Package 'bdribs'

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Title Bayesian Detection of Potential Risk Using Inference on Blinded Safety Data

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Description Implements Bayesian inference to detect signal from blinded clinical trial when total number of adverse events of special concerns and total risk exposures from all patients are available in the study. For more details see the article by Mukhopadhyay et. al. (2018) titled 'Bayesian Detection of Potential Risk Using Inference on Blinded Safety Data', in Pharmaceutical Statistics (to appear).

Depends R (>= 3.1.0), rjags

Note Package 'rjags' requires JAGS executabe file (compatiable version) should be already installed.

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LazyData TRUE

RoxygenNote 6.0.1

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R topics documented:

bdribs *bdribs (Bayesian Detection of Risk using Inference on Blinded Safety data)*

Description

Bayesian Detection of Risk using Inference on Blinded Safety data

Usage

```
bdribs(y, pyr, bg.events, bg.pyr, bg.rate = NULL, k = 1, p.params = list(a
  = 1, b = 1), r.params = list(mu = 0, sd = 2), adj.k = FALSE,
  mc.params = list(burn = 1000, iter = 10000, nc = 2), inf.type = 1,
  plots = TRUE, prnt = TRUE)
```

Arguments

y	observed pooled events (combined active and control group) e.g., y = 20
pyr	total payr exposure (combined active and control group) e.g., pyr = 2000
bg.events	background (historical) events for the control group e.g., bg.events = 5
bg.pyr	background (historical) pyr exposure for the control group e.g., bg.pyr = 1000
bg.rate	when specified used as the true background rate for the control group and ignores bg.events and bg.pyr, default: bg.rate=NULL
k	allocation ratio of treatment vs. control group, default: k=1
p.params	paramaters of beta prior of p (used only when inf.type = 1 or = 2); default: p.param= list(a=1,b=1). See details below.
r.params	paramaters of log-normal prior of r (used only when p.params=NULL); default: r.param= list(mu=0,sd=2). See details below.
adj.k	when TRUE adjusts the prior specification for k >1 (or for k <1), default: adj.k = FALSE . See deatil below.
mc.params	contains detials of MCMC parameters, default: mc.params=list(burn=1000, iter=10000, nc=2)
inf.type	indicate inference type, default: inf.type =1 (gives conditional inference for fixed background rate). See deatil below.
plots	indicates whether standard plots to be generated, default: plots= TRUE
prnt	indicates whether inputs to be printed, default: prnt= TRUE

Details

This 'bdribs' package obtains Bayesian inferences on blinded pooled safety data ...

Values of p.params are used to specify a beta prior for p - default is Jeffreys non-informative prior: Beta(a=0.5,b=0.5).

If inf.type=1, then conditional posterior inference on r is obtained for a given fixed values of del0 = bg.rate = bg.events/bg.pyr.

If inf.type=2, then an average (marginal) Bayesian inference on r is obtained with respect to a prior on del0, where del0 ~ Gamma(bg.events, bg.pyr).

If prior on r must be specified directly it can be done by using a log-normal prior. To do that, p.params must be set to NULL and and then r.params should be specifed as a list to supply mean and sd of the lognormal. For example, to have a lognormal prior with log-mean 0 and log-sd = 2, we should set r.params = list(mu=0, sd=2) and p.params=NULL.

when adj.k = TRUE, and k is not 1 (that is, allocation ratio is not 1:1), then a non-informative prior such as (beta(.5, .5) is first specified on p, assuming equal allocation ratio and then adjusted for the give k. When adj.k = F, then no such adjustment is made on the prior for p. Note that no such adjustments needed if prior on r is directly specified (as discussed above). However, it is always difficult to specify a non-informative prior on r and therefore a a prior on p with adj.k =T is recommended in most cases.

Value

returns a dataframe of MCMC output from the posterior distribution for parameters of interests

Author(s)

Saurabh Mukhopadhyay

Examples

```
## Sample calls
    #run 1: simple case with a fixed background rate of 0.45 per 100 pyr.
    bdribs(y=5,pyr=500, bg.rate=0.0045,k=2)

    #run 2: same as run 1; here bg.rate gets computed as bg.events/bg.pyr
    bdribs(y=5,pyr=500, bg.events = 18, bg.pyr = 4000, k=2)

   # run3: when inf.type = 2, uses a Gamma distribution for del0; e.g. here Gamma(18, 4000)
    bdribs(y=5,pyr=500, bg.events = 18, bg.pyr = 4000, k=2, inf.type = 2)

    #run4: similar to run1, but instead of default p~u(0,1) using p~beta(.5,.5)
    bdribs(y=5,pyr=500, , bg.rate=0.0045,k=2, p.params=list(a=.5,b=.5))

   #run5: similar to run1, but instead of default p ~ beta(.5,.5) using r ~ lognormal(mu=0,sd=2)
    bdribs(y=5,pyr=500, , bg.rate=0.0045,k=2, p.params= NULL, r.params=list(mu=0,sd=2))
```

`bdribs.contour` *contour plot - draws plot (optional) and returns a matrix/grid of posterior values*

Description

Contour plot of posterior probabilities on a range of (y, E) values

Usage

```
bdribs.contour(ymax, pyrmax, eincr, tol, k, bg.rate, plt = TRUE, ...)
```

Arguments

ymax	maximum number of AESI event for which contour plot to be drawn
pyrmax	maximum risk exposure (in patient-year)
eincr	increment of patient-year exposures (default = 50)
tol	the maximum tolerance value of relative risk r (default =1)
k	allocation ratio (T:C)
bg.rate	estimated background rate (historical control rate) per patient-year (using inf.type=1)
plt	whether a contour plot to be drawn (default = TRUE)
...	to supply remaining parameters for bdribs call when supplied will override the default values

Value

returns contour plot matrix over the grid specified

Examples

```
## Sample calls
     #run 1: The contour plot

     bdribs.contour(ymax=15,pyrmax=2000,eincr=250,tol=1.5,k=2, bg.rate=0.0045)
     #run 2: Monitoring blinded AE over time using contour plot
     bdribs.contour(ymax=15,pyrmax=2000,eincr=250,tol=1.5,k=2, bg.rate=0.0045)
     obs.pyr=c(300,570,650,800, 1200, 1500)
     obs.y=c(2,4,5,6,10,12)
     points(obs.pyr, obs.y,type="p",pch=16, cex=1.4,col="maroon")
     if (length(obs.y)>1) points(c(0,obs.pyr), c(0,obs.y), type="s", lty=3, lwd=2,
     col="black")
```

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bdribs.sensitivity — *sensitivity plot - plot of range of posterior probability corresponding to a range of background rate*

Description

plot of range of posterior probability corresponding to a range of background rate

Usage

```
bdribs.sensitivity(Y = 5:9, pyr = 800, k = 1, tol = 1.2, bg.evnt = 18,
  bg.pyr = 4000, bg.ci.coef = 0.9, bg.rng = NULL, add.mid = FALSE, ...)
```

Arguments

Y	range on number of AESI events for which sensitivity range to be drawn (default = 5:9)
pyr	total patient-year exposure where AESI events occurred (default =800)
k	allocation ratio (T:C) (default =1)
tol	clinically meaningful relative risk (default =1.2)
bg.evnt	background (historical) number of events in the control group (default =18)
bg.pyr	background (historical) patient-year exposure in the control group (default =4000)
bg.ci.coef	range of background rate estimate to be obtained from bg.ci.coef*100% CI (default =0.9); takes any value between 0.5 and 0.999.
bg.rng	range of background rate - if specified then bg.evnt, bg.pyr, and bg.ci.coef will be ignored (default =NULL)
add.mid	indicator variable to plot P(r>tol | Y, pyr) under inf.type=2 - requires related parameters to be supplied (default =F)
...	to supply remaining parameters of bdribs call (other than y, pyr, k, bg.events, bg.pyr) for bdribs call when supplied will override the default values

Value

returns a plot of P(r>tol | Y, pyr) over the range of background rate

Examples

```
## Sample calls
     #run 1: The sensitivity plot
    bdribs.sensitivity(Y=5:9,pyr=800,k=1, tol=1.2, bg.evnt=18, bg.pyr=4000,bg.ci.coef=0.90)
     #run 2: The sensitivity plot
    bdribs.sensitivity(Y=5:9,pyr=800,k=1, tol=1.2, bg.evnt=18, bg.pyr=4000,bg.ci.coef=0.90,
     add.mid=TRUE)
     #run 3: Using bg.rng parameter
     bdribs.sensitivity(Y=5:9,pyr=800,k=1, tol=1.2, bg.rng = c(0.0030, 0.0045, 0.0065))
```

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