

# Package ‘HCTDesign’

August 29, 2025

**Title** Group Sequential Design for Historical Control Trial with Survival Outcome

**Version** 0.7.3

**Imports** Rdpack, diversitree, mvtnorm, flexsurv, stats, survival, crayon

**RdMacros** Rdpack

## Description

It provides functions to design historical controlled trials with survival outcome by group sequential method. The options for interim look boundaries are efficacy only, efficacy & futility or futility only. It also provides the function to monitor the trial for any unplanned look. The package is based on Jianrong Wu, Xiaoping Xiong (2016) <[doi:10.1002/pst.1756](https://doi.org/10.1002/pst.1756)> and Jianrong Wu, Yimei Li (2020) <[doi:10.1080/10543406.2019.1684305](https://doi.org/10.1080/10543406.2019.1684305)>.

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| EffDesign | <i>HCT design with interim monitoring for efficacy only</i> |
|-----------|-------------------------------------------------------------|

---

**Description**

The group sequential design for historical controlled survival outcome trials with efficacy boundaries only.

**Usage**

```
EffDesign(
  k,
  alpha,
  beta,
  delta,
  delta0,
  d1,
  option = "OBF",
  param = 4,
  trial = "Superiority"
)
```

**Arguments**

|        |                                                                                                                                                                               |
|--------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| k      | vector of time fraction for all planned looks: $k=c(1/3,2/3,1)$ if the three planned looks will be carried out at 1/3, 2/3 and all of the total events in the experiment arm. |
| alpha  | type I error.                                                                                                                                                                 |
| beta   | type II error.                                                                                                                                                                |
| delta  | hazard ratio: hazard of experiment group over hazard of control group.                                                                                                        |
| delta0 | Non-inferiority margin.                                                                                                                                                       |
| d1     | total number of events in the historical control group.                                                                                                                       |
| option | type of spending function: "OBF", "Gamma", "Rho" or "Pocock". Default is "OBF".                                                                                               |
| param  | Parameter for Gamma family or Rho family. Default value is 4.                                                                                                                 |
| trial  | Type of trial: "Superiority" or "Non-inferiority". Default is "Superiority".                                                                                                  |

**Value**

List of dataframes and vectors containing the details about the following: design of the trial which includes the number of looks and events; details about futility and efficacy boundaries which include transformed information time at each look, cumulative beta and alpha respectively, p-values and crossing probabilities; etam(drift parameter); d2max(maximum number of events in the experimental group); delta\_used(hazard ratio used in the design).

**Author(s)**

Tushar Patni, Yimei Li, Jianrong Wu, and Arzu Onar-Thomas.

**References**

Wu J, Xiong X (2016). "Survival trial design and monitoring using historical controls." *Pharmaceutical Statistics*, **15**(5), 405-411.

Wu J, Li Y (2020). "Group sequential design for historical control trials using error spending functions." *Journal of Biopharmaceutical Statistics*, **30**(2), 351-363.

**Examples**

```
#Superiority trial with three equally spaced looks for efficacy using OBF spending function.
gg<-EffDesign(k=c(0.3,0.6,1),alpha=0.05,beta=0.1,delta=0.57,d1=65,option="OBF",trial="Superiority")
```

---

EffIM

*Monitoring the trial at interim looks for a trial with efficacy monitoring only*

---

**Description**

Calculates one-sided efficacy boundary values at the observed number of events.

**Usage**

```
EffIM(
  d2,
  dmax,
  last.look = FALSE,
  d1,
  etam,
  alpha,
  beta,
  opt = "OBF",
  param = 4
)
```

**Arguments**

|           |                                                                                                                                        |
|-----------|----------------------------------------------------------------------------------------------------------------------------------------|
| d2        | vector of number of events at which you want to monitor the trial.                                                                     |
| dmax      | maximum number of events in the experimental group calculated from design function.                                                    |
| last.look | logical which indicates whether the current look is the last look or not. Default is FALSE. If true, the post hoc power is calculated. |
| d1        | total number of events in the historical control group.                                                                                |
| etam      | value of the drift parameter obtained from design function.                                                                            |

|       |                                                                                 |
|-------|---------------------------------------------------------------------------------|
| alpha | type I error.                                                                   |
| beta  | type II error.                                                                  |
| opt   | type of spending function: "OBF", "Gamma", "Rho" or "Pocock". Default is "OBF". |
| param | Parameter for "gamma family" or rho family. Default value is 4.                 |

### Details

The number of events have to be entered sequentially. See example.

### Value

A list containing efficacy boundary values along with the p-values and transformed information time for the current look. Post-hoc power is also calculated in case of early stopping of the trial.

### Author(s)

Tushar Patni, Yimei Li, Jianrong Wu, and Arzu Onar-Thomas.

### References

Wu J, Xiong X (2016). "Survival trial design and monitoring using historical controls." *Pharmaceutical Statistics*, **15**(5), 405-411.

Wu J, Li Y (2020). "Group sequential design for historical control trials using error spending functions." *Journal of Biopharmaceutical Statistics*, **30**(2), 351-363.

### Examples

```
#Interim look for the trial when the number of events is 13(first look).
gg<-EffIM(c(13),dmax=57,alpha=0.05,beta=0.1,etam=3.0726,d1=65,opt="OBF",last.look=FALSE)
#Interim look for the trial when the number of events is 35(second look).
gg<-EffIM(c(13,35),dmax=57,alpha=0.05,beta=0.1,etam=3.0726,d1=65,opt="OBF",last.look=FALSE)
```

---

FutDesign

*HCT design with interim monitoring for futiity only*

---

### Description

The group sequential design for historical controlled survival outcome trials with futility boundaries only.

**Usage**

```
FutDesign(
  k,
  alpha,
  beta,
  delta,
  d1,
  option = "OBF",
  param = 4,
  trial = "Superiority",
  delta0
)
```

**Arguments**

|        |                                                                                                                                                                                 |
|--------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| k      | vector of time fraction for all planned looks: $k=c(1/3, 2/3, 1)$ if the three planned looks will be carried out at 1/3, 2/3 and all of the total events in the experiment arm. |
| alpha  | type I error.                                                                                                                                                                   |
| beta   | type II error.                                                                                                                                                                  |
| delta  | hazard ratio: hazard of experiment group over hazard of control group.                                                                                                          |
| d1     | total number of events in the historical control group.                                                                                                                         |
| option | type of spending function: "OBF", "Gamma", "Rho" or "Pocock". Default is "OBF".                                                                                                 |
| param  | Parameter for Gamma family or Rho family. Default value is 4.                                                                                                                   |
| trial  | Type of trial: "Superiority" or "Non-inferiority". Default is "Superiority".                                                                                                    |
| delta0 | Non-inferiority margin.                                                                                                                                                         |

**Value**

List of dataframes and vectors containing the details about the following: design of the trial which includes the number of looks and events; details about futility and efficacy boundaries which include transformed information time at each look, cumulative beta and alpha respectively, p-values and crossing probabilities; etam(drift parameter); d2max(maximum number of events in the experimental group); delta\_used(hazard ratio used in the design).

**Author(s)**

Tushar Patni, Yimei Li, Jianrong Wu, and Arzu Onar-Thomas.

**References**

- Wu J, Xiong X (2016). "Survival trial design and monitoring using historical controls." *Pharmaceutical Statistics*, **15**(5), 405-411.
- Wu J, Li Y (2020). "Group sequential design for historical control trials using error spending functions." *Journal of Biopharmaceutical Statistics*, **30**(2), 351-363.

## Examples

```
#Sequential superiority trial for three equally spaced looks for OBF spending function.
gg<-FutDesign(k=c(0.3,0.6,1),alpha=0.05,beta=0.1,delta=0.57,d1=65,option="OBF",trial="Superiority")
```

---

|       |                                                                                        |
|-------|----------------------------------------------------------------------------------------|
| FutIM | <i>Monitoring the trial at interim looks for a trial with futility monitoring only</i> |
|-------|----------------------------------------------------------------------------------------|

---

## Description

Calculates one-sided futility boundary values at the observed number of events.

## Usage

```
FutIM(
  d2,
  dmax,
  last.look = FALSE,
  d1,
  etam,
  alpha,
  beta,
  opt = "OBF",
  param = 4
)
```

## Arguments

|           |                                                                                             |
|-----------|---------------------------------------------------------------------------------------------|
| d2        | vector of number of events at which you want to monitor the trial.                          |
| dmax      | maximum number of events in the experimental group calculated from design function.         |
| last.look | logical which indicates whether the current look is the last look or not. Default is FALSE. |
| d1        | total number of events in the historical control group.                                     |
| etam      | value of the drift parameter obtained from design function.                                 |
| alpha     | type I error.                                                                               |
| beta      | type II error.                                                                              |
| opt       | type of spending function: "OBF", "Gamma", "Rho" or "Pocock". Default is "OBF".             |
| param     | Parameter for Gamma family or Rho family. Default value is 4.                               |

## Details

The number of events have to be entered sequentially. See example.

**Value**

A list containing futility boundary values along with the p-values and transformed information time for the current look. Post-hoc power is also calculated in case of early stopping of the trial.

**Author(s)**

Tushar Patni, Yimei Li, Jianrong Wu, and Arzu Onar-Thomas.

**References**

Wu J, Xiong X (2016). "Survival trial design and monitoring using historical controls." *Pharmaceutical Statistics*, **15**(5), 405-411.

Wu J, Li Y (2020). "Group sequential design for historical control trials using error spending functions." *Journal of Biopharmaceutical Statistics*, **30**(2), 351-363.

**Examples**

```
#Interim look for the trial when the number of events is 13(first look).
gg<-FutIM(c(13),dmax=57,alpha=0.05,beta=0.1,etam=3.0726,d1=65,opt="OBF",last.look=FALSE)
#Interim look for the trial when the number of events is 35(second look).
gg<-FutIM(c(13,35),dmax=57,alpha=0.05,beta=0.1,etam=3.0726,d1=65,opt="OBF",last.look=FALSE)
```

---

HCTSurvDesign

*HCT design with interim monitoring for both efficacy and futility*


---

**Description**

The group sequential design for historical controlled survival outcome trials with both efficacy and futility boundaries.

**Usage**

```
HCTSurvDesign(
  k,
  alpha,
  beta,
  delta,
  d1,
  option = "OBF",
  param = 4,
  trial = "Superiority",
  delta0
)
```

**Arguments**

|        |                                                                                                                                                                                 |
|--------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| k      | vector of time fraction for all planned looks: $k=c(1/3, 2/3, 1)$ if the three planned looks will be carried out at 1/3, 2/3 and all of the total events in the experiment arm. |
| alpha  | type I error.                                                                                                                                                                   |
| beta   | type II error.                                                                                                                                                                  |
| delta  | hazard ratio: hazard of experiment group over hazard of control group.                                                                                                          |
| d1     | total number of events in the historical control group.                                                                                                                         |
| option | type of spending function: "OBF", "Gamma", "Rho" or "Pocock". Default is "OBF".                                                                                                 |
| param  | Parameter for Gamma family or Rho family. Default value is 4.                                                                                                                   |
| trial  | Type of trial: "Superiority" or "Non-inferiority". Default is "Superiority".                                                                                                    |
| delta0 | Non-inferiority margin.                                                                                                                                                         |

**Value**

List of dataframes and vectors containing the details about the following: design of the trial which includes the number of looks and events; details about futility and efficacy boundaries which include transformed information time at each look, cumulative beta and alpha respectively, p-values and crossing probabilities; etam(drift parameter); d2max(maximum number of events in the experimental group); delta\_used(hazard ratio used in the design).

**Author(s)**

Tushar Patni, Yimei Li, Jianrong Wu, and Arzu Onar-Thomas.

**References**

- Wu J, Xiong X (2016). "Survival trial design and monitoring using historical controls." *Pharmaceutical Statistics*, **15**(5), 405-411.
- Wu J, Li Y (2020). "Group sequential design for historical control trials using error spending functions." *Journal of Biopharmaceutical Statistics*, **30**(2), 351-363.

**Examples**

```
#Sequential superiority trial for three equally spaced looks for OBF spending function.
gg<-HCTSurvDesign(k=c(0.3,0.6,1),alpha=0.05,beta=0.1,delta=0.57,d1=65,option="OBF")
```

---

|    |                                                                                                |
|----|------------------------------------------------------------------------------------------------|
| IM | <i>Monitoring the trial at interim looks for a trial with efficacy and futility boundaries</i> |
|----|------------------------------------------------------------------------------------------------|

---

### Description

Calculates one-sided boundary values at the observed number of events.

### Usage

```
IM(d2, dmax, last.look = FALSE, d1, etam, alpha, beta, opt = "OBF", param = 4)
```

### Arguments

|           |                                                                                             |
|-----------|---------------------------------------------------------------------------------------------|
| d2        | vector of number of events at which you want to monitor the trial.                          |
| dmax      | maximum number of events in the experimental group calculated from design function.         |
| last.look | logical which indicates whether the current look is the last look or not. Default is FALSE. |
| d1        | total number of events in the historical control group.                                     |
| etam      | value of the drift parameter obtained from design function.                                 |
| alpha     | type I error.                                                                               |
| beta      | type II error.                                                                              |
| opt       | type of spending function: "OBF", "Gamma", "Rho" or "Pocock". Default is "OBF".             |
| param     | Parameter for Gamma family or Rho family. Default value is 4.                               |

### Details

The number of events have to be entered sequentially. See example.

### Value

A list containing efficacy and futility boundary values along with the p-values and transformed information time for the current look. Post-hoc power is also calculated in case of early stopping of the trial.

### Author(s)

Tushar Patni, Yimei Li, Jianrong Wu, and Arzu Onar-Thomas.

### References

- Wu J, Xiong X (2016). "Survival trial design and monitoring using historical controls." *Pharmaceutical Statistics*, **15**(5), 405-411.
- Wu J, Li Y (2020). "Group sequential design for historical control trials using error spending functions." *Journal of Biopharmaceutical Statistics*, **30**(2), 351-363.

## Examples

```
#Interim look for the trial when the number of events is 13(first look).
gg<-IM(c(13),dmax=57,alpha=0.05,beta=0.1,etam=3.0726,d1=65,opt="OBF",last.look=FALSE)
#Interim look for the trial when the number of events is 35(second look).
gg<-IM(c(13,35),dmax=57,alpha=0.05,beta=0.1,etam=3.0726,d1=65,opt="OBF",last.look=FALSE)
```

---

sf

*Log rank test for non-inferiority trial*

---

## Description

Calculates the score function of the log rank test for non-inferiority trial

## Usage

```
sf(event, status, delta0, group, experiment, control)
```

## Arguments

|            |                                                                                               |
|------------|-----------------------------------------------------------------------------------------------|
| event      | event time vector from person level trial data.                                               |
| status     | numeric vector indicating the status of event from person level trial data.                   |
| delta0     | Non-inferiority margin.                                                                       |
| group      | group string vector indicating the assignment of patients into control or experimental group. |
| experiment | name of experimental group as character string.                                               |
| control    | name of control group as character string.                                                    |

## Value

Returns the value of score statistic.

## Author(s)

Tushar Patni, Yimei Li, Jianrong Wu, and Arzu Onar-Thomas.

## Examples

```
time<-c(20,65,12,50,58,65,45,44)
event<-c(1,0,0,0,1,1,1,1)
group<-c(rep("exp",4),rep("cont",4))
gg<-sf(event=time,status=event,delta0=1.3,group=group,experiment="exp",control="cont")
```

SM

*Sample size in terms of number of subjects in the experimental group***Description**

Calculates the total number of subjects for the experimental group using the total number of events(d2max:the output from design functions) and the estimated failure probability based on the person level historical control data and proportional hazard assumption.

**Usage**

```
SM(time, event, d2max, opt = "KM", event_ind, ta, tf, delta)
```

**Arguments**

|           |                                                                                                          |
|-----------|----------------------------------------------------------------------------------------------------------|
| time      | event time vector from person level historical control data.                                             |
| event     | numeric vector indicating the status of event from person level historical control data.                 |
| d2max     | maximum number of events in the experimental group calculated from the design function.                  |
| opt       | the method of fitting survival curve-"log_normal" or "KM" (log-normal or Kaplan Meier). Default is "KM". |
| event_ind | numeric value indicating the occurrence of event.                                                        |
| ta        | enrollment time.                                                                                         |
| tf        | follow-up time.                                                                                          |
| delta     | hazard ratio.                                                                                            |

**Value**

Returns the value of sample size.

**Author(s)**

Tushar Patni, Yimei Li, Jianrong Wu, and Arzu Onar-Thomas.

**References**

Wu J, Xiong X (2016). "Survival trial design and monitoring using historical controls." *Pharmaceutical Statistics*, **15**(5), 405-411.

Wu J, Li Y (2020). "Group sequential design for historical control trials using error spending functions." *Journal of Biopharmaceutical Statistics*, **30**(2), 351-363.

**Examples**

```
time<-c(20,65,12,50,58,65,45,44)
event<-c(1,0,0,0,1,1,1,1)
d2max=57
gg<-SM(time,event,d2max,opt="log_normal",ta=4,tf=3,delta=0.57,event_ind=1)
```

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