Survival Analysis on Linking Drug Dependent Adults to Primary Care

Introduction

Survival analysis estimates an outcome on an observation or experimental study. The dataset, HELPFUL, contains . The paper "Linking alcohol- and drug-dependent adults to primary medical care: a randomized controlled trial of a multi-disciplinary health intervention in a detoxification unit"

What is survival analysis? What does it do?

What is the dataset, key variables, and what do we want to do with it

(Basically, why do we want to research anything about the HELPfull data? any applications or insights?)

What are some of the initial goals we have in mind? What do we plan to do (exploration of variables, focus on a specific target, building a model, new thing)?

in the introduction: have you gotten a chance to play around much with the other variables (not the treatment or response)? Ideally you can make a bunch of plots just to have a sense of the dataset. How are the variables coded? What do you do with factor variables? Lots of missingness… what should be done about that? Which variables are most interesting?

Methods

first paragraph method: what is our goal? can we replicate the results & process? (yes, because we will use the same dataset and the same code)

Exploratory Data Analysis

second paragraph (and more): how we approached the data exploration & cox.ph model building

include dataset and packages used (lines of code)

For our exploratory data analysis, we will observe relationship the explanatory variables have with the response vairables, linkstatus. Analyzing the relationship between the explantory and response variable will help indicate which variables we want to include in the final model.

First, we will import the packages and dataset.

```
library(mosaic)
library(readr)
library(tidyverse)
library(broom)
library(survival)
library(survminer)
library(praise)
```

```r
# import the dataset HELPFUL. Encode NAs as "*"
df <- read_csv("HELPdata.csv", na="*")
```

Now that the dataset is imported, we can select our variables of interest. Note that the original dataset has some variables encoded as characters types. We converted these variables to a factor type so categorical variables are easily distinguishable in our plots.

```r
df <- df %>%
  mutate(yrs_education = as.numeric(a9),
         gender=a1,
         alcq_30 = as.numeric(alcq_30),
         marriage = as.factor(a10),
         employment = as.factor(a13),
         income = as.factor(case_when(a18 == 1 ~ "<5000",
                                      a18 == 2 ~ "5000-10000",
                                      a18 == 3 ~ "11000-19000",
                                      a18 == 4 ~ "20000-29000",
                                      a18 == 5 ~ "30000-39000",
                                      a18 == 6 ~ "40000-49000",
                                      a18 == 7 ~ "50000+")),
         income_1yr = as.factor(case_when(a18_rec1 == 0 ~ "$19,000",
                                      a18_rec1 == 1 ~ "$20,000-$49,000",
                                      a18_rec1 == 2 ~ "$50,000")),
         any_util = as.factor(case_when(any_util == 0 ~ "No", any_util == 1 ~ "Yes")),
         attempted_suicide = as.factor(case_when(g1c == 0 ~ "No", g1c == 1 ~ "Yes")),
         employment = as.factor(
           case_when(a13 == 1 ~ "Full time",
                     a13 == 2 ~ "Part time",
                     a13 == 3 ~ "Student",
                     a13 == 4 ~ "Unemployed",
                     a13 == 5 ~ "Ctrl_envir")),
         homeless = as.factor(case_when(homeless == 0 ~ "No", homeless == 1 ~ "Yes")),
         hs_grad = as.factor(case_when(hs_grad == 0 ~ "No", hs_grad == 1 ~ "Yes")),
         group = as.factor(case_when(group == 0 ~ "Control", group == 1 ~ "Clinic")),
         # linkstatus = as.factor(case_when(linkstatus == 0 ~ "Did not link to primary care", linkstatu
         alcohol = as.factor(case_when(alcohol == 0 ~ "Not First Drug", alcohol == 1 ~ "First Drug Alco
         money_spent_on_alcohol = as.numeric(h16a),
         mh_index = as.numeric(mh),
         num_med_problems = as.numeric(d3),
         num_hospitilizations = as.numeric(d1),
         bothered_by_med = as.factor(case_when(d4 == 0 ~ "Not at all",
                                               d4 == 1 ~ "Slightly",
                                               d4 == 2 ~ "Moderately",
                                               d4 == 3 ~ "Considerably",
                                               d4 == 4 ~ "Extremely")),
         bothered = as.factor(case_when(d4_rec == 0 ~ "No",
                                        d4_rec == 1 ~ "Yes"))) %>%
  select(group, dayslink, linkstatus, yrs_education, gender, age, alcohol, alcq_30, marriage, employmen
```

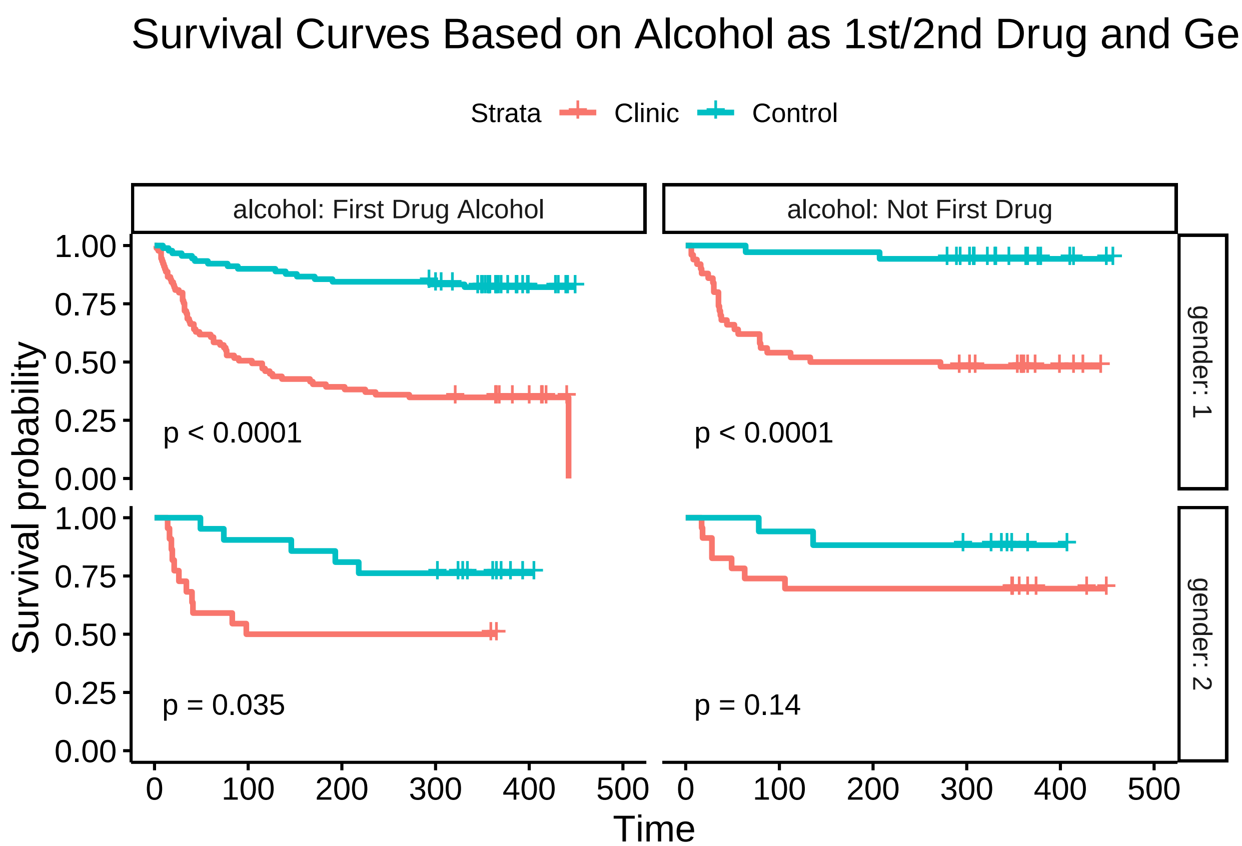
We begin by exploring some general variables in clinical research, such as age, gender, education level, and trial-specific variables, such as alcohol usage and medical conditions, etc.

We want to create different data visualizations, in order to understand the relationship between variables and get more clues on the model building part.

Since we are working with multiple categorical binary variables, we used the facet functionality to look at multiple survival probability plots simultaneously.

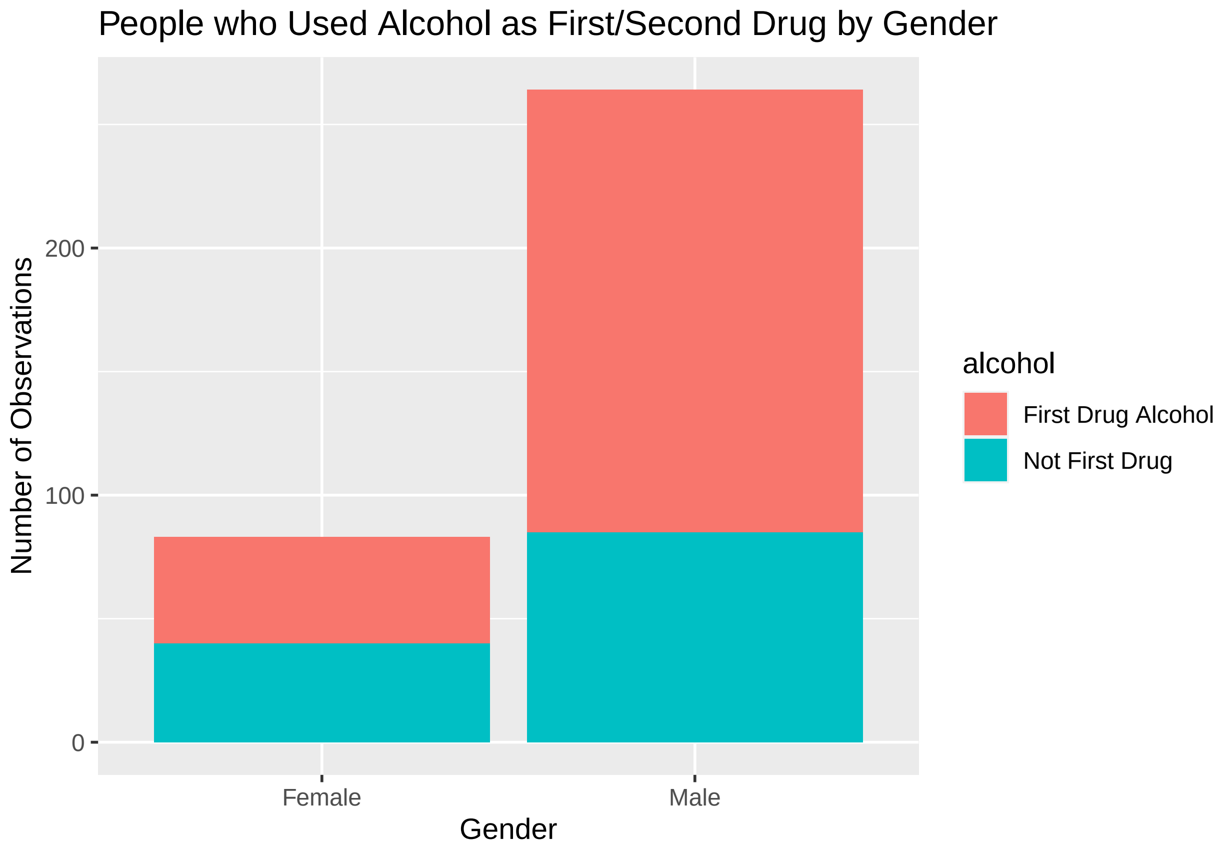
The plot below shows four survival probability plots separated by whether the individual's first drug was alcohol and gender. Gender is encoded as 1=Male and 2=Female. The p-values represent significance for the log-rank test. A p-value less than 0.05 suggests evidence that the survival curves are not equal in favor of the alternative hypothesis, $H_0:$ the survival curves are equal.

```
care_fit <- survfit(Surv(dayslink, linkstatus) ~ group, data=df)
ggsurvplot_facet(care_fit, df, facet.by = c("gender", "alcohol"), pval = TRUE) + ggtitle("Survival Curve
```



Looking at the plot, we see a p-value greater than 0.05 for observations who's first drug was not alcohol and gender is female. This means we fail to reject the null hypothesis that the survival curves are equal.

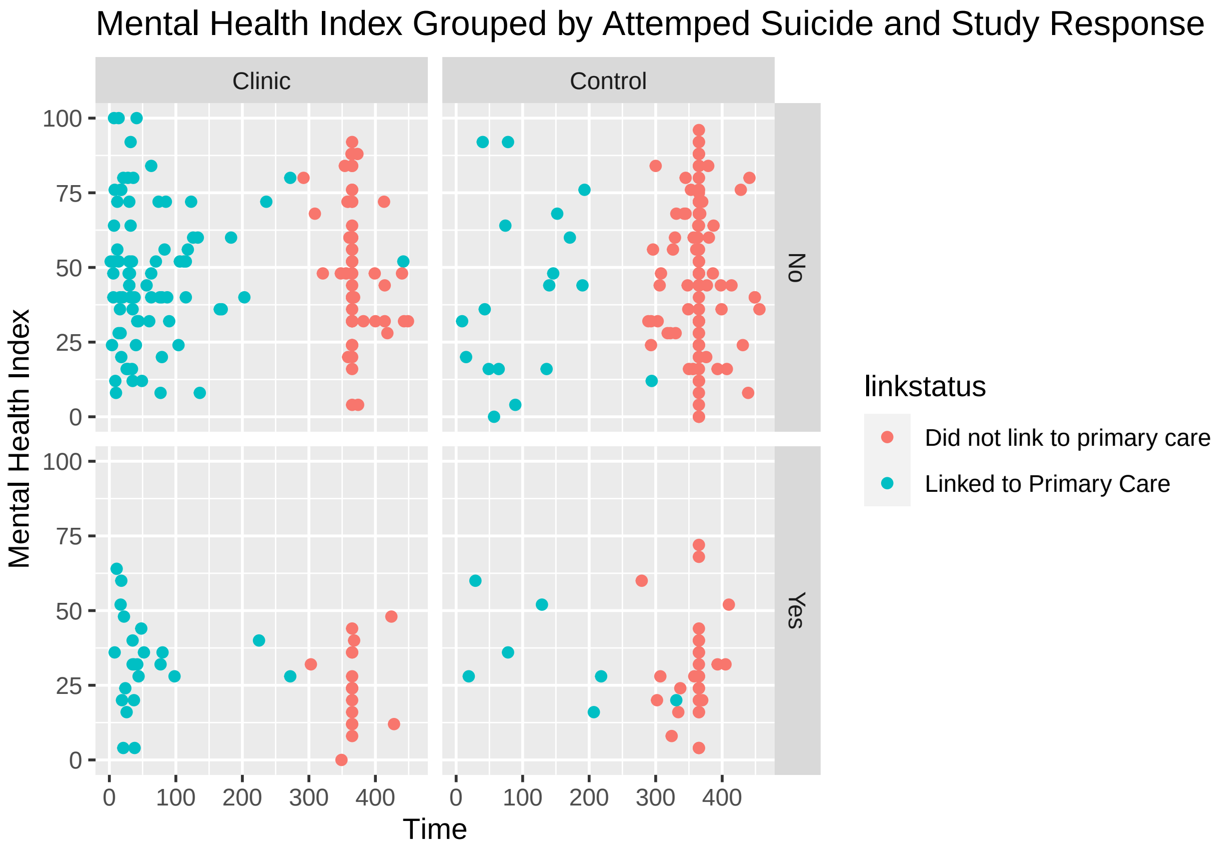
```
df %>%
  select(gender, alcohol) %>%
  mutate(gender_str = as.factor(case_when(gender == 1 ~ "Male", gender == 2 ~ "Female"))) %>%
  mutate(alcohol_str = as.factor(case_when(alcohol == 0 ~ "Not First Drug", alcohol == 1 ~ "First Drug A
  ggplot() + geom_bar(aes(x=gender_str, fill=alcohol)) + xlab("Gender") + ylab("Number of Observations")
```



Note that the number of female participants are way less than the number of male participants.

Here we observe the relationships mental health index and attempted suicide have on the link status.

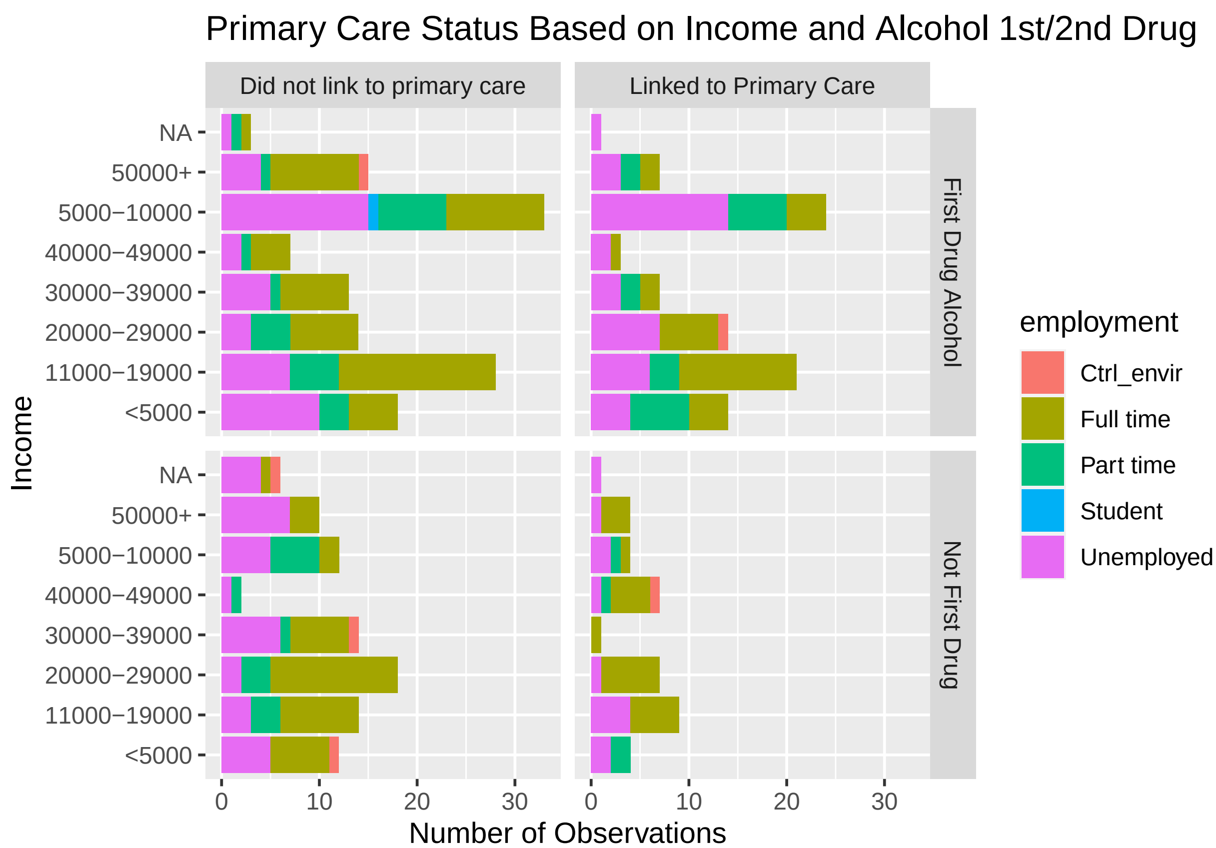
```
df %>%
  mutate(linkstatus = as.factor(case_when(linkstatus == 0 ~ "Did not link to primary care", linkstatus =
  select(group, linkstatus, dayslink, income, mh_index, attempted_suicide) %>%
  ggplot() + geom_point(aes(x=dayslink, y=mh_index, color=linkstatus)) + facet_grid(vars(attempted_suic
```



We see a distinct separation in response variable divided by the clinic and control group. In general, more individuals in the clinic group linked to primary care sooner than the control group. On the y-axis, a lower mental health index seems to be associated with more suicide attempts.

Next, we look at income and first drug alcohol and relation to the linkstatus.

```
df %>%
  select(income, employment, alcohol, group, linkstatus) %>%
  mutate(linkstatus = as.factor(case_when(linkstatus == 0 ~ "Did not link to primary care", linkstatus =
  ggplot() + geom_bar(aes(x=income, fill=employment)) + facet_grid(vars(alcohol), vars(linkstatus)) + co
```



Observe that the number of people in the $\$40,000 - \$49,000$ income bracket is much smaller than the other brackets. This could pose statistical confusion in our model building progress as the small number in that group could skew the results.

Based on the exploratory data analysis, medical and variables can influence the primary care link status. For our model building process, we will separate the medical and socioeconomic variables. We hypothesize that patients with more medical related problems would be inclinded to connect to primary care.

Stepwise Regression

We proceed with stepwise regression. For each potential variable, we build a coxph model including it and a model without the additional variable. Then, we take the loglik deviation from the models and run a drop-in-deviance test. The drop-in-deviance test will help us determine if an additional variable, x_i, should be included in the model. The G statistic equals $2 * (logLik_{biggermodel} - logLik_{smallermodel})$. Calculating degrees of freedom is taking the difference in the number of parameters of the full model minus the restricted model. Finding the p-value is the "percentage of the X^2 distribution that exceeds G". We calculate the p-value by finding the converse of $phcisq(...)$, so $1 - pchisq(...)$. The null and alternative hypothesis for this test is $H_0 : \beta_i = 0$ and $H_a : \beta_i \neq 0$.

Medical Explanatory Variables

```
coxph(Surv(dayslink, linkstatus) ~ group + attempted_suicide, data=df) %>% glance()
```

```
## # A tibble: 1 x 18
```

```
##       n nevent statistic.log p.value.log statistic.sc p.value.sc statistic.wald
##   <int>  <dbl>         <dbl>       <dbl>        <dbl>      <dbl>          <dbl>
## 1   347    128          70.0    6.44e-16         67.1   2.65e-15           54.2
## # ... with 11 more variables: p.value.wald <dbl>, statistic.robust <dbl>,
## #   p.value.robust <dbl>, r.squared <dbl>, r.squared.max <dbl>,
## #   concordance <dbl>, std.error.concordance <dbl>, logLik <dbl>, AIC <dbl>,
## #   BIC <dbl>, nobs <int>
```

```
coxph(Surv(dayslink, linkstatus) ~ group, data=df) %>% glance()
```

```
## # A tibble: 1 x 18
##       n nevent statistic.log p.value.log statistic.sc p.value.sc statistic.wald
##   <int>  <dbl>         <dbl>       <dbl>        <dbl>      <dbl>          <dbl>
## 1   347    128          69.6    7.30e-17         66.8   3.06e-16           53.9
## # ... with 11 more variables: p.value.wald <dbl>, statistic.robust <dbl>,
## #   p.value.robust <dbl>, r.squared <dbl>, r.squared.max <dbl>,
## #   concordance <dbl>, std.error.concordance <dbl>, logLik <dbl>, AIC <dbl>,
## #   BIC <dbl>, nobs <int>
```

```
base_loglik <- -683.2197
```

Socioeconomic Explanatory Variables

Results

The Cox PH analysis should include: an interpretation of your final survival model including a discussion of the sign of the coefficients (note: feel free to use interactions) Which variable(s) are in? Which are out? What do you conclude about linking to primary care? Is there anything worth mentioning about how you got to your final model? What can you say about causation? What can you say about generalizing to a larger population?

New Ideas

Cox.zph

Bootstrapping the Survival Model