Package ‘WLreg’

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Type Package

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Title Regression Analysis Based on Win Loss Endpoints

Description Use various regression models for the analysis of win loss endpoints adjusting for non-binary and multivariate covariates.

Depends R (>= 3.1.2)

Imports inline, stats, survival

License GPL (>= 2)

RoxygenNote 5.0.1

LazyData true

NeedsCompilation yes

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R topics documented:

`winreg` *Double Cox regression for win product*

Description

Use two Cox regression models (one for the terminal event and the other for the non-trminal event) to model the win product adjusting for covariates

Usage

```
winreg(y1,y2,d1,d2,z)
```

Arguments

`y1`	a numeric vector of event times denoting the minimum of event times T_1, T_2 and censoring time C, where the endpoint T_2, corresponding to the terminal event, is considered of higher clinical importance than the endpoint T_1, corresponding to the non-terminal event. Note that the terminal event may censor the non-terminal event, resulting in informative censoring.
`y2`	a numeric vector of event times denoting the minimum of event time T_2 and censoring time C. Clearly, y2 is not smaller than y1.
`d1`	a numeric vector of event indicators with 1 denoting the non-terminal event is observed and 0 else.
`d2`	a numeric vector of event indicators with 1 denoting the terminal event is observed and 0 else.
`z`	a numeric matrix of covariates.

Details

This function uses two Cox regression models (one for the terminal event and the other for the non-trminal event) to model the win product adjusting for covariates.

Value

`beta1`	Estimated regression parameter based on the non-terminal event times `y1`, $\exp($`beta1`$)$ is the adjusted hazard ratio
`sigma1`	Estimated variance of `beta1` using the residual method instead of the inverse of Fisher information
`tb1`	Wald test statistics based on `beta1` and `sigma1`
`pb1`	Two-sided p-values of the Wald test statistics `tb1`
`beta2`	Estimated regression parameter based on the terminal event times `y2`, $\exp($`beta2`$)$ is the adjusted hazard ratio
`sigma2`	Estimated variance of `beta2` using the residual method instead of the inverse of Fisher information

tb2	Wald test statistics based on beta2 and sigma2
pb2	Two-sided p-values of the Wald test statistics tb2
beta	beta1+beta2,exp(-beta) is the adjusted win product
sigma	Estimated variance of beta using the residual method
tb	Wald test statistics based on beta and sigma
pb	Two-sided p-values of the Wald test statistics tb

Author(s)

Xiaodong Luo

References

Pocock S.J., Ariti C.A., Collier T. J. and Wang D. 2012. The win ratio: a new approach to the analysis of composite endpoints in clinical trials based on clinical priorities. European Heart Journal, 33, 176-182.

Luo X., Tian H., Mohanty S. and Tsai W.-Y. 2015. An alternative approach to confidence interval estimation for the win ratio statistic. Biometrics, 71, 139-145.

Luo X., Qiu J., Bai S. and Tian H. 2017. Weighted win loss approach for analyzing prioritized outcomes. Statistics in Medicine, to appear.

See Also

wrlogistic

Examples

```
###Generate data
n<-300
rho<-0.5
b2<-c(1.0,-1.0)
b1<-c(0.5,-0.9)
bc<-c(1.0,0.5)
lambda10<-0.1;lambda20<-0.08;lambdac0<-0.09
lam1<-rep(0,n);lam2<-rep(0,n);lamc<-rep(0,n)
z1<-rep(0,n)
z1[1:(n/2)]<-1
z2<-rnorm(n)
z<-cbind(z1,z2)

lam1<-lam2<-lamc<-rep(0,n)
for (i in 1:n){
    lam1[i]<-lambda10*exp(-sum(z[i,]*b1))
    lam2[i]<-lambda20*exp(-sum(z[i,]*b2))
    lamc[i]<-lambdac0*exp(-sum(z[i,]*bc))
}
tem<-matrix(0,ncol=3,nrow=n)

y2y<-matrix(0,nrow=n,ncol=3)
```

```
y2y[,1]<-rnorm(n);y2y[,3]<-rnorm(n)
y2y[,2]<-rho*y2y[,1]+sqrt(1-rho^2)*y2y[,3]
tem[,1]<--log(1-pnorm(y2y[,1]))/lam1
tem[,2]<--log(1-pnorm(y2y[,2]))/lam2
tem[,3]<--log(1-runif(n))/lamc

y1<-apply(tem,1,min)
y2<-apply(tem[,2:3],1,min)
d1<-as.numeric(tem[,1]<=y1)
d2<-as.numeric(tem[,2]<=y2)

y<-cbind(y1,y2,d1,d2)
z<-as.matrix(z)
aa<-winreg(y1,y2,d1,d2,z)
aa
```

`wrlogistic` *Logistic regression for win ratio*

Description

Use a logistic regression model to model win ratio adjusting for covariates with the user-supplied comparison results

Usage

```
wrlogistic(aindex,z,b0=rep(0,ncol(z)),tol=1.0e-04,maxiter=20)
```

Arguments

`aindex`	a vector that collects the pairwise comparison results. Suppose there are a total of n subjects in the study, there are $n(n-1)/2$ elements in `aindex`. The $(i-1)*(i-2)/2+j$-th element, denoted by C_{ij}, is the comparison result between subject i and subject j, where $i=2,\ldots,n$ and $j=1,\ldots,i-1$. The element C_{ij} is equal to 1 if subject i wins over subject j on the most important outcome, C_{ij} is equal to -1 if subject i loses against subject j on the most important outcome; C_{ij} is equal to 2 if subject i wins over subject j on the second most important outcome after tie on the most important outcome, C_{ij} is equal to -2 if subject i loses against subject j on the second most important outcome after tie on the most important outcome; and so forth until all the outcomes have been used for comparison; then C_{ij} is equal to 0 if an ultimate tie is resulted.
`z`	a matrix of covariates
`b0`	the initial value of the regression parameter
`tol`	error tolerence
`maxiter`	maximum number of iterations

Details

This function uses a logistic regression model to model win ratio adjusting for covaraites. This function uses the pairwise comparision result supplied by the user which hopefully will speed up the program.

Value

b	Estimated regression parameter, $\exp(\mathrm{b})$ is the adjusted win ratio
Ubeta	The score function
Vbeta	The estimated varaince of $\sqrt{n}\times$b
Wald	Wald test statistics for the estimated parameter b
pvalue	Two-sided p-values of the Wald statistics
Imatrix	The information matrix
Wtotal	Total wins
Ltotal	Total losses
err	err at convergence
iter	number of iterations performed before covergence

Author(s)

Xiaodong Luo

References

Pocock S.J., Ariti C.A., Collier T. J. and Wang D. 2012. The win ratio: a new approach to the analysis of composite endpoints in clinical trials based on clinical priorities. European Heart Journal, 33, 176-182.

Luo X., Tian H., Mohanty S. and Tsai W.-Y. 2015. An alternative approach to confidence interval estimation for the win ratio statistic. Biometrics, 71, 139-145.

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See Also

winreg

Examples

```
###Generate data
n<-300
rho<-0.5
b2<-c(1.0,-1.0)
b1<-c(0.5,-0.9)
bc<-c(1.0,0.5)
lambda10<-0.1;lambda20<-0.08;lambdac0<-0.09
lam1<-rep(0,n);lam2<-rep(0,n);lamc<-rep(0,n)
```

```
z1<-rep(0,n)
z1[1:(n/2)]<-1
z2<-rnorm(n)
z<-cbind(z1,z2)

lam1<-lam2<-lamc<-rep(0,n)
for (i in 1:n){
    lam1[i]<-lambda10*exp(-sum(z[i,]*b1))
    lam2[i]<-lambda20*exp(-sum(z[i,]*b2))
    lamc[i]<-lambdac0*exp(-sum(z[i,]*bc))
}
tem<-matrix(0,ncol=3,nrow=n)

y2y<-matrix(0,nrow=n,ncol=3)
y2y[,1]<-rnorm(n);y2y[,3]<-rnorm(n)
y2y[,2]<-rho*y2y[,1]+sqrt(1-rho^2)*y2y[,3]
tem[,1]<--log(1-pnorm(y2y[,1]))/lam1
tem[,2]<--log(1-pnorm(y2y[,2]))/lam2
tem[,3]<--log(1-runif(n))/lamc

y1<-apply(tem,1,min)
y2<-apply(tem[,2:3],1,min)
d1<-as.numeric(tem[,1]<=y1)
d2<-as.numeric(tem[,2]<=y2)

y<-cbind(y1,y2,d1,d2)
z<-as.matrix(z)
###################

#####Define the comparison function
comp<-function(y,x){
  y1i<-y[1];y2i<-y[2];d1i<-y[3];d2i<-y[4]
  y1j<-x[1];y2j<-x[2];d1j<-x[3];d2j<-x[4]
  w2<-0;w1<-0;l2<-0;l1<-0

  if (d2j==1 & y2i>=y2j) w2<-1
  else if (d2i==1 & y2j>=y2i) l2<-1

  if (w2==0 & l2==0 & d1j==1 & y1i>=y1j) w1<-1
  else if (w2==0 & l2==0 & d1i==1 & y1j>=y1i) l1<-1

  comp<-0
  if (w2==1) comp<-1
  else if (l2==1) comp<-(-1)
  else if (w1==1) comp<-2
  else if (l1==1) comp<-(-2)

  comp
}
bin<-rep(0,n*(n-1)/2)
for (i in 2:n)for (j in 1:(i-1))bin[(i-1)*(i-2)/2+j]<-comp(y[i,],y[j,])
###Use the win loss indicator matrix to calculate the general win loss statistics
bb2<-wrlogistic(bin,z,b0=rep(0,ncol(z)),tol=1.0e-04,maxiter=20)
```

```
bb2


####Calculate the win, loss, tie result using Fortran loops to speed up the process
####Using the "inline" package to convert the code into Fortran

#install.packages("inline") #Install the package "inline''
library("inline") ###Load the package "inline"

########################################################
# The use of ``inline'' needs ``rtools'' and ``gcc''
# in the PATH environment of R.
# The following code will put these two into
# the PATH for the current R session ONLY.
########################################################

#rtools <- "C:\Rtools\bin"
#gcc <- "C:\Rtools\gcc-4.6.3\bin"
#path <- strsplit(Sys.getenv("PATH"), ";")[[1]]
#new_path <- c(rtools, gcc, path)
#new_path <- new_path[!duplicated(tolower(new_path))]
#Sys.setenv(PATH = paste(new_path, collapse = ";"))

codex4 <- "
integer::i,j,indexij,d1i,d2i,d1j,d2j,w2,w1,l2,l1
double precision::y1i,y2i,y1j,y2j
do i=2,n,1
   y1i=y(i,1);y2i=y(i,2);d1i=dnint(y(i,3));d2i=dnint(y(i,4))
   do j=1,(i-1),1
      y1j=y(j,1);y2j=y(j,2);d1j=dnint(y(j,3));d2j=dnint(y(j,4))
      indexij=(i-1)*(i-2)/2+j
      w2=0;w1=0;l2=0;l1=0
      if (d2j==1 .and. y2i>=y2j) then
         w2=1
      else if (d2i==1 .and. y2j>=y2i) then
         l2=1
      else if (d1j==1 .and. y1i>=y1j) then
         w1=1
      else if (d1i==1 .and. y1j>=y1i) then
         l1=1
      end if
      aindex(indexij)=0
      if (w2==1) then
         aindex(indexij)=1
      else if (l2==1) then
         aindex(indexij)=-1
      else if (w2==0 .and. l2==0 .and. w1==1) then
         aindex(indexij)=2
      else if (w2==0 .and. l2==0 .and. l1==1) then
         aindex(indexij)=-2
      end if
   end do
end do
```

```
"
###Convert the above code into Fortran
cubefnx4<-cfunction(sig = signature(n="integer", p="integer", y="numeric", aindex="integer"),
         implicit = "none",dim = c("", "", "(n,p)", "(n*(n-1)/2)"), codex4, language="F95")

###Use the converted code to calculate the win, loss and tie indicators
options(object.size=1.0E+10)
ain<-cubefnx4(length(y[,1]),length(y[1,]), y, rep(0,n*(n-1)/2))$aindex

####Perform the logistic regression
aa2<-wrlogistic(ain,z,b0=rep(0,ncol(z)),tol=1.0e-04,maxiter=20)
aa2
```

`zinv` *Inverse matrix*

Description

This will calculate the inverse matrix by Gauss elimination method

Usage

```
zinv(y)
```

Arguments

`y` a sqaure matrix

Details

Inverse matrix

Value

`yi` the inverse of `y`

Note

This provides the inverse matrix using Gauss elimination method, this program performs satisfactorily when the size of the matrix is less than 50

Author(s)

Xiaodong Luo

Examples

```
y<-matrix(c(1,2,0,1),ncol=2,nrow=2)
zinv(y)
```

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