P8108 Homework 9 & 10

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Homework 9

Problem 1

Since $T_i \sim LN(\mu, \sigma^2)$, we have the p.d.f. of the log-normal:

$$f(t) = \frac{1}{t\sigma\sqrt{2\pi}} \exp\left(-\frac{(\ln t - \mu)}{2\sigma^2}\right)$$

The log-likelihood of the sample $\{t_1, t_2, \ldots, t_n\}$ is:

$$LL = -\frac{n}{2}\ln(2\pi) - \frac{n}{2}\ln\sigma^2 - \frac{1}{2\sigma^2}\sum_{i=1}^{n}(\ln t_i - \mu)^2 - \sum_{i=1}^{n}\ln t_i$$

Taking the F.O.C. with respect to μ and σ, and set them to zero, we can get:

$$\frac{\partial LL}{\partial \mu} = \frac{1}{\sigma^2}\left(\sum_{i=1}^{n}\ln t_i - \mu\right) = 0$$
$$\frac{\partial LL}{\partial \sigma^2} = -\frac{n}{2\sigma^2} + \frac{\sum_{i=1}^{n}(\ln t_i - \mu)^2}{2\sigma^4} = 0$$

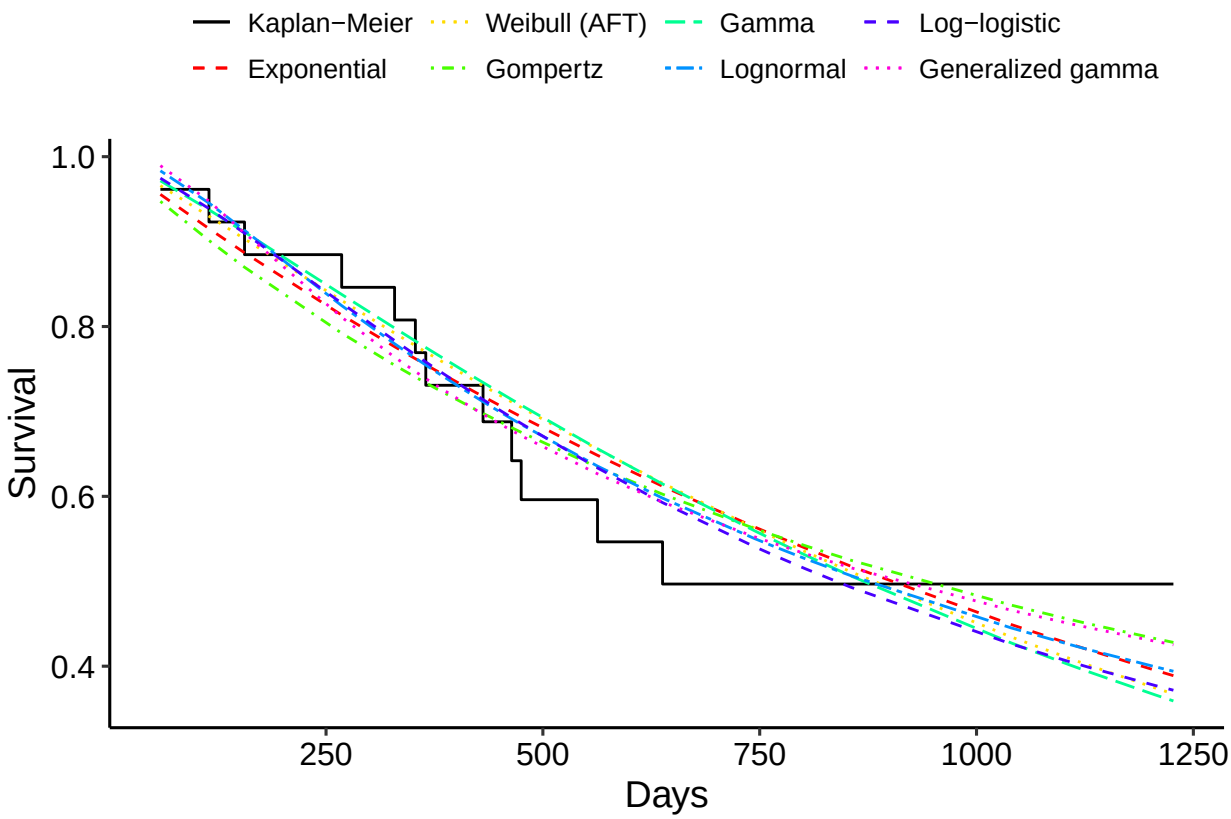
We can solve them MLE $\hat{\mu}, \hat{\sigma}^2$ from the above equations:

$$\hat{\mu} = \frac{1}{n}\sum_{i=1}^{n}\ln t_i$$
$$\hat{\sigma}^2 = \frac{1}{n}\sum_{i=1}^{n}(\ln t_i - \hat{\mu})^2$$

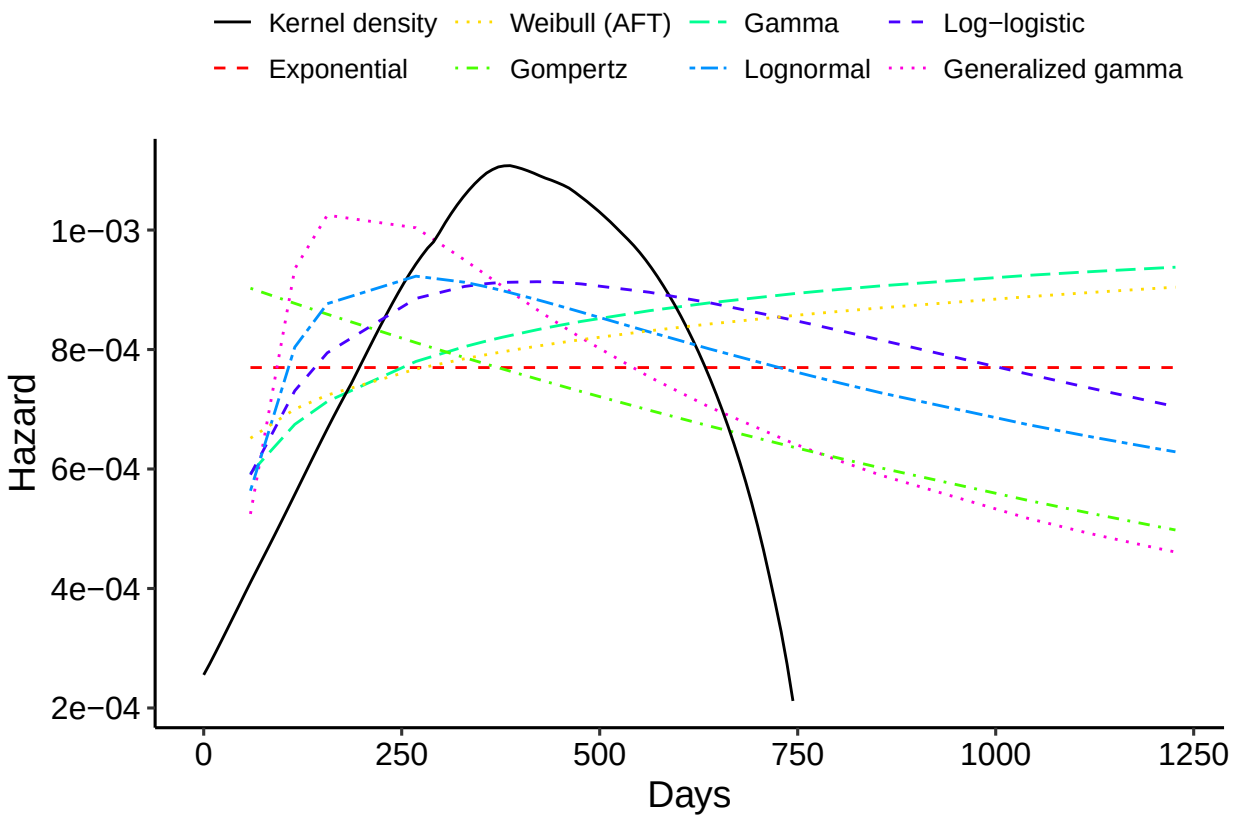
Therefore, MLEs have closed form.

Problem 2

I plot the survival function using K-M estimator and the survival functions from parametric models.



From the above plot, we see that the survival function estimates from parametric models are pretty close (at least visually), and none of them seems similar to the K-M estimator visually. Therefore, I plot the hazard functions corresponding to these survival functions to see if there exists any similarity.



From the hazard function plot above, although there is diffence between different parametric models, none of them is similar to the non-parametric estimator.

Problem 3

The likelihood of Weibull distribution is:

$$
\begin{aligned}
L(\beta) &= \prod_{i=1}^{n} h\left(T_i \mid Z_i\right)^{\Delta_i} S\left(T_i\right) \\
&= \prod_{i=1}^{n} \left(h_0(T_i) e^{\beta Z_i}\right)^{\Delta_i} e^{-\lambda T_i^{\alpha}} \\
&= \prod_{i=1}^{n} \left(\lambda \alpha T_i^{\alpha-1} e^{\beta Z_i}\right)^{\Delta_i} e^{-\lambda T_i^{\alpha}} \\
&= \left(\lambda\alpha \times 16^{\alpha-1} e^{\beta}\right)^{1} e^{-\lambda \times 16^{\alpha}} \times e^{-\lambda \times 20^{\alpha}} \\
&\times \left(\lambda\alpha \times 12^{\alpha-1}\right)^{1} e^{-\lambda \times 12^{\alpha}} \times e^{-\lambda \times 14^{\alpha}} \\
&\times \left(\lambda\alpha \times 11^{\alpha-1}\right)^{1} e^{-\lambda \times 11^{\alpha}} \\
&\times \left(\lambda\alpha \times 9^{\alpha-1} e^{\beta}\right)^{1} e^{-\lambda \times 9^{\alpha}} \\
&= (\lambda\alpha)^4 (16^{\alpha-1} 12^{\alpha-1} 11^{\alpha-1} 9^{\alpha-1}) e^{2\beta - \lambda(16^{\alpha} + 20^{\alpha} + 12^{\alpha} + 14^{\alpha} + 11^{\alpha} + 9^{\alpha})}
\end{aligned}
$$

Problem 4

```
##
## Call:
## survreg(formula = Surv(time, event == 1) ~ trt, data = leu_dat,
##     dist = "loglogistic")
##              Value Std. Error     z       p
## (Intercept)  1.893      0.208  9.12 < 2e-16
## trt6-MP      1.265      0.326  3.89   1e-04
## Log(scale)  -0.604      0.150 -4.02 5.7e-05
##
## Scale= 0.547
##
## Log logistic distribution
## Loglik(model)= -107.7   Loglik(intercept only)= -115.4
##  Chisq= 15.38 on 1 degrees of freedom, p= 8.8e-05
## Number of Newton-Raphson Iterations: 4
## n= 42
```

From the AFT model summary, we can see that the coefficient corresponds to the treatment effect is significant, which means that the treatment 6-MP has a significant effect on the survival of patients with Acute Myelogenous Leukemia.

The corresponding model is:

$$\log T_i = 1.8927 + 1.2655 \times I(\text{trt}_i = \text{ 6-MP})$$

Homework 10

Problem 1

Write down the definition of the overall hazards, cause specific hazards,and sub-distribution hazards. Describe the relationship and differences.

- Hazard Function :

$$h(t) = \lim_{\Delta t \to 0} \frac{P(t < T \leq t + \Delta t \mid T \geq t)}{\Delta t}$$

- Cause Specific Hazards:

$$h_k(t) = \lim_{\Delta t \to 0} \frac{P(t < T \leq t + \Delta t, \Delta = k \mid T \geq t)}{\Delta t}$$

  for $k = 1, 2, \ldots, K$ and no overlapping among the different types of events

- Sub-distribution hazard functions

$$h_k^s(\mathrm{t}) = \lim_{\Delta t \to 0} \frac{P(t \leq T < t + \Delta t, \Delta = k \mid T \geq t \cup (T < t \cap \Delta \neq k))}{\Delta t}$$

  Relationship

$$h(t) = \sum_{k=1}^{K} \lim_{\Delta t \to 0} \frac{P(t < T \leq t + \Delta t, \Delta = k \mid T \geq t)}{\Delta t} = \sum_{k=1}^{K} h_k(t)$$

and

$$h_k(t) \neq h_k^s(t)$$

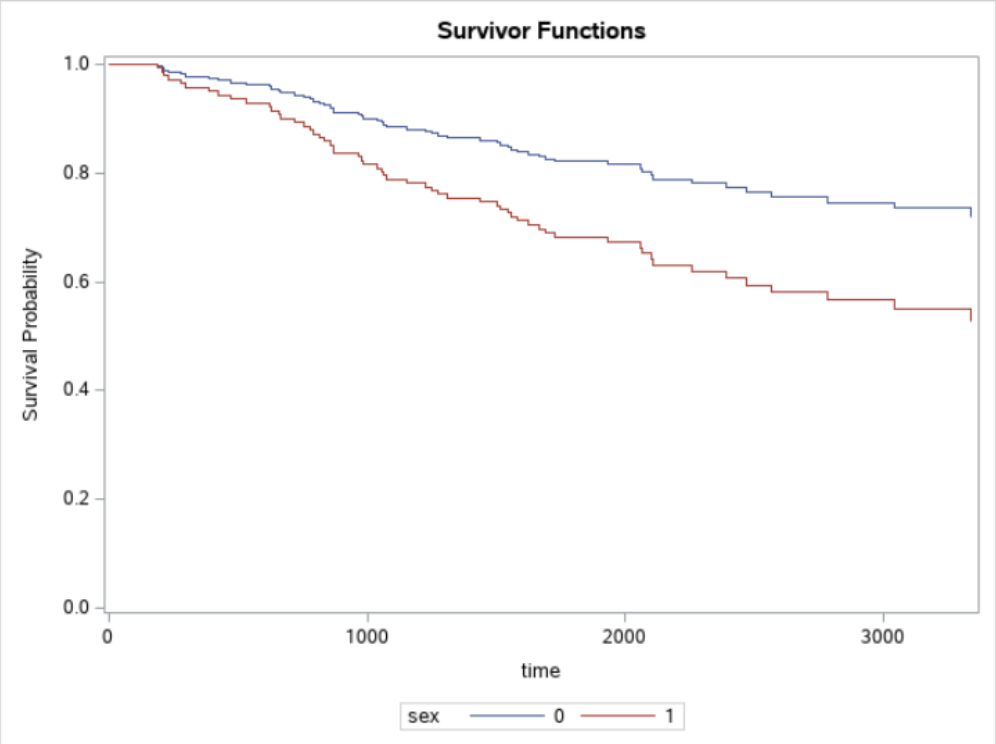
Problem 2

Here is the cause-specific proportional hazard model results.

Testing Global Null Hypothesis: BETA=0			
Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	6.1506	1	0.0131
Score	6.4680	1	0.0110
Wald	6.2370	1	0.0125

Type 3 Tests			
Effect	DF	Wald Chi-Square	Pr > ChiSq
sex	1	6.2370	0.0125

Analysis of Maximum Likelihood Estimates								
Parameter		DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio	Label
sex	1	1	0.66214	0.26513	6.2370	0.0125	1.939	sex 1



From the results above, we can see that the effect of sex on the death from melanoma is a risk increase about 93.9%.

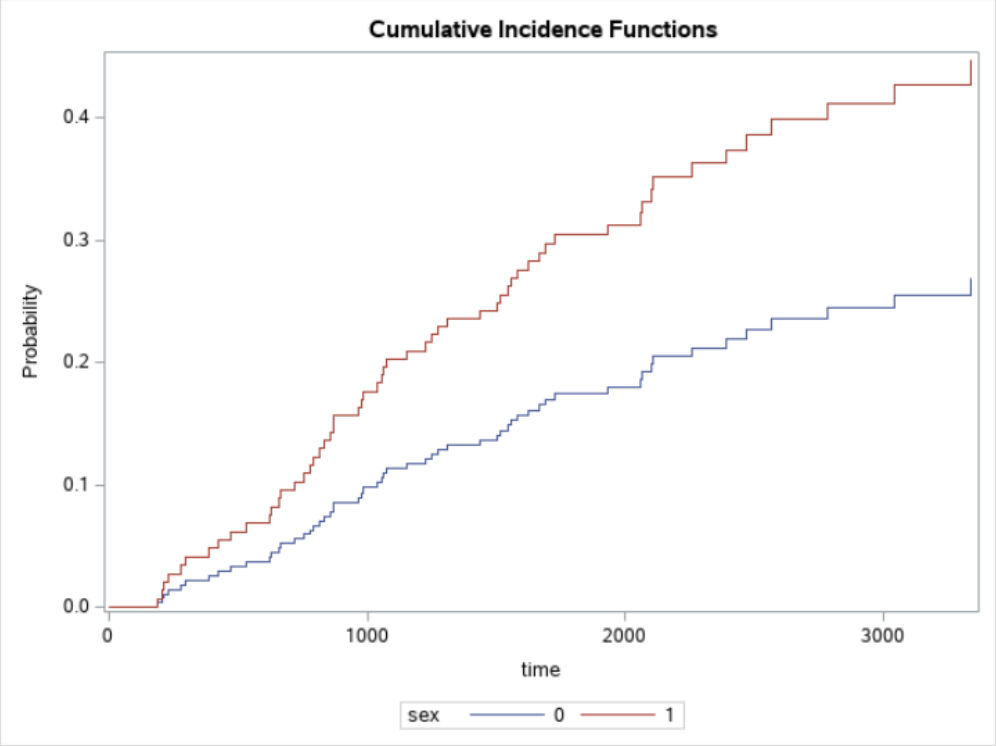
Problem 3

Here is the results of proportional hazard model using sub-distribution hazards, which is the Fine and Gray's method.

Testing Global Null Hypothesis: BETA=0			
Test	Chi-Square	DF	Pr > ChiSq
Wald	5.8363	1	0.0157

Type 3 Tests			
Effect	DF	Wald Chi-Square	Pr > ChiSq
sex	1	5.8363	0.0157

Analysis of Maximum Likelihood Estimates								
Parameter		DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio	Label
sex	1	1	0.63651	0.26347	5.8363	0.0157	1.890	sex 1



From the results above, we can see that the effect of sex on the death from melanoma is a risk increase about 89.0%.

Appendix: Code for this report

```
knitr::opts_chunk$set(echo = FALSE, message = FALSE, warning = FALSE)
library(tidyverse)
library(knitr)
library(kableExtra)
library(survival)
library(flexsurv)
library(survminer)
library(survMisc)
library(MASS)
dists <- c("exp", "weibull", "gompertz", "gamma",
           "lognormal", "llogis", "gengamma")
dists_long <- c("Exponential", "Weibull (AFT)",
                "Gompertz", "Gamma", "Lognormal", "Log-logistic",
                "Generalized gamma")
parametric_surv <- vector(mode = "list", length = length(dists))
for (i in 1:length(dists)){
  fit <- flexsurvreg(Surv(futime, fustat) ~ 1, data = ovarian, dist = dists[i])
  parametric_surv[[i]] <- summary(fit, type = "survival",
                                  ci = FALSE, tidy = TRUE)
  parametric_surv[[i]]$method <- dists_long[i]
}

parametric_surv_df <- do.call("rbind", parametric_surv)
#parametric_surv <- rbind(parametric_surv[[1]], parametric_surv[[2]], parametric_surv[[3]],parametric_s

km.fit <- survfit(Surv(futime, fustat) ~ 1, data = ovarian)
km_surv <- data.frame(time = km.fit$time, est = km.fit$surv, method = "Kaplan-Meier")
surv_df <- rbind(km_surv, parametric_surv_df)

surv_df$method = factor(surv_df$method,
                        levels = c("Kaplan-Meier",
                                   dists_long))

ggplot(surv_df, aes(x = time, y = est, col = method, linetype = method)) +
  geom_step(data = surv_df[surv_df$method == "Kaplan-Meier",], aes(x =time, y = est, col = method, linet
  geom_line(data = surv_df[surv_df$method != "Kaplan-Meier",], aes(x = time, y = est, col = method, linet
  xlab("Days") + ylab("Survival") +
  scale_colour_manual(name = "",
                      values = c("black", rainbow(7)),
                      breaks = c("Kaplan-Meier", dists_long)) +
  scale_linetype_manual(name = "",
                        values = c(1,rep_len(2:6, 7)),
                        breaks = c("Kaplan-Meier", dists_long)) +
  theme_survminer()


library("muhaz")
kernel_haz_est <- muhaz(ovarian$futime, ovarian$fustat)
kernel_haz <- data.frame(time = kernel_haz_est$est.grid,
                         est = kernel_haz_est$haz.est,
                         method = "Kernel density")
```

```
parametric_haz <- vector(mode = "list", length = length(dists))
for (i in 1:length(dists)){
  fit <- flexsurvreg(Surv(futime, fustat) ~ 1, data = ovarian, dist = dists[i])
  parametric_haz[[i]] <- summary(fit, type = "hazard",
                                 ci = FALSE, tidy = TRUE)
  parametric_haz[[i]]$method <- dists_long[i]
}

parametric_haz_df <- do.call("rbind", parametric_haz)
#parametric_surv <- rbind(parametric_surv[[1]], parametric_surv[[2]], parametric_surv[[3]],parametric_s

#km_haz <- data.frame(time = km.fit$time, est = km.fit$cumhaz, method = "Kaplan-Meier")
#km_haz$est = c(km_haz$est[1],diff(km_haz$est))
haz_df <- rbind(kernel_haz, parametric_haz_df)

ggplot(haz_df, aes(x = time, y = est, col = method, linetype = method)) +
  geom_line() +
  xlab("Days") + ylab("Hazard") +
  scale_colour_manual(name = "",
                      values = c("black", rainbow(7)),
                      breaks = c("Kernel density", dists_long)) +
  scale_linetype_manual(name = "",
                        values = c(1,rep_len(2:6, 7)),
                        breaks = c("Kernel density", dists_long)) +
  theme_survminer()


leu_dat = readxl::read_excel("Datasets.xlsx", sheet = "Leukaemia")
leu_dat$trt = relevel(factor(leu_dat$trt), ref = "Control")
leuk.aft <- survreg(Surv(time, event == 1) ~ trt, leu_dat,
                    dist = "loglogistic")
summary(leuk.aft)
knitr::include_graphics("./hw10_p2_a.png")
knitr::include_graphics("./hw10_p2_b.png")
knitr::include_graphics("./hw10_p3_a.png")
knitr::include_graphics("./hw10_p3_b.png")
proc import out = melanoma
    datafile="/home/u62725158/Datasets.xlsx"
    dbms=xlsx
    replace;
    sheet = "Melanoma";
    GETNAMES=yes;
run;

data Risk;
    sex = 0; output;
    sex = 1; output;
    format sex BEST.;
run;

* Problem 2 ;

proc phreg data = melanoma plots(overlay = stratum) = survival;
```

```
class sex (order = internal ref = first);
model time*status(2, 3) = sex;
Hazardratio 'Pairwise' sex / diff=pairwise;
baseline covariates=Risk out=out1 cif=_all_ /
seed = 8108;
run;


* Problem 3 ;

proc phreg data = melanoma plots(overlay = stratum) = cif;
class sex (order = internal ref = first);
model time*status(2) = sex/ eventcode = 1;
Hazardratio 'Pairwise' sex / diff=pairwise;
baseline covariates=Risk out=out1 cif=_all_ /
seed = 8108;
run;

proc lifetest data = melanoma plots= cif(test);
time time*status(2)/ eventcode = 1;
strata sex/ order=internal;
run;
```