

이 supplementary document는 예기치 않은 오류가 발생하는 경우 차이를 비교하는데 사용할 수 있도록 본문에 제공된 R code를 시행한 뒤, 편집없이 R console의 내용을 인용하였다. 따라서 명령어 앞의 “>”표시가 함께 실행되는 경우에는 R에서 명령어를 인식할 수 없음을 주의한다. 이 글의 코드를 R에서 사용하는 경우에는 “>”를 제거하여야 한다.

This supplementary document provides whole R code and R console contents without any editing, to be used for comparison in case of an unexpected error. Be careful that R software cannot recognize “>” which is placed in front of each command. If one wants to use the codes in this document, every “>” should be removed first.

```
<R code and R console contents>
> # Read data
> PONV.raw <- read.csv (“d:/Survival2_PONV.csv”, TRUE, sep = “;”)
> # Check imported data
> head(PONV.raw)
  No Antiemetics Age  Wt Inopioid Time PONV
1 1      0 48 78.5    0  4  0
2 3      0 54 88.3   100 21  0
3 4      0 22 49.4    0 14  0
4 5      1 67 59.0    0 12  0
5 7      1 45 64.5    0 19  0
6 8      0 44 65.9    0  8  0
>
>
> #Load Package: survival, survminer
> library(survival)
> library(survminer)
Loading required package: ggplot2
Loading required package: ggpubr
Loading required package: magrittr
>
>
> ### Kaplan-Meier Estimation (KME)
> #Add survival object
> PONV.raw$Survobj <- with(PONV.raw, Surv(Time, PONV == 1))
> head (PONV.raw)
  No Antiemetics Age  Wt Inopioid Time PONV Survobj
1 1      0 48 78.5    0  4  0  4+
2 3      0 54 88.3   100 21  0  21+
3 4      0 22 49.4    0 14  0  14+
4 5      1 67 59.0    0 12  0  12+
5 7      1 45 64.5    0 19  0  19+
6 8      0 44 65.9    0  8  0  8+
> ## Single KME. The log-log confidence interval is preferred.
> km.one <- survfit(Survobj ~1, data = PONV.raw, conf.type = “log-log”)
> # Result of KME
> km.one
Call: survfit(formula = Survobj ~ 1, data = PONV.raw, conf.type = “log-log”)

      n events median 0.95LCL 0.95UCL
104   63   10      7    16
> # Survival table
> summary (km.one)
```

Call: survfit(formula = Survobj ~ 1, data = PONV.raw, conf.type = "log-log")

time	n.risk	n.event	survival	std.err	lower 95% CI	upper 95% CI
1	104	8	0.923	0.0261	0.852	0.961
2	96	7	0.856	0.0345	0.772	0.910
3	89	3	0.827	0.0371	0.739	0.887
4	86	8	0.750	0.0425	0.655	0.822
5	76	3	0.720	0.0441	0.623	0.797
6	70	8	0.638	0.0477	0.537	0.723
7	60	5	0.585	0.0493	0.482	0.674
8	53	2	0.563	0.0498	0.460	0.654
9	49	4	0.517	0.0508	0.413	0.611
10	43	4	0.469	0.0514	0.366	0.565
11	39	2	0.445	0.0515	0.342	0.542
12	35	2	0.419	0.0516	0.318	0.518
13	32	1	0.406	0.0517	0.305	0.505
16	28	2	0.377	0.0519	0.277	0.477
17	24	2	0.346	0.0521	0.246	0.447
18	22	1	0.330	0.0521	0.231	0.432
19	21	1	0.314	0.0519	0.216	0.417

> # Survival curve

```
> ggsurvplot(km.one, data = PONV.raw, conf.int = TRUE, palette = "grey", surv.median.line = "hv",
+           break.time.by = 4, censor = TRUE, legend = "none", xlab = "Time (hour)",
+           risk.table = TRUE, tables.height = 0.2,
+           tables.theme = theme_cleantable(), risk.table.y.text = FALSE)
>
>
```

> ### KME by Antiemetics

```
> km.antiemetics <- survfit(Survobj ~ Antiemetics, data = PONV.raw, conf.type = "log-log")
```

> # Result of KME by Antiemetics

```
> km.antiemetics
```

Call: survfit(formula = Survobj ~ Antiemetics, data = PONV.raw, conf.type = "log-log")

	n	events	median	0.95LCL	0.95UCL
Antiemetics=0	51	25	13	9	NA
Antiemetics=1	53	38	6	4	10

> # Survival table of KME by Antiemetics

```
> summary(km.antiemetics)
```

Call: survfit(formula = Survobj ~ Antiemetics, data = PONV.raw, conf.type = "log-log")

Antiemetics=0						
time	n.risk	n.event	survival	std.err	lower 95% CI	upper 95% CI
1	51	1	0.980	0.0194	0.869	0.997
2	50	2	0.941	0.0329	0.829	0.981
3	48	1	0.922	0.0376	0.804	0.970
4	47	2	0.882	0.0451	0.757	0.945
6	41	3	0.818	0.0551	0.679	0.901
7	37	3	0.751	0.0625	0.603	0.851
8	32	2	0.705	0.0669	0.551	0.814
9	28	2	0.654	0.0709	0.496	0.773

10	24	3	0.572	0.0762	0.410	0.705
11	21	1	0.545	0.0773	0.383	0.681
12	19	1	0.516	0.0783	0.355	0.656
13	18	1	0.488	0.0791	0.327	0.631
17	14	1	0.453	0.0807	0.292	0.601
18	13	1	0.418	0.0817	0.258	0.570
19	12	1	0.383	0.0820	0.227	0.538

Antiemetics=1

time n.risk n.event survival std.err lower 95% CI upper 95% CI

1	53	7	0.868	0.0465	0.743	0.935
2	46	5	0.774	0.0575	0.636	0.865
3	41	2	0.736	0.0606	0.595	0.834
4	39	6	0.623	0.0666	0.478	0.738
5	33	3	0.566	0.0681	0.423	0.687
6	29	5	0.468	0.0689	0.330	0.595
7	23	2	0.428	0.0687	0.292	0.556
9	21	2	0.387	0.0679	0.256	0.516
10	19	1	0.367	0.0673	0.238	0.496
11	18	1	0.346	0.0666	0.220	0.476
12	16	1	0.325	0.0659	0.201	0.454
16	12	2	0.271	0.0650	0.153	0.402
17	10	1	0.243	0.0639	0.131	0.375

> # KM estimation, log-rank test

> survdiff (formula = Surv(Time, PONV == 1) ~ Antiemetics, data = PONV.raw)

Call:

survdiff(formula = Surv(Time, PONV == 1) ~ Antiemetics, data = PONV.raw)

N Observed Expected (O-E)^2/E (O-E)^2/V

Antiemetics=0	51	25	34.9	2.83	6.8
Antiemetics=1	53	38	28.1	3.53	6.8

Chisq= 6.8 on 1 degrees of freedom, p= 0.009

> # Survival curve of KME by Antiemetics

> ggsvplot (km.antiemetics, data = PONV.raw, fun = "pct", pval = TRUE, conf.int = TRUE, surv.median.line = "hv", linetype = "strata", palette = "grey", xlab="Time (hour)",

+ legend.title = "Antiemetics", legend.labs = c("Drug A", "Drug B"), legend = c(.1, .2),

+ break.time.by = 4, risk.table = TRUE, tables.height = 0.2,

+ tables.theme = theme_cleantable(), risk.table.y.text.col = TRUE, risk.table.y.text = TRUE)

>

>

> # LML plot

> plot (survfit(Surv(Time, PONV == 1) ~ Antiemetics, data = PONV.raw), fun = "cloglog")

> # Non-log scaled LML plot

> ponvsurv <- Surv(PONV.raw\$Time, PONV.raw\$PONV)

> NLML.fun <- function(p){return(log(-log(p)))}

> plot(survfit(ponvsurv ~ PONV.raw\$Antiemetics), fun=NLML.fun)

>

>

```

> # Univariate Cox proportional hazard model
> # for a single covariate
> cph.antiemetics <- coxph(Surv(Time, PONV == 1) ~ Antiemetics , data = PONV.raw)
> summary(cph.antiemetics)
Call:
coxph(formula = Surv(Time, PONV == 1) ~ Antiemetics, data = PONV.raw)

```

```

n= 104, number of events= 63

      coef exp(coef) se(coef)  z Pr(>|z|)
Antiemetics 0.6664  1.9471  0.2581 2.582 0.00983 **
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

```

```

      exp(coef) exp(-coef) lower .95 upper .95
Antiemetics  1.947  0.5136  1.174  3.229

```

```

Concordance= 0.615 (se = 0.032 )
Rsquare= 0.064 (max possible= 0.993 )
Likelihood ratio test= 6.85 on 1 df, p=0.009
Wald test      = 6.67 on 1 df, p=0.01
Score (logrank) test = 6.91 on 1 df, p=0.009

```

```

>
>
> # Multivariate Cox regression
> cph.full <- coxph(Surv(Time, PONV == 1) ~ Antiemetics + Age + Wt + Inopioid,
+      data = PONV.raw)
> summary(cph.full)
Call:
coxph(formula = Surv(Time, PONV == 1) ~ Antiemetics + Age + Wt +
      Inopioid, data = PONV.raw)

```

```

n= 104, number of events= 63

      coef exp(coef) se(coef)  z Pr(>|z|)
Antiemetics 0.706453  2.026790  0.271136  2.606 0.00917 **
Age      -0.006871  0.993153  0.009312 -0.738 0.46060
Wt      -0.004329  0.995681  0.010855 -0.399 0.69006
Inopioid  0.013038  1.013123  0.002454  5.312 1.08e-07 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

```

```

      exp(coef) exp(-coef) lower .95 upper .95
Antiemetics  2.0268  0.4934  1.1913  3.448
Age      0.9932  1.0069  0.9752  1.011
Wt      0.9957  1.0043  0.9747  1.017
Inopioid  1.0131  0.9870  1.0083  1.018

```

```

Concordance= 0.7 (se = 0.031 )
Rsquare= 0.288 (max possible= 0.993 )
Likelihood ratio test= 35.3 on 4 df, p=4e-07
Wald test      = 34.66 on 4 df, p=5e-07
Score (logrank) test = 38.89 on 4 df, p=7e-08

```

```

> # Variables selection
> cph.selection <- step( coxph(Surv(Time, PONV == 1) ~ Antiemetics + Age + Wt + Inopiod,
+ data = PONV.raw), direction = "both")
Start: AIC=491.4
Surv(Time, PONV == 1) ~ Antiemetics + Age + Wt + Inopiod

```

```

      Df  AIC
- Wt    1 489.56
- Age   1 489.93
<none>  491.40
- Antiemetics 1 496.39
- Inopiod   1 517.85

```

```

Step: AIC=489.56
Surv(Time, PONV == 1) ~ Antiemetics + Age + Inopiod

```

```

      Df  AIC
- Age   1 488.01
<none>  489.56
+ Wt    1 491.40
- Antiemetics 1 495.58
- Inopiod   1 515.85

```

```

Step: AIC=488.01
Surv(Time, PONV == 1) ~ Antiemetics + Inopiod

```

```

      Df  AIC
<none>  488.01
+ Age   1 489.56
+ Wt    1 489.93
- Antiemetics 1 493.61
- Inopiod   1 513.85
> summary(cph.selection)

```

```

Call:
coxph(formula = Surv(Time, PONV == 1) ~ Antiemetics + Inopiod,
      data = PONV.raw)

```

n= 104, number of events= 63

```

      coef exp(coef) se(coef)  z Pr(>|z|)
Antiemetics 0.703650 2.021116 0.258971 2.717 0.00659 **
Inopiod    0.012740 1.012821 0.002417 5.271 1.35e-07 ***

```

```

---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

```

```

      exp(coef) exp(-coef) lower .95 upper .95
Antiemetics 2.021 0.4948 1.217 3.358
Inopiod    1.013 0.9873 1.008 1.018

```

```

Concordance= 0.694 (se = 0.03 )
Rsquare= 0.284 (max possible= 0.993 )
Likelihood ratio test= 34.69 on 2 df, p=3e-08
Wald test      = 34.09 on 2 df, p=4e-08

```

Score (logrank) test = 38.29 on 2 df, p=5e-09

```
> # Final model selected
> cph.selected <- coxph(Surv(Time, PONV == 1) ~ Antiemetics + Inopiod, data = PONV.raw)
> summary(cph.selected)
```

Call:

```
coxph(formula = Surv(Time, PONV == 1) ~ Antiemetics + Inopiod,
      data = PONV.raw)
```

n= 104, number of events= 63

```
      coef exp(coef) se(coef)  z Pr(>|z|)
Antiemetics 0.703650 2.021116 0.258971 2.717 0.00659 **
Inopiod      0.012740 1.012821 0.002417 5.271 1.35e-07 ***
```

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

```
      exp(coef) exp(-coef) lower .95 upper .95
Antiemetics  2.021  0.4948  1.217  3.358
Inopiod      1.013  0.9873  1.008  1.018
```

Concordance= 0.694 (se = 0.03)

Rsquare= 0.284 (max possible= 0.993)

Likelihood ratio test= 34.69 on 2 df, p=3e-08

Wald test = 34.09 on 2 df, p=4e-08

Score (logrank) test = 38.29 on 2 df, p=5e-09

>

>

```
> # Survival curves of Cox PH model
```

```
> # grouped by Antiemetics
```

```
> new.cph.antiemetics <- with (PONV.raw, data.frame(Antiemetics = c(0, 1), Inopiod = c(0,0)))
```

```
> new.cph.antiemetics.fit <- survfit(cph.selected, newdata = new.cph.antiemetics)
```

```
> ggssurvplot(new.cph.antiemetics.fit, data = PONV.raw, conf.int = TRUE, conf.int.style = "step",
```

```
+   censor = FALSE, palette = "grey", break.time.by = 4, linetype = "solid",
```

```
+   axes.offset = FALSE, xlab = "Time (hour)", legend = c(0.1, 0.15),
```

```
+   legend.labs = c("Drug A", "Drug B"), legend.title = "Antiemetics")
```

>

>

```
> #LML for CoxPH
```

```
> plot (survfit(coxph(Surv(Time, PONV == 1) ~ strata(Antiemetics), data = PONV.raw)), fun = "cloglog")
```

>

>

```
> # Schoenfeld residual test
```

```
> sf.residual <- cox.zph(cph.selected)
```

```
> print(sf.residual) # display the results
```

```
      rho chisq  p
```

```
Antiemetics -0.275 4.50 0.0340
```

```
Inopiod      0.307 5.36 0.0206
```

```
GLOBAL      NA 10.26 0.0059
```

```
> par (mfrow = c(2,1))
```

```
> plot(sf.residual[1]) # plot curves
```

```
> abline (h = coef(cph.selected)[1], lty = "dotted", lwd = 1)
```

```
> plot(sf.residual[2])
```

```

> abline (h = coef(cph.selected)[2], lty = "dotted", lwd = 1)
>
>
> ##### Stratified Cox regression
> ### Add categorical variables from Inopioid
> PONV.raw <- transform(PONV.raw, Inopioid_c = ifelse(Inopioid == 0, 0, 1))
> head (PONV.raw)
  No Antiemetics Age  Wt Inopioid Time PONV Survobj Inopioid_c
1 1      0 48 78.5   0 4 0 4+      0
2 3      0 54 88.3  100 21 0 21+     1
3 4      0 22 49.4   0 14 0 14+     0
4 5      1 67 59.0   0 12 0 12+     0
5 7      1 45 64.5   0 19 0 19+     0
6 8      0 44 65.9   0 8 0 8+      0
>
>
> ### Stratified Cox proportional hazard modeling
> cph.strata <- coxph(Surv(Time, PONV == 1) ~ Antiemetics + strata(Inopioid_c), data = PONV.raw)
> summary (cph.strata)
Call:
coxph(formula = Surv(Time, PONV == 1) ~ Antiemetics + strata(Inopioid_c),
      data = PONV.raw)

n= 104, number of events= 63

      coef exp(coef) se(coef)  z Pr(>|z|)
Antiemetics 0.7282  2.0714  0.2625 2.774 0.00553 **
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

      exp(coef) exp(-coef) lower .95 upper .95
Antiemetics  2.071  0.4828  1.238  3.465

Concordance= 0.634 (se = 0.034 )
Rsquare= 0.074 (max possible= 0.979 )
Likelihood ratio test= 7.96 on 1 df, p=0.005
Wald test      = 7.7 on 1 df, p=0.006
Score (logrank) test = 8.03 on 1 df, p=0.005

> ggsvplot(survfit(cph.strata), data = PONV.raw, risk.table = TRUE, palette = c("black","black")
+           , linetype = c("solid","dashed"))
> par(mfrow = c(1,1))
> plot (survfit(cph.strata), fun = "cloglog", main = "Antiemetics")
> sf.residual.strata <- cox.zph(cph.strata)
> print(sf.residual.strata)
      rho chisq  p
Antiemetics -0.265 4.26 0.039
> plot(sf.residual.strata)
> abline(h = coef(cph.strata), lty = "dotted", lwd = 1)
>
>
> ### Time-dependent coefficient Cox regression model: step function
> tdc <- survSplit (Surv(Time, PONV) ~., data = PONV.raw, cut=c(3, 6),
+                  episode = "tgroup", id = "id")

```

```

> head(tdc)
  No Antiemetics Age Wt Inopioid Survobj Inopioid_c id tstart Time PONV tgroup
1 1      0 48 78.5   0  4+      0 1   0 3 0 1
2 1      0 48 78.5   0  4+      0 1   3 4 0 2
3 3      0 54 88.3  100 21+      1 2   0 3 0 1
4 3      0 54 88.3  100 21+      1 2   3 6 0 2
5 3      0 54 88.3  100 21+      1 2   6 21 0 3
6 4      0 22 49.4   0 14+      0 3   0 3 0 1
>
> # Fitting Cox regression
> fit.tdc <- coxph(Surv(tstart,Time, PONV) ~ Antiemetics:strata(tgroup) + Inopioid, data = tdc)
> summary(fit.tdc)
Call:
coxph(formula = Surv(tstart, Time, PONV) ~ Antiemetics:strata(tgroup) +
      Inopioid, data = tdc)

n= 250, number of events= 63

              coef exp(coef) se(coef)  z Pr(>|z|)
Inopioid          0.012477 1.012556 0.002413 5.172 2.32e-07 ***
Antiemetics:strata(tgroup)tgroup=1 1.295949 3.654464 0.567181 2.285 0.02232 *
Antiemetics:strata(tgroup)tgroup=2 1.360185 3.896914 0.521567 2.608 0.00911 **
Antiemetics:strata(tgroup)tgroup=3 -0.063743 0.938247 0.404993 -0.157 0.87494
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

              exp(coef) exp(-coef) lower .95 upper .95
Inopioid          1.0126  0.9876  1.0078  1.017
Antiemetics:strata(tgroup)tgroup=1  3.6545  0.2736  1.2024 11.107
Antiemetics:strata(tgroup)tgroup=2  3.8969  0.2566  1.4020 10.831
Antiemetics:strata(tgroup)tgroup=3  0.9382  1.0658  0.4242  2.075

Concordance= 0.67 (se = 0.031 )
Rsquare= 0.152 (max possible= 0.874 )
Likelihood ratio test= 41.35 on 4 df, p=2e-08
Wald test      = 38.92 on 4 df, p=7e-08
Score (logrank) test = 44.61 on 4 df, p=5e-09

> # GOF test
> sf.tdc <- cox.zph(fit.tdc)
> print(sf.tdc)

              rho chisq p
Inopioid          0.29948 5.150327 0.0232
Antiemetics:strata(tgroup)tgroup=1 -0.02755 0.047411 0.8276
Antiemetics:strata(tgroup)tgroup=2 -0.00368 0.000845 0.9768
Antiemetics:strata(tgroup)tgroup=3  0.02486 0.038692 0.8441
GLOBAL              NA 5.199691 0.2674
> par(mfrow=c(2,2))
> plot(sf.tdc[1])
> abline(h = coef(fit.tdc)[1], lty = "dotted")
> plot(sf.tdc[2])
> abline(h = coef(fit.tdc)[2], lty = "dotted")
> plot(sf.tdc[3])
> abline(h = coef(fit.tdc)[3], lty = "dotted")

```



```

> plot(sf.tdc[4])
> abline (h = coef(fit.tdc)[4], lty = "dotted")
>
>
> # Combined results
> combine.tdc <- data.frame(tstart = rep(c(0,3,6), 2), Time = rep(c(3,6, 24), 2), PONV = rep(0,12),
+       tgroup= rep(1:3,4), trt = rep(1,12), prior= rep(0,12), Antiemetics = rep(c(0,1), each = 6),
+       Inopioid = rep (c(0,1), each = 3), parameter = rep(0:1, each = 6))
> combine.tdc
  tstart Time PONV tgroup trt prior Antiemetics Inopioid parameter
1     0  3  0    1  1  0     0  0  0
2     3  6  0    2  1  0     0  0  0
3     6 24  0    3  1  0     0  0  0
4     0  3  0    1  1  0     0  1  0
5     3  6  0    2  1  0     0  1  0
6     6 24  0    3  1  0     0  1  0
7     0  3  0    1  1  0     1  0  1
8     3  6  0    2  1  0     1  0  1
9     6 24  0    3  1  0     1  0  1
10    0  3  0    1  1  0     1  1  1
11    3  6  0    2  1  0     1  1  1
12    6 24  0    3  1  0     1  1  1
> cfit.tdc <- survfit(fit.tdc, newdata = combine.tdc, id = parameter)
> cfit.tdc
Call: survfit(formula = fit.tdc, newdata = combine.tdc, id = parameter)

```

```

      n events median 0.95LCL 0.95UCL
0 104 126 31 17 40
1 104 126 16 10 26
> km <- survfit(Surv(Time, PONV) ~Antiemetics, data = PONV.raw)
> summary (km)
Call: survfit(formula = Surv(Time, PONV) ~ Antiemetics, data = PONV.raw)

```

```

      Antiemetics=0
time n.risk n.event survival std.err lower 95% CI upper 95% CI
1  51  1  0.980 0.0194  0.943  1.000
2  50  2  0.941 0.0329  0.879  1.000
3  48  1  0.922 0.0376  0.851  0.998
4  47  2  0.882 0.0451  0.798  0.975
6  41  3  0.818 0.0551  0.717  0.933
7  37  3  0.751 0.0625  0.638  0.885
8  32  2  0.705 0.0669  0.585  0.849
9  28  2  0.654 0.0709  0.529  0.809
10 24  3  0.572 0.0762  0.441  0.743
11 21  1  0.545 0.0773  0.413  0.720
12 19  1  0.516 0.0783  0.384  0.695
13 18  1  0.488 0.0791  0.355  0.670
17 14  1  0.453 0.0807  0.319  0.642
18 13  1  0.418 0.0817  0.285  0.613
19 12  1  0.383 0.0820  0.252  0.583

```

```

      Antiemetics=1
time n.risk n.event survival std.err lower 95% CI upper 95% CI
1  53  7  0.868 0.0465  0.781  0.964

```

2	46	5	0.774	0.0575	0.669	0.895
3	41	2	0.736	0.0606	0.626	0.865
4	39	6	0.623	0.0666	0.505	0.768
5	33	3	0.566	0.0681	0.447	0.717
6	29	5	0.468	0.0689	0.351	0.625
7	23	2	0.428	0.0687	0.312	0.586
9	21	2	0.387	0.0679	0.274	0.546
10	19	1	0.367	0.0673	0.256	0.525
11	18	1	0.346	0.0666	0.237	0.505
12	16	1	0.325	0.0659	0.218	0.483
16	12	2	0.271	0.0650	0.169	0.433
17	10	1	0.243	0.0639	0.146	0.407

> km

Call: survfit(formula = Surv(Time, PONV) ~ Antiemetics, data = PONV.raw)

```

      n events median 0.95LCL 0.95UCL
Antiemetics=0 51  25  13  10  NA
Antiemetics=1 53  38   6   5  12
>
> par(mfrow = c(1,1))
> plot(km, xmax= 24, col="Black", lty = c("solid","dashed"), lwd=2, xlab="Postoperative hours",
+      ylab="PONV free")
> lines(cfit.tdc, col="Grey", lty= c("solid","dashed"), lwd=2)
> legend (x = 0.15, y = 0.25, c("Drug A, Kaplan-Meier estimation",
+                               "Drug B, Kaplan-Meier estimation",
+                               "Drug A, Cox regression with time-dependent coefficient",
+                               "Drug B, Cox regression with time-dependent coefficient"),
+       col = c("black", "black", "grey", "grey"),
+       lty = c("solid", "dashed", "solid", "dashed"))

```