## Package 'CMFCAM'

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Title	Copula,	Multistate,	Frailty	for	Causal	Analysis	Modle

## Version 1.0

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**Description** The packages for 'Unified semicompeting risks analysis of hepatitis natural history through mediation modeling'. The main functions are CP\_MLE (calculate the causal effect from copula model by MLE), CP\_Ustat (calculate the causal effect from copula model by Ustatistics), Frailty (calculate the causal effect from frailty model) and M\_state (calculate the causal effect from multistate model).

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## **R** topics documented:

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## Description

Estimating the direct and indirect of the Copula model by MLE

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#### Usage

```
CP_MLE(data, P.time, int_theta, tol, step)
```

## **Arguments**

data data.frame(X1,X2,D,Z)

P. time interpolation time can be vector or scalar

## **Examples**

```
 \begin{array}{l} {\rm data=meta.gen(500,theta\_0=0.5,theta\_1=0.5,L1=0.5,L2=0.5,L3=1,b01=1,b02=0,b03=0,cc=2,dd="uniform")} \\ {\rm P.time=seq(0,1,by=0.01)} \\ {\rm ans=CP\_MLE(data,P.time,int\_theta=c(0.5,0.5),tol=0.01,step=50)} \\ {\rm plot(P.time,ans\$DE,type="l",ylim=c(-0.5,0.5))} \\ {\rm points(P.time,ans\$DE-ans\$DE\_sd,type="l",ylim=c(-0.5,0.5))} \\ {\rm points(P.time,ans\$DE-ans\$DE\_sd,type="l",ylim=c(-0.5,0.5))} \\ {\rm points(P.time,ans\$IE,type="l",ylim=c(-0.5,0.5),col=2)} \\ {\rm points(P.time,ans\$IE+ans\$IE\_sd,type="l",ylim=c(-0.5,0.5),col=2)} \\ {\rm points(P.time,ans\$IE-ans\$IE\_sd,type="l",ylim=c(-0.5,0.5),col=2)} \\ {\rm legend(0,0.45,c("direct effect","indirect effect"),col=1:2,lty=1)} \\ \end{array}
```

cp\_u

Estimating the direct and indirect of the Copula model by U-statistics

## **Description**

Estimating the direct and indirect of the Copula model by U-statistics

## Usage

```
cp_u(data, P.time)
```

## **Arguments**

 $\begin{array}{ll} \text{data} & \text{data.frame}(X1,\!X2,\!D,\!Z) \\ \text{interpolation} & \text{time can be vector or scalar} \end{array}$ 

 $int\_theta$  initial value of theta for iteration, nonnegative values vector of length 2

tol maximum tolerance of change during the iteration

step maximum number of the iteration

## **Examples**

```
 \begin{array}{l} {\rm data=meta.gen(500,theta\_0=0.5,theta\_1=0.5,L1=0.5,L2=0.5,L3=1,b01=1,b02=0,b03=0,cc=2,dd="uniform")} \\ {\rm P.time=seq(0,1,by=0.01)} \\ {\rm ans=cp\_u(data,P.time)} \\ {\rm plot(P.time,ans\$DE,type="l",ylim=c(-0.5,0.5))} \\ {\rm points(P.time,ans\$IE,type="l",ylim=c(-0.5,0.5),col=2)} \\ {\rm legend(0,0.45,c("direct effect","indirect effect"),col=1:2,lty=1)} \\ \end{array}
```

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CP_Ustat	Estimating the direct and indirect of the Copula model by U-statistics,
	calculate the variance by bootstrapping

## **Description**

Estimating the direct and indirect of the Copula model by U-statistics, calculate the variance by bootstrapping

## Usage

```
CP_Ustat(data, P.time)
```

## **Arguments**

data data.frame(X1,X2,Z,D)

P. time interpolation time can be vector or scalar

## **Examples**

```
 \begin{array}{l} {\rm data=meta.gen(500,theta\_0=0.5,theta\_1=0.5,L1=0.5,L2=0.5,L3=1,b01=1,b02=0,b03=0,cc=2,dd="uniform")} \\ {\rm P.time=seq(0,1,by=0.01)} \\ {\rm ans=CP\_Ustat(data,P.time)} \\ {\rm plot(P.time,ans\$DE,type="l",ylim=c(-0.5,0.5))} \\ {\rm points(P.time,ans\$DE-ans\$DE\_sd,type="l",ylim=c(-0.5,0.5))} \\ {\rm points(P.time,ans\$DE-ans\$DE\_sd,type="l",ylim=c(-0.5,0.5))} \\ {\rm points(P.time,ans\$IE,type="l",ylim=c(-0.5,0.5),col=2)} \\ {\rm points(P.time,ans\$IE-ans\$IE\_sd,type="l",ylim=c(-0.5,0.5),col=2)} \\ {\rm points(P.time,ans\$IE-ans\$IE\_sd,type="l",ylim=c(-0.5,0.5),col=2)} \\ {\rm legend(0,0.45,c("direct effect","indirect effect"),col=1:2,lty=1)} \\ \end{array}
```

Frailty

Estimating the direct and indirect of the frailty model

## **Description**

Estimating the direct and indirect of the frailty model

## Usage

```
Frailty(data, P.time, int_theta, tol, step)
```

## Arguments

data.frame(X1, X2, D, Z)

 $\verb|int_theta| initial value of theta for iteration, nonnegative values vector of length 2$ 

tol maximum tolerance of change during the iteration

step maximum number of the iteration interpolation time can be vector or scalar

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#### **Examples**

```
 \begin{array}{l} {\rm data=meta.gen(500,theta\_0=0.5,theta\_1=0.5,L1=0.5,L2=0.5,L3=1,b01=1,b02=0,b03=0,cc=2,dd="uniform")} \\ {\rm P.time=seq(0,1,by=0.01)} \\ {\rm ans=Frailty(data,P.time,int\_theta=c(0.5,0.5),tol=0.01,step=50)} \\ {\rm plot(P.time,ans\$DE,type="l",ylim=c(-0.5,0.5))} \\ {\rm points(P.time,ans\$DE-ans\$DE\_sd,type="l",ylim=c(-0.5,0.5))} \\ {\rm points(P.time,ans\$DE-ans\$DE\_sd,type="l",ylim=c(-0.5,0.5))} \\ {\rm points(P.time,ans\$IE,type="l",ylim=c(-0.5,0.5),col=2)} \\ {\rm points(P.time,ans\$IE+ans\$IE\_sd,type="l",ylim=c(-0.5,0.5),col=2)} \\ {\rm points(P.time,ans\$IE-ans\$IE\_sd,type="l",ylim=c(-0.5,0.5),col=2)} \\ {\rm legend(0,0.45,c("direct effect","indirect effect"),col=1:2,lty=1)} \\ \end{array}
```

meta.gen

generating the data with 1/2 bivariate exposure from the frailty model by three exponential distributions

## **Description**

generating the data with 1/2 bivariate exposure from the frailty model by three exponential distributions

## Usage

```
meta.gen(
    n,
    theta_0,
    theta_1,
    L1,
    L2,
    L3,
    b01,
    b02,
    b03,
    cc = 2,
    dd = "uniform"
)
```

## **Arguments**

```
sample size (even)
n
theta_0
                   theta for Z=1
theta_1
                   theta for Z=2
                   lambda for genarate T1
L1
L2
                   lambda for generate T2 without given T1
L3
                   lambda for generate T2 given T1
                   effect from Z to T1
b01
                   effect from Z to T2
b02
b03
                   effect from T1 to T2
                   parameter for generating the censoring time, the regulator censoring rate
СС
```

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dd set "uniform" for U(0,cc); set weibull for weibull(shape=5,scale=cc)

output X1,X2,Z and D are observed mediated, terminal event times exposure and cen-

soring index (1/0 for failure and censored)

## **Examples**

```
meta.gen(500,theta_0=1,theta_1=0.5,L1=1,L2=1,L3=1,b01=0.5,b02=0,b03=1,cc=2,dd="uniform")
```

ms

Estimating the direct and indirect of the Multistate model.

## Description

Estimating the direct and indirect of the Multistate model.

## Usage

```
ms(data, P.time)
```

## **Arguments**

data data.frame(X1,X2,D,Z)

P. time interpolation time can be vector or scalar

## **Examples**

```
 \begin{array}{l} {\rm data=meta.gen(500,theta\_0=0.5,theta\_1=0.5,L1=0.5,L2=0.5,L3=1,b01=1,b02=0,b03=0,cc=2,dd="uniform")} \\ {\rm P.time=seq(0,1,by=0.01)} \\ {\rm ans=ms(data,P.time)} \\ {\rm plot(P.time,ans\$DE,type="l",ylim=c(-0.5,0.5))} \\ {\rm points(P.time,ans\$IE,type="l",ylim=c(-0.5,0.5),col=2)} \\ {\rm legend(0,0.45,c("direct effect","indirect effect"),col=1:2,lty=1)} \\ \end{array}
```

M state

Estimating the direct and indirect of the Multistate model. Obtaining the variance by bootstrapping

## **Description**

Estimating the direct and indirect of the Multistate model. Obtaining the variance by bootstrapping

#### **Usage**

```
M_state(data, P.time)
```

## **Arguments**

data data.frame(X1,X2,D,Z)

P. time interpolation time can be vector or scalar

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## **Examples**

```
 \begin{array}{l} {\rm data=meta.gen(500,theta\_0=0.5,theta\_1=0.5,L1=0.5,L2=0.5,L3=1,b01=1,b02=0,b03=0,cc=2,dd="uniform")} \\ {\rm P.time=seq(0,1,by=0.01)} \\ {\rm ans=M\_state(data,P.time)} \\ {\rm plot(P.time,ans\$DE,type="l",ylim=c(-0.5,0.5))} \\ {\rm points(P.time,ans\$DE-ans\$DE\_sd,type="l",ylim=c(-0.5,0.5))} \\ {\rm points(P.time,ans\$DE-ans\$DE\_sd,type="l",ylim=c(-0.5,0.5))} \\ {\rm points(P.time,ans\$IE,type="l",ylim=c(-0.5,0.5),col=2)} \\ {\rm points(P.time,ans\$IE-ans\$IE\_sd,type="l",ylim=c(-0.5,0.5),col=2)} \\ {\rm points(P.time,ans\$IE-ans\$IE\_sd,type="l",ylim=c(-0.5,0.5),col=2)} \\ {\rm points(P.time,ans\$IE-ans\$IE\_sd,type="l",ylim=c(-0.5,0.5),col=2)} \\ {\rm legend(0,0.45,c("direct effect","indirect effect"),col=1:2,lty=1)} \\ \end{array}
```

pLA

predicting the value for one to one vector

## **Description**

predicting the value for one to one vector

## Usage

```
pLA(yy, tt, LL)
```

## **Arguments**

yy any time you want to interpolate

tt time or x value with same length of LL, must >0

LL value as f(tt)

## **Examples**

```
x=seq(0,0.5,by=0.01)
LL=pnorm(x,0,1)
pLA(c(0,0.1,0.25,0.01,3),x,LL)
```

Xu2010

Estimating the parameters of the frailty model

## **Description**

Estimating the parameters of the frailty model

## Usage

```
Xu2010(T1, T2, d2, int\_theta, tol = tol, step)
```

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## **Arguments**

T1	observed mediator event time (vector)
T2	observed terminal event time (vector)
d2	1 for terminal event occured 0 for censored (vector)

int\_theta initial value (>0) for theta used for iteration

tol maximum tolerance of change during the iteration

step maximum number of the iteration

## **Examples**

Xu2010\_rest

Estimating the parameters of the frailty model

## **Description**

Estimating the parameters of the frailty model

## Usage

```
Xu2010_rest(T1, T2, d2, int_theta, tol = 0.01, step)
```

## **Arguments**

T1	observed mediator event time (vector)
T2	observed terminal event time (vector)

d2 1 for terminal event occured 0 for censored (vector)

int\_theta initial value (>0) for theta used for iteration

tol maximum tolerance of change during the iteration

step maximum number of the iteration

## **Examples**

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