TTEAnalysis

```r
gc()
```

```
          used (Mb) gc trigger (Mb) max used (Mb)
Ncells  598614 32.0    1364202 72.9   692245 37.0
Vcells 1103446  8.5    8388608 64.0  1923819 14.7
```

```r
rm(list = ls())
cat('\014')
```

```r
graphics.off()

if(!require(haven)) {install.packages("haven"); library(haven)}
if(!require(tidyverse)) {install.packages("tidyverse"); library(tidyverse)}
if(!require(ggplot2)) {install.packages("ggplot2"); library(ggplot2)}
if(!require(survival)) {install.packages("survival"); library(survival)} # for MNRM
if(!require(survminer)) {install.packages("survminer"); library(survminer)} # for model means
if(!require(officer)) {install.packages("officer"); library(officer)} # for reporting
if(!require(flextable)) {install.packages("flextable"); library(flextable)} # for reporting
if(!require(Hmisc)) {install.packages("Hmisc"); library(Hmisc)}
if(!require(openxlsx)) {install.packages("openxlsx"); library(openxlsx)}
if(!require(epiR)) {install.packages("epiR"); library(epiR)}
if(!require(Barnard)) {install.packages("Barnard"); library(Barnard)}


adtte <- read_xpt("~/Documents/Coding/Website/biostatistics/Data/adtte.xpt")
adsl <- read_xpt("~/Documents/Coding/Website/biostatistics/Data/adsl.xpt")

doc.KM <- read_docx()
```

```r
adtte <- adtte %>%
  mutate(Evt = ifelse(CNSR == 0, 1, 0),
         Treatment = TRTP,
         Treat = recode(TRTAN, '54' = '1', '81' = '2', '0' = '0'))

master = adsl %>%
  filter(ITTFL == "Y") %>%
  group_by(TRT01P) %>%
  summarise(Treat = first(TRT01PN), N.Pop = n()) %>%
  rename(Treatment = TRT01P) %>%
  mutate(Treat = recode(Treat, '54' = '1', '81' = '2', '0' = '0'))

pop <- adsl %>%
  filter(ITTFL == "Y") %>%
  select(USUBJID)

#check adtte has
adtte <- merge(pop, adtte, by ="USUBJID")

res <- data.frame()

doc.KM = read_docx()
```

```r
param <-  unique(adtte$PARAM)
p=1

tte <- adtte

doc.KM = body_add_par(x = doc.KM,
                      value = param[[p]],
                      style = 'heading 2')

NEvt = data.frame('Treatment' = NA, 'N.eligible' = NA, 'Evt' = NA, 'RR' = NA, 'LCL.RR' = NA,
                  'OR' = NA, 'LCL.OR' = NA, 'UCL.OR' = NA,
                  'RD' = NA, 'LCL.RD' = NA, 'UCL.RD' = NA, 'p.fisher' = NA, 'p.barnard' = NA)

noEvt = 0
AEFilter = 0
time = NULL
fup  = NULL
hr   = NULL
logrank = data.frame('Log-rank Test' = NA, 'Treatment' = NA)
KM  = data.frame('median' = NA, '0.95LCL' = NA, '0.95UCL' = NA, 'Treatment' = NA, 'AD' = NA)
FUP = data.frame('median' = NA, '0.95LCL' = NA, '0.95UCL' = NA, 'Treatment' = NA)
HR  = data.frame('exp.(coef)' = NA, 'lower .95' = NA, 'upper .95' = NA, 'Treatment' = NA)
scoretest = data.frame('Score Test' = NA, 'Treatment' = NA)
foo = NULL

error0 = try({NEvt = tte %>%
  group_by(Treatment) %>%
  summarise(N.eligible = n_distinct(USUBJID),
            Evt = sum(Evt))}, silent = T)

TAB = NEvt %>% mutate(CNSR = N.eligible - Evt) %>% #Umstrukturieren für epi-tools - s. Help
  arrange(desc(Treatment)) %>% # Leri muss oben stehen (Expose+)
  dplyr::select(Treatment, Evt, CNSR, N.eligible) # Disease +, Disease -, Total


if(any(TAB$Evt == 0)){
  TAB$Evt = TAB$Evt + 0.5
  TAB$CNSR = TAB$CNSR + 0.5
  TAB$N.eligible = TAB$N.eligible + 1
}
```

```r
vec = c(TAB$Evt[1], TAB$CNSR[1], TAB$Evt[2], TAB$CNSR[2])
RR_OR_RD = epi.2by2(vec, method = 'cohort.count')$massoc.summary[1:3,]


RR = RR_OR_RD[1, 2:4]
RR$Treatment = 'Xanomeline Low Dose'
names(RR) = c('RR', 'LCL.RR', 'UCL.RR', 'Treatment')
OR = RR_OR_RD[2, 2:4]
OR$Treatment = 'Xanomeline Low Dose'
names(OR) = c('OR', 'LCL.OR', 'UCL.OR', 'Treatment')
RD = RR_OR_RD[3, 2:4]
RD$Treatment = 'Xanomeline Low Dose'
names(RD) = c('RD', 'LCL.RD', 'UCL.RD', 'Treatment')

p.fisher = data.frame('p.fisher' = fisher.test(TAB[,2:3])$p.value, 'Treatment' = 'Xanomeline

NEvt = NEvt %>%
  left_join(RR, by = 'Treatment') %>%
  left_join(OR, by = 'Treatment') %>%
  left_join(RD, by = 'Treatment') %>%
  left_join(p.fisher, by = 'Treatment')


#Survival Stats
error1 = try({time   <- survfit(Surv(AVAL, Evt)     ~ Treat, data = tte)}, silent = T)
error2 = try(fup    <- survfit(Surv(AVAL, CNSR) ~ Treat, data = tte), silent = T)
error3 = try(hr     <- coxph(Surv(AVAL, Evt)        ~ Treat, data = tte), silent = T)

if(sum(NEvt$Evt) == 0 | is.na(sum(NEvt$Evt))){
  noEvt = 1
}

# Kaplan Meier Plots

KM = as.data.frame(summary(time)$table)

# stimmt die erwartete Spaltenzahl, wird weiter aufbereitet

KM = subset(KM, select = -c(1, 2, 3, 4, 5, 6))
KM$Treatment[row.names(KM) == 'Treat=0'] = "Placebo"
KM$Treatment[row.names(KM) == 'Treat=1'] = "Xanomeline Low Dose"
KM$Treatment[row.names(KM) == 'Treat=2'] = "Xanomeline High Dose"
```

```r
KM <- KM %>%
  mutate(Treatment = case_when(
    row.names(KM) == "Treat=0" ~ "Placebo",
    row.names(KM) == "Treat=1" ~ "Xanomeline Low Dose",
    row.names(KM) == "Treat=2" ~ "Xanomeline High Dose",
    TRUE ~ Treatment  # Keeps existing values for other rows
  ))
if (noEvt == 0){
  logrank <- as.data.frame(surv_pvalue(time)$pval)
  names(logrank) = 'Log-rank Test'
  logrank$Treatment = 'Xanomeline Low Dose'
}

filename = paste0('~/Documents/Coding/Website/biostatistics/Images/KM/KM_', p, '_TTE','.png')
tit = str_to_title(tte$PARAM[1])
subtit = '(MITT Set)'
# device öffnen
png(filename, height = 480, width = 640)


foo = ggsurvplot(time, data = tte, risk.table = T, palette = 'lancet', ggtheme = theme_pubcle
                 title = str_wrap(tit, 70),
                 pval = T,
                 subtitle = paste0(subtit),
                 legend.title = 'Treatment',
                 legend.labs = c("Placebo", "Xanomeline Low Dose", "Xanomeline High Dose"),
                 risk.table.y.text = F,
                 risk.table.title = 'Number at risk',
                 ylab = 'Probability of no event', xlab = 'Time since therapy start (Days)',
                 break.time.by = 180)
print(foo)
dev.off()
```

```
pdf
  2
```

```r
doc.KM = doc.KM %>%
  body_add_par(value = '') %>%
  body_add_img(src = filename, height = 3.5, width = 4.66666667)
fig_num.KM = run_autonum(seq_id = 'Figure', pre_label = 'Figure ', post_label = ': ')
doc.KM <- body_add_caption(x = doc.KM,
                           value = block_caption(paste0(tit, ' - ', subtit), autonum = fig_nu
```