Package 'IPWsurvival'

April 22, 2015

Type Package

Title Adjusted survival curves and corresponding log-rank statistic

Version 0.3

Date 2014-09-02

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Description In observational studies, the presence of confounding factors is common and the comparison of different groups of subjects requires adjustment. In this package, we propose to R-users simple functions to estimate adjusted survival curves and log-rank test based on inverse probability weighting (IPW).

License GPL (>=2)

LazyLoad yes

Depends splines, survival

URL www.r-project.org, www.divat.fr

R topics documented:

`IPWsurvival-package` *Adjusted Kaplan-Meier estimator and log-rank statistic*

Description

This package computes adjusted Kaplan-Meier estimator and log-rank statistic by using inverse probability weighting (IPW).

Details

In observational studies, the presence of confounding factors is common and the comparison of different groups of subjects requires adjustment. In the presence of survival data, this adjustment can be achieved with a multivariate model. A recent alternative solution is the use of adjusted survival curves and log-rank test based on inverse probability weighting (IPW). By using the approach proposed by Xie and Liu (2005), we illustrate the usefulness of such methodology by studying the patient and graft survival of kidney transplant recipients according to the expanded donor criteria (ECD).

Package:	IPWsurvival
Type:	Package
Version:	0.1
Date:	2014-03-14
License:	GPL (>=2)
LazyLoad:	yes

adjustedKM	Compute adjusted survival curves by weighting the indvidual contributions by the inverse of the probability to be in the group.
adjustedLR	Propose the log-rank test adapted to the corresponding adjusted survival curves.
DIVAT	These data extracted from the DIVAT data bank of kidney transplant recipients.

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References

Le Borgne F, Giraudeau B, Querard AH, Giral M and Foucher Y. Comparisons of the performances of different statistical tests for time-to-event analysis with confounding factors: practical illustrations in kidney transplantation. Manuscript submitted.

Cole S and Hernan M. Adjusted survival curves with inverse probability weights. Computer methods and programs in biomedicine, 75(1):45-49, 2004.

Jun Xie and Chaofeng Liu. Adjusted Kaplan-Meier estimator and log-rank test with inverse probability of treatment weighting for survival data. Statistics in medicine, 24(20):3089-3110, October 2005.

See Also

URL: http://www.divat.fr

`adjustedKM` *Adjusted survival curves by using IPW and Kaplan-Meier estimator*

Description

This function allows for computing adjusted survival curves by weighting the individual contributions by the inverse of the probability to be in the group. The user enters individual survival data and the weights previously calculated (by using logistic regression for instance). The usual Kaplan-Meier estimator is adapted in order to obtain the adjusted survival.

Usage

```
adjustedKM(times, failures, variable, weights)
```

Arguments

`times`	A numeric vector with the follow up times.
`failures`	A numeric vector with the event indicators (0=right censored, 1=event).
`variable`	A numeric vector with the binary variable under interest (only two groups).
`weights`	The weights for correcting the contribution of each individual. By default, the weights are all equalled to 1 and the survival curves correspond to the usual Kaplan-Meier estimator.

Details

For instance, `w` may be equal to `1/p`, where `p` is the estimated probability of the individual to be in its group. The probabilities `p` are often estimated by a logistic regression in which the dependent binary variable is the group. The possible confounding factors are the explanatory variables of this model.

Value

`Table`	This data frame presents the survival probabilities (`survival`) in each group (`variable`) according to the `times`. The number of individuals at risk (`n.risk`) and the number of observed events are also provided (`n.event`).

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References

Le Borgne F, Giraudeau B, Querard AH, Giral M and Foucher Y. Comparisons of the performances of different statistical tests for time-to-event analysis with confounding factors: practical illustrations in kidney transplantation. Manuscript submitted.

Cole S and Hernan M. Adjusted survival curves with inverse probability weights. Computer methods and programs in biomedicine, 75(1):45-49, 2004.

Examples

```
data(DIVAT)

# Kaplan-Meier estimator
res.km <- adjustedKM(times=DIVAT$times, failures=DIVAT$failures,
  variable=DIVAT$ecd, weights=NULL)
plot(NULL,xlim=c(0,13),ylim=c(0,1),ylab="Graft and patient survival",
 xlab="Time post-transplantation (years)")
lines(res.km$times[res.km$variable==1], res.km$survival[res.km$variable==1],
type="s",col=2,lty=2,lwd=2)
lines(res.km$times[res.km$variable==0], res.km$survival[res.km$variable==0],
type="s",col=1,lty=2,lwd=2)

# adjusted Kaplan-Meier estimator by IPW
Pr0 <- glm(ecd ~ 1, family = binomial(link="logit"), data=DIVAT)$fitted.values[1]
Pr1 <- glm(ecd ~ age + hla + retransplant, data=DIVAT,
 family=binomial(link = "logit"))$fitted.values
W <- (DIVAT$ecd==1) * (1/Pr1) + (DIVAT$ecd==0) * (1)/(1-Pr1)
res.akm <- adjustedKM(times=DIVAT$times, failures=DIVAT$failures,
 variable=DIVAT$ecd, weights=W)
lines(res.akm$times[res.akm$variable==1], res.akm$survival[res.akm$variable==1],
 type="s",col=2,lwd=2)
lines(res.akm$times[res.akm$variable==0], res.akm$survival[res.akm$variable==0],
 type="s",col=1,lwd=2)

nb.risk1<-function(x) {sum(DIVAT$times[DIVAT$ecd==0]>x)}
nb.risk2<-function(x) {sum(DIVAT$times[DIVAT$ecd==1]>x)}
segments(x0=0, y0=0.1, x1=13, y1=0.1)
text(x=6, y=0.12, "number of at-risk patients", cex=0.8)
tps <- seq(1,12,by=1)
text(x=tps, y=rep(0.07,length(tps)), as.character(sapply(tps, FUN="nb.risk1")),
 cex=0.8, col=1)
text(x=tps, y=rep(0.02,length(tps)), as.character(sapply(tps, FUN="nb.risk2")),
 cex=0.8, col=2)
legend("topright", legend=c("Unadjusted estimator for SCD",
 "Adjusted estimator for SCD", "Unadjusted estimator for ECD",
 "Adjusted estimator for ECD"), col=c(1,1,2,2),
 lty=c(2,1,2,1), lwd=2, cex=0.8)
```

`adjustedLR` *Log-rank test for adjusted survival curves*

Description

The user enters individual survival data and the weights previously calculated (by using logistic regression for instance). The usual log-rank test is adapted to the corresponding adjusted survival curves.

Usage

```
adjustedLR(times, failures, variable, weights)
```

Arguments

`times`	A numeric vector with the follow up times.
`failures`	A numeric vector with the event indicator (0=right censored, 1=event).
`variable`	A numeric vector with the binary variable under interest (only two groups).
`weights`	The weigths for correcting the contribution of each individual. By default, the weights are all equalled to 1 and the survival curves correspond to the usual Kaplan-Meier estimator.

Details

For instance, `w` may be equal to 1/`p`, where `p` is the estimated probability of the individual to be in its group. The probabilities `p` are often estimated by a logistic regression in which the dependent binary variable is the group. The possible confounding factors are the explanatory variables of this model.

Value

`statistic`	This parameter corresponds to the value of estimated log-rank statistic. If the weights are all equalled to 1, this value corresponds to the usual log-rank test.
`p.value`	The p-value associated to the previous log-rank statistic.

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References

Le Borgne F, Giraudeau B, Querard AH, Giral M and Foucher Y. Comparisons of the performances of different statistical tests for time-to-event analysis with confounding factors: practical illustrations in kidney transplantation. Manuscript submitted.

Jun Xie and Chaofeng Liu. Adjusted Kaplan-Meier estimator and log-rank test with inverse probability of treatment weighting for survival data. Statistics in medicine, 24(20):3089-3110, October 2005.

Examples

```
data(DIVAT)

# adjusted log-rank test
Pr0 <- glm(ecd ~ 1, family = binomial(link="logit"), data=DIVAT)$fitted.values[1]
Pr1 <- glm(ecd ~ age + hla + retransplant, data=DIVAT,
 family=binomial(link = "logit"))$fitted.values
W <- (DIVAT$ecd==1) * (1/Pr1) + (DIVAT$ecd==0) * (1)/(1-Pr1)

adjustedLR(DIVAT$times, DIVAT$failures, DIVAT$ecd, W)
```

DIVAT — *These data were extracted from the DIVAT data bank of kidney transplant recipients.*

Description

Data were extracted from the DIVAT cohort. The nephrology department of the Nantes University Hospital has developed DIVAT: a database which includes the monitoring of medical records for kidney transplant recipients. For more details or requesting the data for your research, please visit the following website: www.divat.fr/en.

Usage

```
data(DIVAT)
```

Format

A data frame with the 4 following variables.

- `age` This numeric vector provides the age of the recipient at the transplantation (in years).
- `hla` This numeric vector provides the indicator of transplantations with at least 4 HLA incompatibilities between the donor and the recipient (1 for high level and 0 otherwise).
- `retransplant` This numeric vector provides the indicator of re-transplantation (1 for more than one transplantation and 0 for first kidney transplantation).
- `ecd` The Expended Criteria Donor (1 for transplantations from ECD and 0 otherwise).
- `times` This numeric vector is the follow up times of each patient.
- `failures` This numeric vector is the event indicator (0=right censored, 1=event). An event is considered when return in dialysis or patient death with functioning graft is observed.

Details

This database is constituted by 1912 patients transplanted between January 1996 and December 2013 and followed in the prospective DIVAT cohort from Nantes University hospital. Adults receiving a first or second kidney transplant alone from a deceased heart beating donor were included. In kidney transplantation, donors are classified into two categories, the expanded criteria donor and the standard criteria donor. ECD are defined by widely accepted criteria, which includes donors older than 60 years of age or 50-59 years of age with two of the following characteristics: history of hypertension, cerebrovascular accident as the cause of death or terminal serum creatinine higher than 1.5 mg/dL.

References

Le Borgne F, Giraudeau B, Querard AH, Giral M and Foucher Y. Comparisons of the performances of different statistical tests for time-to-event analysis with confounding factors: practical illustrations in kidney transplantation. Manuscript submitted.

Port F, Bragg-Gresham J, Metzger R, Dykstra D, Gillespie B, Young E, Delmonico F, Wynn J, Merion R, Wolfe R and Held P. Donor characteristics associated with reduced graft survival: an approach to expanding the pool of kidney donors. Transplantation, 74(9):1281-86, November 2002.

Examples

```
data(DIVAT)

# Compute the non-adjusted Cox PH model
cox.ECD0<-coxph(Surv(times, failures) ~ ecd, data=DIVAT)
summary(cox.ECD0) # Hazard Ratio = 1.97

# Compute the adjusted Cox PH model
cox.ECD1<-coxph(Surv(times, failures) ~ age + hla + retransplant + ecd, data=DIVAT)
summary(cox.ECD1) # Hazard Ratio = 1.66
```

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