Package 'survmixer'

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Title Design of Clinical Trials with Survival Endpoints Based on
Binary Responses

Version 1.3

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Description Sample size and effect size calculations for survival endpoints based on mixture survival-
by-response model. The methods imple-
mented can be found in Bofill, Shen & Gómez (2021) <arXiv:2008.12887>.

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survmixture_f   *Mixture survival function*

Description

The function 'survmixture_f' computes the survival distribution as a mixture of responders and non-responders. The responders and non-responders distributions are assumed to be Weibull distributions.

Usage

```
survmixture_f(t, ascale_r, ascale_nr, bshape = 1, p)
```

Arguments

t	time at which the survival distribution is evaluated
ascale_r	scale parameter for the Weibull distribution for responders
ascale_nr	scale parameter for the Weibull distribution for non-responders
bshape	shape parameter for the Weibull distribution
p	event rate for the response

Value

This function returns the survival function evaluated at t based on a mixture model of responders and non-responders.

Author(s)

Marta Bofill Roig.

References

Design of phase III trials with long-term survival outcomes based on short-term binary results. Marta Bofill Roig, Yu Shen, Guadalupe Gomez Melis. arXiv:2008.12887

Examples

```
survmixture_f(t=0.2,ascale_r=8,ascale_nr=5.6,p=0.2)
```

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survm_effectsize	*Effect size calculation for mixture survival distributions*

Description

The function 'survm_effectsize' calculates the effect size in terms of the difference of restricted mean survival times (RMST) according to the information on responders and non-responders.

Usage

```
survm_effectsize(
  ascale0_r,
  ascale0_nr,
  delta_p,
  p0,
  bshape0 = 1,
  bshape1 = 1,
  ascale1_r,
  ascale1_nr,
  tau,
  Delta_r = NULL,
  Delta_0 = NULL,
  Delta_nr = NULL,
  anticipated_effects = FALSE
)
```

Arguments

ascale0_r	scale parameter for the Weibull distribution in the control group for responders
ascale0_nr	scale parameter for the Weibull distribution in the control group for non-responders
delta_p	effect size for the response rate
p0	event rate for the response
bshape0	shape parameter for the Weibull distribution in the control group
bshape1	shape parameter for the Weibull distribution in the intervention group
ascale1_r	scale parameter for the Weibull distribution in the intervention group for responders
ascale1_nr	scale parameter for the Weibull distribution in the intervention group for non-responders
tau	follow-up
Delta_r	RMST difference between intervention and control groups for responders
Delta_0	RMST difference between responders and non-responders in the control group
Delta_nr	RMST difference between intervention and control groups for non-responders

anticipated_effects

Logical parameter. If it is TRUE then the effect size is computed based on previous information on the effect sizes on response rate and survival-by-responses (that is, based on Delta_r, Delta_0, Delta_nr); otherwise is based on the distributional parameters (ascale0_r, ascale0_nr, ascale1_r, ascale1_nr, bshape0, bshape1).

Value

This function returns the overall mean survival improvement (RMST difference between groups) and it also includes the mean survival improvement that would be assumed for each responders and non-responders.

Author(s)

Marta Bofill Roig.

References

Design of phase III trials with long-term survival outcomes based on short-term binary results. Marta Bofill Roig, Yu Shen, Guadalupe Gomez Melis. arXiv:2008.12887

Examples

```
survm_effectsize(ascale0_r=8,ascale0_nr=5.6,ascale1_r=36,ascale1_nr=5.6,delta_p=0.2,p0=0.2,tau=5)
```

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survm_samplesize   *Sample size calculation for mixture survival distributions*

Description

The function 'survm_samplesize' calculates the sample size according to the distributional parameters of the responders and non-responders.

Usage

```
survm_samplesize(
  ascale0_r,
  ascale0_nr,
  ascale1_r,
  ascale1_nr,
  delta_p,
  p0,
  m0_r,
  m0_nr,
  diffm_r,
  diffm_nr,
  S0_r,
```

```
        S0_nr,
        diffS_r,
        diffS_nr,
        Delta_r,
        Delta_nr,
        ascale_cens,
        tau,
        bshape0 = 1,
        bshape1 = 1,
        all_ratio = 0.5,
        alpha = 0.025,
        beta = 0.2,
        set_param = 0
    )
```

Arguments

ascale0_r	scale parameter for the Weibull distribution in the control group for responders
ascale0_nr	scale parameter for the Weibull distribution in the control group for non-responders
ascale1_r	scale parameter for the Weibull distribution in the intervention group for responders
ascale1_nr	scale parameter for the Weibull distribution in the intervention group for non-responders
delta_p	effect size for the response rate
p0	event rate for the response
m0_r	survival mean for responders in the control group
m0_nr	survival mean for non-responders in the control group
diffm_r	difference in survival means between groups for responders
diffm_nr	difference in survival means between groups for responders
S0_r	tau-year survival rates for responders in the control group
S0_nr	tau-year survival rates for non-responders in the control group
diffS_r	difference in tau-year survival rates for responders
diffS_nr	difference in tau-year survival rates for non-responders
Delta_r	restricted mean survival times (RMST) difference between intervention and control groups for responders
Delta_nr	RMST difference between intervention and control groups for non-responders
ascale_cens	distributional parameter for the exponential distribution for the censoring
tau	follow-up
bshape0	shape parameter for the Weibull distribution in the control group
bshape1	shape parameter for the Weibull distribution in the intervention group
all_ratio	allocation ratio. The ratio of numbers of participants allocated in the control group. By default is assumed 1:1 (i.e., all_ratio=0.5)

alpha	type I error
beta	type II error
set_param	Set of parameters to be used for the responders/non-responders survival functions If the set of parameters is =1, then the sample size is computed using the survival means (m0_r,m0_nr,diffm _r,diffm_nr); if set_param=2, it is computed using the tau-year survival rates (S0_r,S0_nr,diffS_r,diffS_nr); if set_param=2, it is computed using the RMSTs and survival rates (Delta_r,Delta_nr,S0_r,S0_nr). If set_param=0, the computation is based on the distributional parameters (ascale0_r, ascale0_nr, ascale1_r, ascale1_nr).

Value

This function returns the total sample size needed and the expected effect size for overall survival (RMST difference between groups).

Author(s)

Marta Bofill Roig.

References

Design of phase III trials with long-term survival outcomes based on short-term binary results. Marta Bofill Roig, Yu Shen, Guadalupe Gomez Melis. arXiv:2008.12887

Index