

# Package ‘survELtest’

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**Title** Comparing Multiple Survival Functions with Crossing Hazards in R

**Version** 1.0.1

**Description** Contains routines for computing the one-sided/two-sided integrated/maximally selected EL statistics for simultaneous testing, the one-sided/two-sided EL tests for pointwise testing, and an initial test that precedes one-sided testing to exclude the possibility of crossings or alternative orderings.

**Depends** R (>= 2.13.0)

**Imports** Iso, nloptr, methods, plyr, survival, stats

**License** GPL (>= 2)

**LazyData** true

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## R topics documented:

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| hepatitis | <i>Severe alcoholic hepatitis data</i> |
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**Description**

The data frame `hepatitis` is obtained by digitizing the published Kaplan-Meier curves in Nguyen-Khac et al (2011). The method of digitizing is described in Guyot et al. (2012). See [intELtest](#) for the application.

**Usage**

```
hepatitis
```

**Format**

The `hepatitis` is a data frame with 174 observations of 3 variables, and has the following columns:

- `time` the observed survival and censoring times
- `sensor` the censoring indicator
- `group` the grouping variable

**Source**

Nguyen-Khac et al., "Glucocorticoids plus N-Acetylcysteine in Severe Alcoholic Hepatitis," *The New England Journal of Medicine*, Vol. 365, No. 19, pp. 1781-1789 (2011). <http://www.nejm.org/doi/full/10.1056/NEJMoa1101214#t=article>

**References**

P. Guyot, A. E. Ades, M. J. N. M. Ouwens, and N. J. Welton, "Enhanced secondary analysis of survival data: reconstructing the data from published Kaplan-Meier survival curves," *BMC Medical Research Methodology*, 12(1):9. <http://bmcmedresmethodol.biomedcentral.com/articles/10.1186/1471-2288-12-9>

**See Also**

[intELtest](#)

intELtest

*The integrated EL test***Description**

intELtest gives a class of integrated EL statistics:

$$\sum_{i=1}^m w_i \cdot \{-2 \log R(t_i)\},$$

where  $R(t)$  is the EL ratio that compares the survival functions at each given time  $t$ ,  $w_i$  is the weight at each  $t_i$ , and  $0 < t_1 < \dots < t_m < \infty$  are the (ordered) observed uncensored times at which the Kaplan–Meier estimate is positive and less than 1 for each sample.

**Usage**

```
intELtest(data, group_order = sort(unique(data[, 3])), t1 = 0,
  t2 = Inf, sided = 2, nboot = 1000, wt = "p.event",
  alpha = 0.05, seed = 1011, nlimit = 200)
```

**Arguments**

|             |  |
|-------------|--|
| data        | a data frame/matrix with 3 columns: column 1 contains the observed survival and censoring times, column 2 the censoring indicator, and column 3 the grouping variable. This is a compulsory input.   |
| group_order | a $k$ -vector containing the values of the grouping variable (in column 3 of the data frame/matrix), with the $j$ -th element being the group hypothesized to have the $j$ -th highest survival rates, $j = 1, \dots, k$ . The default is the vector of sorted grouping variables. |
| t1          | the first endpoint of a prespecified time interval, if any, during which the comparison of the survival functions is restricted to. The default value is 0.  |
| t2          | the second endpoint of a prespecified time interval, if any, during which the comparison of the survival functions is restricted to. The default value is $\infty$ .   |
| sided       | 2 if two-sided test, and 1 if one-sided test. The default value is 2.  |
| nboot       | the number of bootstrap replications in calculating critical values for the tests. The default value is 1000.  |
| wt          | the name of the weight for the integrated EL statistics: "p.event", "dF", or "dt". The default is "p.event".   |
| alpha       | the pre-specified significance level of the tests. The default value is 0.05.  |
| seed        | the seed of random number generation in R for generating bootstrap samples needed to calculate critical values for the tests. The default value is 1011.   |
| nlimit      | a number used to calculate <code>nsplit = m/nlimit</code> , the number of parts we split the calculation of the nboot bootstrap replications into. This can make computation faster when the number of time points $m$ is too large. The default value for nlimit is 200.          |

## Details

There are three options for the weight  $w_i$ :

- (wt = "p.event")  
This default option is an objective weight,

$$w_i = \frac{d_i}{n},$$

which assigns weight proportional to the number of events  $d_i$  at each observed uncensored time  $t_i$ . Here  $n$  is the total sample size.

- (wt = "dF")  
Inspired by the integral-type statistics considered in Barmi and McKeague (2013), another weight function is

$$w_i = \hat{F}(t_i) - \hat{F}(t_{i-1}),$$

for  $i = 1, \dots, m$ , where  $\hat{F}(t) = 1 - \hat{S}(t)$ ,  $\hat{S}(t)$  is the pooled KM estimator, and  $t_0 \equiv 0$ . This reduces to the objective weight when there is no censoring. The resulting  $I_n$  can be seen as an empirical version of the expected negative two times log EL ratio under  $H_0$ .

- (wt = "dt")  
Inspired by the integral-type statistics considered in Pepe and Fleming (1989), another weight function is

$$w_i = t_{i+1} - t_i,$$

for  $i = 1, \dots, m$ , where  $t_{m+1} \equiv t_m$ . This gives more weight to the time intervals where there are fewer observed uncensored times, but can be affected by extreme observations.

## Value

intELtest returns a list with three elements:

- teststat the resulting integrated EL statistics
- critval the critical value based on bootstrap
- pvalue the p-value of the test

## References

- H. Chang, I.W. McKeague, "Nonparametric testing for multiple survival functions with non-inferiority margins," *Annals of Statistics*, accepted (2018).
- M. S. Pepe and T. R. Fleming, "Weighted Kaplan-Meier Statistics: A Class of Distance Tests for Censored Survival Data," *Biometrics*, Vol. 45, No. 2, pp. 497-507 (1989). [https://www.jstor.org/stable/2531492?seq=1#page\\_scan\\_tab\\_contents](https://www.jstor.org/stable/2531492?seq=1#page_scan_tab_contents)
- H. E. Barmi and I.W. McKeague, "Empirical likelihood-based tests for stochastic ordering," *Bernoulli*, Vol. 19, No. 1, pp. 295-307 (2013). <https://projecteuclid.org/euclid.bj/1358531751>

## See Also

[hepatitis](#), [ptwiseELtest](#), [supELtest](#)

**Examples**

```

library(survELtest)
intELtest(hepatitis)

## OUTPUT:
## $teststat
## [1] 1.406029
##
## $critval
## [1] 0.8993514
##
## $pvalue
## [1] 0.012

```

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|             |   |
|-------------|---|
| nocrossings | <i>The test that excludes the possibility of crossings or alternative orderings</i> |
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**Description**

The test `nocrossings` should be used before one-sided testing via `intELtest` or `supELtest` to exclude the possibility of crossings or alternative orderings.

**Usage**

```

nocrossings(data, group_order = sort(unique(data[, 3])), t1 = 0,
  t2 = Inf, sided = 2, nboot = 1000, alpha = 0.05, seed = 1011,
  nlimit = 200)

```

**Arguments**

|                          |  |
|--------------------------|--|
| <code>data</code>        | a data frame/matrix with 3 columns: column 1 contains the observed survival and censoring times, column 2 the censoring indicator, and column 3 the grouping variable. This is a compulsory input.   |
| <code>group_order</code> | a $k$ -vector containing the values of the grouping variable (in column 3 of the data frame/matrix), with the $j$ -th element being the group hypothesized to have the $j$ -th highest survival rates, $j = 1, \dots, k$ . The default is the vector of sorted grouping variables. |
| <code>t1</code>          | the first endpoint of a prespecified time interval, if any, during which the comparison of the survival functions is restricted to. The default value is 0.  |
| <code>t2</code>          | the second endpoint of a prespecified time interval, if any, during which the comparison of the survival functions is restricted to. The default value is $\infty$ .   |
| <code>sided</code>       | 2 if two-sided test, and 1 if one-sided test. The default value is 2.  |
| <code>nboot</code>       | the number of bootstrap replications in calculating critical values for the tests. The default value is 1000.  |

|        |  |
|--------|--|
| alpha  | the pre-specified significance level of the tests. The default value is 0.05.  |
| seed   | the seed of random number generation in R for generating bootstrap samples needed to calculate critical values for the tests. The default value is 1011.   |
| nlimit | a number used to calculate $nsplit = m/nlimit$ , the number of parts we split the calculation of the nboot bootstrap replications into. This can make computation faster when the number of time points $m$ is too large. The default value for nlimit is 200. |

**Value**

- decision 1 for rejection of the null hypothesis that there are crossings or alternative orderings, and 0 otherwise

**References**

- H. Chang, I.W. McKeague, "Empirical likelihood based tests for stochastic ordering under right censorship," *Electronic Journal of Statistics*, Vol. 10, No. 2, pp. 2511-2536 (2016).
- H. Chang, I.W. McKeague, "Nonparametric testing for multiple survival functions with non-inferiority margins," *Annals of Statistics*, accepted (2018).

**See Also**

[intELtest](#), [supELtest](#), [threearm](#)

**Examples**

```
library(survELtest)
nocrossings(threearm[1:30,],group_order=c(3,2,1),sided=1)
## OUTPUT:
## $decision
## [1] 1
```

---

ptwiseELtest

*The pointwise EL testing*

---

**Description**

ptwiseELtest gives pointwise EL testing to compare the survival curves at each time point.

**Usage**

```
ptwiseELtest(data, group_order = sort(unique(data[, 3])), t1 = 0,
  t2 = Inf, sided = 2, nboot = 1000, alpha = 0.05, seed = 1011,
  nlimit = 200)
```

**Arguments**

|                          |   |
|--------------------------|---|
| <code>data</code>        | a data frame/matrix with 3 columns: column 1 contains the observed survival and censoring times, column 2 the censoring indicator, and column 3 the grouping variable. This is a compulsory input.  |
| <code>group_order</code> | a $k$ -vector containing the values of the grouping variable (in column 3 of the data frame/matrix), with the $j$ -th element being the group hypothesized to have the $j$ -th highest survival rates, $j = 1, \dots, k$ . The default is the vector of sorted grouping variables.                  |
| <code>t1</code>          | the first endpoint of a prespecified time interval, if any, during which the comparison of the survival functions is restricted to. The default value is 0.   |
| <code>t2</code>          | the second endpoint of a prespecified time interval, if any, during which the comparison of the survival functions is restricted to. The default value is $\infty$ .  |
| <code>sided</code>       | 2 if two-sided test, and 1 if one-sided test. The default value is 2.   |
| <code>nboot</code>       | the number of bootstrap replications in calculating critical values for the tests. The default value is 1000.   |
| <code>alpha</code>       | the pre-specified significance level of the tests. The default value is 0.05.   |
| <code>seed</code>        | the seed of random number generation in R for generating bootstrap samples needed to calculate critical values for the tests. The default value is 1011.  |
| <code>nlimit</code>      | a number used to calculate <code>nsplit = m/nlimit</code> , the number of parts we split the calculation of the <code>nboot</code> bootstrap replications into. This can make computation faster when the number of time points $m$ is too large. The default value for <code>nlimit</code> is 200. |

**Value**

`ptwiseELtest` returns a list with four elements:

- `time_pts` a vector containing the observed uncensored time points at which the Kaplan—Meier estimate is positive and less than 1 for each sample.
- `decision` a vector containing the decisions of the pointwise EL tests at `time_pts`. The decision at each of `time_pts` is 1 for rejection of the null hypothesis that the survival functions are the same at the specific time point, and 0 otherwise.
- `stat_ptwise` a vector containing the pointwise EL statistics at `time_pts`.
- `critval_ptwise` a vector containing the critical values for pointwise EL testing at `time_pts`.

**See Also**

[intELtest](#), [supELtest](#), [threearm](#)

**Examples**

```
## Not run:
library(survELtest)
ptwiseELtest(threearm[1:30,],group_order=c(3,2,1),sided=1)
## It produces the estimates at 2 observed uncensored time points.

## End(Not run)
```

---

supELtest

*The maximally selected EL test*


---

### Description

supELtest provides the maximally selected EL statistics that is better adapted at detecting local differences:

$$\sup_{i=1,\dots,m} \{-2 \log R(t_i)\},$$

where  $R(t)$  is the EL ratio that compares the survival functions at each given time  $t$ , and  $0 < t_1 < \dots < t_m < \infty$  are the (ordered) observed uncensored times at which the Kaplan–Meier estimate is positive and less than 1 for each sample.

### Usage

```
supELtest(data, group_order = sort(unique(data[, 3])), t1 = 0,
  t2 = Inf, sided = 2, nboot = 1000, alpha = 0.05, seed = 1011,
  nlimit = 200)
```

### Arguments

|             |  |
|-------------|--|
| data        | a data frame/matrix with 3 columns: column 1 contains the observed survival and censoring times, column 2 the censoring indicator, and column 3 the grouping variable. This is a compulsory input.   |
| group_order | a $k$ -vector containing the values of the grouping variable (in column 3 of the data frame/matrix), with the $j$ -th element being the group hypothesized to have the $j$ -th highest survival rates, $j = 1, \dots, k$ . The default is the vector of sorted grouping variables. |
| t1          | the first endpoint of a prespecified time interval, if any, during which the comparison of the survival functions is restricted to. The default value is 0.  |
| t2          | the second endpoint of a prespecified time interval, if any, during which the comparison of the survival functions is restricted to. The default value is $\infty$ .   |
| sided       | 2 if two-sided test, and 1 if one-sided test. The default value is 2.  |
| nboot       | the number of bootstrap replications in calculating critical values for the tests. The default value is 1000.  |
| alpha       | the pre-specified significance level of the tests. The default value is 0.05.  |
| seed        | the seed of random number generation in R for generating bootstrap samples needed to calculate critical values for the tests. The default value is 1011.   |
| nlimit      | a number used to calculate $n_{split} = m/nlimit$ , the number of parts we split the calculation of the nboot bootstrap replications into. This can make computation faster when the number of time points $m$ is too large. The default value for nlimit is 200.                  |



**Value**

supELtest returns a list with three elements:

- teststat the resulting maximally selected EL statistics
- critval the critical value based on bootstrap
- pvalue the p-value of the test

**References**

- H. Chang, I.W. McKeague, "Empirical likelihood based tests for stochastic ordering under right censorship," *Electronic Journal of Statistics*, Vol. 10, No. 2, pp. 2511-2536 (2016).
- H. Chang, I.W. McKeague, "Nonparametric testing for multiple survival functions with non-inferiority margins," *Annals of Statistics*, accepted (2018).

**See Also**

[intELtest](#), [nocrossings](#), [ptwiseELtest](#), [threearm](#)

**Examples**

```
library(survELtest)
nocrossings(threearm[1:30,],group_order=c(3,2,1),sided=1)

## $decision
## [1] 1
## The decision 1 means the case of crossing or alternative orderings is excluded.
## Thus, we can proceed to the one-sided test.

supELtest(threearm[1:30,],group_order=c(3,2,1),sided=1)

## OUTPUT:
## $teststat
## [1] 4.246498
## $critval
## [1] 3.424961
## $pvalue
## [1] 0.026
```

---

threearm

*Time to first remission data*

---

**Description**

The data frame threearm is obtained by perturbing the time-to-remission data from patients in a three-arm randomized clinical trial for the treatment of major depression. See [nocrossings](#), [ptwiseELtest](#) and [supELtest](#) for the application.

**Usage**

`threearm`

**Format**

The `threearm` is a data frame with 664 observations of 3 variables, and has the following columns:

- `time` the observed times to first remission and censoring times
- `censor` the censoring indicator
- `group` the grouping variable

**See Also**

[nocrossings](#), [ptwiseELtest](#), [supELtest](#)

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