Package 'ToxCrit'

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Type Package

Title Calculates Safety Stopping Boundaries for a Single-Arm Trial
using Bayes

Version 1.0

Author NCT Trial Center, Heidelberg [aut],
Lisa-Marie Lanz [cre]

Maintainer Lisa-Marie Lanz <studienzentrale@nct-heidelberg.de>

Description Computation of stopping boundaries for a single-arm trial using a
Bayesian criterion; i.e., for each m<=n (n= total patient number of the
trial) the smallest number of observed toxicities is calculated
leading to the termination of the trial/accrual according to the specified
criteria. The probabilities of stopping the trial/accrual at and up until
(resp.) the m-th patient (m<=n) is also calculated. This design is more
conservative than the frequentist approach (using Clopper Pearson CIs)
which might be preferred as it concerns safety.See also Aamot et.al.(2010)
``Continuous monitoring of toxicity in clinical trials - simulating the risk
of stopping prematurely'' <doi:10.5414/cpp48476>.

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R topics documented:

ToxCrit   *ToxCrit*

Description

Calculates critical values for continuous monitoring of toxicity using a Bayesian approach. It also simulates the probability for stopping the trial for each recruited patient given a true toxicity rate passed in this function.

To calculate the posterior distribution of the toxicity rate r, the binomial-beta model is used. Thus, if y cases of toxicities have been observed among the first k patients, the posterior distribution of r is beta(1+y, 1+k-y). The formal stopping criterion is reached if the posterior probability (Pr) that the true toxicity rate r exceeds the unacceptable toxicity rate.

Please note: The trial must be stopped or modified if the observed number of toxicities is >= the critical value for the respective number of recruited patients. This method is mostly used for early phase clinical trials and validated according to GCP. It was firstly presented at the 54th annual meeting of GMDS.

Assumptions:

1. The prior distribution of the toxicity rate is assumed to be beta(a,b).

2. No stopping at the first patient.

IMPORTANT INFORMATION:

The program is closed automatically after each execution on a server. Therefore, always the same pseudo random numbers are used and simulation based on the the same parameters will always yield identical output! In order to fix this, an additional random number is generated based on a time-dependent seed point.

Usage

```
ToxCrit(npat, ptoxcrit, pstop, nsim, ptox, a = 1, b = 1)
```

Arguments

npat	number of patients to be included in the trial.
ptoxcrit	critical (minimal unacceptable) toxicity rate (%).
pstop	critical posterior probability of unacceptable toxicity; higher values lead to the termination of the trial/accrual.
nsim	number of simulation runs (simulated studies).
ptox	assumed true toxicity rate used for simulations (%).
a	first parameter of the Beta distribution.
b	second parameter of the Beta distribution.

Value

A table containing information on critical boundaries per patient, the probability to stop the trial given the assumed true toxicity rate and the cumulative probability to stop the trial given the assumed true toxicity rate.

Examples

```
#Pr(r>30%)>=95%) --> The posterior probability that the true toxicity rate exceeds the
#unacceptable toxicity rate of 30% is at least 95% (with 9 patients, an assumed true
#toxicity rate of 20% and 100,000 simulation runs):
ToxCrit(9, 30, 95, 100000, 20)
```

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