

BST 210 Project: Survival Analysis

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```
library(tidyverse)

## -- Attaching packages ----- tidyverse 1.3.1 --

## v ggplot2 3.3.5      v purrr  0.3.4
## v tibble  3.1.4      v dplyr  1.0.7
## v tidyr   1.1.3      v stringr 1.4.0
## v readr   2.0.1      v forcats 0.5.1

## -- Conflicts ----- tidyverse_conflicts() --
## x dplyr::filter() masks stats::filter()
## x dplyr::lag()     masks stats::lag()

library(survival)
library(survminer)

## Warning: package 'survminer' was built under R version 4.1.2

## Loading required package: ggpubr

## Warning: package 'ggpubr' was built under R version 4.1.2
```

Stem Cell Source

Read in Data

```
bone <- read.csv("data.csv")

# remove HLA_match_raw (was already converted into a different column)
bone <- select(bone, -HLA_match_raw)

# convert numeric columns to numeric
bone_num <- c("donor_age", "recipient_age", "recipient_body_mass", "CD34_x1e6_per_kg...CD34kgx10d6",
              "CD3_x1e8_per_kg", "CD3_to_CD34_ratio", "ANC_recovery", "PLT_recovery",
              "time_to_acute_GvHD_III_IV", "survival_time", "survival_status")

bone[,bone_num] <- lapply(bone_num, function(x) as.numeric(bone[[x]]))
```

```
## Warning in FUN(X[[i]], ...): NAs introduced by coercion
## Warning in FUN(X[[i]], ...): NAs introduced by coercion
## Warning in FUN(X[[i]], ...): NAs introduced by coercion
```

Compare Kaplan-Meier curves for the two stem cell sources

filter data

```
# sources <- bone %>% select(stem_cell_source, survival_time, survival_status)
# head(sources)
#
# pb <- sources %>% filter(stem_cell_source == "peripheral_blood")
# bm <- sources %>% filter(stem_cell_source == "bone_marrow")
```

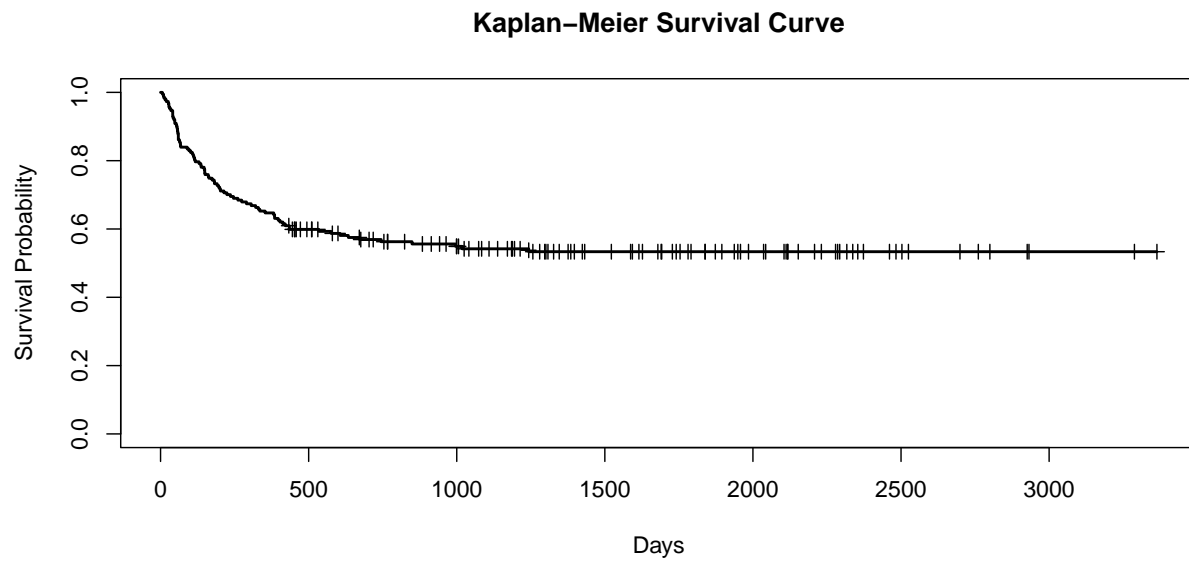
plot two separate curves

```
### peripheral blood
# survival.pb.obj <- Surv(pb$survival_time, pb$survival_status)
# KM.ph.fit <- survfit(survival.pb.obj ~ 1, data = pb)
#
# plot(KM.ph.fit, xlab = "Days", ylab = "Survival Probability", conf.int=,
# mark.time = TRUE, main = "Peripheral Blood Group Survival")
#
#
# ### bone marrow
# survival.bm.obj <- Surv(bm$survival_time, bm$survival_status)
# KM.bm.fit <- survfit(survival.bm.obj ~ 1, data = bm)
#
# plot(KM.bm.fit, xlab = "Days", ylab = "Survival Probability", conf.int=,
# mark.time = TRUE, main = "Bone Marrow Group Survival")
```

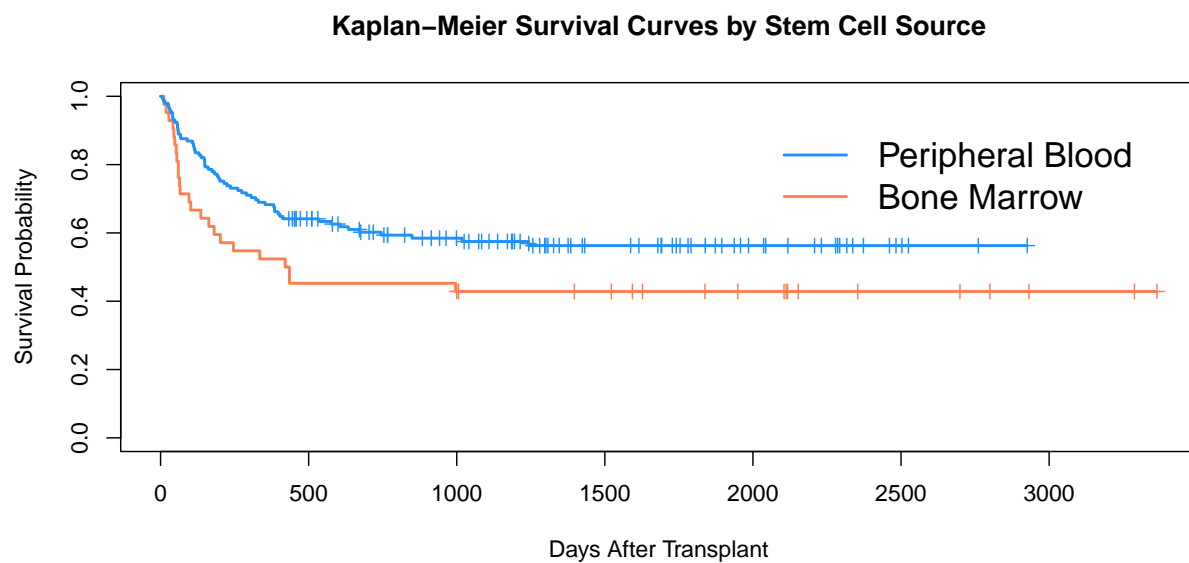
plot both curves together

```
survival.obj <- Surv(time = bone$survival_time, event = bone$survival_status)

# Overall
KM.fit1 <- survfit(survival.obj ~ 1, data = bone)
plot(KM.fit1, xlab = "Days", ylab = "Survival Probability", conf.int = FALSE,
mark.time = TRUE, main = "Kaplan-Meier Survival Curve", lwd = 2)
```



```
# By treatment
KM.fit2 <- survfit(survival.obj ~ stem_cell_source, data = bone)
plot(KM.fit2, xlab = "Days After Transplant", ylab = "Survival Probability", mark.time = TRUE, conf.int = TRUE,
     col = c("coral", "dodgerblue"), main = "Kaplan–Meier Survival Curves by Stem Cell Source", lwd = 2,
     legend(x = 2000, y = 0.95,
           legend = c("Peripheral Blood", "Bone Marrow"),
           col = c("dodgerblue", "coral"),
           bty = "n",
           lty = 1:1,
           lwd = 2,
           cex = 1.5))
```



can we get CIs on this plot??

no confounders with KM

```
survdif(Surv(bone$survival_time, bone$survival_status) ~ stem_cell_source, data=bone)
```

log-rank test to compare these two curves

```
## Call:
## survdiff(formula = Surv(bone$survival_time, bone$survival_status) ~
##     stem_cell_source, data = bone)
##
##               N Observed Expected (O-E)^2/E (O-E)^2/V
## stem_cell_source=bone_marrow      42      24      16.8      3.065      3.83
## stem_cell_source=peripheral_blood 145      61      68.2      0.756      3.83
##
##  Chisq= 3.8  on 1 degrees of freedom, p= 0.05
```

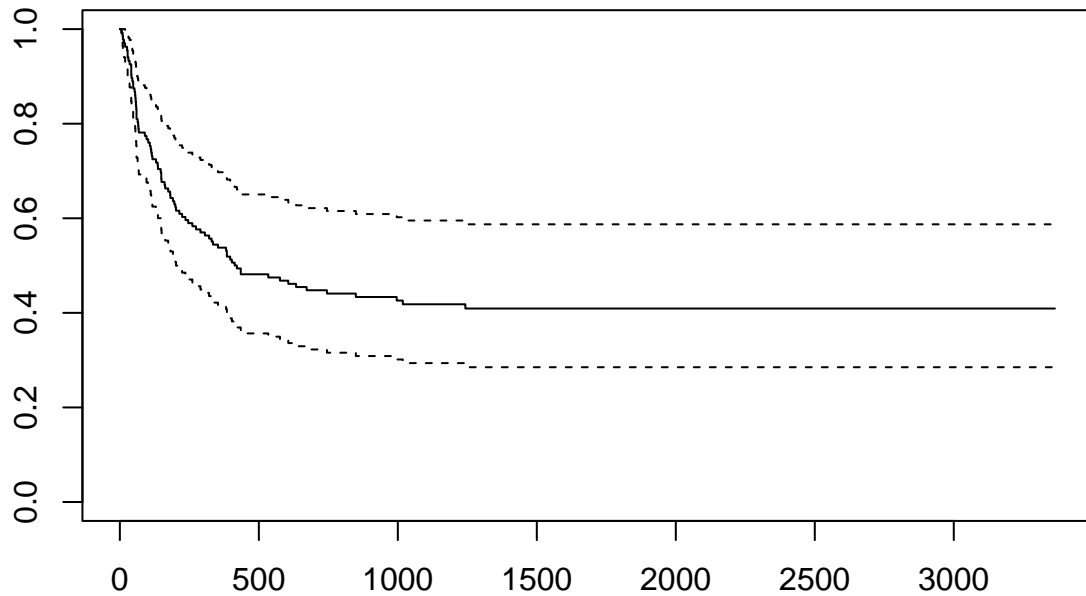
p-value is exactly 0.5—this means that the curves are (approximately) statistically significantly different

Cox Proportional Hazards Model

```
cox_model_source <- coxph(survival.obj ~ as.factor(stem_cell_source), data = bone, ties = "exact")
summary(cox_model_source)
```

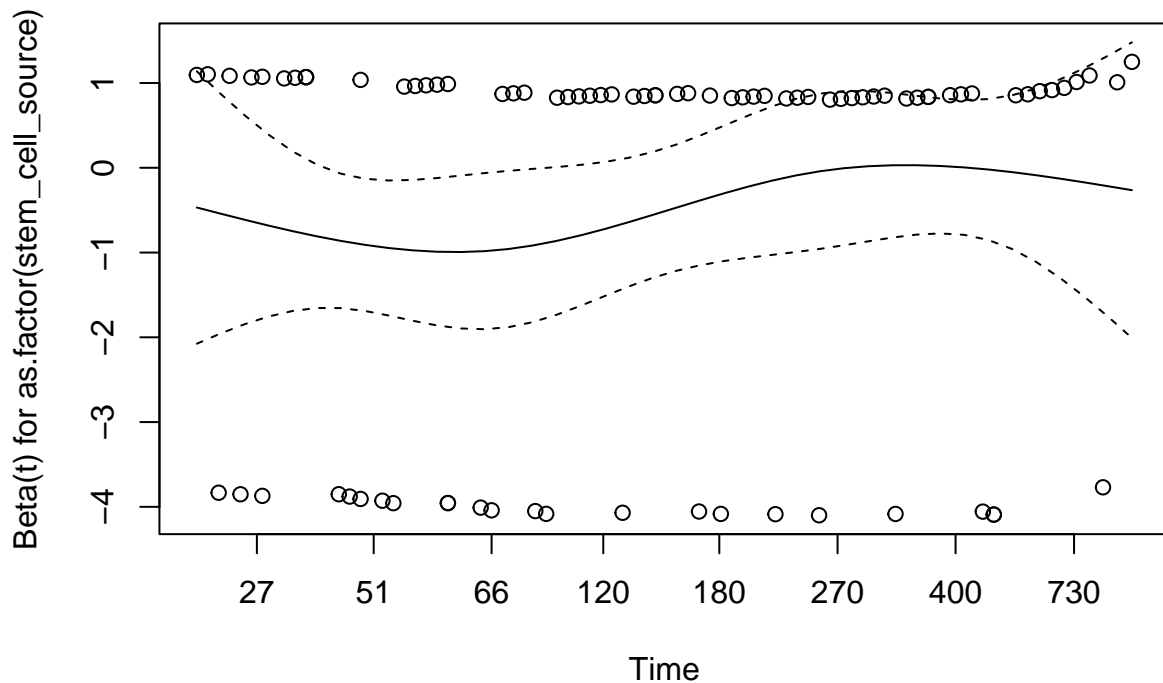
```
## Call:
## coxph(formula = survival.obj ~ as.factor(stem_cell_source), data = bone,
##     ties = "exact")
##
##    n= 187, number of events= 85
##
##               coef exp(coef) se(coef)      z
## as.factor(stem_cell_source)peripheral_blood -0.4686    0.6259    0.2415 -1.941
##               Pr(>|z|)
## as.factor(stem_cell_source)peripheral_blood  0.0523 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##               exp(coef) exp(-coef) lower .95
## as.factor(stem_cell_source)peripheral_blood  0.6259    1.598    0.3899
##               upper .95
## as.factor(stem_cell_source)peripheral_blood  1.005
##
## Concordance= 0.549 (se = 0.025 )
## Likelihood ratio test= 3.5  on 1 df,  p=0.06
## Wald test              = 3.77  on 1 df,  p=0.05
## Score (logrank) test = 3.83  on 1 df,  p=0.05
```

```
plot(survfit(cox_model_source))
```



check Schoenfeld residuals

```
# create plot of schoenfeld resids  
wt_sch_source <- cox.zph(cox_model_source)  
plot(wt_sch_source) # slight decrease then increase over time
```



```
# check summary to see if problematic
wt_sch_source
```

```
##               chisq df    p
## as.factor(stem_cell_source)  1.5  1 0.22
## GLOBAL                      1.5  1 0.22
```

confounders??

did the authors adjust for confounders? no, it was an RCT

we can look at the covariates that are most strongly associated with survival

looking for common causes of stem cell type and survival

we had selected for our prediction model: - CD3 dosage (is this related to stem cell source?) - rh factor - disease type - recipient body mass (which is probably closely related to age)

DIFFERENT IDEA: - disease type (Anasetti article says that this could be an effect modifier)

###try some models with possible confounders

```
cox_model_source2 <- coxph(survival.obj ~ as.factor(stem_cell_source) + recipient_age + CD3_x1e8_per_kg
                           data = bone, ties = "exact")
summary(cox_model_source2)
```

```
## Call:
## coxph(formula = survival.obj ~ as.factor(stem_cell_source) +
##       recipient_age + CD3_x1e8_per_kg, data = bone, ties = "exact")
##
##      n= 182, number of events= 81
##      (5 observations deleted due to missingness)
##
##               coef exp(coef) se(coef)      z
## as.factor(stem_cell_source)peripheral_blood -0.18045    0.83489  0.30931 -0.583
## recipient_age                               0.04226    1.04317  0.02421  1.745
## CD3_x1e8_per_kg                             -0.07077    0.93168  0.04466 -1.584
##
##               Pr(>|z|)
## as.factor(stem_cell_source)peripheral_blood  0.5596
## recipient_age                               0.0809 .
## CD3_x1e8_per_kg                             0.1131
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##               exp(coef) exp(-coef) lower .95
## as.factor(stem_cell_source)peripheral_blood  0.8349    1.1978    0.4553
## recipient_age                               1.0432    0.9586    0.9948
## CD3_x1e8_per_kg                             0.9317    1.0733    0.8536
##
##               upper .95
## as.factor(stem_cell_source)peripheral_blood  1.531
## recipient_age                               1.094
## CD3_x1e8_per_kg                             1.017
##
## Concordance= 0.615 (se = 0.034 )
## Likelihood ratio test= 13.61 on 3 df,  p=0.003
## Wald test              = 12.44 on 3 df,  p=0.006
## Score (logrank) test = 12.9 on 3 df,  p=0.005
```

this would imply that source doesn't matter as much once we adjust for dosage and age - need to adjust for age when we use dosage (previous authors did) - why do people get different doses?

```
cox_model_source3 <- coxph(survival.obj ~ as.factor(stem_cell_source):as.factor(disease_group),
                          data = bone, ties = "exact")
summary(cox_model_source3)
```

```
## Call:
## coxph(formula = survival.obj ~ as.factor(stem_cell_source):as.factor(disease_group),
##       data = bone, ties = "exact")
##
##      n= 187, number of events= 85
##
##
##               coef
## as.factor(stem_cell_source)bone_marrow:as.factor(disease_group)malignant  0.7916
## as.factor(stem_cell_source)peripheral_blood:as.factor(disease_group)malignant 0.5181
## as.factor(stem_cell_source)bone_marrow:as.factor(disease_group)nonmalignant  1.7811
## as.factor(stem_cell_source)peripheral_blood:as.factor(disease_group)nonmalignant NA
##
##               exp(coef)
## as.factor(stem_cell_source)bone_marrow:as.factor(disease_group)malignant  2.2070
## as.factor(stem_cell_source)peripheral_blood:as.factor(disease_group)malignant 1.6789
```

```

## as.factor(stem_cell_source)bone_marrow:as.factor(disease_group)nonmalignant      5.9362
## as.factor(stem_cell_source)peripheral_blood:as.factor(disease_group)nonmalignant    NA
##                                                                 se(coef)
## as.factor(stem_cell_source)bone_marrow:as.factor(disease_group)malignant          0.4188
## as.factor(stem_cell_source)peripheral_blood:as.factor(disease_group)malignant      0.3797
## as.factor(stem_cell_source)bone_marrow:as.factor(disease_group)nonmalignant        0.6159
## as.factor(stem_cell_source)peripheral_blood:as.factor(disease_group)nonmalignant    0.0000
##                                                                 z
## as.factor(stem_cell_source)bone_marrow:as.factor(disease_group)malignant          1.890
## as.factor(stem_cell_source)peripheral_blood:as.factor(disease_group)malignant      1.365
## as.factor(stem_cell_source)bone_marrow:as.factor(disease_group)nonmalignant        2.892
## as.factor(stem_cell_source)peripheral_blood:as.factor(disease_group)nonmalignant    NA
##                                                                 Pr(>|z|)
## as.factor(stem_cell_source)bone_marrow:as.factor(disease_group)malignant          0.05873
## as.factor(stem_cell_source)peripheral_blood:as.factor(disease_group)malignant      0.17237
## as.factor(stem_cell_source)bone_marrow:as.factor(disease_group)nonmalignant        0.00383
## as.factor(stem_cell_source)peripheral_blood:as.factor(disease_group)nonmalignant    NA
##
## as.factor(stem_cell_source)bone_marrow:as.factor(disease_group)malignant          .
## as.factor(stem_cell_source)peripheral_blood:as.factor(disease_group)malignant
## as.factor(stem_cell_source)bone_marrow:as.factor(disease_group)nonmalignant      **
## as.factor(stem_cell_source)peripheral_blood:as.factor(disease_group)nonmalignant
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                                                                 exp(coef)
## as.factor(stem_cell_source)bone_marrow:as.factor(disease_group)malignant          2.207
## as.factor(stem_cell_source)peripheral_blood:as.factor(disease_group)malignant      1.679
## as.factor(stem_cell_source)bone_marrow:as.factor(disease_group)nonmalignant        5.936
## as.factor(stem_cell_source)peripheral_blood:as.factor(disease_group)nonmalignant    NA
##                                                                 exp(-coef)
## as.factor(stem_cell_source)bone_marrow:as.factor(disease_group)malignant          0.4531
## as.factor(stem_cell_source)peripheral_blood:as.factor(disease_group)malignant      0.5956
## as.factor(stem_cell_source)bone_marrow:as.factor(disease_group)nonmalignant        0.1685
## as.factor(stem_cell_source)peripheral_blood:as.factor(disease_group)nonmalignant    NA
##                                                                 lower .95
## as.factor(stem_cell_source)bone_marrow:as.factor(disease_group)malignant          0.9712
## as.factor(stem_cell_source)peripheral_blood:as.factor(disease_group)malignant      0.7977
## as.factor(stem_cell_source)bone_marrow:as.factor(disease_group)nonmalignant        1.7753
## as.factor(stem_cell_source)peripheral_blood:as.factor(disease_group)nonmalignant    NA
##                                                                 upper .95
## as.factor(stem_cell_source)bone_marrow:as.factor(disease_group)malignant          5.015
## as.factor(stem_cell_source)peripheral_blood:as.factor(disease_group)malignant      3.534
## as.factor(stem_cell_source)bone_marrow:as.factor(disease_group)nonmalignant        19.849
## as.factor(stem_cell_source)peripheral_blood:as.factor(disease_group)nonmalignant    NA
##
## Concordance= 0.572 (se = 0.029 )
## Likelihood ratio test= 8.19  on 3 df,  p=0.04
## Wald test              = 9.44  on 3 df,  p=0.02
## Score (logrank) test = 10.49  on 3 df,  p=0.01

```

previous research mentioned interaction between disease type and stem cell source—many of these interactions are significant


```

cox_model_source4 <- coxph(survival.obj ~ as.factor(stem_cell_source) +
                           recipient_age + CD3_x1e8_per_kg,
                           data = bone, ties = "exact")
summary(cox_model_source4)

## Call:
## coxph(formula = survival.obj ~ as.factor(stem_cell_source) +
##       recipient_age + CD3_x1e8_per_kg, data = bone, ties = "exact")
##
## n= 182, number of events= 81
## (5 observations deleted due to missingness)
##
##               coef exp(coef) se(coef)      z
## as.factor(stem_cell_source)peripheral_blood -0.18045    0.83489  0.30931 -0.583
## recipient_age                               0.04226    1.04317  0.02421  1.745
## CD3_x1e8_per_kg                             -0.07077    0.93168  0.04466 -1.584
##               Pr(>|z|)
## as.factor(stem_cell_source)peripheral_blood  0.5596
## recipient_age                               0.0809 .
## CD3_x1e8_per_kg                             0.1131
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##               exp(coef) exp(-coef) lower .95
## as.factor(stem_cell_source)peripheral_blood  0.8349    1.1978    0.4553
## recipient_age                               1.0432    0.9586    0.9948
## CD3_x1e8_per_kg                             0.9317    1.0733    0.8536
##               upper .95
## as.factor(stem_cell_source)peripheral_blood  1.531
## recipient_age                               1.094
## CD3_x1e8_per_kg                             1.017
##
## Concordance= 0.615 (se = 0.034 )
## Likelihood ratio test= 13.61 on 3 df,  p=0.003
## Wald test              = 12.44 on 3 df,  p=0.006
## Score (logrank) test = 12.9 on 3 df,  p=0.005

```

CD3/CD34 dosage

plot KM curves by dosage

```

# add new columns based on previous research
bone$CD3_over_4 <- ifelse(bone$CD3_x1e8_per_kg >= 4, 1, 0)
bone$CD34_over10 <- ifelse(bone$CD34_x1e6_per_kg...CD34kgx10d6 >= 10, 1, 0)

KM.fit4 <- survfit(survival.obj ~ CD3_over_4, data = bone)
summary(KM.fit4)

## Call: survfit(formula = survival.obj ~ CD3_over_4, data = bone)
##

```

```

## 5 observations deleted due to missingness
##
##      CD3_over_4=0
## time n.risk n.event survival std.err lower 95% CI upper 95% CI
##  10      87       1   0.989  0.0114      0.966      1.000
##  11      86       1   0.977  0.0161      0.946      1.000
##  15      85       1   0.966  0.0196      0.928      1.000
##  19      84       1   0.954  0.0225      0.911      0.999
##  28      83       1   0.943  0.0250      0.895      0.993
##  35      82       1   0.931  0.0272      0.879      0.986
##  42      81       1   0.920  0.0292      0.864      0.979
##  48      80       1   0.908  0.0310      0.849      0.971
##  53      79       1   0.897  0.0327      0.835      0.963
##  55      78       1   0.885  0.0342      0.821      0.955
##  58      77       1   0.874  0.0356      0.806      0.946
##  60      76       2   0.851  0.0382      0.779      0.929
##  64      74       1   0.839  0.0394      0.765      0.920
##  66      73       1   0.828  0.0405      0.752      0.911
##  68      72       1   0.816  0.0415      0.739      0.902
##  96      71       1   0.805  0.0425      0.725      0.892
## 102      70       1   0.793  0.0434      0.712      0.883
## 111      69       1   0.782  0.0443      0.699      0.873
## 115      68       1   0.770  0.0451      0.687      0.864
## 117      67       1   0.759  0.0459      0.674      0.854
## 130      66       1   0.747  0.0466      0.661      0.844
## 136      65       1   0.736  0.0473      0.649      0.834
## 149      64       1   0.724  0.0479      0.636      0.824
## 150      63       1   0.713  0.0485      0.624      0.814
## 161      62       1   0.701  0.0491      0.611      0.804
## 163      61       1   0.690  0.0496      0.599      0.794
## 181      60       1   0.678  0.0501      0.587      0.784
## 182      59       1   0.667  0.0505      0.575      0.773
## 196      58       1   0.655  0.0510      0.563      0.763
## 202      57       1   0.644  0.0513      0.551      0.753
## 224      56       1   0.632  0.0517      0.539      0.742
## 246      55       1   0.621  0.0520      0.527      0.732
## 261      54       1   0.609  0.0523      0.515      0.721
## 274      53       1   0.598  0.0526      0.503      0.710
## 290      52       1   0.586  0.0528      0.491      0.699
## 335      51       1   0.575  0.0530      0.480      0.689
## 353      50       1   0.563  0.0532      0.468      0.678
## 382      49       1   0.552  0.0533      0.457      0.667
## 403      48       1   0.540  0.0534      0.445      0.656
## 413      47       1   0.529  0.0535      0.434      0.645
## 421      46       1   0.517  0.0536      0.422      0.634
## 435      45       2   0.494  0.0536      0.400      0.611
## 534      40       1   0.482  0.0537      0.387      0.599
## 576      39       1   0.470  0.0537      0.375      0.588
## 996      35       1   0.456  0.0538      0.362      0.575
##
##      CD3_over_4=1
## time n.risk n.event survival std.err lower 95% CI upper 95% CI
##   6      95       1   0.989  0.0105      0.969      1.000
##  28      94       1   0.979  0.0147      0.951      1.000
##  31      93       1   0.968  0.0179      0.934      1.000

```

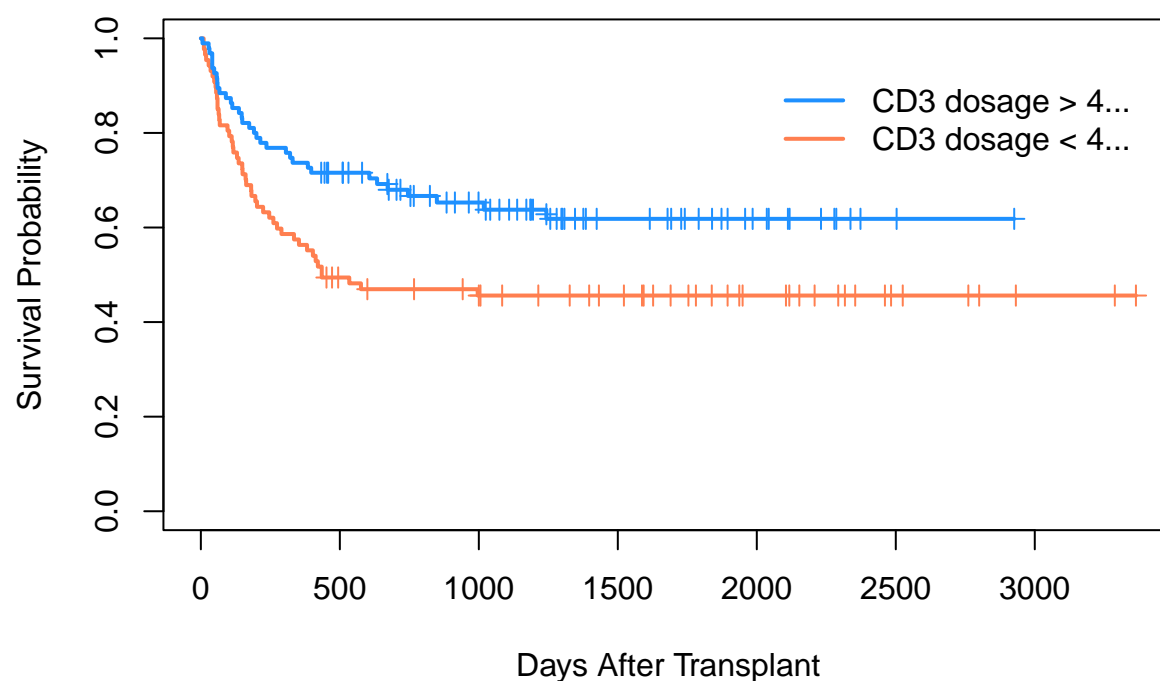
| | | | | | | | |
|----|------|----|---|-------|--------|-------|-------|
| ## | 41 | 92 | 3 | 0.937 | 0.0250 | 0.889 | 0.987 |
| ## | 48 | 89 | 1 | 0.926 | 0.0268 | 0.875 | 0.980 |
| ## | 57 | 88 | 1 | 0.916 | 0.0285 | 0.862 | 0.973 |
| ## | 59 | 87 | 1 | 0.905 | 0.0300 | 0.848 | 0.966 |
| ## | 60 | 86 | 1 | 0.895 | 0.0315 | 0.835 | 0.959 |
| ## | 67 | 85 | 1 | 0.884 | 0.0328 | 0.822 | 0.951 |
| ## | 90 | 84 | 1 | 0.874 | 0.0341 | 0.809 | 0.943 |
| ## | 108 | 83 | 1 | 0.863 | 0.0353 | 0.797 | 0.935 |
| ## | 113 | 82 | 1 | 0.853 | 0.0364 | 0.784 | 0.927 |
| ## | 137 | 81 | 1 | 0.842 | 0.0374 | 0.772 | 0.919 |
| ## | 147 | 80 | 1 | 0.832 | 0.0384 | 0.760 | 0.910 |
| ## | 149 | 79 | 1 | 0.821 | 0.0393 | 0.747 | 0.902 |
| ## | 174 | 78 | 1 | 0.811 | 0.0402 | 0.735 | 0.893 |
| ## | 191 | 77 | 1 | 0.800 | 0.0410 | 0.723 | 0.885 |
| ## | 200 | 76 | 1 | 0.789 | 0.0418 | 0.712 | 0.876 |
| ## | 214 | 75 | 1 | 0.779 | 0.0426 | 0.700 | 0.867 |
| ## | 236 | 74 | 1 | 0.768 | 0.0433 | 0.688 | 0.858 |
| ## | 306 | 73 | 1 | 0.758 | 0.0439 | 0.676 | 0.849 |
| ## | 321 | 72 | 1 | 0.747 | 0.0446 | 0.665 | 0.840 |
| ## | 330 | 71 | 1 | 0.737 | 0.0452 | 0.653 | 0.831 |
| ## | 385 | 70 | 1 | 0.726 | 0.0457 | 0.642 | 0.822 |
| ## | 397 | 69 | 1 | 0.716 | 0.0463 | 0.631 | 0.812 |
| ## | 606 | 60 | 1 | 0.704 | 0.0470 | 0.617 | 0.802 |
| ## | 634 | 59 | 1 | 0.692 | 0.0477 | 0.604 | 0.792 |
| ## | 672 | 57 | 1 | 0.680 | 0.0484 | 0.591 | 0.782 |
| ## | 745 | 52 | 1 | 0.667 | 0.0492 | 0.577 | 0.770 |
| ## | 849 | 48 | 1 | 0.653 | 0.0501 | 0.562 | 0.759 |
| ## | 1018 | 43 | 1 | 0.638 | 0.0512 | 0.545 | 0.746 |
| ## | 1243 | 33 | 1 | 0.618 | 0.0531 | 0.522 | 0.732 |

```

plot(KM.fit4, xlab = "Days After Transplant", ylab = "Survival Probability", mark.time = TRUE, conf.int = TRUE,
      col = c("coral", "dodgerblue"), main = "Kaplan-Meier Survival Curves by CD3 Dosage per kg", lwd = 2)
legend(x = 2000, y = 0.95,
      legend = c("CD3 dosage > 4...", "CD3 dosage < 4..."),
      col = c("dodgerblue", "coral"),
      bty = "n",
      lty = 1:1,
      lwd = 2,
      cex = 1)

```

Kaplan–Meier Survival Curves by CD3 Dosage per kg



```
survdif(Surv(bone$survival_time, bone$survival_status) ~ CD3_over_4, data=bone)
```

log-rank test to compare these two curves

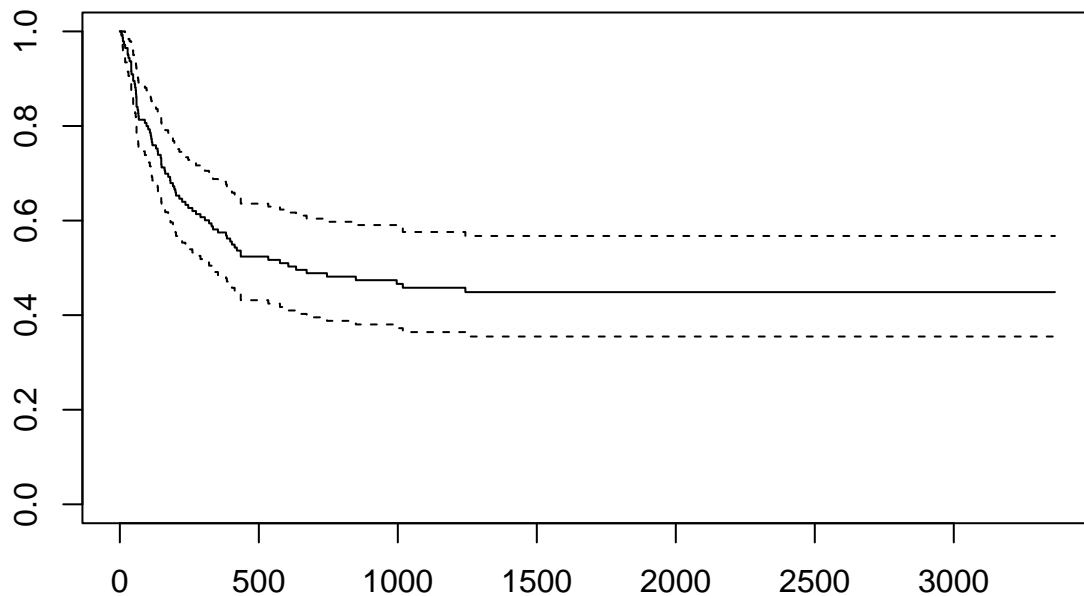
```
## Call:
## survdiff(formula = Surv(bone$survival_time, bone$survival_status) ~
##     CD3_over_4, data = bone)
##
## n=182, 5 observations deleted due to missingness.
##
##           N Observed Expected (O-E)^2/E (O-E)^2/V
## CD3_over_4=0 87      47    35.8      3.49      6.28
## CD3_over_4=1 95      34    45.2      2.76      6.28
##
## Chisq= 6.3  on 1 degrees of freedom, p= 0.01
```

Cox Proportional Hazards Model

```
cox_model_dose <- coxph(survival.obj ~ as.factor(CD3_over_4), data = bone, ties = "exact")
summary(cox_model_dose)
```

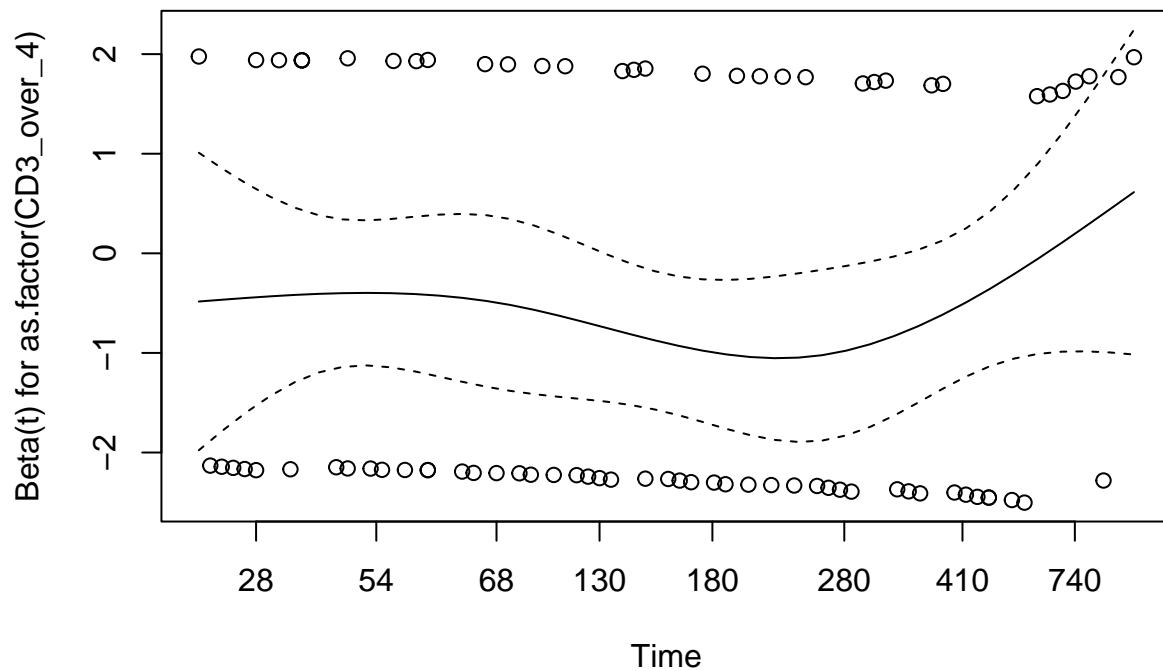
```
## Call:
## coxph(formula = survival.obj ~ as.factor(CD3_over_4), data = bone,
##       ties = "exact")
##
## n= 182, number of events= 81
## (5 observations deleted due to missingness)
##
##               coef exp(coef) se(coef)      z Pr(>|z|)
## as.factor(CD3_over_4)1 -0.5581    0.5723  0.2256 -2.474  0.0134 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##               exp(coef) exp(-coef) lower .95 upper .95
## as.factor(CD3_over_4)1  0.5723      1.747   0.3678   0.8906
##
## Concordance= 0.573 (se = 0.028 )
## Likelihood ratio test= 6.22 on 1 df,  p=0.01
## Wald test               = 6.12 on 1 df,  p=0.01
## Score (logrank) test = 6.28 on 1 df,  p=0.01
```

```
plot(survfit(cox_model_dose))
```



check Schoenfeld residuals

```
# create plot of schoenfeld resids
wt_sch_dose <- cox.zph(cox_model_dose)
plot(wt_sch_dose) # slight decrease then increase over time
```



```
# check summary to see if problematic
wt_sch_dose
```

```
##               chisq df    p
## as.factor(CD3_over_4) 0.0491  1 0.82
## GLOBAL                0.0491  1 0.82
```

confounders

```
cox_model_dose2 <- coxph(survival.obj ~ as.factor(CD3_over_4) + recipient_age_below_10, data = bone, ties = "exact")
summary(cox_model_dose2)
```

```
## Call:
## coxph(formula = survival.obj ~ as.factor(CD3_over_4) + recipient_age_below_10,
##       data = bone, ties = "exact")
```

```
##
##   n= 182, number of events= 81
##   (5 observations deleted due to missingness)
##
##               coef exp(coef) se(coef)      z Pr(>|z|)
## as.factor(CD3_over_4)1  -0.4718    0.6239   0.2356 -2.002   0.0453 *
## recipient_age_below_10yes -0.2972    0.7429   0.2333 -1.274   0.2027
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##               exp(coef) exp(-coef) lower .95 upper .95
## as.factor(CD3_over_4)1    0.6239    1.603    0.3931    0.9901
## recipient_age_below_10yes  0.7429    1.346    0.4702    1.1736
##
## Concordance= 0.588 (se = 0.031 )
## Likelihood ratio test= 7.85 on 2 df,  p=0.02
## Wald test              = 7.74 on 2 df,  p=0.02
## Score (logrank) test = 7.93 on 2 df,  p=0.02
```

need to remove people who are missing CD3