorolac$BadPain)

hist(ketorolac$LongStay)

hist(ketorolac$HYS)

hist(ketorolac$OV)

hist(ketorolac$LNS)

hist(ketorolac$TOR)

hist(ketorolac$AddPro)

hist(ketorolac$Comps)

hist(ketorolac$Morphine)

```

### Scatter plot of predictors with long stay responce

```{r}

par(mfrow = c(2,2))

plot(ketorolac$LongStay ~ ketorolac$Age)

plot(ketorolac$LongStay ~ ketorolac$DOS.yr)

plot(ketorolac$LongStay ~ ketorolac$duration)

plot(ketorolac$LongStay ~ ketorolac$Diagnosis)

plot(ketorolac$LongStay ~ ketorolac$Stage)

plot(ketorolac$LongStay ~ ketorolac$HYS)

plot(ketorolac$LongStay ~ ketorolac$OV)

plot(ketorolac$LongStay ~ ketorolac$LNS)

plot(ketorolac$LongStay ~ ketorolac$TOR)

plot(ketorolac$LongStay ~ ketorolac$AddPro)

plot(ketorolac$LongStay ~ ketorolac$Comps)

plot(ketorolac$LongStay ~ ketorolac$Morphine)

plot(ketorolac$LongStay ~ ketorolac$General.diet)

plot(ketorolac$LongStay ~ ketorolac$BadPain)

```

### Scatter plot of predictors with bad pain responce

```{r}

par(mfrow = c(2,2))

plot(ketorolac$BadPain ~ ketorolac$Age)

plot(ketorolac$BadPain ~ ketorolac$DOS.yr)

plot(ketorolac$BadPain ~ ketorolac$duration)

plot(ketorolac$BadPain ~ ketorolac$Diagnosis)

plot(ketorolac$BadPain ~ ketorolac$Stage)

plot(ketorolac$BadPain ~ ketorolac$HYS)

plot(ketorolac$BadPain ~ ketorolac$OV)

plot(ketorolac$BadPain ~ ketorolac$LNS)

plot(ketorolac$BadPain ~ ketorolac$TOR)

plot(ketorolac$BadPain ~ ketorolac$AddPro)

plot(ketorolac$BadPain ~ ketorolac$Comps)

plot(ketorolac$BadPain ~ ketorolac$Morphine)

plot(ketorolac$BadPain ~ ketorolac$General.diet)

plot(ketorolac$BadPain ~ ketorolac$LongStay)

### Odds Ratio of the two responce variables with different predictors

```{r}

mats <- matrix(c(length(which(ketorolac$BadPain == 1 & ketorolac$TOR == 0)),length(which(ketorolac$BadPain == 0 & ketorolac$TOR == 0)),length(which(ketorolac$BadPain == 1 & ketorolac$TOR == 1)),length(which(ketorolac$BadPain == 0 & ketorolac$TOR == 1))),ncol=2, byrow=T)

row.names(mats) <- c("Toradol Not Given","Toradol Given")

colnames(mats) <- c("Expierenced Pain Greater than 4/10", "Did Not Expierence Pain Greater than 4/10")

mats

OR.est = mats[1,1] \* mats[2,2] / (mats[1,2] \* mats[2,1])

logOR.se = sqrt(sum(1/mats))

logOR.CI <- log(OR.est) + c(-1,1) \* qnorm(1-0.05/2) \* logOR.se

OR.est

exp(logOR.CI)

# Anova comparison

anova(back\_stay\_probitmod, stay\_probitmod, test = "Chisq")

### Test for outliers and high influence points in the model

```{r}

par(mfrow = c(2,3))

plot(hatvalues(back\_stay\_mod), type="h")

plot(hatvalues(back\_stay\_probitmod), type="h")

plot(hatvalues(back\_stay\_cloglogmod), type="h")

plot(cooks.distance(back\_stay\_mod))

plot(cooks.distance(back\_stay\_probitmod))

plot(cooks.distance(back\_stay\_cloglogmod))

### cloglog Link Model

stay\_cloglogmod = glm(LongStay ~. - BadPain, family = binomial(link = "cloglog") ,data = ketorolac)

### Backwards AIC Variable Selection

back\_stay\_cloglogmod <- step(stay\_cloglogmod, direction="backward",trace = F)

summary(back\_stay\_cloglogmod)

### Goodness of Fit Tests and Anova Model Comparision

# G^2 Test for homogeneous association

1 - pchisq(deviance(stay\_cloglogmod), df.residual(stay\_cloglogmod))

1 - pchisq(deviance(back\_stay\_cloglogmod), df.residual(back\_stay\_cloglogmod))