

Package ‘seqmon’

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Title Sequential Monitoring of Clinical Trials

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Description A program that computes the probability of crossing sequential boundaries in a clinical trial. It implements the Armitage-McPherson and Rowe Algorithm using the method described in Schoenfeld D. (2001)“ A simple Algorithm for Designing Group Sequential Clinical Trials” Biometrics 27: pp,972-974

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Description

A program that computes the probabilities of crossing boundaries in a group sequential clinical trial. It implements the Armitage-McPherson and Rowe (1969) algorithm using the method described in Schoenfeld D. (2001). Assume that there is a sequence of test statistics z_1, \dots, z_m in a clinical trial. Each statistic has a standard normal distribution under the null hypothesis. Let a_1, \dots, a_m and b_1, \dots, b_m be a lower and an upper boundary and let t_1, \dots, t_m be the amount of information that was used to calculate each statistic. The function calculates the probability that $z_j < a_j, j \leq i$ and $b_j < z_j, j \leq i$ for $i = 1, \dots, m$. Probabilities for an alternative hypothesis can be found by adding an offset to a_1, \dots, a_m and b_1, \dots, b_m equal to the expected value of the statistic.

Usage

```
seqmon(a,b,t,int)
```

Arguments

a	A vector of the lower boundaries at information time t1,t2,...,tm
b	A vector of the upper boundaries at the information times t1,t2,...,tm
t	A vector of the information times, usually 1:m
int	A vector of the number of intervals to divide up (a[k],b[k]), 500 should be adequate

Value

A $m \times 2$ matrix giving the the cumulative probabilities of crossing the lower boundary and the probabilities of crossing the upper boundary.

Note

The test statistic is assumed to be standardized so that it's value at any point in time is normally distributed random variable with mean zero and variance one. The numerator of the test statistic is assumed to be a gaussian process with independent increments.

References

Armitage, P., McPherson, C. K. and Rowe, B. C. (1969) "Repeated significance tests on accumulating data" *Journal of the Royal Statistical Society, Series A, General*, 132, 235-244

Schoenfeld D. (2001) "A simple Algorithm for Designing Group Sequential Clinical Trials" *Biometrics* 27 , pp, 972-974.

O'Brien, Peter C. , and Fleming, Thomas R. (1979), "A multiple testing procedure for clinical trials", *Biometrics*, 35 , 549-556

Examples

```
##The following gives the probability of crossing
##the boundaries for a O'Brien Fleming (1979) lower and upper bound
##with five looks at the data under the null hypothesis.
z<-2.04
```

```
a<- -z*sqrt(5/(1:5))
b<- +z*sqrt(5/(1:5))
t<- 1:5
int<- 500* array(c(1),5)
seqmon(a,b,t,int)
##This gives the probabilities under the alternative hypothesis if the expected value of the mean difference over it
##standard error for one group is 1.5
u<-1.5
seqmon(a+u*sqrt(1:5),b+u*sqrt(1:5),t,int)
```

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