Package ‘gsMAMS’

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Title  Group Sequential Designs of Multi-Arm Multi-Stage Trials
Version  0.7.1
Imports  mvtnorm, stats, survival
Description  
It provides functions to generate operating characteristics and to calculate Sequential Conditional Probability Ratio Tests (SCPRT) efficacy and futility boundary values along with sample/event size of Multi-Arm Multi-Stage (MAMS) trials for different outcomes. The package is based on Jianrong Wu, Yimei Li, Liang Zhu (2023) <doi:10.1002/sim.9682>, Jianrong Wu, Yimei Li (2023) "Group Sequential Multi-Arm Multi-Stage Survival Trial Design with Treatment Selection" (Manuscript accepted for publication) and Jianrong Wu, Yimei Li, Shengping Yang (2023) "Group Sequential Multi-Arm Multi-Stage Trial Design with Ordinal Endpoints" (In preparation).

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design_cont

Description
This function generates the design parameters of a clinical trial for continuous outcome.

Usage
design_cont(delta0, delta1, alpha, beta, K, frac)

Arguments
- delta0: Standardized effect size in ineffective arm.
- delta1: Standardized effect size in effective arm.
- alpha: Type I error.
- beta: Type II error.
- K: Number of treatment arms.
- frac: Vector of fractions for information time at each look.

Value
List of cumulative sample size for each stage of treatment and control groups along with maximum total sample size of the trial. It also provides efficacy and futility boundaries of the trial.

Examples
design_cont(delta0=0.178, delta1=0.545, alpha = 0.05, beta = 0.1, K = 4, frac=c(1/2,1))

design_ord

Description
This function generates the design parameters of a clinical trial for ordinal outcome.

Usage
design_ord(alpha, beta, K, prob, or0, or, frac)
Arguments

alpha       Type I error.
beta        Type II error.
K           Number of treatment arms.
prob        Probability of ordinal outcomes in control group.
or0         Odds ratio of ineffective treatment group vs control.
or           Odds ratio of effective treatment group vs control.
frac        Vector of fractions for information time at each look.

Value

List of cumulative sample size for each stage of treatment and control groups along with maximum total sample size of the trial. It also provides efficacy and futility boundaries of the trial.

Examples

design_ord(0.05,0.1,K=4,c(0.075, 0.182, 0.319, 0.243, 0.015, 0.166),or=3.06,or0=1.32,c(1/2,1))

design_surv(m0, alpha, beta, K, HR0, HR1, ta, tf, kappa, eta, frac)
Value

List of cumulative number of events for each stage of combined treatment and control groups along with total number of subjects and maximum total number of events for the trial. It also provides efficacy and futility boundaries of the trial.

Examples

design_surv(m0=20, HR0=1, HR1=0.65, ta=20, tf=40, alpha=0.05, beta=0.1, K=3, kappa=1, eta=0, frac=c(1/2,1))

\begin{verbatim}

\texttt{op_fwer_cont} \hspace{1cm} \textit{Provides operating characteristics of group sequential MAMS trial for continuous outcome under null hypothesis}

\end{verbatim}

Description

Computes FWER and other characteristics for group-sequential MAMS trial for continuous outcome.

Usage

\begin{verbatim}

\texttt{op_fwer_cont(alpha, beta, K, frac, delta0, delta1, nsim, seed)}

\end{verbatim}

Arguments

- \texttt{alpha}: Type I error.
- \texttt{beta}: Type II error.
- \texttt{K}: Number of treatment arms.
- \texttt{frac}: Vector of fractions for information time at each look.
- \texttt{delta0}: Standardized effect size in ineffective arm.
- \texttt{delta1}: Standardized effect size in effective arm.
- \texttt{nsim}: Number of simulations.
- \texttt{seed}: Random seed number.

Value

A list of FWER, stage-wise type I error, average sample size used per arm, stopping probability, probability of futility.

Examples

\begin{verbatim}

\texttt{op_fwer_cont(0.05,0.1,2,c(0.5,1),0.178,0.545,15,1)}

\end{verbatim}
**op_fwer_ord**

*Provides operating characteristics of group sequential MAMS trial for ordinal outcome under null hypothesis*

---

**Description**

Computes FWER and other characteristics for group-sequential MAMS trial for ordinal outcome.

**Usage**

```r
op_fwer ORD(alpha, beta, K, frac, or0, or, nsim, prob, seed)
```

**Arguments**

- `alpha`: Type I error.
- `beta`: Type II error.
- `K`: Number of treatment arms.
- `frac`: Vector of fractions for information time at each look.
- `or0`: Odds ratio of ineffective treatment group vs control.
- `or`: Odds ratio of effective treatment group vs control.
- `nsim`: Number of simulations.
- `prob`: Probability of ordinal outcomes in control group.
- `seed`: Random seed number.

**Value**

A list of FWER, stage-wise type I error, average sample size used per arm, stopping probability, probability of futility.

**Examples**

```r
op_fwer ORD(0.05, 0.1, 4, c(0.5, 1), 1.32, 3.06, 15, c(0.075, 0.182, 0.319, 0.243, 0.015, 0.166), 13)
```

---

**op_fwer_surv**

*Provides operating characteristics of group sequential MAMS trial for survival outcome under null hypothesis*

---

**Description**

Computes FWER and other characteristics for group-sequential MAMS trial for survival outcome.
Usage

\texttt{op\_fwer\_surv(}
  \texttt{m0, alpha, beta, K, frac, HR0, HR1, nsim, ta, tf, kappa, eta, seed)}
\texttt{)}

Arguments

\begin{itemize}
  \item \texttt{m0} \hspace{1cm} Median survival time in control group.
  \item \texttt{alpha} \hspace{1cm} Type I error.
  \item \texttt{beta} \hspace{1cm} Type II error.
  \item \texttt{K} \hspace{1cm} Number of treatment arms.
  \item \texttt{frac} \hspace{1cm} Vector of fractions for information time at each look.
  \item \texttt{HR0} \hspace{1cm} Hazard ratio of ineffective treatment group vs control.
  \item \texttt{HR1} \hspace{1cm} Hazard ratio of effective treatment group vs control.
  \item \texttt{nsim} \hspace{1cm} Number of simulations.
  \item \texttt{ta} \hspace{1cm} Accrual time.
  \item \texttt{tf} \hspace{1cm} Follow-up time.
  \item \texttt{kappa} \hspace{1cm} Shape parameter (Kappa=1 for exponential distribution).
  \item \texttt{eta} \hspace{1cm} Rate of loss to follow-up.
  \item \texttt{seed} \hspace{1cm} Random seed number.
\end{itemize}

Value

A list of FWER, stage-wise type I error, stopping probability, probability of futility, average number of events happened per arm, average duration of trial.

Examples

\texttt{op\_fwer\_surv(20, 0.05, 0.1, c(1/2, 1), 1, 0.75, 12, 40, 20, 1, 0, 12)}
op_power_cont

Provides operating characteristics of group sequential MAMS trial for continuous outcome

Description
Computes power and other characteristics for group-sequential MAMS trial for continuous outcome.

Usage
op_power_cont(alpha, beta, K, frac, delta0, delta1, nsim, seed)

Arguments
alpha Type I error.
beta Type II error.
K Number of treatment arms.
frac Vector of fractions for information time at each look.
delta0 Standardized effect size in ineffective arm.
delta1 Standardized effect size in effective arm.
nsim Number of simulations.
seed Random seed number.

Value
A list of power, stage-wise probability of success, average sample size used per arm, stopping probability, probability of futility.

Examples
op_power_cont(0.05,0.1,4,c(1/5,2/5,3/5,4/5,1),0.178,0.545,12,12)

op_power_ord
Provides operating characteristics of group sequential MAMS trial for ordinal outcome

Description
Computes power and other characteristics for group-sequential MAMS trial for ordinal outcome.

Usage
op_power_ord(alpha, beta, K, frac, or0, or, nsim, prob, seed)
Arguments

- **alpha**: Type I error.
- **beta**: Type II error.
- **K**: Number of treatment arms.
- **frac**: Vector of fractions for information time at each look.
- **or0**: Odds ratio of ineffective treatment group vs control.
- **or**: Odds ratio of effective treatment group vs control.
- **nsim**: Number of simulations.
- **prob**: Probability of ordinal outcomes in control group.
- **seed**: Random seed number.

Value

A list of power, stage-wise probability of success, average sample size used per arm, stopping probability, probability of futility.

Examples

```r
op_power_ord(0.05, 0.1, 4, c(0.5, 1), 1.32, 3.06, 12, c(0.075, 0.182, 0.319, 0.243, 0.015, 0.166), 13)
```

---

**op_power_surv**: Provides operating characteristics of group sequential MAMS trial for survival outcome

Description

Computes power and other characteristics for group-sequential MAMS trial for survival outcome.

Usage

```r
op_power_surv(
  m0,
  alpha,
  beta,
  K,
  frac,
  HR0,
  HR1,
  nsim,
  ta,
  tf,
  kappa,
  eta,
  seed
)
```
**Arguments**

- \( m_0 \): Median survival time of control group.
- \( \alpha \): Type I error.
- \( \beta \): Type II error.
- \( K \): Number of treatment arms.
- \( \text{frac} \): Vector of fractions for information time at each look.
- \( HR_0 \): Hazard ratio of ineffective treatment group vs control.
- \( HR_1 \): Hazard ratio of effective treatment group vs control.
- \( \text{nsim} \): Number of simulations.
- \( \text{ta} \): Accrual time.
- \( tf \): Follow-up time.
- \( \text{kappa} \): Shape parameter (kappa=1 for exponential distribution).
- \( \text{eta} \): Rate of loss to follow-up.
- \( \text{seed} \): Random seed number.

**Value**

A list of power, stage-wise probability of success, stopping probability, probability of futility, average number of events happened per arm, average duration of trial.

**Examples**

```r
op_power_surv(20, 0.05, 0.1, 4, c(1/2, 1), 1, 0.74, 12, 40, 20, 1, 0, 12)
```
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