Does TDT affect prognosis of Acute Myeloid Leukemia (AML)

This document will serve as a hub for all the charts, tests, and conclusions made for this experiment based on our AML Data. The background of this study will be in the TDT-AML document.

Pre-processing

We loaded full-set data and check for missing data.

```
# Load required libraries
library(survival)
library(ggplot2)
library(rms)

# Load packages
library(readxl)
library(survival)
library(survminer)
library(rms)

# Read the csv file
data <- read.csv("Complete TDT AML Data.csv", header = TRUE)

new_colnames <- c(
  "PatientID", "Age", "Male", "ECOG", "HCTCI", "ENLrisk", "AMLtype", "CytoredAgent",
  "TDT", "WBC", "LDH", "BMblast", "Karyotype", "RxRegimen",
  "SCT", "DelayCause", "TxResponse", "SurvivalEFS", "SurvivalOS", "EFS"
)

# Apply the new column names to the dataset
colnames(data) <- new_colnames
```

Descriptive Statistics

This section will include the calculations that produces 3 tables for summary statistics:

1) Patient and treatment characteristics of all 10 patients and according to TDT groups.
2) Treatment outcomes CR/CRi, ED, and 2-year OS of all patients stratified for TDT groups and age less than or equal to 60 years vs $>$ 60 years.
3) ORs for the achievement of CR/CRi, ED, HRs for OS according to the linear multivariable logistic regression models.

Table 1: Patient and treatment characteristics

```r
library(dplyr)
library(knitr)

# Useful functions for calculations:

calculate_mean_sd <- function(dataset, variable_name) {
  variable <- dataset[[variable_name]]
  paste(round(mean(variable, na.rm = TRUE), 2),
        "(", round(sd(variable, na.rm = TRUE), 2), ")",
        sep = "")
}

calculate_median_IQR <- function(dataset, variable_name) {
  variable <- dataset[[variable_name]]
  paste(round(median(variable, na.rm = TRUE), 2),
        "(", round(IQR(variable, na.rm = TRUE), 2), ")",
        sep = "")
}

calculate_percentage <- function(dataset, condition_column, condition_value) {
  condition <- dataset[[condition_column]] == condition_value
  total_rows <- nrow(dataset)
  count <- sum(condition, na.rm = TRUE)
  paste(count, "/", total_rows, " (",
        round(count * 100 / total_rows, 2), ")",
        sep = "")
}

calculate_frequency <- function(dataset, column_name, keyword) {
  column <- dataset[[column_name]]
  count <- sum(grepl(keyword, column, ignore.case = TRUE), na.rm = TRUE)
  paste(count, "/", length(column), " (",
        round(count * 100 / length(column), 2), ")",
        sep = "")
}

# Patient diagnostics:
age_mean_sd <- calculate_mean_sd(data, "Age")
age_median_IQR <- calculate_median_IQR(data, "Age")
female_sex <- calculate_percentage(data, "Male", 0)


ecog_status <- paste(sum(data$ECOG <= 1), "/", nrow(data), " (",
                     sum(data$ECOG <= 1)*100/nrow(data),  ")" , sep = "")

hctci_score <- calculate_percentage(data, "HCTCI", 0)

enl_favorable <- calculate_frequency(data, "ENLrisk","favorable")
enl_intermediate <- calculate_frequency(data, "ENLrisk","intermediate")
enl_adverse <- calculate_frequency(data, "ENLrisk","adverse")
enl_unknown <- calculate_frequency(data, "ENLrisk","unknown")

aml_denovo <- calculate_frequency(data, "AMLtype","de novo")
aml_s <- calculate_frequency(data, "AMLtype","sAML")
aml_t <- calculate_frequency(data, "AMLtype","unknown")
```

```r
cytor_hydro <- calculate_frequency(data, "CytoredAgent", "hydroxyurea")
cytor_cytarabine <- calculate_frequency(data, "CytoredAgent", "cytarabine")
cytor_none <- calculate_frequency(data, "CytoredAgent", "no cytoreduction given")

tdt_mean_sd <- calculate_mean_sd(data, "TDT")
tdt_median_IQR <- calculate_median_IQR(data, "TDT")

wbc_mean_sd <- calculate_mean_sd(data, "WBC")
wbc_median_IQR <- calculate_median_IQR(data, "WBC")

ldh_mean_sd <- calculate_mean_sd(data, "LDH")
ldh_median_IQR <- calculate_median_IQR(data, "LDH")

bone_mean_sd <-  calculate_mean_sd(data, "BMblast")
bone_median_IQR <- calculate_median_IQR(data, "BMblast")

karyo_abnormal <- calculate_frequency(data, "Karyotype", "no growth")
karyo_normal <- calculate_frequency(data, "Karyotype", "normal")
karyo_undone <- calculate_frequency(data, "Karyotype", "not done")

regimen_37 <- calculate_percentage(data, "RxRegimen", "3+7")
regimen_hidac <- calculate_percentage(data, "RxRegimen", "HiDAC + Doxo")
regimen_ham <- calculate_percentage(data, "RxRegimen", "HAM")

allogenic_CR1 <- calculate_frequency(data, "SCT", "CR1")
allogenic_salvage <- calculate_frequency(data, "SCT", "salvage")
allogenic_none <- calculate_frequency(data, "SCT", "not done")

delay_infection <- calculate_frequency(data, "DelayCause", "infection")
delay_nutritional <- calculate_frequency(data, "DelayCause", "nutritional upbuilding")
delay_cost <- calculate_frequency(data, "DelayCause", "cost of treatment")
delay_access <- calculate_frequency(data, "DelayCause", "lack of access")
delay_unfamiliar <- calculate_frequency(data, "DelayCause", "unfamiliarity to treatment")
delay_pregnancy <- calculate_frequency(data, "DelayCause", "pregnancy")
delay_diagdilemma <- calculate_frequency(data, "DelayCause", "diagnostic dilemma")
delay_unknown <- calculate_frequency(data, "DelayCause", "unknown")
delay_none <- calculate_frequency(data, "DelayCause", "none")

# Patient diagnostics 0-30:
data_30 <- data %>% filter(!is.na(TDT) & TDT >= 0 & TDT <= 30)

age_mean_sd_30 <- calculate_mean_sd(data_30, "Age")
age_median_IQR_30 <- calculate_median_IQR(data_30, "Age")
female_sex_30 <- calculate_percentage(data_30, "Male", 0)

ecog_status_30 <- paste(sum(data_30$ECOG <= 1), "/", nrow(data_30), " (",
                    sum(data_30$ECOG <= 1)*100/nrow(data_30),  ")" , sep = "")

hctci_score_30 <- calculate_percentage(data_30, "HCTCI", 0)

enl_favorable_30 <- calculate_frequency(data_30, "ENLrisk","favorable")
enl_intermediate_30 <- calculate_frequency(data_30, "ENLrisk","intermediate")
enl_adverse_30 <- calculate_frequency(data_30, "ENLrisk","adverse")
enl_unknown_30 <- calculate_frequency(data_30, "ENLrisk","unknown")

aml_denovo_30 <- calculate_frequency(data_30, "AMLtype","de novo")
```

```r
aml_s_30 <- calculate_frequency(data_30, "AMLtype","sAML")
aml_t_30 <- calculate_frequency(data_30, "AMLtype","unknown")

cytor_hydro_30 <- calculate_frequency(data_30, "CytoredAgent", "hydroxyurea")
cytor_cytarabine_30 <- calculate_frequency(data_30, "CytoredAgent", "cytarabine")
cytor_none_30 <- calculate_frequency(data_30, "CytoredAgent", "no cytoreduction given")

tdt_mean_sd_30 <- calculate_mean_sd(data_30, "TDT")
tdt_median_IQR_30 <- calculate_median_IQR(data_30, "TDT")

wbc_mean_sd_30 <- calculate_mean_sd(data_30, "WBC")
wbc_median_IQR_30 <- calculate_median_IQR(data_30, "WBC")

ldh_mean_sd_30 <- calculate_mean_sd(data_30, "LDH")
ldh_median_IQR_30 <- calculate_median_IQR(data_30, "LDH")

bone_mean_sd_30 <-  calculate_mean_sd(data_30, "BMblast")
bone_median_IQR_30 <- calculate_median_IQR(data_30, "BMblast")

karyo_abnormal_30 <- calculate_frequency(data_30, "Karyotype", "no growth")
karyo_normal_30 <- calculate_frequency(data_30, "Karyotype", "normal")
karyo_undone_30 <- calculate_frequency(data_30, "Karyotype", "not done")

regimen_37_30 <- calculate_percentage(data_30, "RxRegimen", "3+7")
regimen_hidac_30 <- calculate_percentage(data_30, "RxRegimen", "HiDAC + Doxo")
regimen_ham_30 <- calculate_percentage(data_30, "RxRegimen", "HAM")

allogenic_CR1_30 <- calculate_frequency(data_30, "SCT", "CR1")
allogenic_salvage_30 <- calculate_frequency(data_30, "SCT", "salvage")
allogenic_none_30 <- calculate_frequency(data_30, "SCT", "not done")

delay_infection_30 <- calculate_frequency(data_30, "DelayCause", "infection")
delay_nutritional_30 <- calculate_frequency(data_30, "DelayCause", "nutritional upbuilding")
delay_cost_30 <- calculate_frequency(data_30, "DelayCause", "cost of treatment")
delay_access_30 <- calculate_frequency(data_30, "DelayCause", "lack of access")
delay_unfamiliar_30 <- calculate_frequency(data_30, "DelayCause", "unfamiliarity to treatment")
delay_pregnancy_30 <- calculate_frequency(data_30, "DelayCause", "pregnancy")
delay_diagdilemma_30 <- calculate_frequency(data_30, "DelayCause", "diagnostic dilemma")
delay_unknown_30 <- calculate_frequency(data_30, "DelayCause", "unknown")
delay_none_30 <- calculate_frequency(data_30, "DelayCause", "none")

# Patient diagnostics 31-60:
data_60 <- data %>% filter(!is.na(TDT) & TDT >= 31 & TDT <= 60)

age_mean_sd_60 <- calculate_mean_sd(data_60, "Age")
age_median_IQR_60 <- calculate_median_IQR(data_60, "Age")
female_sex_60 <- calculate_percentage(data_60, "Male", 0)

ecog_status_60 <- paste(sum(data_60$ECOG <= 1), "/", nrow(data_60), " (",
                    sum(data_60$ECOG <= 1)*100/nrow(data_60),  ")" , sep = "")

hctci_score_60 <- calculate_percentage(data_60, "HCTCI", 0)

enl_favorable_60 <- calculate_frequency(data_60, "ENLrisk","favorable")
enl_intermediate_60 <- calculate_frequency(data_60, "ENLrisk","intermediate")
enl_adverse_60 <- calculate_frequency(data_60, "ENLrisk","adverse")
```

```r
enl_unknown_60 <- calculate_frequency(data_60, "ENLrisk","unknown")

aml_denovo_60 <- calculate_frequency(data_60, "AMLtype","de novo")
aml_s_60 <- calculate_frequency(data_60, "AMLtype","sAML")
aml_t_60 <- calculate_frequency(data_60, "AMLtype","unknown")

cytor_hydro_60 <- calculate_frequency(data_60, "CytoredAgent", "hydroxyurea")
cytor_cytarabine_60 <- calculate_frequency(data_60, "CytoredAgent", "cytarabine")
cytor_none_60 <- calculate_frequency(data_60, "CytoredAgent", "no cytoreduction given")

tdt_mean_sd_60 <- calculate_mean_sd(data_60, "TDT")
tdt_median_IQR_60 <- calculate_median_IQR(data_60, "TDT")

wbc_mean_sd_60 <- calculate_mean_sd(data_60, "WBC")
wbc_median_IQR_60 <- calculate_median_IQR(data_60, "WBC")

ldh_mean_sd_60 <- calculate_mean_sd(data_60, "LDH")
ldh_median_IQR_60 <- calculate_median_IQR(data_60, "LDH")

bone_mean_sd_60 <-  calculate_mean_sd(data_60, "BMblast")
bone_median_IQR_60 <- calculate_median_IQR(data_60, "BMblast")

karyo_abnormal_60 <- calculate_frequency(data_60, "Karyotype", "no growth")
karyo_normal_60 <- calculate_frequency(data_60, "Karyotype", "normal")
karyo_undone_60 <- calculate_frequency(data_60, "Karyotype", "not done")

regimen_37_60 <- calculate_percentage(data_60, "RxRegimen", "3+7")
regimen_hidac_60 <- calculate_percentage(data_60, "RxRegimen", "HiDAC + Doxo")
regimen_ham_60 <- calculate_percentage(data_60, "RxRegimen", "HAM")

allogenic_CR1_60 <- calculate_frequency(data_60, "SCT", "CR1")
allogenic_salvage_60 <- calculate_frequency(data_60, "SCT", "salvage")
allogenic_none_60 <- calculate_frequency(data_60, "SCT", "not done")

delay_infection_60 <- calculate_frequency(data_60, "DelayCause", "infection")
delay_nutritional_60 <- calculate_frequency(data_60, "DelayCause", "nutritional upbuilding")
delay_cost_60 <- calculate_frequency(data_60, "DelayCause", "cost of treatment")
delay_access_60 <- calculate_frequency(data_60, "DelayCause", "lack of access")
delay_unfamiliar_60 <- calculate_frequency(data_60, "DelayCause", "unfamiliarity to treatment")
delay_pregnancy_60 <- calculate_frequency(data_60, "DelayCause", "pregnancy")
delay_diagdilemma_60 <- calculate_frequency(data_60, "DelayCause", "diagnostic dilemma")
delay_unknown_60 <- calculate_frequency(data_60, "DelayCause", "unknown")
delay_none_60 <- calculate_frequency(data_60, "DelayCause", "none")

# Patient diagnostics > 60:
data_big60 <- data %>% filter(!is.na(TDT) & TDT >= 61)

age_mean_sd_big60 <- calculate_mean_sd(data_big60, "Age")
age_median_IQR_big60 <- calculate_median_IQR(data_big60, "Age")
female_sex_big60 <- calculate_percentage(data_big60, "Male", 0)

ecog_status_big60 <- paste(sum(data_big60$ECOG <= 1), "/", nrow(data_big60), " (",
                     sum(data_big60$ECOG <= 1)*100/nrow(data_big60),  ")" , sep = "")

hctci_score_big60 <- calculate_percentage(data_big60, "HCTCI", 0)
```

```r
enl_favorable_big60 <- calculate_frequency(data_big60, "ENLrisk","favorable")
enl_intermediate_big60 <- calculate_frequency(data_big60, "ENLrisk","intermediate")
enl_adverse_big60 <- calculate_frequency(data_big60, "ENLrisk","adverse")
enl_unknown_big60 <- calculate_frequency(data_big60, "ENLrisk","unknown")

aml_denovo_big60 <- calculate_frequency(data_big60, "AMLtype","de novo")
aml_s_big60 <- calculate_frequency(data_big60, "AMLtype","sAML")
aml_t_big60 <- calculate_frequency(data_big60, "AMLtype","unknown")

cytor_hydro_big60 <- calculate_frequency(data_big60, "CytoredAgent", "hydroxyurea")
cytor_cytarabine_big60 <- calculate_frequency(data_big60, "CytoredAgent", "cytarabine")
cytor_none_big60 <- calculate_frequency(data_big60, "CytoredAgent", "no cytoreduction given")

tdt_mean_sd_big60 <- calculate_mean_sd(data_big60, "TDT")
tdt_median_IQR_big60 <- calculate_median_IQR(data_big60, "TDT")

wbc_mean_sd_big60 <- calculate_mean_sd(data_big60, "WBC")
wbc_median_IQR_big60 <- calculate_median_IQR(data_big60, "WBC")

ldh_mean_sd_big60 <- calculate_mean_sd(data_big60, "LDH")
ldh_median_bigIQR_60 <- calculate_median_IQR(data_big60, "LDH")

bone_mean_sd_big60 <-  calculate_mean_sd(data_big60, "BMblast")
bone_median_IQR_big60 <- calculate_median_IQR(data_big60, "BMblast")

karyo_abnormal_big60 <- calculate_frequency(data_big60, "Karyotype", "no growth")
karyo_normal_big60 <- calculate_frequency(data_big60, "Karyotype", "normal")
karyo_undone_big60 <- calculate_frequency(data_big60, "Karyotype", "not done")

regimen_37_big60 <- calculate_percentage(data_big60, "RxRegimen", "3+7")
regimen_hidac_big60 <- calculate_percentage(data_big60, "RxRegimen", "HiDAC + Doxo")
regimen_ham_big60 <- calculate_percentage(data_big60, "RxRegimen", "HAM")

allogenic_CR1_big60 <- calculate_frequency(data_big60, "SCT", "CR1")
allogenic_salvage_big60 <- calculate_frequency(data_big60, "SCT", "salvage")
allogenic_none_big60 <- calculate_frequency(data_big60, "SCT", "not done")

delay_infection_big60 <- calculate_frequency(data_big60, "DelayCause", "infection")
delay_nutritional_big60 <- calculate_frequency(data_big60, "DelayCause", "nutritional upbuilding")
delay_cost_big60 <- calculate_frequency(data_big60, "DelayCause", "cost of treatment")
delay_access_big60 <- calculate_frequency(data_big60, "DelayCause", "lack of access")
delay_unfamiliar_big60 <- calculate_frequency(data_big60, "DelayCause", "unfamiliarity to treatment")
delay_pregnancy_big60 <- calculate_frequency(data_big60, "DelayCause", "pregnancy")
delay_diagdilemma_big60 <- calculate_frequency(data_big60, "DelayCause", "diagnostic dilemma")
delay_unknown_big60 <- calculate_frequency(data_big60, "DelayCause", "unknown")
delay_none_big60 <- calculate_frequency(data_big60, "DelayCause", "none")
```

Create the Table

```r
# Adding indent:
add_indent <- function(text) {
  indent = "      "
  paste(indent, text, sep = "")
}
```

```r
# Create the data frame
table_data <- data.frame(
  Parameter = c("Age at initial diagnosis (years)",
                  add_indent("Mean (SD)"),
                  add_indent("Median (IQR)"),
                "Female sex, no./no.available (%)",
                "ECOG status 0-1, no./no.available (%) ",
                "HCT-CI score 0-2, no./no.available (%)",
                "ENL Risk 2022 Group, no./no.available (%)",
                  add_indent("Favorable"),
                  add_indent("Intermediate"),
                  add_indent("Adverse"),
                  add_indent("Unknown"),
                "AML type, no./no. available (%)",
                  add_indent("De novo AML"),
                  add_indent("sAML"),
                  add_indent("unknown"),
                "Cytoreductive pretreatment, no./no. available (%)",
                  add_indent("Hydroxyurea"),
                  add_indent("Cytarabine"),
                  add_indent("None given"),
                "TDT, d",
                  add_indent("Mean (SD)"),
                  add_indent("Median (IQR)"),
                "WBC, x10^9/L",
                  add_indent("Mean (SD)"),
                  add_indent("Median (IQR)"),
                "LDH (U/L)",
                  add_indent("Mean (SD)"),
                  add_indent("Median (IQR)"),
                "Bone marrow blasts (%)",
                  add_indent("Mean (SD)"),
                  add_indent("Median (IQR)"),
                "Karyotype, no./no. available (%)",
                  add_indent("No growth"),
                  add_indent("Normal"),
                  add_indent("Not Done"),
                "Treatment regimen (%)",
                  add_indent("H7+3"),
                  add_indent("HIDAC +/- Doxo"),
                  add_indent("HAM"),
                "Allogeneic SCT, no./no. available (%)",
                  add_indent("AlloSCT in CR1"),
                  add_indent("AlloSCT salvage"),
                  add_indent("Not done"),
                "Cause of delay of treatment, no./no. available (%)",
                  add_indent("Infection"),
                  add_indent("Nutritional upbuilding"),
                  add_indent("Cost of treatment"),
                  add_indent("Lack of access"),
                  add_indent("Unfamiliarity to Treatment"),
                  add_indent("Pregnancy"),
                  add_indent("Diagnostic Dilemma"),
                  add_indent("Unknown"),
                  add_indent("No Treatment Delay")
                ),
```

```
  All_patients =  c("",
                    age_mean_sd,
                    age_median_IQR,
                  female_sex,
                  ecog_status,
                  hctci_score,
                  "",
                    enl_favorable,
                    enl_intermediate,
                    enl_adverse,
                    enl_unknown,
                  "",
                    aml_denovo,
                    aml_s,
                    aml_t,
                  "",
                    cytor_hydro,
                    cytor_cytarabine,
                    cytor_none,
                  "",
                    tdt_mean_sd,
                    tdt_median_IQR,
                  "",
                    wbc_mean_sd,
                    wbc_median_IQR,
                  "",
                    ldh_mean_sd,
                    ldh_median_IQR,
                  "",
                    bone_mean_sd,
                    bone_median_IQR,
                  "",
                    karyo_abnormal,
                    karyo_normal,
                    karyo_undone,
                  "",
                    regimen_37,
                    regimen_hidac,
                    regimen_ham,
                  "",
                    allogenic_CR1,
                    allogenic_salvage,
                    allogenic_none,
                  "",
                    delay_infection,
                    delay_nutritional,
                    delay_cost,
                    delay_access,
                    delay_unfamiliar,
                    delay_pregnancy,
                    delay_diagdilemma,
                    delay_unknown,
                    delay_none
                  ),
     TDT_0_30 = c("",
                    age_mean_sd_30,
```

```
                   age_median_IQR_30,
                 female_sex_30,
                 ecog_status_30,
                 hctci_score_30,
                 "",
                   enl_favorable_30,
                   enl_intermediate_30,
                   enl_adverse_30,
                   enl_unknown_30,
                 "",
                   aml_denovo_30,
                   aml_s_30,
                   aml_t_30,
                 "",
                   cytor_hydro_30,
                   cytor_cytarabine_30,
                   cytor_none_30,
                 "",
                   tdt_mean_sd_30,
                   tdt_median_IQR_30,
                 "",
                   wbc_mean_sd_30,
                   wbc_median_IQR_30,
                 "",
                   ldh_mean_sd_30,
                   ldh_median_IQR_30,
                 "",
                   bone_mean_sd_30,
                   bone_median_IQR_30,
                 "",
                   karyo_abnormal_30,
                   karyo_normal_30,
                   karyo_undone_30,
                 "",
                   regimen_37_30,
                   regimen_hidac_30,
                   regimen_ham_30,
                 "",
                   allogenic_CR1_30,
                   allogenic_salvage_30,
                   allogenic_none_30,
                 "",
                   delay_infection_30,
                   delay_nutritional_30,
                   delay_cost_30,
                   delay_access_30,
                   delay_unfamiliar_30,
                   delay_pregnancy_30,
                   delay_diagdilemma_30,
                   delay_unknown_30,
                   delay_none_30
                 ),
TDT_31_60 = c("",
                   age_mean_sd_60,
                   age_median_IQR_60,
                 female_sex_60,
```

```
                  ecog_status_60,
                  hctci_score_60,
                  "",
                     enl_favorable_60,
                     enl_intermediate_60,
                     enl_adverse_60,
                     enl_unknown_60,
                  "",
                     aml_denovo_60,
                     aml_s_60,
                     aml_t_60,
                  "",
                     cytor_hydro_60,
                     cytor_cytarabine_60,
                     cytor_none_60,
                  "",
                     tdt_mean_sd_60,
                     tdt_median_IQR_60,
                  "",
                     wbc_mean_sd_60,
                     wbc_median_IQR_60,
                  "",
                     ldh_mean_sd_60,
                     ldh_median_IQR_60,
                  "",
                     bone_mean_sd_60,
                     bone_median_IQR_60,
                  "",
                     karyo_abnormal_60,
                     karyo_normal_60,
                     karyo_undone_60,
                  "",
                     regimen_37_60,
                     regimen_hidac_60,
                     regimen_ham_60,
                  "",
                     allogenic_CR1_60,
                     allogenic_salvage_60,
                     allogenic_none_60,
                  "",
                     delay_infection_60,
                     delay_nutritional_60,
                     delay_cost_60,
                     delay_access_60,
                     delay_unfamiliar_60,
                     delay_pregnancy_60,
                     delay_diagdilemma_60,
                     delay_unknown_60,
                     delay_none_60
                  ),
TDT_61_inf     = c("",
                     age_mean_sd_big60,
                     age_median_IQR_big60,
                  female_sex_big60,
                  ecog_status_big60,
                  hctci_score_big60,
```

```
                    "",
                       enl_favorable_big60,
                       enl_intermediate_big60,
                       enl_adverse_big60,
                       enl_unknown_big60,
                    "",
                       aml_denovo_big60,
                       aml_s_big60,
                       aml_t_big60,
                    "",
                       cytor_hydro_big60,
                       cytor_cytarabine_big60,
                       cytor_none_big60,
                    "",
                       tdt_mean_sd_60,
                       tdt_median_IQR_60,
                    "",
                       wbc_mean_sd_60,
                       wbc_median_IQR_60,
                    "",
                       ldh_mean_sd_60,
                       ldh_median_IQR_60,
                    "",
                       bone_mean_sd_big60,
                       bone_median_IQR_big60,
                    "",
                       karyo_abnormal_big60,
                       karyo_normal_big60,
                       karyo_undone_big60,
                    "",
                       regimen_37_big60,
                       regimen_hidac_big60,
                       regimen_ham_big60,
                    "",
                       allogenic_CR1_big60,
                       allogenic_salvage_big60,
                       allogenic_none_big60,
                    "",
                       delay_infection_big60,
                       delay_nutritional_big60,
                       delay_cost_big60,
                       delay_access_big60,
                       delay_unfamiliar_big60,
                       delay_pregnancy_big60,
                       delay_diagdilemma_big60,
                       delay_unknown_big60,
                       delay_none_big60
                    )
)

# Format the table using kable
kable(table_data, format = "markdown", align = "l")
```

Parameter	All_patients	TDT_0_30	TDT_31_60	TDT_61_inf
Age at initial diagnosis (years)				

Parameter	All_patients	TDT_0_30	TDT_31_60	TDT_61_inf
Mean (SD)	37.35(12.2)	36.57(12.66)	40.88(12.02)	35.11(9.71)
Median (IQR)	37(18.75)	35(18.5)	44(12.75)	37(7)
Female sex, no./no.available (%)	40/72 (55.56)	22/47 (46.81)	14/16 (87.5)	4/9 (44.44)
ECOG status 0-1, no./no.available (%)	72/72 (100)	47/47 (100)	16/16 (100)	9/9 (100)
HCT-CI score 0-2, no./no.available (%)	69/72 (95.83)	46/47 (97.87)	16/16 (100)	7/9 (77.78)
ENL Risk 2022 Group, no./no.available (%)				
Favorable	3/72 (4.17)	2/47 (4.26)	0/16 (0)	1/9 (11.11)
Intermediate	27/72 (37.5)	13/47 (27.66)	9/16 (56.25)	5/9 (55.56)
Adverse	2/72 (2.78)	2/47 (4.26)	0/16 (0)	0/9 (0)
Unknown	40/72 (55.56)	30/47 (63.83)	7/16 (43.75)	3/9 (33.33)
AML type, no./no. available (%)				
De novo AML	68/72 (94.44)	44/47 (93.62)	16/16 (100)	8/9 (88.89)
sAML	2/72 (2.78)	2/47 (4.26)	0/16 (0)	0/9 (0)
unknown	2/72 (2.78)	1/47 (2.13)	0/16 (0)	1/9 (11.11)
Cytoreductive pretreatment, no./no. available (%)				
Hydroxyurea	29/72 (40.28)	22/47 (46.81)	4/16 (25)	3/9 (33.33)
Cytarabine	13/72 (18.06)	10/47 (21.28)	2/16 (12.5)	1/9 (11.11)
None given	41/72 (56.94)	24/47 (51.06)	11/16 (68.75)	6/9 (66.67)
TDT, d				
Mean (SD)	33.56(35.41)	16(9.03)	42.5(9.49)	42.5(9.49)
Median (IQR)	26.5(27.5)	15(17.5)	42(17.75)	42(17.75)
WBC, x10^9/L				
Mean (SD)	51.74(78.87)	64.03(89.41)	22.6(37.63)	22.6(37.63)
Median (IQR)	15.66(55.55)	21.92(74.8)	11.65(17.88)	11.65(17.88)
LDH (U/L)				
Mean (SD)	726.23(792.2)	841.05(932.39)	461.19(287.11)	461.19(287.11)
Median (IQR)	487(601)	573(610.25)	334(258.5)	334(258.5)
Bone marrow blasts (%)				
Mean (SD)	50.83(21.28)	55.65(19.94)	43.69(22.5)	38.37(19.25)
Median (IQR)	52.67(39.23)	56.52(28.7)	45.52(34.07)	30(18.61)
Karyotype, no./no. available (%)				
No growth	38/72 (52.78)	27/47 (57.45)	9/16 (56.25)	2/9 (22.22)
Normal	25/72 (34.72)	12/47 (25.53)	7/16 (43.75)	6/9 (66.67)
Not Done	4/72 (5.56)	3/47 (6.38)	0/16 (0)	1/9 (11.11)
Treatment regimen (%)				
H7+3	70/72 (97.22)	45/47 (95.74)	16/16 (100)	9/9 (100)
HIDAC +/- Doxo	2/72 (2.78)	2/47 (4.26)	0/16 (0)	0/9 (0)
HAM	0/72 (0)	0/47 (0)	0/16 (0)	0/9 (0)
Allogeneic SCT, no./no. available (%)				
AlloSCT in CR1	0/72 (0)	0/47 (0)	0/16 (0)	0/9 (0)
AlloSCT salvage	0/72 (0)	0/47 (0)	0/16 (0)	0/9 (0)
Not done	72/72 (100)	47/47 (100)	16/16 (100)	9/9 (100)
Cause of delay of treatment, no./no. available (%)				

Parameter	All_patients	TDT_0_30	TDT_31_60	TDT_61_inf
Infection	22/72 (30.56)	14/47 (29.79)	6/16 (37.5)	2/9 (22.22)
Nutritional upbuilding	0/72 (0)	0/47 (0)	0/16 (0)	0/9 (0)
Cost of treatment	16/72 (22.22)	8/47 (17.02)	5/16 (31.25)	3/9 (33.33)
Lack of access	15/72 (20.83)	7/47 (14.89)	5/16 (31.25)	3/9 (33.33)
Unfamiliarity to Treatment	2/72 (2.78)	1/47 (2.13)	0/16 (0)	1/9 (11.11)
Pregnancy	1/72 (1.39)	1/47 (2.13)	0/16 (0)	0/9 (0)
Diagnostic Dilemma	1/72 (1.39)	1/47 (2.13)	0/16 (0)	0/9 (0)
Unknown	4/72 (5.56)	4/47 (8.51)	0/16 (0)	0/9 (0)
No Treatment Delay	11/72 (15.28)	11/47 (23.4)	0/16 (0)	0/9 (0)

Table 2: Treatment outcomes CR/CRi, ED, and 2-year OS of all patients

Note that Age > 60 table is not shown because no patient is Age > 60 in sample dataset

```r
# Load necessary libraries
library(dplyr)
library(tidyr)
library(DescTools)  # For calculating confidence intervals
library(survival)   # For Kaplan-Meier survival analysis

# Preprocess the data: Create age and TDT categories
data_table2 <- data %>%
  mutate(
    AgeGroup = ifelse(Age <= 60, "Age <= 60 y", "Age >60 y"),
    TDTGroup = case_when(
      TDT <= 30 ~ "TDT 0-30 d",
      TDT >= 31 & TDT <= 60 ~ "TDT 31-60 d",
      TDT > 60 ~ "TDT 60+ d",
      TRUE ~ "All TDTs"
    )
  )

# Function to calculate CR/CRi rates with confidence intervals
calculate_cr_cri <- function(data) {
  total <- nrow(data)
  cr_cri_count <- sum(data$TxResponse == "CR", na.rm = TRUE)
  ci <- BinomCI(cr_cri_count, total, conf.level = 0.95, method = "wilson")
  paste0(
    cr_cri_count, "/", total, " (", round(100 * cr_cri_count / total, 1),
    "%) [", round(100 * ci[2], 1), "-", round(100 * ci[3], 1), "]"
  )
}

# Function to calculate ED rates with confidence intervals
calculate_ed <- function(data) {
  total <- nrow(data)
  ed_count <- sum(data$EFS == "Death", na.rm = TRUE)
  ci <- BinomCI(ed_count, total, conf.level = 0.95, method = "wilson")
  paste0(
    ed_count, "/", total, " (", round(100 * ed_count / total, 1),
```

```
    "%) [", round(100 * ci[2], 1), "-", round(100 * ci[3], 1), "]"
  )
}

# Function to calculate 2-year OS percentages
calculate_2y_os <- function(data) {
  total <- nrow(data)
  os_count <- sum(data$SurvivalOS > 730, na.rm = TRUE)  # 730 days = 2 years
  ci <- BinomCI(os_count, total, conf.level = 0.95, method = "wilson")
  paste0(
    round(100 * os_count / total, 1), "% [",
    round(100 * ci[2], 1), "-", round(100 * ci[3], 1), "]"
  )
}
```

```
# Generate metrics for every combination of Age and TDT groups
metrics_table <- data_table2 %>%
  group_by(AgeGroup, TDTGroup) %>%
  summarize(
    CR_CRI = calculate_cr_cri(cur_data()),
    ED = calculate_ed(cur_data()),
    OS_2Y = calculate_2y_os(cur_data()),
    .groups = "drop"
  ) %>%
  pivot_longer(
    cols = c(CR_CRI, ED, OS_2Y),
    names_to = "Metric",
    values_to = "Value"
  ) %>%
  pivot_wider(
    names_from = TDTGroup,
    values_from = Value
  )

# Add "All Patients" row for each metric (not stratified by AgeGroup)
all_patients_table <- data_table2 %>%
  group_by(TDTGroup) %>%
  summarize(
    CR_CRI = calculate_cr_cri(cur_data()),
    ED = calculate_ed(cur_data()),
    OS_2Y = calculate_2y_os(cur_data()),
    .groups = "drop"
  ) %>%
  pivot_longer(
    cols = c(CR_CRI, ED, OS_2Y),
    names_to = "Metric",
    values_to = "Value"
  ) %>%
  pivot_wider(
    names_from = TDTGroup,
    values_from = Value
  ) %>%
  mutate(AgeGroup = "All Patients")


## Can't use this yet because no columns of Age > 60 exist
```

```
# # Add "All TDTs" row for Age >60 specifically
# age_gt_60_table <- data_table2 %>%
#   filter(Age > 60) %>%
#   summarize(
#     CR_CRI = calculate_cr_cri(cur_data()),
#     ED = calculate_ed(cur_data()),
#     OS_2Y = calculate_2y_os(cur_data()),
#     .groups = "drop"
#   ) %>%
#   pivot_longer(
#     cols = c(CR_CRI, ED, OS_2Y),
#     names_to = "Metric",
#     values_to = "Value"
#   ) %>%
#   pivot_wider(
#     names_from = TDTGroup,
#     values_from = Value
#   ) %>%
#   mutate(AgeGroup = "Age >60 y with All TDT Groups")

# Combine the tables
final_table <- bind_rows(all_patients_table, metrics_table)

final_table <- final_table %>%
  select(AgeGroup, Metric, everything())  # Move AgeGroup and Metric to the front

# Format the table using kable
kable(final_table, format = "markdown", align = "l")
```

AgeGroup	Metric	TDT 0-30 d	TDT 31-60 d	TDT 60+ d
All Patients	CR_CRI	26/47 (55.3%) [41.2-68.6]	7/16 (43.8%) [23.1-66.8]	4/9 (44.4%) [18.9-73.3]
All Patients	ED	19/47 (40.4%) [27.6-54.7]	9/16 (56.2%) [33.2-76.9]	6/9 (66.7%) [35.4-87.9]
All Patients	OS_2Y	2.1% [0.4-11.1]	12.5% [3.5-36]	0% [0-29.9]
Age <= 60 y	CR_CRI	25/45 (55.6%) [41.2-69.1]	6/15 (40%) [19.8-64.3]	4/9 (44.4%) [18.9-73.3]
Age <= 60 y	ED	18/45 (40%) [27-54.5]	9/15 (60%) [35.7-80.2]	6/9 (66.7%) [35.4-87.9]
Age <= 60 y	OS_2Y	2.2% [0.4-11.6]	6.7% [1.2-29.8]	0% [0-29.9]
Age >60 y	CR_CRI	1/2 (50%) [9.5-90.5]	1/1 (100%) [20.7-100]	NA
Age >60 y	ED	1/2 (50%) [9.5-90.5]	0/1 (0%) [0-79.3]	NA
Age >60 y	OS_2Y	0% [0-65.8]	100% [20.7-100]	NA

Table 3: ORs for the achievement of CR/CRi, ED, HRs for OS

The reason why this table does not include AML type and HCTCI yet is because they only contain one unique value (AML type as de novo and HCTCI as 0). So cannot extract odds ratio from it.

```
# Load necessary libraries
library(dplyr)
library(broom)      # For tidy model outputs
library(survival)   # For Cox proportional hazards regression
library(survminer)  # For survival analysis visualization (optional)

# add AML type and HCTCI to both models for full dataset. Can't add now since there is only the one value f

# Logistic regression for CR/CRi
```

```r
model_cr <- glm(TxResponse == "CR" ~ TDT + ENLrisk + Age + WBC + LDH + ECOG,
                data = data, family = binomial(link = "logit"))

# Logistic regression for ED (early death)
model_ed <- glm(EFS == "Death" ~ TDT + ENLrisk + Age + WBC + LDH + ECOG,
                data = data, family = binomial(link = "logit"))

# Extract ORs, CIs, and P-values for CR/CRi and ED

# Calculate odds ratio and confidence intervals
confint_cr <- exp(confint.default(model_cr))
confint_ed <- exp(confint.default(model_ed))
p_values_cr <- summary(model_cr)$coefficients[, "Pr(>|z|)"]
p_values_ed <- summary(model_ed)$coefficients[, "Pr(>|z|)"]

results_cr <- exp(cbind(OddsRatio = coef(model_cr), confint_cr, p_values_cr))
results_ed <- exp(cbind(OddsRatio = coef(model_ed), confint_ed, p_values_ed))
```

```r
# Cox proportional hazards model for OS
# Add AMLtype and HCTCI later
model_os <- coxph(Surv(SurvivalOS, TxResponse != "CR") ~
                  TDT + ENLrisk + Age + WBC + LDH + ECOG, data = data)

# Extract HRs, CIs, and P-values for OS
results_os <- summary(model_os)
```

```r
cr_table <- data.frame(
  Predictor = rownames(results_cr)[-1],
  OR_CR = round(results_cr[-1,1], 3),
  CI_CR = paste0(round(results_cr[-1,2], 3), "-", round(results_cr[-1,3], 3)),
  P_CR = round(results_cr[-1,4], 3)
)

ed_table <- data.frame(
  Predictor = rownames(results_ed)[-1],
  OR_ED = round(results_ed[-1,1], 3),
  CI_ED = paste0(round(results_ed[-1,2], 3), "-", round(results_cr[-1,3], 3)),
  P_ED = round(results_ed[-1,4], 3)
)
ed_table$OR_ED <- format(ed_table$OR_ED, nsmall = 3)


os_table <- data.frame(
  Predictor = rownames(results_ed)[-1],
  HR_OS = round(results_os$conf.int[,1],1),
  CI_OS = paste0(round(results_os$conf.int[,3], 3), "-", round(results_os$conf.int[,4],3), 3),
  P_OS = results_os$coefficients[,5]
)

# Round values for cleaner presentation
os_table$HR_OS <- round(os_table$HR_OS, 3)
os_table$P_OS <- round(os_table$P_OS, 3)

# Merge the tables into a single table
table3 <- merge(cr_table, ed_table, by = "Predictor", all = TRUE)
table3 <- merge(table3, os_table, by = "Predictor", all = TRUE)
```

```r
library(knitr)
kable(table3, format = "markdown", align = "l")
```

Predictor	OR_CR	CI_CR	P_CR	OR_ED	CI_ED	P_ED	HR_OS	CI_OS	P_OS
Age	0.995	2.591-2.829	2.289	0.997	2.594-2.829	2.407	1.0	0.974-1.0343	0.814
ECOG	2.239	1.962-1699.335	1.207	0.659	1.205-1699.335	1.676	0.6	0.236-1.4533	0.248
ENLriskfavorable	0.000	1-Inf	2.698	0.239	1-Inf	2.717	16818405.4	0-Inf3	0.997
ENLriskintermediate	0.000	1-Inf	2.697	20746222.039	1-Inf	2.705	27336357.1	0-Inf3	0.997
ENLriskunknown	0.000	1-Inf	2.696	42462735.043	1-Inf	2.705	41266825.0	0-Inf3	0.997
LDH	1.001	2.718-2.722	1.196	1.000	2.717-2.722	1.962	1.0	0.999-13	0.317
TDT	0.995	2.665-2.744	1.593	1.020	2.714-2.744	1.072	1.0	0.99-1.0113	0.946
WBC	0.998	2.695-2.733	1.941	1.006	2.713-2.733	1.166	1.0	0.997-1.0083	0.343

I am not sure why the OR results of ENL are odd. You may discard these.

Tests Performed

For the purposes of this analysis, I will not be doing any stratification (breaking up TDT into groups) due to low sample size (difficult to draw conclusions).

So for example, I did not perform the propensity score weighting test since that determines the treatment effects for each treatment TDT group.

Test 1: Chi-sqaure Test for CR and ED

Basic Overview

- **Technical Definition:** The chi-squared test is used to compare observed frequencies of categorical data across groups to expected frequencies under the null hypothesis of no association.
- **What It Is**: This test checks if there's a relationship between two categories. For example, it can test if remission rates are different for patients who started treatment earlier versus later.
- **How It Was Used:** To compare binary outcomes like complete remission (CR) and early death (ED) between TDT groups.
- **Why It Was Used:** To see if starting treatment sooner or later affected outcomes like remission or early death.
- **Purpose:** To test whether there is a significant association between TDT categories and binary outcomes.
- **Example of Interpreting Results:** If the p-value is small (less than 0.05), it means there's a strong relationship between the timing of treatment and outcomes. For example, p = 0.169 for remission rates, meaning there was no significant difference between groups.

Execution and Analysis First, we create a contingency table to count how many observations fall into each category

```r
table_CR <- table(data$TDT, data$TxResponse)
```

Then we run the chisq-test to determine the p-value:

- The null hypothesis is: The two variables (TDT & Treatment Response) are independent
- The alternative hypothesis is: The two variables are dependent

```r
# Run chi-square test, correct = FALSE for small sample sizes
chi_test_CR <- chisq.test(table_CR, correct=FALSE)

# Output results
print(chi_test_CR)
```

```
##
##  Pearson's Chi-squared test
##
## data:  table_CR
## X-squared = 118.08, df = 135, p-value = 0.8498
```

Results and Conclusions For complete remission (CR), since p = 0.8498 (greater than 0.05), we fail to reject the null hypothesis. This means there's no strong evidence that TDT affects Treatment Response

Test 2: Survival Tests

Test 2a: Kaplan-Meier Survival Curves

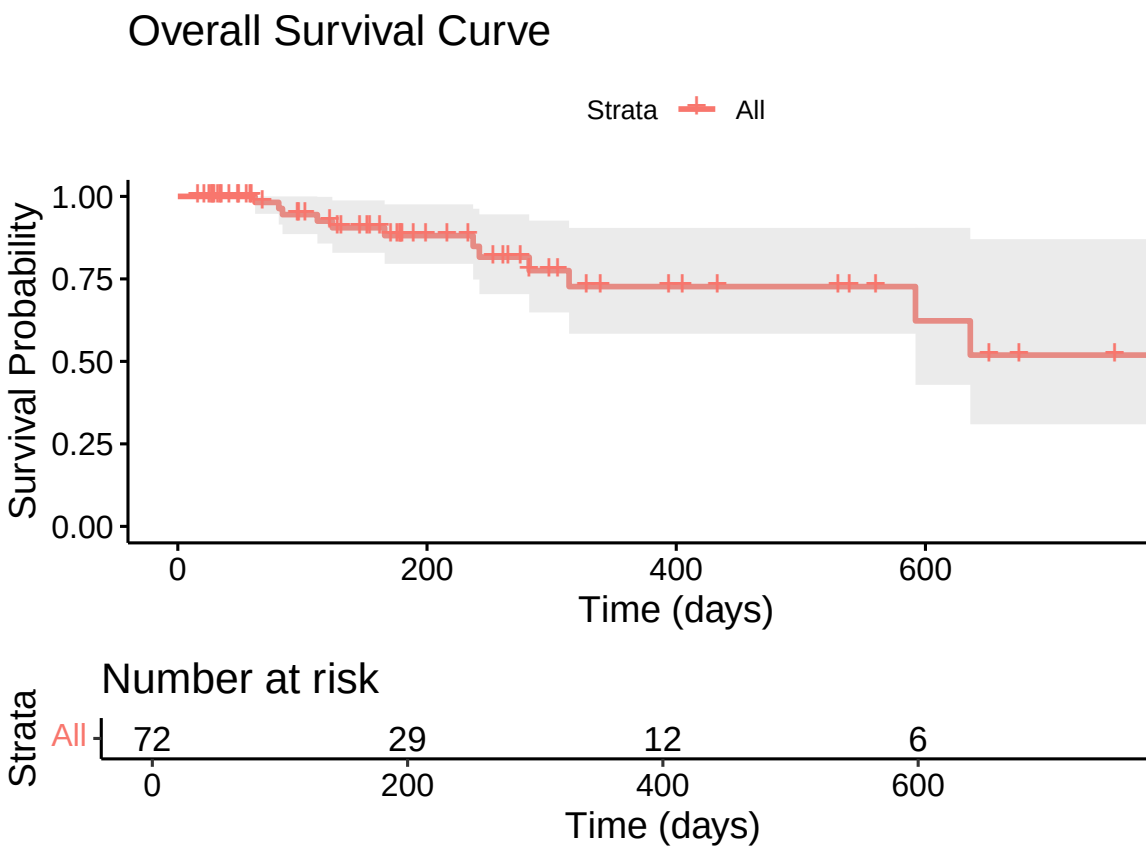
This will serve as a setup (visual representation) for the log-ranked test (Test 2b)

Basic Overview

- **Technical Definition:** Kaplan-Meier survival curves estimate the probability of survival over time while accounting for censored data (patients lost to follow-up or still alive at the end of the study).
- **What It Is:** This method shows how long patients survive over time. It creates a graph (called a survival curve) that shows the percentage of people still alive at different points in time.
- **Why It Was Used:** To check if patients who started treatment earlier lived longer than those who started later.
- **How It Was Used:** To compare overall survival (OS) across TDT groups. Log-rank tests were used to assess whether survival differences between groups were statistically significant.
- **Purpose:** To visualize and test differences in survival probabilities over time.
- **Example of Interpreting Results:** The survival curves showed no big differences between groups based on TDT. A p-value of 0.211 means there's no evidence that starting treatment earlier improves survival.

```r
# Load packages
library(survival)
library(survminer)
library(ggplot2)

# Create survival object
surv_object <- Surv(
  time = data$SurvivalOS,
```

```r
  event = data$TxResponse == 'Primary Refractory Disease')
## 1 = death, 0 - alive

# Fit Kaplan-Meier curve for all data
km_fit <- survfit(surv_object ~ 1, data = data)  # ~1 means no grouping

# Plot survival curve
par(mar = c(5, 12, 4, 2))
ggsurvplot(
  km_fit,
  data = data,
  conf.int = TRUE,
  xlab = "Time (days)",
  ylab = "Survival Probability",
  title = "Overall Survival Curve",
  risk.table = TRUE
)
```



Execution and Analysis

Results and Conclusions

- Early Phase (0–200 Days)
  - Survival Probability: Starts at 1.00 and declines to approximately 0.80 within the first 200 days.
  - Note that there is a significant decrease in the number at risk between 0 and 200 days compared to the other ones.
  - Interpretation: There is a notable early mortality rate, indicating that a subset of patients experience events (e.g., death or relapse) relatively soon after diagnosis or treatment initiation.

- Mid-Phase (200–600 days)
  - Survival Probability: Continues to decline slowly, but reaches a standstill from 320 to 600 days, reaching around 0.75.
  - Interpretation: There is a gradual reduction in the proportion of patients surviving during this period after a slight decrease/
- Late Decline (600+ days)
  - Survival Probability: The curve flattens out after approximately 625 days and stabilizes around 0.5.
  - Interpretation: The mortality rate decreases substantially beyond this point. Patients who survive past the 625-day mark have a relatively stable long-term survival probability.
- Median Survival Time Estimation: The median survival time (when the survival probability reaches 0.50) appears to be around 625 days.
- Confidence Interval (Gray Shaded Area): A wide confidence interval suggests high variability, particularly at later time points, indicating a limited sample size

Test 2b: Cox-regression

Note: We did not perform the Log-rank test because I did not split up TDT into groups due to low sample size.

This is also an extension of the survival test performed in test 2a.

Basic Overview

- **Technical Definition:** Cox regression models the relationship between survival time and one or more predictors while assuming proportional hazards (i.e., hazard ratios are constant over time).
- **What It Is:** Cox regression looks at how different factors (like age or TDT) affect survival time while accounting for other variables.
- **Why It Was Used:** To see if TDT affects survival when considering other things like patient age or lab results.
- **How It Was Used:** Univariable Cox regression assessed the effect of TDT on OS. Multivariable Cox regression adjusted for confounders like age, WBC, genetic risk, etc.
- **Purpose:** To quantify the effect of predictors (e.g., TDT) on survival outcomes while controlling for other variables.
- **Example of Interpreting Results:** A hazard ratio (HR) tells you how much a factor changes the risk of dying. An HR of 1 means no effect. For ex: an HR for TDT was 1.00 (p=0.617), meaning TDT had no impact on survival.

```
# Fit Cox model (adjust for covariates like Age, WBC, etc.)
cox_model <- coxph(
  Surv(
    time = SurvivalOS,
    event = TxResponse == "Primary Refractory Disease")
  ~ TDT + Age + WBC + ECOG, data = data
)

# Summarize results
summary(cox_model)
```

Execution and Analysis

```
## Call:
## coxph(formula = Surv(time = SurvivalOS, event = TxResponse ==
##     "Primary Refractory Disease") ~ TDT + Age + WBC + ECOG, data = data)
##
##   n= 72, number of events= 12
##
##            coef exp(coef)  se(coef)      z Pr(>|z|)
## TDT   0.006567  1.006589  0.006765  0.971    0.332
## Age  -0.015707  0.984416  0.025870 -0.607    0.544
## WBC  -0.001031  0.998969  0.005441 -0.190    0.850
## ECOG -0.969626  0.379225  0.828256 -1.171    0.242
##
##      exp(coef) exp(-coef) lower .95 upper .95
## TDT     1.0066     0.9935    0.9933     1.020
## Age     0.9844     1.0158    0.9357     1.036
## WBC     0.9990     1.0010    0.9884     1.010
## ECOG    0.3792     2.6370    0.0748     1.923
##
## Concordance= 0.592  (se = 0.107 )
## Likelihood ratio test= 2.15  on 4 df,   p=0.7
## Wald test            = 2.01  on 4 df,   p=0.7
## Score (logrank) test = 1.99  on 4 df,   p=0.7
```

```
# Key outputs:
# - Hazard Ratios (HR): exp(coef) > 1 indicates increased risk.
# - Confidence Intervals (CI): HR CI excluding 1 implies significance.
# - p-values: Variables with p < 0.05 are significant predictors.
```

Results and Conclusions Key outputs:

- Hazard Ratios (HR): exp(coef) > 1 indicates increased risk.
- Confidence Intervals (CI): HR CI excluding 1 implies significance.
- p-values: Variables with p < 0.05 are significant predictors.
- No Significant Predictors: All predictors have p > 0.05, meaning none are independently associated with survival.
- Concordance: 0.592 (moderate ability to rank survival times correctly)
- Global Tests: Likelihood ratio, Wald, and score tests all show p=0.7, confirming the model does not significantly explain survival variation.
- Hazard Ratios:
  - TDT: HR = 1.0066. For every additional hour of TDT, the hazard of death increases by 0.7%, but this is non-significant (p=0.332)
  - Age: HR = 0.9844. For every year increase, the hazard of death decreases by 1.6%, which is non-significant (p=0.544)
  - WBC: HR = 0.9990. For every unit increase in WBC, the hazard of death decreases by 0.1%, which is non-significant (p=0.850)
  - ECOG: HR = 0.3792. This is non-significant (p=0.242)

Test 3: Logistic Regression

To analyze whether TDT affects early death (ED) or complete remission (CR), while accounting for other covariates like age and WBC, you would use multivariable logistic regression.

Basic Overview

- **Technical Definition:** Logistic regression models binary outcomes (e.g., CR or ED) as a function of one or more predictors.
- **What It Is:** Logistic regression predicts outcomes that have two possibilities—like whether a patient achieved remission (yes/no) or died early (yes/no).
- **Why It Was Used:** To check if TDT affects the chances of remission or early death while considering other factors like age and lab results.
- **How It Was Used:** Univariable logistic regression tested associations between TDT and binary outcomes. Multivariable logistic regression adjusted for confounders like age, genetic risk, etc.
- **Purpose:** To estimate odds ratios (ORs) for binary outcomes based on predictors while accounting for other variables.
- **Example on Interpreting Results:** An odds ratio (OR) tells you how much a factor changes the odds of an outcome. measure the strength of association between a categorical outcome (e.g., early death or complete remission) and one or more predictors (e.g., TDT, age, WBC).
  - OR = 1: No effect; the predictor does not change the odds of the outcome. (Ex: an OR of 0.99 (p=0.254) for remission shows that each extra day of TDT didn't change the odds of remission significantly.)
  - OR > 1: Increased odds; the predictor makes the outcome more likely. (Ex: An OR of 1.5 for TDT means that for every additional day of TDT, the odds of early death increase by 50%.)
  - OR < 1: Decreased odds; the predictor makes the outcome less likely. (Ex: An OR of 0.8 for TDT means that for every additional day of TDT, the odds of early death decrease by 20%.)
  - If OR $\neq$ 1 and p $<$ 0.05, TDT significantly affects ED or CR.

Execution and Analysis

Univariable Analysis We want to try examining the relationship between TDT & Treatment Response. We do this by first excluding all other variables from the models.

Univariate Logistic Regression model for CR:

```
# Fit univariate logistic regression model for CR
cr_uni_model <- glm(TxResponse == 'CR' ~ TDT, family = binomial(link = "logit"), data = data)

# 1 = CR.

# Summary of the model
summary(cr_uni_model)
```

```
##
## Call:
## glm(formula = TxResponse == "CR" ~ TDT, family = binomial(link = "logit"),
##     data = data)
##
## Coefficients:
##              Estimate Std. Error z value Pr(>|z|)
## (Intercept)  0.154931   0.327054   0.474    0.636
## TDT         -0.002964   0.006771  -0.438    0.662
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 99.758  on 71  degrees of freedom
## Residual deviance: 99.564  on 70  degrees of freedom
```

```
## AIC: 103.56
##
## Number of Fisher Scoring iterations: 3
```

```
# Calculate odds ratio and confidence intervals
exp(cbind(OddsRatio = coef(cr_uni_model), confint(cr_uni_model)))
```

```
##             OddsRatio     2.5 %   97.5 %
## (Intercept) 1.1675770 0.6154167 2.239575
## TDT         0.9970409 0.9829259 1.010482
```

Interpretation:

- TDT Effect: Coefficient = -0.003 (p = 0.662)
- Odds Ratio: 0.997 (95% CI: 0.982 - 1.91) (no effect)
- Interpretation: For each additional day of TDT, the odds of achieving CR decrease by approximately 0.3% (1 - 0.997).
- Statistical Significance: The effect is not statistically significant ($p > 0.05$), and the the confidence interval covers 1.0, indicating no effect that TDT has an effect on Treatment response.

Model Fit:

- AIC: 103.56. Doesn't suggest a strong model fit in terms explanatory power.
- Residual Deviance: 99.564 on 70 degrees of freedom
  - The null deviance (99.758) and residual deviance (99.564) are nearly identical.
  - A large drop in deviance would indicate that the model improves prediction—but here, the difference is minimal.
  - This suggests that TDT doesn't explain much of the variability in treatment response (CR).

Conclusion: TDT does not significant predict treament response (CR)

Multivariable Analysis Now we consider whether other factors such as age, WBC, etc. affect our conclusions.

First we create the multivariable logistic regression for complete remission (CR)

- We exclude the ED variable from the CR model because it is an outcome variable, not a predictor (vice versa applies later for the ED model)

```
# Fit logistic regression model for CR
cr_multi_model <- glm(TxResponse == 'CR' ~ TDT + Age + WBC + ECOG,
                 family = binomial(link = "logit"), data = data)

# Summary of the model
summary(cr_multi_model)
```

```
##
## Call:
## glm(formula = TxResponse == "CR" ~ TDT + Age + WBC + ECOG, family = binomial(link = "logit"),
##     data = data)
##
## Coefficients:
```

```
##               Estimate Std. Error z value Pr(>|z|)
## (Intercept)  0.3869678  0.8725832   0.443    0.657
## TDT         -0.0041151  0.0069038  -0.596    0.551
## Age         -0.0093407  0.0200046  -0.467    0.641
## WBC         -0.0003477  0.0030943  -0.112    0.911
## ECOG         0.6738030  0.5617210   1.200    0.230
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 99.758  on 71  degrees of freedom
## Residual deviance: 97.728  on 67  degrees of freedom
## AIC: 107.73
##
## Number of Fisher Scoring iterations: 4
```

```
# Calculate odds ratios and confidence intervals
exp(cbind(OddsRatio = coef(cr_multi_model), confint(cr_multi_model)))
```

```
##             OddsRatio     2.5 %   97.5 %
## (Intercept) 1.4725091 0.2651032 8.383917
## TDT         0.9958934 0.9816845 1.009706
## Age         0.9907027 0.9519980 1.030485
## WBC         0.9996523 0.9934596 1.005862
## ECOG        1.9616834 0.6654663 6.179323
```

Interpretation:

- None of the predictors (TDT, Age, WBC, ECOG) have p-values below 0.05, meaning none are significant.
- Even ECOG, which has the highest odds ratio (1.96), has a p-value of 0.230, indicating it does not significantly predict CR.
- Odds ratios: TDT (0.9959), Age (0.9901), WBC (0.997) all have odds very close to 1. Suggests minimal impact on whether a patients achieves CR.
- Confidence intervals: All the 95% predictors contain 1, indicating that none of them are significant predictors of CR.
- Sample Size Issues: The small sample size (n=72) severely limits the reliability of the multivariate model.
- AIC of 107.73 indicates model does not have explanatory power. So we decide to not use the multivatiate model due to sample size

Results and Conclusions From all the univariate tests, we can conclude that there is no significant association between TDT & Treatment Response (with a potential negative effect but not significant)

Optional Check: You may skip this section

I will run a few tests to determine whether it is stable and fits our data appropriately:

```
# Check VIF for CR model
# Load required package
library(car)

# Fit the CR model
cr_model <- glm(TxResponse == 'CR' ~ TDT + Age + WBC + ECOG,
```

```
                family = binomial(link = "logit"), data = data)

# Check VIF
vif(cr_model)
```

```
##      TDT      Age      WBC     ECOG
## 1.034425 1.019667 1.036107 1.032364
```

```
# If VIF > 10 - severe multicollinearity
# If VIF < 5 - generally acceptable
```

So multicollinearity is not the cause of instability of these models since all VIF's are < 10.

We can conclude the extreme confidence intervals in multivariate model and odds ratios (OR) are most likely due to sample size.

Test 4: Restricted Cubic Spline (RCS)

Basic Overview

- **Technical Definition:** RCS is a flexible modeling technique that allows for nonlinear relationships between a predictor and an outcome by dividing the predictor into segments joined by "knots."
- **What It Is:** RCS is a fancy way to look at relationships that aren't straight lines—it helps find patterns that might be curved or complex.
- **Why It Was Used:** To see if there's a more complicated relationship between TDT and outcomes like survival or remission.
- **How It Was Used:** To model potential nonlinear relationships between TDT and outcomes like OS or CR without categorizing continuous variables.
- **Purpose:** To avoid loss of information from categorization and better capture complex relationships between variables.
- **Example of Interpreting Results:** Likelihood ratio tests compared models with linear vs RCS terms. Non-significant results suggest that even with RCS modeling, there was no evidence that TDT influenced outcomes significantly. The analysis found no evidence that using RCS improved predictions about outcomes.This means there wasn't a complicated relationship between TDT and patient results—it was pretty straightforward.

Execution and Analysis Model TDT as a nonlinear predictor. For example, to analyze CR (using 4 knots):

```
# Load packages
library(rms)
library(ggplot2)

# Fit logistic regression model with RCS for TDT
cr_rcs_model <- lrm(TxResponse == 'CR' ~ rcs(TDT, 4) + Age + Male + WBC + ECOG,
                    data = data)

# Print model summary
print(cr_rcs_model)
```

```
## Logistic Regression Model
##
## lrm(formula = TxResponse == "CR" ~ rcs(TDT, 4) + Age + Male +
##     WBC + ECOG, data = data)
##
##                       Model Likelihood    Discrimination    Rank Discrim.
```

```
##                             Ratio Test           Indexes          Indexes
## Obs            72    LR chi2      3.61    R2       0.065    C       0.632
##  FALSE         35    d.f.            7    R2(7,72) 0.000    Dxy     0.265
##  TRUE          37    Pr(> chi2) 0.8232    R2(7,54) 0.000    gamma   0.265
## max |deriv| 2e-07                         Brier    0.237    tau-a   0.134
##
##           Coef    S.E.   Wald Z Pr(>|Z|)
## Intercept  0.9893 1.3072  0.76  0.4492
## TDT       -0.0289 0.0795 -0.36  0.7161
## TDT'      -0.0272 0.8299 -0.03  0.9738
## TDT''      0.1415 1.6334  0.09  0.9310
## Age       -0.0081 0.0204 -0.39  0.6935
## Male      -0.0895 0.5174 -0.17  0.8626
## WBC       -0.0015 0.0034 -0.46  0.6482
## ECOG       0.5666 0.5935  0.95  0.3398
```

```r
# Compare linear vs RCS models using likelihood ratio test
linear_model <- lrm(TxResponse == 'CR' ~ TDT + Age + Male + WBC + ECOG,
                    data = data)
lrtest(cr_rcs_model, linear_model)
```

```
##
## Model 1: TxResponse == "CR" ~ rcs(TDT, 4) + Age + Male + WBC + ECOG
## Model 2: TxResponse == "CR" ~ TDT + Age + Male + WBC + ECOG
##
## L.R. Chisq       d.f.          P
##  1.5785953  2.0000000  0.4541637
```

Interpretation:

- No nonlinear relationships:
  - The RCS terms (TDT, TDT', TDT'') are not significant ($p > 0.1$), and the likelihood ratio test confirms the RCS model does not improve fit over a linear model.
  - All the other predictors have weak or insignificant effects, except for ECOG (0.5666) with the strongest effect but no significance.
- Likelihood Ratio Test (chisquare = 1.58, $p = 0.45$). The RCS model does not significantly improve fit over a linear model.
- R squared value of 0.065 is very low, indicating the model captures little variation in the outcome (CR)
- Moderate Discrimination ($C = 0.632$): The model weakly distinguishes CR vs. non-CR patients. Slightly better than random guessing but far from ideal (closer to 0.5 is worse, closer to 1 is normal).

Results and Conclusions

- No significant predictors: Age, WBC, Male, or ECOG do not independently affect CR.
- TDT's relationship with CR is weak and does not benefit from this spline transformation. Model performance is weak.

Other tests not mentioned in the study

Test 5: Correlation Analysis:

Assess relationships between continuous variables (e.g., TDT, WBC, LDH). Stronger relationships are higher numbers that are further away from 0. 0 indicates no relationship.

```
cor_matrix <- cor(data[, c("TDT", "WBC", "ECOG", "SurvivalEFS", "SurvivalOS")], use = "complete.obs")
print(cor_matrix)
```

```
##                    TDT         WBC        ECOG SurvivalEFS  SurvivalOS
## TDT          1.0000000 -0.12492553  0.12407486  -0.0266559  0.10143550
## WBC         -0.1249255  1.00000000 -0.09276117  -0.1488567 -0.17846969
## ECOG         0.1240749 -0.09276117  1.00000000   0.1208513  0.06822502
## SurvivalEFS -0.0266559 -0.14885667  0.12085133   1.0000000  0.88474843
## SurvivalOS   0.1014355 -0.17846969  0.06822502   0.8847484  1.00000000
```

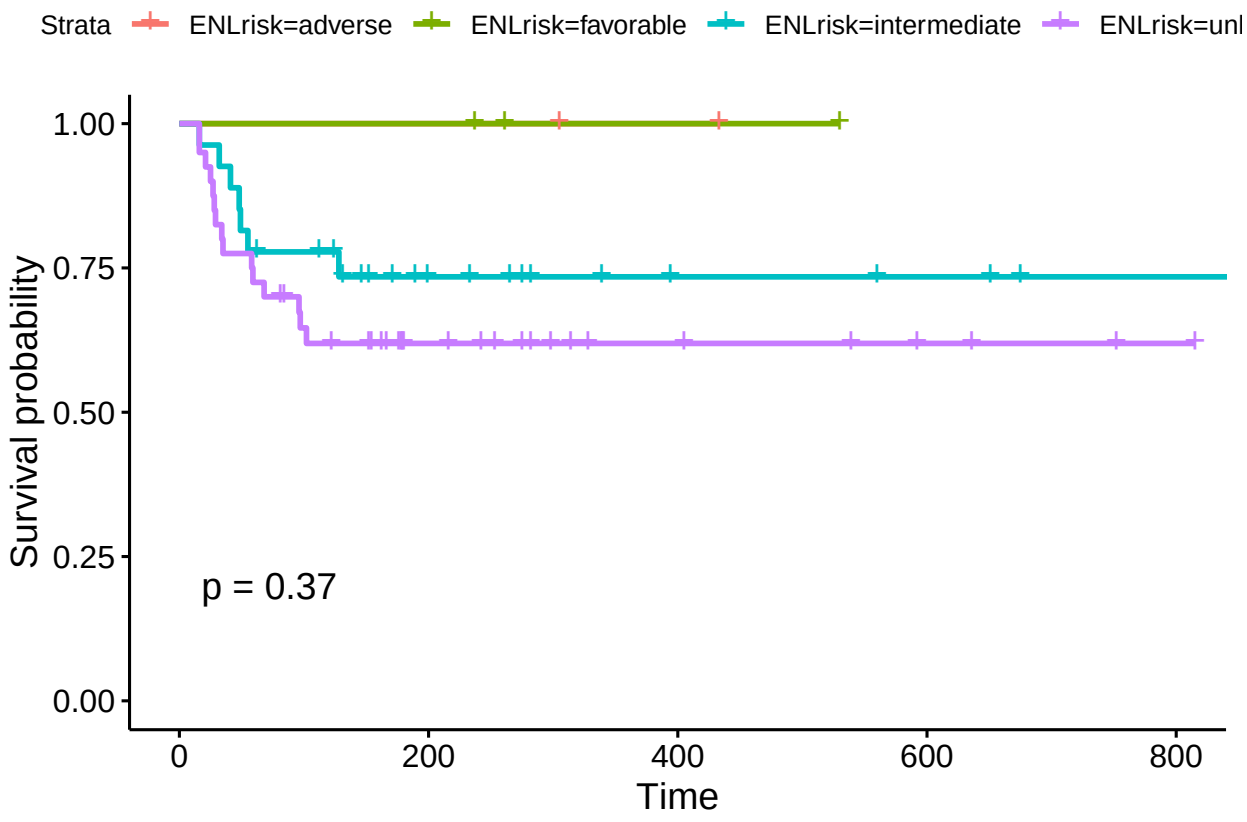
Interpretation

- The strongest relationship is between SurvivalEFS and SurvivalOS. This suggests these measures are tightly linked and may provide complementary information about patient survival.
- TDT's almost 0 correlation (-0.03) with SurvivalEFS hints at that there is no relationship between TDT and Survival.
- Other correlations are relatively weak, which might suggest low interdependence between those variables.

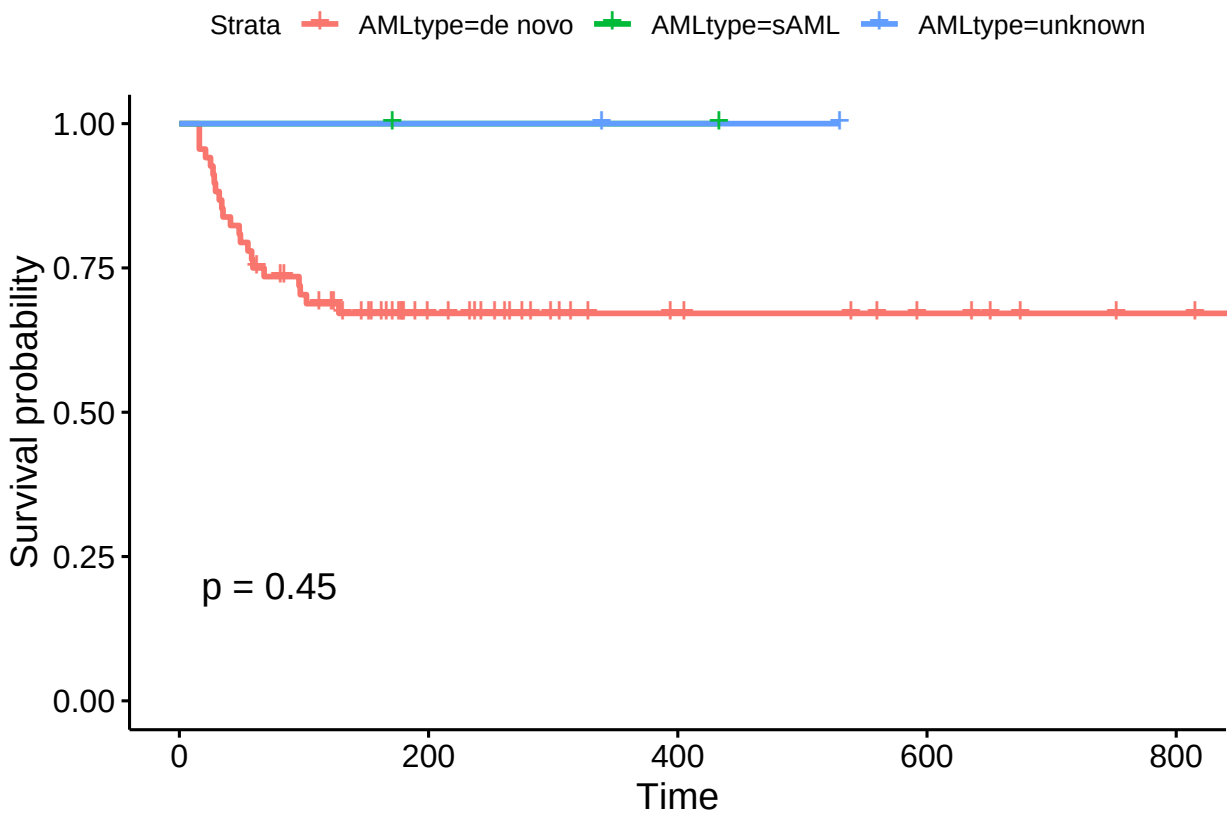
Test 6: SUrvival Analysis by Subgroups

Analyze survival curves stratified by categorical variables such as: - ENL risk group (e.g., favorable, intermediate, adverse, unknown). - AML type (e.g., de novo vs. secondary AML). - Use of CytoredAgent (e.g. hydroxyurea, cytarabine, no cytoreduction given)

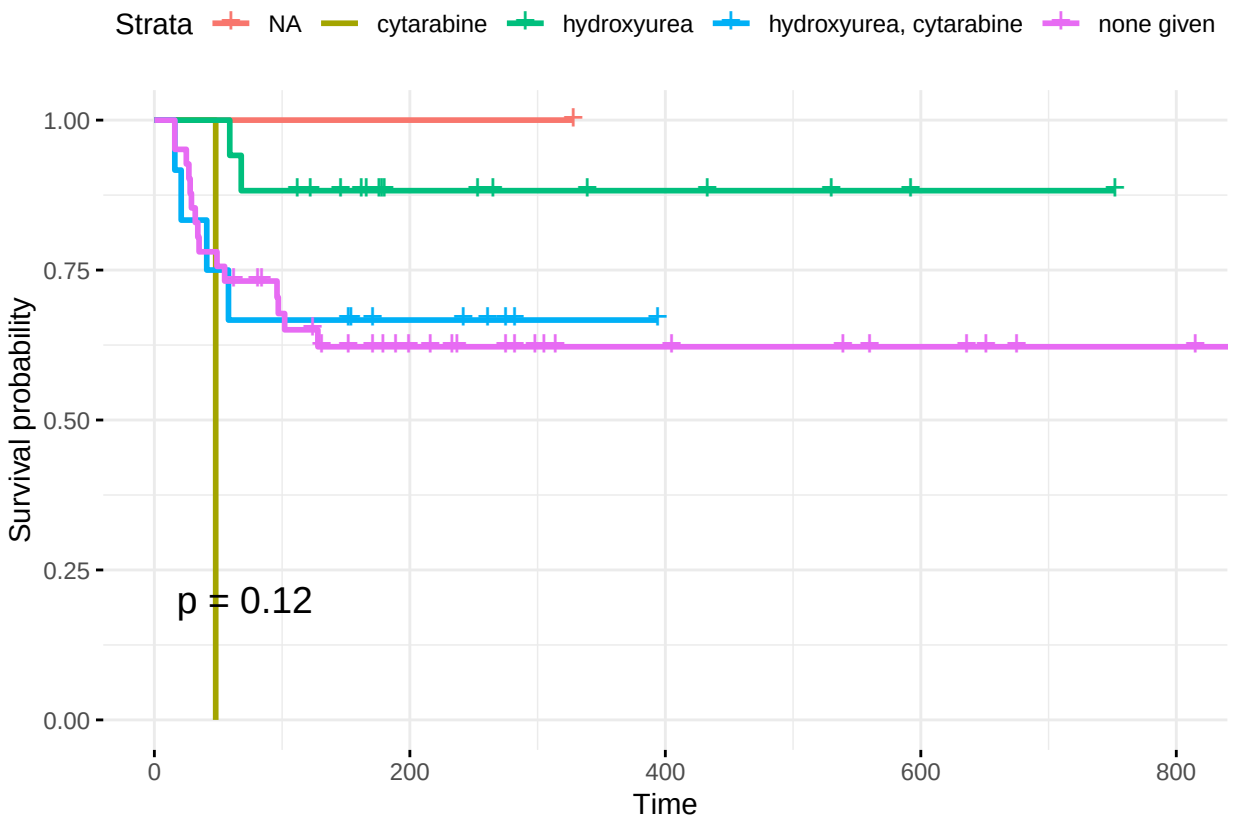
```
library(survminer)
library(ggplot2)
surv_object <- Surv(
  time = data$SurvivalOS,
  event = data$TxResponse == 'Early Death')
#1 - death. 0 - alive

par(mar = c(5, 12, 4, 2))

km_fit_risk <- survfit(surv_object ~ ENLrisk, data = data)
ggsurvplot(km_fit_risk, data = data, pval = TRUE)
```




```
par(mar = c(5, 12, 4, 2))

km_fit_AML <- survfit(surv_object ~ AMLtype, data = data)
ggsurvplot(km_fit_AML, data = data, pval = TRUE)
```




```
par(mar = c(5, 12, 4, 2))

km_fit_cyto <- survfit(surv_object ~ CytoredAgent, data = data)
ggsurvplot(km_fit_cyto, data = data, pval = TRUE,
           legend.labs = c("NA","cytarabine", "hydroxyurea", "hydroxyurea, cytarabine", "none given"),
           ggtheme = theme_minimal() + theme(legend.position = "bottom"))
```



Results and Interpretation For ENL Risk:

- The green group (ENLrisk = favorable) appears to have the best survival probability over time, followed by the blue group (ENLrisk = intermediate) while the purple group (ENLrisk = unknown) drops faster.
- The p-value (log-rank test) of 0.37 suggests that the differences between these ENL risk levels do not significantly impact survival outcomes.
- There is not enough data to determine survival probability for ENLrisk = adverse
- The lack of statistical significance could be due to small sample size, high variability, or overlapping survival patterns.

For AML Type:

- The red group (AMLtype = de novo), appears to have varying levels of survival probability within the early stages of 0-150 days, but it becomes flattened out from 150+ days onwards with survival probability around 0.65.
- The p-value (log-rank test) of 0.45 suggests that there is no strong evidence that AML type significantly impact survival outcomes.
- There is not enough data to determine survival probability for AMLtype = unknown or AMLtype = sAML.

For CytoredAgent:

- The green group (hydroxyurea) looks to have the best survival probability overtime followed by the blue group (both hydroxyurea and cytarabine)
- The purple group (CytoredAgent = no cytoreduction given) appears to have the worst survival probability over time
- Log-Rank Test (p-value): The p-value = 0.12 suggests that there is no statistically significant difference in survival between the three groups.

Conclusion There is no significant difference in survival between the different groups for ENL Risk, AML Type, and Cytored Agent.

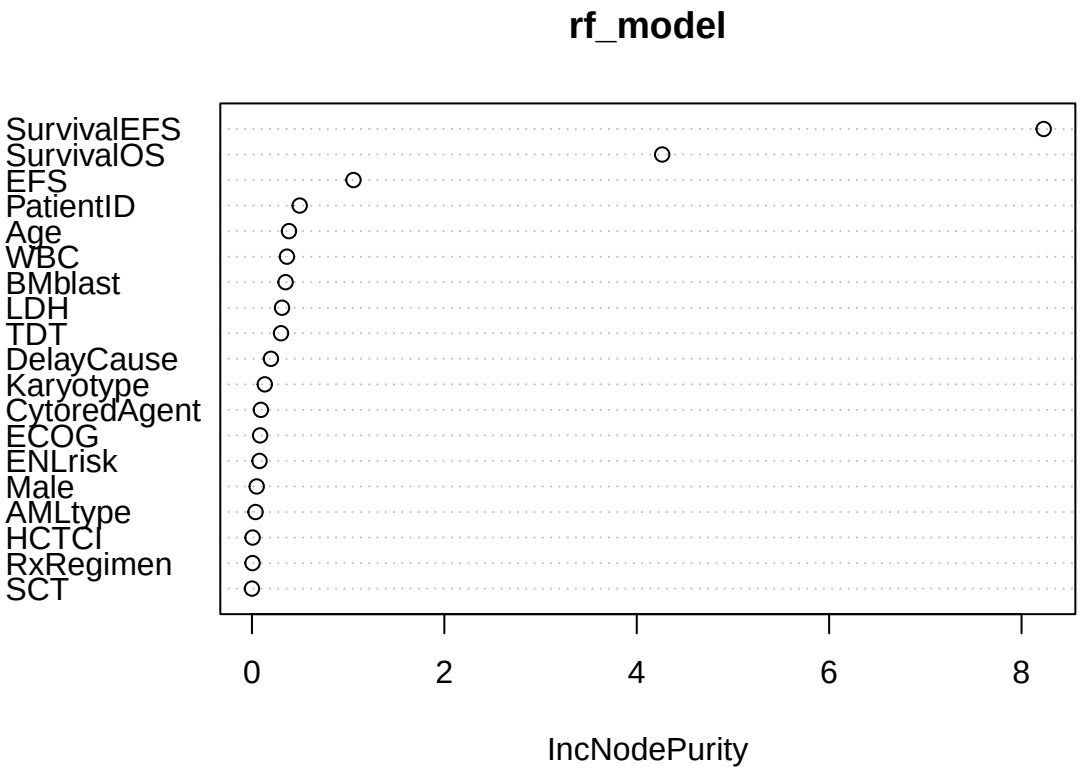
Test 7: Machine Learning for Feature Importance

Using machine learning (random forests) to determine the most important predictors of survival or treatment response:

```
library(randomForest)
# Remove rows with NA values
data_clean <- na.omit(data)

# Run the random forest model on the cleaned dataset
rf_model <- randomForest(TxResponse == "CR" ~ ., data = data_clean) #1 - alive. 0 - death

print(rf_model)
```

```
##
## Call:
##  randomForest(formula = TxResponse == "CR" ~ ., data = data_clean)
##                Type of random forest: regression
##                      Number of trees: 500
## No. of variables tried at each split: 6
##
##           Mean of squared residuals: 0.05146391
##                     % Var explained: 79.41
```

```
# Variable importance plot
varImpPlot(rf_model)
```



It looks like SurvivalEFS is the most important predictor for survival, followed by: SuvivalOS, EFS, TDT

Test 8: LASSO Model

Also try using the LASSO model to determine the key predictors of treatment response:

Definition: LASSO (Least Absolute Shrinkage and Selection Operator) is a special type of regression that helps select the most important variables.

- Standard models (like logistic regression) might include many variables, even if some don't contribute much.
- LASSO effectively removes unnecessary predictors/factors
- This prevents overfitting (making a model too complex) and improves accuracy

```
library(glmnet)

# Remove rows with NA values
data_clean <- na.omit(data)

# Prepare matrix for LASSO
x <- model.matrix(TxResponse == 'CR' ~ Age + TDT + WBC + LDH + ECOG + Male, data = data_clean)
y <- as.numeric(data_clean$TxResponse == 'CR')

# Fit LASSO model
lasso_model <- cv.glmnet(x, y, family = "binomial", alpha = 1)
print(lasso_model)
```

```
##
```

```
## Call:  cv.glmnet(x = x, y = y, family = "binomial", alpha = 1)
##
## Measure: Binomial Deviance
##
##      Lambda Index Measure     SE Nonzero
## min 0.07994     1   1.414 0.0124       0
## 1se 0.07994     1   1.414 0.0124       0
```

Results & Interpretation

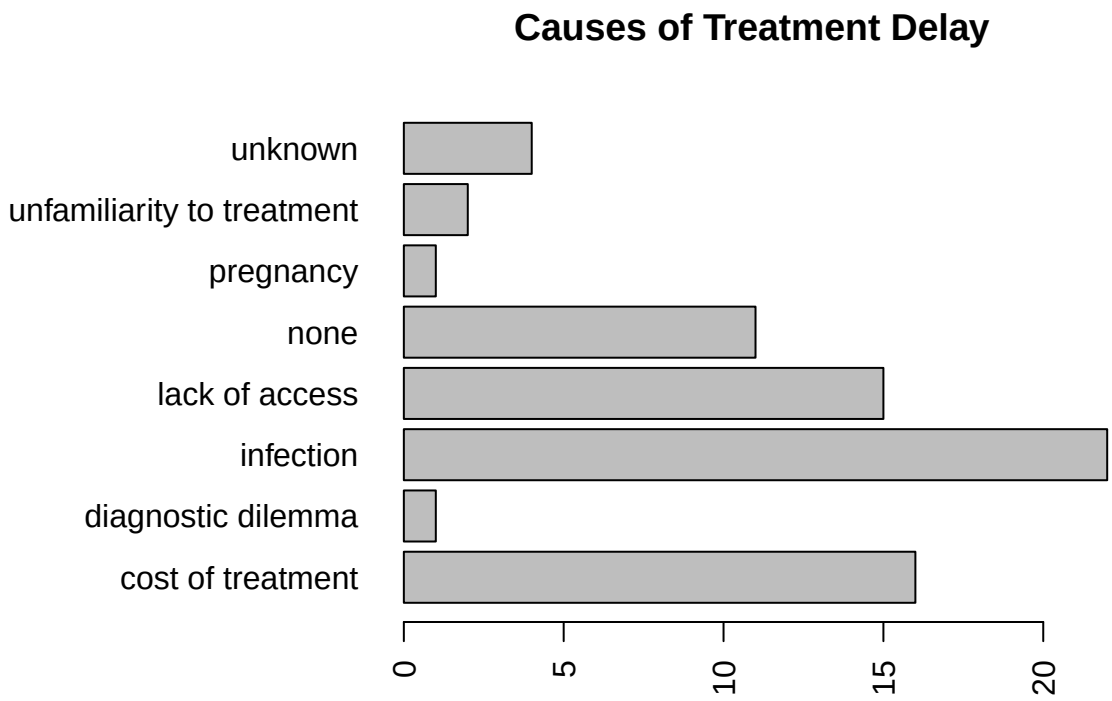
- Measure (Binomial Deviance): Indicates the goodness of fit. Lower values represent better model performance.

Lambda Values (min and 1se):

- Lambda Min (0.07994): Minimizes the binomial deviance, representing the most predictive model, but may include more coefficients.
- Lambda 1-SE (0.07994): A simpler model within one standard error of Lambda Min. This balances accuracy and complexity.
- For both lambda.min and lambda.se, the model selected 0 non-zero coefficients, implying none of the predictors had strong predictive power for treatment response. This might indicate potential issues with variable selection (previous test) or data quality
- Since both selected lambdas resulted in zero predictors, it's worth trying alternative models.

Test 9: Cause of Treatment Delay Analysis

```r
table_delay <- table(data$DelayCause)

par(mar = c(5, 12, 4, 2))
barplot(table_delay, main="Causes of Treatment Delay", horiz = TRUE, cex.names = 1, las = 2)
```



Looks like the most frequent cause of treatment delay is infection.

Impact on Outcomes: Assess how different causes of delay affect early death. Using 2 different models:

1. Cox model - for survival analysis: estimates how different predictors (e.g., TDT, ECOG, LDH) affect the likelihood of early death over time. Hazard ratio (HR) tells you if a predictor increases or decreases the risk of an event happening sooner.
2. Logistic Regression - used to predict the probability of an event happening— whether a patient achieves CR (Complete Response) or experiences Early Death (ED). It takes predictors (like age, WBC, ECOG, and delay causes) and estimates their impact on the outcome.

```
cox_delay <- coxph(Surv(SurvivalOS, TxResponse == 'Early Death') ~ DelayCause,
                   data = data)
summary(cox_delay)
```

```
## Call:
## coxph(formula = Surv(SurvivalOS, TxResponse == "Early Death") ~
##     DelayCause, data = data)
##
##   n= 72, number of events= 22
##
##                                          coef  exp(coef)   se(coef)      z
## DelayCausediagnostic dilemma         -1.878e+01  6.965e-09  1.832e+04 -0.001
## DelayCauseinfection                  -4.323e-01  6.490e-01  6.057e-01 -0.714
## DelayCauselack of access              1.372e-01  1.147e+00  5.775e-01  0.238
## DelayCausenone                        1.792e-01  1.196e+00  6.462e-01  0.277
## DelayCausepregnancy                   1.713e+00  5.545e+00  1.105e+00  1.550
## DelayCauseunfamiliarity to treatment -1.878e+01  6.965e-09  1.295e+04 -0.001
```

```
## DelayCauseunknown                    -1.878e+01  6.964e-09  9.234e+03 -0.002
##                                     Pr(>|z|)
## DelayCausediagnostic dilemma           0.999
## DelayCauseinfection                    0.475
## DelayCauselack of access               0.812
## DelayCausenone                         0.782
## DelayCausepregnancy                    0.121
## DelayCauseunfamiliarity to treatment   0.999
## DelayCauseunknown                      0.998
##
##                                     exp(coef) exp(-coef) lower .95 upper .95
## DelayCausediagnostic dilemma        6.965e-09  1.436e+08    0.0000       Inf
## DelayCauseinfection                 6.490e-01  1.541e+00    0.1980     2.127
## DelayCauselack of access            1.147e+00  8.718e-01    0.3699     3.557
## DelayCausenone                      1.196e+00  8.359e-01    0.3371     4.245
## DelayCausepregnancy                 5.545e+00  1.803e-01    0.6354    48.395
## DelayCauseunfamiliarity to treatment 6.965e-09  1.436e+08    0.0000       Inf
## DelayCauseunknown                   6.964e-09  1.436e+08    0.0000       Inf
##
## Concordance= 0.63  (se = 0.06 )
## Likelihood ratio test= 8.49  on 7 df,   p=0.3
## Wald test            = 3.92  on 7 df,   p=0.8
## Score (logrank) test = 8.3  on 7 df,   p=0.3
```

```
glm_delay <- glm(TxResponse == 'Early Death' ~ DelayCause,
                 family = binomial(link="logit"), data=data)
summary(glm_delay)
```

```
##
## Call:
## glm(formula = TxResponse == "Early Death" ~ DelayCause, family = binomial(link = "logit"),
##     data = data)
##
## Coefficients:
##                                      Estimate Std. Error z value Pr(>|z|)
## (Intercept)                          -0.51083    0.51640  -0.989    0.323
## DelayCausediagnostic dilemma        -17.05524 3956.18036  -0.004    0.997
## DelayCauseinfection                  -0.71295    0.72491  -0.984    0.325
## DelayCauselack of access              0.10536    0.73786   0.143    0.886
## DelayCausenone                       -0.04879    0.81211  -0.060    0.952
## DelayCausepregnancy                  18.07689 3956.18036   0.005    0.996
## DelayCauseunfamiliarity to treatment -17.05524 2797.44199  -0.006    0.995
## DelayCauseunknown                    -17.05524 1978.09023  -0.009    0.993
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 88.632  on 71  degrees of freedom
## Residual deviance: 79.363  on 64  degrees of freedom
## AIC: 95.363
##
## Number of Fisher Scoring iterations: 16
```

Conclusion: For the first test (coxph):

- All p-values exceed 0.05, meaning no delay factor shows strong statistical significance

- Pregnancy (p = 0.121) has the largest effect size (HR = 5.545), but it's not statistically significant
- Some predictors (Diagnostic dilemma, Unfamiliarity with treatment, Unknown) have standard errors in the thousands, leading to unrealistic HR values near 0 or infinity
- Concordance (C = 0.63, SE = 0.06) suggests moderate discrimination (higher C would indicate stronger model performance).
- Likelihood Ratio Test (p = 0.3), Wald Test (p = 0.8), and Score Test (p = 0.3) all show weak model significance

Conclusion: DelayCause does not strongly influence early death in this dataset

For the second test (glm): to determine relationship between survival and cause of delay.

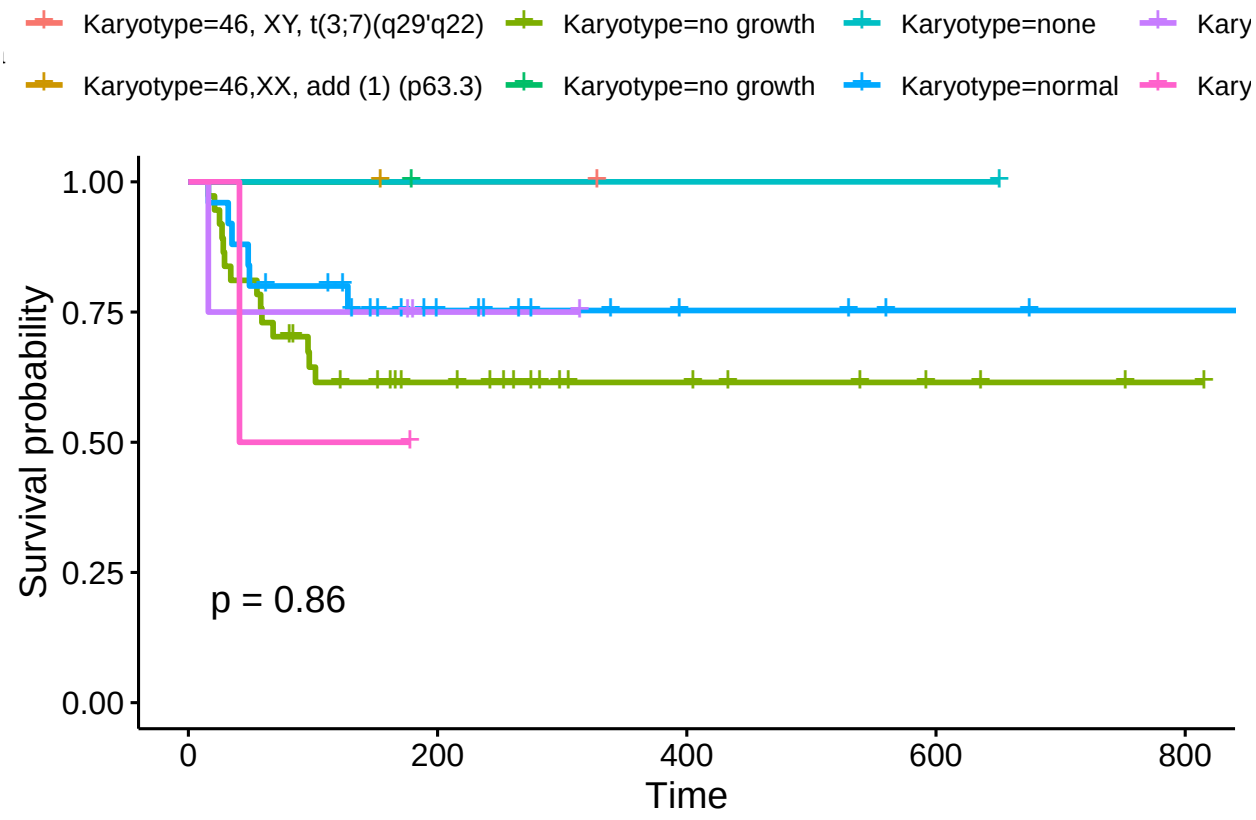
- None of the predictors are statistically significant (p-values all > 0.05), meaning DelayCause does not strongly impact Early Death (CR) in this dataset.
- Residual Deviance (79.36) vs. Null Deviance (88.63) indicates only a minor improvement, meaning DelayCause explains very little of the variation in TxResponse.
- Extreme coefficient values for pregnancy, diagnostic dilemma, unfamiliarity with treatment, and unknown suggest data sparsity in those categories.
- AIC (95.36) suggests the model is not strongly optimized for predicting Early Death.

Conclusion: DelayCause does not significantly predict Early Death in TxResponse

Test 10: Test KaryoType and Response

Compare survival outcomes based on karyotype results (e.g., normal vs. no growth).

```
km_fit_karyo <- survfit(Surv(SurvivalOS, TxResponse == 'Early Death') ~ Karyotype,
                        data = data)
ggsurvplot(km_fit_karyo, data=data, pval=TRUE)
```



Also perform chi-square test for Karyotype and response

```
table_karyo_response <- table(data$Karyotype, data$TxResponse == 'CR')
chisq.test(table_karyo_response)
```

```
##
##  Pearson's Chi-squared test
##
## data:  table_karyo_response
## X-squared = 4.984, df = 7, p-value = 0.6619
```

Conclusion

From the plot, it looks like karyotype = normal has the best survival probability followed by no growth, but it is not significant (p = 0.986).

From Chisquare test, since p-value is 0.6619, it is not significant.

Summary: What Did All These Tests Show?

To answer one big question: Does starting treatment sooner improve patient outcomes? Here's what they found:

- Patients who started treatment later didn't have worse remission rates or survival times compared to those who started earlier.
- Statistical tests confirmed that TDT didn't significantly affect outcomes like remission, early death, or overall survival—even after adjusting for other factors like age and lab results.

These findings suggest it might be okay to wait for important test results before starting treatment in some cases—especially if patients are stable—so doctors can choose the best possible treatment plan for each individual.