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library(survival)

# Klein and Moeschberger (1997)
library(KMsurv)

## Data from Section 1.2

data(drug6mp)

? drug6mp

drug6mp[1:7, ]

time <- c(drug6mp$t1, drug6mp$t2)
irelapse <- c(rep(1,21), drug6mp$relapse)
# 1: placebo e 2: 6-MP
grupo <- c(rep(1, 21), rep(2, 21))

kmc <- survfit(Surv(time, irelapse) ~ grupo)
plot(kmc, mark.time = TRUE, xlab = "Tempo até recidiva (meses)",
     col = c("black", "blue"), ylab = "Função sobrevivência")
legend("topright", lty = 1, col = c("black", "blue"),
     c("Placebo", "6-MP"), bty = "n")

wst <- log(-log(kmc$surv))
wt <- log(kmc$time)
plot(wt, wst, pch = 20, xlab = "log(t)", ylab = "log(-log(S(t)))")
survdiff(Surv(time, irelapse) ~ grupo)

est <- log(kmc$surv)
plot(kmc$time, est, pch = 20, xlab = "t", ylab = "log(S(t))")

mwei <- survreg(Surv(time, irelapse) ~ grupo, dist = "weibull")
summary(mwei)
confint(mwei)

# Fator de aceleração (gama)
exp(mwei$coeff[2])

1 / mwei$scale # alfa^

mediana <- predict(mwei, newdata = list(grupo = c(0, 1)),
                  type = "quantile", p = 0.5)
mediana
mediana[2] / mediana[1]

plot(kmc, mark.time = TRUE, xlab = "Tempo até recidiva (meses)",
     col = c("black", "blue"), ylab = "Função sobrevivência")
legend("topright", lty = 1, col = c("black", "blue"),
     c("Placebo", "6-MP"), bty = "n")

varexp <- unique(mwei$linear.predictors)
# Placebo
curve(pweibull(x, shape = 1/ mwei$scale,
              scale = exp(varexp[1]),
              lower.tail = FALSE), add = TRUE)
# 6-MP
curve(pweibull(x, shape = 1/ mwei$scale,
              scale = exp(varexp[2]),
              lower.tail = FALSE), add = TRUE, col = "blue")

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mexp <- survreg(Surv(time, irelapse) ~ grupo, dist = "exponential")
summary(mexp)

plot(kmc, mark.time = TRUE, xlab = "Tempo até recidiva (meses)",
     col = c("black", "blue"), ylab = "Função sobrevivência")
legend("topright", lty = 1, col = c("black", "blue"),
      legend = c("Placebo", "6-MP"), bty = "n")

varexp <- unique(mexp$linear.predictors)
# Placebo
curve(pexp(x, rate = 1 / exp(varexp[1]),
        lower.tail = FALSE), add = TRUE)
# 6-MP
curve(pexp(x, rate = 1 / exp(varexp[2]),
        lower.tail = FALSE), add = TRUE, col = "blue")

# Teste da RV: exponencial x Weibull
rv <- 2 * (mwei$loglik[2] - mexp$loglik[2])
cat("\n Estatística de teste =", rv, "(p =", pchisq(rv, 1,
        lower.tail = FALSE), ")")

## Data from Section 1.8
data(larynx)

? larynx

mycolors <- rainbow(length(unique(larynx$stage)))
kmc <- survfit(Surv(time, delta) ~ stage, data = larynx)
plot(kmc, mark.time = TRUE, xlab = "Tempo até óbito (meses)",
     col = mycolors, ylab = "Função sobrevivência")
legend("topright", lty = 1, col = mycolors,
      legend = unique(larynx$stage), bty = "n")

wst <- log(-log(kmc$surv))
wt <- log(kmc$time)
plot(wt, wst, pch = 20, xlab = "log(t)", ylab = "log(-log(S(t)))")
survdif(Surv(time, delta) ~ stage, data = larynx)

est <- log(kmc$surv)
plot(kmc$time, est, pch = 20, xlab = "t", ylab = "log(S(t))")

cstage <- factor(larynx$stage)
mwei <- survreg(Surv(time, delta) ~ cstage * age, dist = "weibull",
              data = larynx)
summary(mwei)
confint(mwei)

## Exercício 1, cap. 4 em Colosimo e Giolo (2006).
tempo <- c(1,2,2,2,2,6,8,8,9,9,13,13,16,17,22,25,29,34,36,43,45,
          1,2,5,7,7,11,12,19,22,30,35,39,42,46,55)
delta <- c(1,1,1,1,0,1,1,1,1,0,1,0,1,1,0,0,1,1,1,0,0,1,1,1,1,0,0,
          1,1,1,1,0,1,1,1,1)
tratamento <- factor(c(rep("A", 21), rep("B", 15)))

kmc0 <- survfit(Surv(tempo, delta) ~ 1)
kmc <- survfit(Surv(tempo, delta) ~ tratamento)
plot(kmc, mark.time = TRUE, xlab = "Tempo de sobrevivência (meses)",
     col = c("black", "blue"), ylab = "Função sobrevivência")
legend("topright", lty = 1, col = c("black", "blue"),
      c("A", "B"), bty = "n")

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survdiff(Surv(tempo, delta) ~ tratamento)

# Linearização exponencial
est <- log(kmc$surv)
plot(kmc$time, est, pch = 20, xlab = "t", ylab = "log(S(t))")

# Linearização Weibull
wst <- log(-log(kmc$surv))
wt <- log(kmc$time)
plot(wt, wst, pch = 20, xlab = "log(t)", ylab = "log(-log(S(t)))")

# Linearização lognormal
lognst <- qnorm(kmc$surv)
lognt <- log(kmc$time)
plot(lognt, lognst, pch = 20, xlab = "log(t)", ylab = "Phi^-1(S(t))")

# Modelos
mexp <- survreg(Surv(tempo, delta) ~ tratamento, dist = "exponential")
summary(mexp)

mwei <- survreg(Surv(tempo, delta) ~ tratamento, dist = "weibull")
summary(mwei)
confint(mwei)

plot(kmc, mark.time = TRUE, xlab = "Tempo de sobrevivência (meses)",
      col = c("black", "blue"), ylab = "Função sobrevivência")
legend("topright", lty = 1, col = c("black", "blue"),
      c("A", "B"), bty = "n")
varexp <- unique(mwei$linear.predictors)
# Tratamento A
curve(pweibull(x, shape = 1/ mwei$scale,
              scale = exp(varexp[1]),
              lower.tail = FALSE), add = TRUE)
# Tratamento b
curve(pweibull(x, shape = 1/ mwei$scale,
              scale = exp(varexp[2]),
              lower.tail = FALSE), add = TRUE, col = "blue")

# Modelo Weibull sem covariável
i0 <- which(kmc0$surv > 0)
wst0 <- log(-log(kmc0$surv[i0]))
wt0 <- log(kmc0$time[i0])
plot(wt0, wst0, pch = 20, xlab = "log(t)", ylab = "log(-log(S(t)))")
abline(lm(wst0 ~ wt0), lty = 2, col = "red")

mwei0 <- survreg(Surv(tempo, delta) ~ 1, dist = "weibull")
summary(mwei0)

plot(kmc0, mark.time = TRUE, xlab = "Tempo de sobrevivência (meses)",
      ylab = "Função sobrevivência", conf.int = FALSE)
curve(pweibull(x, shape = 1 / mwei0$scale,
              scale = exp(coef(mwei0)),
              lower.tail = FALSE), add = TRUE, col = "blue")

# Modelo exponencial sem covariável
plot(kmc0, mark.time = TRUE, xlab = "Tempo de sobrevivência (meses)",
      ylab = "Função sobrevivência", conf.int = FALSE)
mexp0 <- survreg(Surv(tempo, delta) ~ 1, dist = "exponential")
summary(mexp0)
curve(pexp(x, rate = 1 / exp(coef(mexp0))),

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        lower.tail = FALSE), add = TRUE, col = "blue")

mlogn <- survreg(Surv(tempo, delta) ~ tratamento, dist = "lognormal")
summary(mlogn)

# Modelo lognormal sem covariável
lognst0 <- qnorm(kmc0$surv[i0])
lognt0 <- log(kmc0$time[i0])
plot(lognt0, lognst0, pch = 20, xlab = "log(t)",
      ylab = "Phi^-1(S(t))")
abline(lm(lognst0 ~ lognt0), lty = 2, col = "red")

plot(kmc0, mark.time = TRUE, xlab = "Tempo de sobrevivência (meses)",
      ylab = "Função sobrevivência", conf.int = FALSE)
mlogn0 <- survreg(Surv(tempo, delta) ~ 1, dist = "lognormal")
summary(mlogn0)
curve(plnorm(x, sdlog = mlogn0$scale,
             meanlog = coef(mlogn0),
             lower.tail = FALSE), add = TRUE, col = "blue")

# Três modelos
plot(kmc0, mark.time = TRUE, xlab = "Tempo de sobrevivência (meses)",
      ylab = "Função sobrevivência", conf.int = FALSE)
curve(pweibull(x, shape = 1 / mwei0$scale,
               scale = exp(coef(mwei0)),
               lower.tail = FALSE), add = TRUE, col = "blue")
curve(pexp(x, rate = 1 / exp(coef(mexp0)),
           lower.tail = FALSE), add = TRUE, col = "red")
curve(plnorm(x, sdlog = mlogn0$scale,
             meanlog = coef(mlogn0),
             lower.tail = FALSE), add = TRUE, col = "darkgreen")
legend("topright", lty = 1, col = c("blue", "red", "darkgreen"),
      c("Weibull", "Exponencial", "Lognormal"), bty = "n")

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