R code

```
> install.packages("BuyseTest", quiet = TRUE)
> library(BuyseTest)
```

R output

```
Loading required package: Rcpp
BuyseTest version 3.0.6
```

R code

```
> set.seed(10)
> data <- simBuyseTest(100, n.strata = 2)
> head(data)
```

R output

```
      id treatment  eventtime status toxicity      score strata
   <num>    <fctr>      <num>  <num>   <fctr>      <num> <fctr>
1:     1         C 0.17392093      1      yes -2.1250686      a
2:     2         C 0.16255166      0      yes  0.5211787      a
3:     3         C 0.08302502      1      yes -0.0464229      b
4:     4         C 0.22204972      0       no -1.1494717      b
5:     5         C 0.11669726      1       no  0.6293383      a
6:     6         C 0.11885540      1      yes -0.7264715      a
```

R code

```
> e.BT <- BuyseTest(treatment ~ tte(eventtime, status = status),
                    data = data)
```

R output

```
         Generalized Pairwise Comparisons

Settings
- 2 groups  : Control = C and Treatment = T
- 1 endpoint:
priority endpoint   type           operator             event
1        eventtime  time to event  higher is favorable  status (0 1)
- right-censored pairs: probabilistic score based on the survival curves

Point estimation and calculation of the iid decomposition

Estimation of the estimator's distribution
- method: moments of the U-statistic

Gather the results in a S4BuyseTest object
```

R code

```
> summary(e.BT)
```

R output

```
       Generalized pairwise comparisons with 1 endpoint

- statistic       : net treatment benefit  (delta: endpoint specific, Delta: global)
- null hypothesis : Delta == 0
- confidence level: 0.95
- inference       : H-projection of order 1 after atanh transformation
- treatment groups: T (treatment) vs. C (control)
- censored pairs  : probabilistic score based on the survival curves
- results
endpoint total(%) favorable(%) unfavorable(%) neutral(%) uninf(%)  Delta CI [2.5% ; 97.5%] p.v
eventtime     100        57.39          42.61          0        0 0.1479  [-0.0293;0.3161] 0.1
```

R code

```
> confint(e.BT, statistic = "winRatio")
```

R output

```
          estimate        se  lower.ci upper.ci null   p.value
eventtime 1.347081 0.2450411 0.9430953 1.924118    1 0.1014458
```

R code

```
> e.BThalf <- BuyseTest(treatment ~ tte(eventtime, status),
                        data = data, add.halfNeutral = TRUE, trace = FALSE)
> model.tables(e.BThalf, statistic = "favorable")
```

R output

```
   endpoint total favorable unfavorable neutral uninf     Delta  lower.ci  upper.ci   p.value
1 eventtime   100  57.39388    42.60612       0     0 0.5739388 0.4852354 0.6581263 0.1019135
```

R code

```
> coef(e.BThalf, statistic = "winRatio")
```

R output

```
[1] 1.347081
```

R code

```
> e.MBT <- BuyseTest(treatment ~ tte(eventtime, status, threshold = 1) + bin(toxicity, operato
                     data = data, trace = 0)
> model.tables(e.MBT)
```

R output

```
   endpoint threshold total favorable unfavorable neutral uninf   delta  Delta lower.ci upper.
1 eventtime     1e+00 100.0      10.2        2.55    87.2     0  0.0768 0.0768 -0.00928    0.1
3  toxicity     1e-12  87.2      18.8       24.72    43.7     0 -0.0590 0.0178 -0.13396    0.1
```

R code

```
plot(e.MBT)
```

R code

```
plot(e.MBT, type = "racetrack")
```

R code

```
> e.BTindiv <- BuyseTest(treatment ~ tte(eventtime, status = status),
                       data = data, keep.pairScore = TRUE)
> getPairScore(e.BTindiv)
```

R output

```
       index.C index.T favorable unfavorable neutral        uninf weight
    1:       1     101 0.9192694  0.08073064       0 0.000000e+00      1
    2:       2     101 0.5695583  0.43044167       0 1.110223e-16      1
    3:       3     101 1.0000000  0.00000000       0 0.000000e+00      1
    4:       4     101 0.4969601  0.50303994       0 0.000000e+00      1
    5:       5     101 1.0000000  0.00000000       0 0.000000e+00      1
   ---
 9996:      96     200 0.2858328  0.71416716       0 0.000000e+00      1
 9997:      97     200 0.8120919  0.18790807       0 0.000000e+00      1
 9998:      98     200 0.6171644  0.38283561       0 0.000000e+00      1
 9999:      99     200 0.6171644  0.38283561       0 0.000000e+00      1
10000:     100     200 0.4596044  0.54039560       0 0.000000e+00      1
```

R code

```
> eBT.perm <- BuyseTest(treatment ~ cont(score), data = data,
                      method.inference = "varexact permutation")
> model.tables(eBT.perm)
```

R output

```
  endpoint total favorable unfavorable neutral uninf  Delta   p.value
1    score   100     53.67       46.33       0     0 0.0734 0.3698664
```

R code

```
> wilcox.test(score ~ treatment, data = data, correct = FALSE)$p.value
```

R output

```
0.3698664
```

R code

```
> rbind(confint(e.BTindiv, transformation = TRUE),
        confint(e.BTindiv, transformation = FALSE))
```

R output

```
            estimate         se    lower.ci  upper.ci null    p.value
eventtime  0.1478776 0.08897931 -0.02931684 0.3160612    0 0.10150573
eventtime1 0.1478776 0.08897931 -0.02651861 0.3222739    0 0.09652625
```

R code

```
> NTB <- coef(e.BTindiv)
> sigma.NTB <- sqrt(crossprod(getIid(e.BTindiv)))
> sigmaTrans.NTB <- sigma.NTB/(1-NTB^2)
> c(estimate = NTB, se = sigmaTrans.NTB, p.value = 2*(1-pnorm(NTB/sigma.NTB)),
    pTrans.value = 2*(1-pnorm(atanh(NTB)/sigmaTrans.NTB)))
```

R output

```
  estimate           se      p.value pTrans.value
0.14787764   0.09096860   0.09652625   0.10150573
```

R code

```
BuyseTest.options(method.inference = "permutation", n.resampling = 1000,
                  statistic = "winRatio")
```

$$U - \Delta = \underbrace{\frac{1}{m}\sum_{i=1}^{m} h_E(i)}_{\text{Experimental group}} + \underbrace{\frac{1}{n}\sum_{j=1}^{n} h_C(j)}_{\text{Control group}} + \underbrace{\frac{1}{mn}\sum_{i=1}^{n}\sum_{j=1}^{m} h_{EC}(i,j)}_{\text{Second order term}}$$

$$\text{where for } i \in \{1,\dots,m\}, h_E(i) = \mathbb{E}[\mathbb{1}_{Y_i > X_j} - \mathbb{1}_{X_i > Y_j} \mid X_i] - \Delta$$

$$j \in \{1,\dots,n\}, h_C(j) = \mathbb{E}[\mathbb{1}_{Y_i > X_j} - \mathbb{1}_{X_i > Y_j} \mid Y_j] - \Delta$$

$$\widehat{\sigma}_U \underbrace{\approx}_{\text{First order}} \frac{1}{m^2}\sum_{i=1}^{m} h_E^2(i) + \frac{1}{n^2}\sum_{j=1}^{n} h_C^2(j)$$

$$p^{\mathcal{P}} = \frac{1}{1+P}\left\{1 + \sum_{p=1}^{P} \mathbb{1}_{\left|\Delta^{\mathcal{P}(p)}\right| \geq |\Delta|}\right\}$$