### BIOST/EPI 537 Final Group Project

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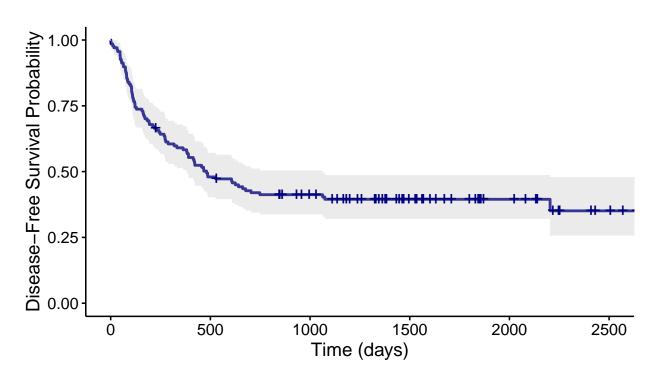
1. Provide an estimate of disease-free survival time for patients enrolled in this study. What are the main characteristics of this summary?

```
library(survival)
library(survminer)
## Loading required package: ggplot2
## Loading required package: ggpubr
##
## Attaching package: 'survminer'
## The following object is masked from 'package:survival':
##
       myeloma
library(ggplot2)
library(dplyr)
## Attaching package: 'dplyr'
## The following objects are masked from 'package:stats':
##
##
       filter, lag
## The following objects are masked from 'package:base':
##
##
       intersect, setdiff, setequal, union
library(knitr)
library(broom)
library(table1)
```

```
##
## Attaching package: 'table1'
## The following objects are masked from 'package:base':
##
##
       units, units<-
library(kableExtra)
##
## Attaching package: 'kableExtra'
## The following object is masked from 'package:dplyr':
##
       group_rows
\textit{\#bmt} \; \textit{<-} \; read.csv("~/Documents/UW \; classes/survival \; analysis/bmt.csv")
bmt <- read.csv("~/Downloads/bmt.csv")</pre>
dfs_surv <- Surv(time = bmt$tdfs, event = bmt$deltadfs)</pre>
km_fit <- survfit(dfs_surv ~ 1)</pre>
survminer::ggsurvplot(
    fit = km_fit,
    data = bmt,
    conf.int = T,
    palette = "navy",
    xlab = "Time (days)",
    ylab = "Disease-Free Survival Probability",
    title = "Kaplan-Meier Curve for Disease-Free Survival of All Participants"
```

### Kaplan-Meier Curve for Disease-Free Survival of All Partic





#### summary(km\_fit)

```
Call: survfit(formula = dfs_surv ~ 1)
##
    time n.risk n.event survival std.err lower 95% CI upper 95% CI
##
                                                     0.979
##
       1
             137
                        1
                              0.993 0.00727
                                                                    1.000
                              0.985 0.01025
##
       2
             136
                        1
                                                     0.966
                                                                    1.000
##
      10
             135
                        1
                              0.978 0.01250
                                                     0.954
                                                                    1.000
##
      16
             134
                              0.971 0.01438
                                                     0.943
                                                                    0.999
                        1
##
      32
             133
                        1
                              0.964 0.01602
                                                     0.933
                                                                    0.995
      35
             132
                              0.956 0.01748
##
                        1
                                                     0.923
                                                                    0.991
      47
             131
                        2
                              0.942 0.02003
                                                                    0.982
##
                                                     0.903
##
             129
                        2
                              0.927 0.02222
                                                     0.884
                                                                    0.972
      48
      53
             127
                        1
                              0.920 0.02322
                                                     0.875
                                                                    0.966
##
##
      55
             126
                        1
                              0.912 0.02415
                                                     0.866
                                                                    0.961
             125
##
      63
                        1
                              0.905 0.02504
                                                     0.857
                                                                    0.956
      64
             124
                        1
                              0.898 0.02588
                                                     0.848
                                                                    0.950
##
##
      74
             123
                        2
                              0.883 0.02744
                                                     0.831
                                                                    0.939
             121
##
      76
                        1
                              0.876 0.02817
                                                     0.822
                                                                    0.933
##
      79
             120
                        1
                              0.869 0.02886
                                                     0.814
                                                                    0.927
##
      80
             119
                        2
                              0.854 0.03017
                                                     0.797
                                                                    0.915
##
      84
             117
                              0.847 0.03078
                                                     0.788
                                                                    0.909
                        1
##
      86
             116
                        1
                              0.839 0.03137
                                                     0.780
                                                                    0.903
##
      93
             115
                        1
                              0.832 0.03193
                                                     0.772
                                                                    0.897
##
     100
             114
                              0.825 0.03248
                                                     0.764
                                                                    0.891
```

##	104	113	1	0.818 0.03300	0.755	0.885
##	105	112	2	0.803 0.03399	0.739	0.872
##	107	110	1	0.796 0.03445	0.731	0.866
##	109	109	1	0.788 0.03490	0.723	0.860
##	110	108	1	0.781 0.03533	0.715	0.853
##	113	107	1	0.774 0.03575	0.707	0.847
##	115	106	1	0.766 0.03615	0.699	0.841
##	120	105	1	0.759 0.03653	0.691	0.834
##	122	104	2	0.745 0.03726	0.675	0.821
##	129	102	1	0.737 0.03760	0.667	0.815
##	157	101	1	0.730 0.03793	0.659	0.808
##	162	100	1	0.723 0.03825	0.651	0.802
##	164	99	1	0.715 0.03855	0.644	0.795
##	168	98	1	0.708 0.03884	0.636	0.788
##	172	97	1	0.701 0.03912	0.628	0.782
##	183	96	1	0.693 0.03939	0.620	0.775
##	192	95	1	0.686 0.03965	0.613	0.768
##	194	94	1	0.679 0.03989	0.605	0.762
##	211	93	1	0.672 0.04013	0.597	0.755
##	219	92	1	0.664 0.04035	0.590	0.748
##	230	90	1	0.657 0.04057	0.582	0.741
##	242	89	1	0.649 0.04078	0.574	0.735
##	248	88	1	0.642 0.04098	0.567	0.728
##	268	87	1	0.635 0.04117	0.559	0.721
##	272	86	1	0.627 0.04134	0.551	0.714
##	273	85	1	0.620 0.04151	0.544	0.707
##	276	84	1	0.613 0.04167	0.536	0.700
##	288	83	1	0.605 0.04181	0.529	0.693
##	318	82	1	0.598 0.04195	0.521	0.686
##	332	81	1	0.590 0.04208	0.513	0.679
##	363	80	1	0.583 0.04219	0.506	0.672
##	381	79	1	0.576 0.04230	0.498	0.665
##	383	78	1	0.568 0.04240	0.491	0.658
##	390	77	2	0.554 0.04256	0.476	0.644
##	414	75	1	0.546 0.04263	0.469	0.636
##	418	74	1	0.539 0.04269	0.461	0.629
##	421	73	1	0.531 0.04273	0.454	0.622
##	422	72	1	0.524 0.04277	0.447	0.615
##	456	71	1	0.517 0.04280	0.439	0.608
##	466	70	1	0.509 0.04282	0.432	0.600
##	467	69	1	0.502 0.04283	0.425	0.593
##	481	68	1	0.494 0.04284	0.417	0.586
##	486	67	1	0.487 0.04283	0.410	0.579
##	487	66	1	0.480 0.04281	0.403	0.571
##	526	65	1	0.472 0.04278	0.396	0.564
##	606	63	1	0.465 0.04275	0.388	0.557
##	609	62	1	0.457 0.04272	0.381	0.549
##	625	61	1	0.450 0.04267	0.374	0.542
##	641	60	1	0.442 0.04261	0.366	0.534
##	662	59	1	0.435 0.04254	0.359	0.527
##	677	58	1	0.427 0.04247	0.352	0.519
##	704	57	1	0.420 0.04238	0.345	0.512
##	748	56	1	0.412 0.04228	0.337	0.504
##	1063	47	1	0.404 0.04228	0.329	0.496

```
## 1074 46 1 0.395 0.04226 0.320 0.487
## 2204 9 1 0.351 0.05587 0.257 0.479
```

2. How do patients in different disease groups or in different FAB classifications compare to each other with respect to other available baseline measurements?

```
baseline_vars <- c("age", "donorage", "waittime")</pre>
cat_vars <- c("male","cmv", "donormale", "donorcmv", "mtx")</pre>
# do hospital on its own since it is 4 categories
group_summary <- bmt %>%
  group_by(disgroup) %>%
  summarise(n = n(), across(all of(baseline vars), list(mean = mean, sd = sd, median = median), na.rm =
            across(all_of(cat_vars), ~ mean(. == 1, na.rm = TRUE) * 100, .names = "percent_{.col}"),
            percent_Ohio=mean(hospital == 1, na.rm = TRUE) * 100,
            percent_Melbourne=mean(hospital == 2, na.rm = TRUE) * 100,
            percent_Sydney=mean(hospital == 3, na.rm = TRUE) * 100,
            percent Philadelphia=mean(hospital == 4, na.rm = TRUE) * 100) %>%
  mutate(disgroup=case_when(disgroup==1 ~ "ALL",
                            disgroup==2 ~ "Low risk AML",
                            disgroup==3 ~ "High risk AML"))
## Warning: There was 1 warning in 'summarise()'.
## i In argument: 'across(...)'.
## i In group 1: 'disgroup = 1'.
## Caused by warning:
## ! The '...' argument of 'across()' is deprecated as of dplyr 1.1.0.
## Supply arguments directly to '.fns' through an anonymous function instead.
##
##
    # Previously
     across(a:b, mean, na.rm = TRUE)
##
##
##
     across(a:b, \x) mean(x, na.rm = TRUE))
##
kable(group_summary, caption = "Baseline Summary by Disease Group (disgroup)")
```

Table 1: Baseline Summary by Disease Group (disgroup)

```
disgroup age_ageasde_doctiedgenortegeorsdeittimeditaimeintispher.ceptedirepteccemperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomperdomper
```

```
# Continuous variables - ANOVA or Kruskal-Wallis
kruskal.test(age ~ disgroup, data = bmt)
##
   Kruskal-Wallis rank sum test
## data: age by disgroup
## Kruskal-Wallis chi-squared = 10.486, df = 2, p-value = 0.005284
kruskal.test(donorage ~ disgroup, data = bmt)
##
   Kruskal-Wallis rank sum test
##
##
## data: donorage by disgroup
## Kruskal-Wallis chi-squared = 2.4723, df = 2, p-value = 0.2905
kruskal.test(waittime ~ disgroup, data = bmt)
##
   Kruskal-Wallis rank sum test
## data: waittime by disgroup
## Kruskal-Wallis chi-squared = 26.105, df = 2, p-value = 2.145e-06
# Categorical variables - Chi-square test
table_male <- table(bmt$male, bmt$disgroup)</pre>
chisq.test(table_male)
##
## Pearson's Chi-squared test
##
## data: table_male
## X-squared = 2.226, df = 2, p-value = 0.3286
table_cmv <- table(bmt$cmv, bmt$disgroup)</pre>
chisq.test(table_cmv)
##
   Pearson's Chi-squared test
##
## data: table_cmv
## X-squared = 3.5512, df = 2, p-value = 0.1694
table_hospital <- table(bmt$hospital, bmt$disgroup)</pre>
fisher.test(table_hospital)
##
## Fisher's Exact Test for Count Data
```

```
##
## data: table_hospital
## p-value = 0.004719
## alternative hypothesis: two.sided
table_mtx <- table(bmt$mtx, bmt$disgroup)</pre>
chisq.test(table_mtx)
##
##
   Pearson's Chi-squared test
##
## data: table_mtx
## X-squared = 6.2014, df = 2, p-value = 0.04502
fab_summary <- bmt %>%
  group_by(fab) %>%
  summarise(n = n(), across(all_of(baseline_vars), list(mean = mean, sd = sd, median = median), na.rm =
            across(all_of(cat_vars), ~ mean(. == 1, na.rm = TRUE) * 100, .names = "percent_{.col}"),
            percent_Ohio=mean(hospital == 1, na.rm = TRUE) * 100,
            percent_Melbourne=mean(hospital == 2, na.rm = TRUE) * 100,
            percent_Sydney=mean(hospital == 3, na.rm = TRUE) * 100,
            percent Philadelphia=mean(hospital == 4, na.rm = TRUE) * 100) %>%
  mutate(fab=case_when(fab==0 ~ "Otherwise",
                            fab==1 ~ "FAB Grade 4 or 5 & AML"))
kable(fab_summary, caption = "Baseline Summary by FAB Classification (fab)")
```

Table 2: Baseline Summary by FAB Classification (fab)

```
fab
      n age ageasge doodiedgeordgeordgeittimedtaimeittisderceptediespdecemperdenterdebtreepter@hporkleiboofgadegPhiladelphia
Otherw 98e 28.597872731 29.00906692865 308.74726.9280
                                                     60.869578268904348.82689.78201173912173915652204348
FAB
      45\ \ 27.8\$8890365\ \ 26.95956132897\ \ \ 206.33353.8540 \qquad 53.333333663667.11117.776722292366667.11120100000
Grade
4 \text{ or}
5 &
AML
# Continuous variables - Wilcoxon test (since fab only has 2 levels)
wilcox.test(age ~ fab, data = bmt)
##
## Wilcoxon rank sum test with continuity correction
##
## data: age by fab
## W = 2075.5, p-value = 0.9817
## alternative hypothesis: true location shift is not equal to 0
wilcox.test(donorage ~ fab, data = bmt)
```

```
##
## Wilcoxon rank sum test with continuity correction
## data: donorage by fab
## W = 2212, p-value = 0.5164
## alternative hypothesis: true location shift is not equal to 0
wilcox.test(waittime ~ fab, data = bmt)
##
## Wilcoxon rank sum test with continuity correction
##
## data: waittime by fab
## W = 2244.5, p-value = 0.4244
## alternative hypothesis: true location shift is not equal to 0
# Categorical variables - Chi-square test
table_male_fab <- table(bmt$male, bmt$fab)</pre>
chisq.test(table_male_fab)
##
   Pearson's Chi-squared test with Yates' continuity correction
## data: table_male_fab
## X-squared = 0.43028, df = 1, p-value = 0.5119
table_cmv_fab <- table(bmt$cmv, bmt$fab)</pre>
chisq.test(table_cmv_fab)
##
## Pearson's Chi-squared test with Yates' continuity correction
## data: table_cmv_fab
## X-squared = 0.17943, df = 1, p-value = 0.6719
table_hospital_fab <- table(bmt$hospital, bmt$fab)</pre>
fisher.test(table_hospital_fab)
##
## Fisher's Exact Test for Count Data
## data: table_hospital_fab
## p-value = 0.2222
## alternative hypothesis: two.sided
table_mtx_fab <- table(bmt$mtx, bmt$fab)</pre>
chisq.test(table_mtx_fab)
##
## Pearson's Chi-squared test with Yates' continuity correction
##
## data: table mtx fab
## X-squared = 3.4444, df = 1, p-value = 0.06346
```

```
# table 1 by disease or FAB classification
bmt <- bmt %>%
  mutate(disgroupCat = factor(disgroup,
                               levels = c(1, 2, 3),
                               labels = c("All", "Low Risk AML", "High Risk AML")),
         maleCat = factor(male,
                           levels = c(0, 1),
                           labels = c("Female", "Male")),
         cmvCat = factor(cmv,
                          levels = c(0, 1),
                          labels = c("CMV Negative", "CMV Positive")),
         donormaleCat = factor(donormale,
                                levels = c(0, 1),
                                labels = c("Female Donor", "Male Donor")),
         donorcmvCat = factor(donorcmv,
                               levels = c(0, 1).
                               labels = c("CMV Negative Donor", "CMV Positive Donor")),
         fabCat = factor(fab,
                          levels = c(0, 1),
                          labels = c("Otherwise", "FAB Grade 4 or 5 and AML")),
         hospitalCat = factor(hospital,
                               levels = c(1, 2, 3, 4),
                               labels = c("OSU", "Alfred", "St. Vincent", "Hahnemann")),
         mtxCat = factor(mtx,
                          levels = c(0, 1),
                          labels = c("No", "Yes")),
         deltasCat = factor(deltas,
                             levels = c(0, 1),
                             labels = c("Alive", "Dead")),
         deltarCat = factor(deltar,
                             levels = c(0,1),
                             labels = c("Disease-free", "Relapse")),
         deltadfsCat = factor(deltadfs,
                             levels = c(0,1),
                             labels = c("Alive and Disease-free", "Dead or Relapsed")),
         deltaaCat = factor(deltaa,
                             levels = c(0,1),
                             labels = c("No aGVHD", "aGVHD")),
         deltapCat = factor(deltap,
                             levels = c(0,1),
                             labels = c("Not Recovered", "Recovered")))
label(bmt$deltarCat) <- "Replase"</pre>
label(bmt$deltasCat) <- "Death"</pre>
label(bmt$deltadfsCat) <- "Disease-free Survival"</pre>
label(bmt$deltaaCat) <- "aGVHD"</pre>
label(bmt$deltapCat) <- "Recovery of Normal Platelet Levels"</pre>
label(bmt$age) <- "Patient Age"</pre>
label(bmt$maleCat) <- "Patient Sex"</pre>
label(bmt$cmvCat) <- "Patient CMV Status"</pre>
label(bmt$donorage) <- "Donor Age"</pre>
label(bmt$donormaleCat) <- "Donor Sex"</pre>
label(bmt$donorcmvCat) <- "Donor CMV Status"</pre>
```

### 3. Are any of the measured baseline variables associated with differences in disease-free survival?

```
baseline_vars <- c("age", "maleCat", "cmvCat", "disgroupCat",</pre>
                   "donorage", "donormaleCat", "donorcmvCat",
                   "waittime", "hospitalCat", "mtxCat")
univariate_results <- lapply(baseline_vars, function(var) {</pre>
    formula <- as.formula(paste("dfs_surv ~", var))</pre>
    cox_model <- coxph(formula, data = bmt)</pre>
    result <- tidy(cox_model, conf.int = TRUE, exponentiate=TRUE) # Ensure confidence intervals are in
    result$variable <- var
    return(result)
})
univariate_results <- do.call(rbind, univariate_results)</pre>
colnames(univariate_results)
## [1] "term"
                   "estimate"
                               "std.error" "statistic" "p.value"
                                                                      "conf.low"
## [7] "conf.high" "variable"
univariate_results <- univariate_results[, c("variable", "term", "estimate", "conf.low", "conf.high", "
kable(univariate_results, digits = 3, caption = "Univariate Cox Regression Results for Disease-Free Sur
```

Table 3: Baseline Descriptive Statistics by Disease Group

	All	Low Risk AML	High Risk AML	Overall
	(N=38)	(N=54)	(N=45)	(N=137)
Replase				
Disease-free	26 (68.4%)	45 (83.3%)	24 (53.3%)	95~(69.3%)
Relapse	12 (31.6%)	9 (16.7%)	$21\ (46.7\%)$	42 (30.7%)
Disease-free Survival				
Alive and Disease-free	14 (36.8%)	29~(53.7%)	$11\ (24.4\%)$	54 (39.4%)
Dead or Relapsed	24 (63.2%)	25~(46.3%)	$34\ (75.6\%)$	83 (60.6%)
aGVHD				
No a $\operatorname{GVHD}$	29~(76.3%)	43~(79.6%)	39 (86.7%)	111 (81.0%)
aGVHD	9(23.7%)	$11\ (20.4\%)$	6~(13.3%)	26 (19.0%)
Death				
Alive	14 (36.8%)	31 (57.4%)	11 (24.4%)	56 (40.9%)
Dead	24~(63.2%)	23~(42.6%)	34 (75.6%)	81 (59.1%)
Recovery of Normal P	latelet Levels			
Not Recovered	4 (10.5%)	6 (11.1%)	7 (15.6%)	17 (12.4%)
Recovered	34~(89.5%)	48 (88.9%)	38 (84.4%)	120~(87.6%)
Patient Age				
Mean (SD)	24.4(7.30)	29.4 (8.76)	30.4 (11.2)	28.4 (9.56)
Median [Min, Max]	22.5 [15.0, 42.0]	29.5 [13.0, 50.0]	32.0 [7.00, 52.0]	28.0 [7.00, 52.0]
Donor Age				
Mean (SD)	26.8 (8.93)	28.1 (9.24)	29.9 (12.1)	28.3 (10.2)
Median [Min, Max]	26.0 [5.00, 48.0]	29.5 [12.0, 54.0]	29.0 [2.00, 56.0]	28.0 [2.00, 56.0]
Wait Time until Trans	splant (Days)			
Mean (SD)	477 (599)	138 (74.5)	269 (211)	275 (365)
Median [Min, Max]	200 [74.0, 2620]	120 [30.0, 450]	210 [24.0, 900]	178 [24.0, 2620]
Patient Sex				
Female	12 (31.6%)	24 (44.4%)	21 (46.7%)	57 (41.6%)
Male	26 (68.4%)	30 (55.6%)	24 (53.3%)	80 (58.4%)
Patient CMV Status				
CMV Negative	23~(60.5%)	28 (51.9%)	18 (40.0%)	69 (50.4%)
CMV Positive	15 (39.5%)	26 (48.1%)	27 (60.0%)	68 (49.6%)
Recruitment Center				
OSU	21~(55.3%)	27 (50.0%)	28~(62.2%)	76~(55.5%)
Alfred	8 (21.1%)	5 (9.3%)	4 (8.9%)	17 (12.4%)
St. Vincent	9~(23.7%)	7~(13.0%)	7~(15.6%)	23~(16.8%)
Hahnemann	0 (0%)	15~(27.8%)	6 (13.3%)	$21\ (15.3\%)$
Prophylactic Methotre				
No	$21\ (55.3\%)$	42 (77.8%)	$34 \ (75.6\%)$	97 (70.8%)
Yes	17 (44.7%)	12 (22.2%)	11 (24.4%)	40 (29.2%)

Table 4: Baseline Descriptive Statistics by FAB Classification

	Otherwise	FAB Grade 4 or 5 and AML $$	Overall
	(N=92)	(N=45)	(N=137)
Replase			
Disease-free	72~(78.3%)	23 (51.1%)	95~(69.3%)
Relapse	20~(21.7%)	22 (48.9%)	42 (30.7%)
Disease-free Survival			
Alive and Disease-free	44 (47.8%)	10 (22.2%)	54 (39.4%)
Dead or Relapsed	48 (52.2%)	35 (77.8%)	83~(60.6%)
aGVHD			
No a $\operatorname{GVHD}$	74 (80.4%)	37 (82.2%)	111 (81.0%)
aGVHD	18 (19.6%)	8 (17.8%)	26 (19.0%)
Death			
Alive	45 (48.9%)	11 (24.4%)	56 (40.9%)
Dead	47 (51.1%)	34 (75.6%)	81 (59.1%)
Recovery of Normal P	latelet Levels		
Not Recovered	12 (13.0%)	5 (11.1%)	17 (12.4%)
Recovered	80 (87.0%)	40 (88.9%)	120(87.6%)
Patient Age			
Mean (SD)	28.6 (9.48)	27.9 (9.81)	28.4 (9.56)
Median [Min, Max]	27.0 [13.0, 52.0]	28.0 [7.00, 50.0]	28.0 [7.00, 52.0]
Donor Age			
Mean (SD)	29.0 (9.67)	27.0 (11.1)	28.3 (10.2)
Median [Min, Max]	28.5 [5.00, 56.0]	28.0 [2.00, 48.0]	28.0 [2.00, 56.0]
Wait Time until Trans	splant (Days)		
Mean (SD)	309 (427)	206 (164)	275 (365)
Median [Min, Max]	180 [24.0, 2620]	150 [60.0, 780]	178 [24.0, 2620]
Patient Sex			
Female	36 (39.1%)	21 (46.7%)	57 (41.6%)
Male	56 (60.9%)	24 (53.3%)	80 (58.4%)
Patient CMV Status			
CMV Negative	48 (52.2%)	21 (46.7%)	69 (50.4%)
CMV Positive	44 (47.8%)	24 (53.3%)	68 (49.6%)
Recruitment Center			
OSU	48 (52.2%)	28 (62.2%)	76 (55.5%)
Alfred	14 (15.2%)	3 (6.7%)	17(12.4%)
St. Vincent	18 (19.6%)	5 (11.1%)	23 (16.8%)
Hahnemann	$12\ (13.0\%)$	9 (20.0%)	$21\ (15.3\%)$
Prophylactic Methotro	exate Use		
No	60~(65.2%)	37 (82.2%)	97 (70.8%)
Yes	32 (34.8%)	8 (17.8%)	40 (29.2%)

Table 5: Univariate Cox Regression Results for Disease-Free Survival

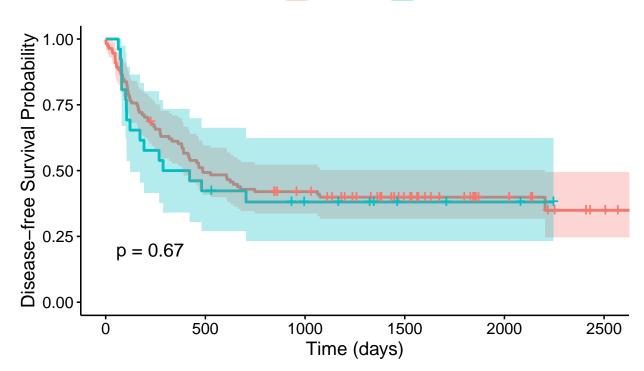
variable	term	estimate	conf.low	conf.high	p.value
age	age	1.011	0.988	1.035	0.338
maleCat	maleCatMale	0.795	0.514	1.228	0.301
cmvCat	cmvCatCMV Positive	1.167	0.759	1.796	0.482
disgroupCat	disgroupCatLow Risk AML	0.563	0.321	0.989	0.046
disgroupCat	disgroupCatHigh Risk AML	1.467	0.869	2.478	0.152
donorage	donorage	1.014	0.990	1.040	0.252
donormaleCat	donormaleCatMale Donor	0.991	0.633	1.552	0.970
donorcmvCat	donorcmvCatCMV Positive Donor	1.047	0.677	1.620	0.836
waittime	waittime	1.000	0.999	1.001	0.791
hospitalCat	hospitalCatAlfred	2.122	1.148	3.922	0.016
hospitalCat	hospitalCatSt. Vincent	0.912	0.495	1.681	0.768
hospitalCat	hospitalCatHahnemann	0.421	0.191	0.930	0.032
mtxCat	mtxCatYes	1.489	0.934	2.373	0.094

4. It is generally thought that aGVHD has an anti-leukemic effect. Based on the available data, is occurrence of aGVHD after transplantation associated with improved disease-free survival? Is it associated with a decreased risk of relapse? In view of this, do you consider aGVHD as an important prognostic event?

```
dfs_surv <- Surv(time = bmt$tdfs, event = bmt$deltadfs)</pre>
relapse_surv <- Surv(time = bmt$tdfs, event = bmt$deltar)</pre>
## univariate Cox for disease-free survival
cox_dfs_unadj <- coxph(dfs_surv ~ deltaa, data = bmt)</pre>
dfs_summary <- tidy(cox_dfs_unadj, conf.int = TRUE, exponentiate = TRUE)</pre>
dfs summary
## # A tibble: 1 x 7
## term estimate std.error statistic p.value conf.low conf.high
   <chr> <dbl> <dbl> <dbl> <dbl>
                                                    <dbl>
                                                               <dbl>
                         0.279
                                   0.428 0.668
                                                    0.653
                                                               1.94
              1.13
## 1 deltaa
km_dfs <- survfit(dfs_surv ~ deltaa, data = bmt)</pre>
ggsurvplot(km_dfs, conf.int = TRUE, pval = TRUE,
           xlab = "Time (days)",
           ylab = "Disease-free Survival Probability",
           legend.labs = c("No aGVHD", "aGVHD"),
           title = "Disease-free Survival by aGVHD Status")
```

### Disease-free Survival by aGVHD Status





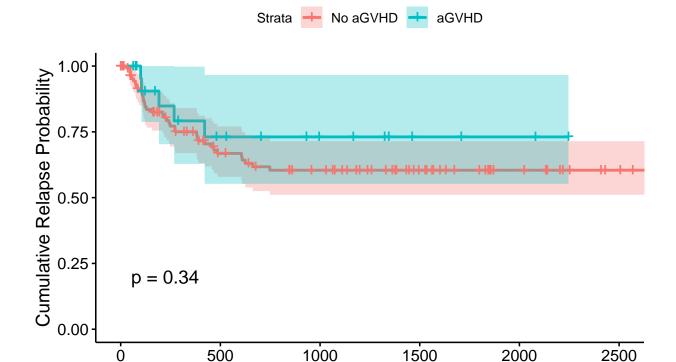
```
## multivariable Cox for dfs
cox_dfs_adj <- coxph(dfs_surv ~ deltaa + age + as.factor(hospital) + male, data = bmt)
dfs_summary_adj <- tidy(cox_dfs_adj, conf.int = T, exponentiate = T)
dfs_summary_adj</pre>
```

```
## # A tibble: 6 x 7
                           estimate std.error statistic p.value conf.low conf.high
     term
                                                                               <dbl>
##
     <chr>>
                              <dbl>
                                        <dbl>
                                                   <dbl>
                                                           <dbl>
                                                                    <dbl>
## 1 deltaa
                              1.24
                                       0.288
                                                   0.742 0.458
                                                                    0.704
                                                                               2.18
## 2 age
                              1.02
                                       0.0129
                                                   1.44
                                                          0.150
                                                                    0.993
                                                                               1.04
## 3 as.factor(hospital)2
                                                          0.0541
                                                                    0.989
                                                                               3.58
                              1.88
                                       0.328
                                                  1.93
## 4 as.factor(hospital)3
                              0.805
                                       0.325
                                                  -0.668 0.504
                                                                    0.425
                                                                               1.52
## 5 as.factor(hospital)4
                              0.342
                                       0.423
                                                  -2.54
                                                          0.0112
                                                                    0.149
                                                                               0.783
## 6 male
                              0.828
                                       0.234
                                                  -0.807 0.419
                                                                    0.524
                                                                               1.31
```

```
## univariate Cox for relapse
cox_relapse_unadj <- coxph(relapse_surv ~ deltaa, data = bmt)
relapse_summary <- tidy(cox_relapse_unadj, conf.int = TRUE, exponentiate=TRUE)
relapse_summary</pre>
```

```
## # A tibble: 1 x 7
##
            estimate std.error statistic p.value conf.low conf.high
                                     <dbl>
                                                                 <dbl>
##
     <chr>
               <dbl>
                          <dbl>
                                             <dbl>
                                                      <dbl>
## 1 deltaa
               0.638
                          0.477
                                   -0.944
                                             0.345
                                                      0.250
                                                                  1.62
```

### Relapse by aGVHD Status



```
## multivariable Cox for relapse
cox_relapse_adj <- coxph(relapse_surv ~ deltaa + age + as.factor(hospital) + male, data = bmt)
relapse_summary_adj <- tidy(cox_relapse_adj, conf.int = T, exponentiate = T)
relapse_summary_adj</pre>
```

Time (days)

```
## # A tibble: 6 x 7
##
     term
                           estimate std.error statistic p.value conf.low conf.high
##
     <chr>>
                              <dbl>
                                         <dbl>
                                                   <dbl>
                                                            <dbl>
                                                                     <dbl>
                                                                                <dbl>
## 1 deltaa
                              0.682
                                        0.491
                                                  -0.778
                                                            0.437
                                                                     0.260
                                                                                 1.79
                              1.01
                                        0.0182
                                                            0.557
                                                                     0.975
## 2 age
                                                   0.587
                                                                                 1.05
## 3 as.factor(hospital)2
                              1.21
                                        0.555
                                                   0.350
                                                            0.726
                                                                     0.409
                                                                                 3.60
## 4 as.factor(hospital)3
                                        0.413
                                                            0.808
                                                                     0.492
                                                                                 2.48
                              1.11
                                                   0.243
## 5 as.factor(hospital)4
                              0.588
                                        0.513
                                                  -1.04
                                                            0.300
                                                                     0.215
                                                                                 1.61
## 6 male
                              0.673
                                        0.320
                                                  -1.24
                                                            0.216
                                                                     0.359
                                                                                 1.26
```

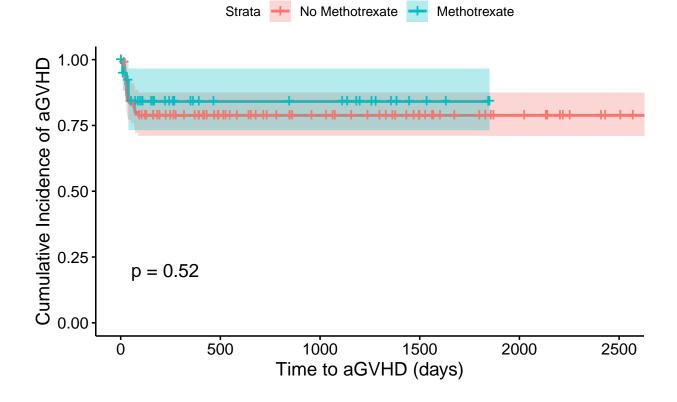
## 5. Among the patients who develop aGVHD, are any of the measured baseline factors associated with differences in disease-free survival?

Table 6: Univariate Cox Regression Results for DFS (aGVHD Patients Only)

variable	term	estimate	conf.low	conf.high	p.value
age	age	1.024	0.978	1.073	0.307
maleCat	maleCatMale	1.323	0.478	3.661	0.590
cmvCat	cmvCatCMV Positive	0.787	0.295	2.102	0.632
disgroupCat	disgroupCatLow Risk AML	1.450	0.424	4.966	0.554
disgroupCat	disgroupCatHigh Risk AML	3.854	1.022	14.531	0.046
donorage	donorage	1.072	0.996	1.153	0.063
donormaleCat	donormaleCatMale Donor	0.837	0.311	2.255	0.725
donorcmvCat	donorcmvCatCMV Positive Donor	1.878	0.647	5.453	0.247
waittime	waittime	1.000	1.000	1.001	0.375
hospitalCat	hospitalCatAlfred	1.147	0.251	5.239	0.859
hospitalCat	hospitalCatSt. Vincent	1.014	0.223	4.612	0.986
hospitalCat	hospitalCatHahnemann	0.118	0.015	0.929	0.042
mtxCat	mtxCatYes	1.718	0.551	5.350	0.351

6. Is prophylactic use of methotrexate associated with an increased or decreased risk of developing aGVHD? Provide an estimate of the survival function of time from transplant until onset of aGVHD separately for patients either administered methotrexate or not. In doing so, consider the importance of accounting for relevant confounding factors.

### Time to aGVHD by Prophylactice Methotrexate Use



## univariate Cox

cox\_mtx <- coxph(agvhd\_surv ~ mtx, data = bmt)</pre>

Table 7: Univariate Cox Regression: Methotrexate and aGVHD Risk

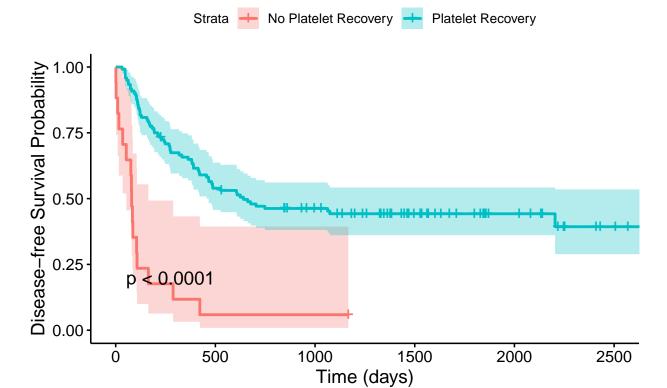
term	estimate	conf.low	conf.high	p.value
mtx	0.742	0.298	1.847	0.521

Table 8: Multivariable Cox Regression: Methotrexate and aGVHD Risk

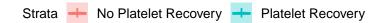
term	estimate	conf.low	conf.high	p.value
mtx	0.470	0.131	1.682	0.246
age	1.074	1.027	1.123	0.002
maleCatMale	0.882	0.390	1.996	0.764
disgroupCatLow Risk AML	0.528	0.177	1.580	0.254
disgroupCatHigh Risk AML	0.303	0.093	0.986	0.047
waittime	1.000	0.999	1.001	0.470
hospitalCatAlfred	1.632	0.316	8.417	0.558
hospitalCatSt. Vincent	NA	NA	NA	NA
hospital Cat Hahnemann	1.606	0.563	4.586	0.376

# 7. Based on the available data, is recovery of normal platelet levels associated with improved disease- free survival? Is it associated with a decreased risk of relapse?

### Disease-free Survival by Platelet Recovery



### Relapse by Platelet Recovery



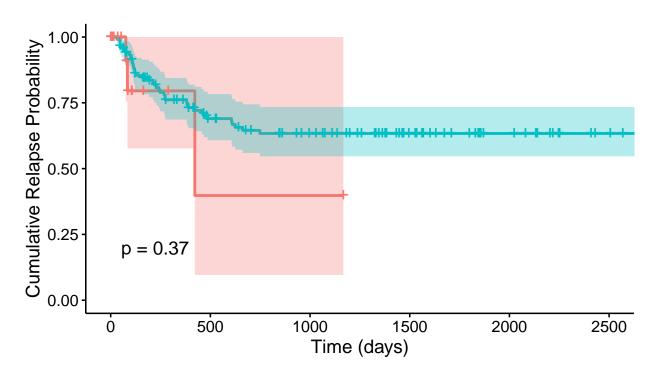


Table 9: Univariate Cox: Platelet Recovery and DFS

term	estimate	conf.low	conf.high	p.value
deltap	0.188	0.107	0.33	0

Table 10: Multivariable Cox: Platelet Recovery and DFS

term	estimate	conf.low	conf.high	p.value
deltap	0.256	0.138	0.476	0.000
age	1.017	0.992	1.044	0.189
as.factor(hospital)2	1.347	0.662	2.739	0.411
as.factor(hospital)3	0.869	0.453	1.667	0.672
as.factor(hospital)4	0.477	0.206	1.102	0.083
as.factor(disgroup)2	0.702	0.375	1.312	0.267
as.factor(disgroup)3	1.496	0.835	2.680	0.176
male	0.928	0.580	1.484	0.756

Table 11: Univariate Cox: Platelet Recovery and Relapse Risk

term	estimate	conf.low	conf.high	p.value
deltap	0.583	0.178	1.916	0.374

Table 12: Multivariable Cox: Platelet Recovery and DFS

term	estimate	conf.low	conf.high	p.value
deltap	0.895	0.256	3.134	0.863
age	0.998	0.960	1.038	0.937
as.factor(hospital)2	1.100	0.359	3.374	0.868
as.factor(hospital)3	1.324	0.575	3.051	0.509
as.factor(hospital)4	0.783	0.274	2.241	0.649
as.factor(disgroup)2	0.415	0.163	1.057	0.065
as.factor(disgroup)3	1.836	0.821	4.106	0.139

term	estimate	conf.low	conf.high	p.value
male	0.637	0.335	1.213	0.170