Example 1. Table 1.

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Example 1. (Table 1.) Single-time Analysis

A hypothetical example with two hypothesis tests of progression-free survival (PFS) for a subgroup (S: PD-L1^+) and overall(O) population $I = \{1, 2\}$. The analysis is performed with 250 PFS events in PD-L1^+ subset and 400 in overall population. Consider one-sided FWER $\alpha = 0.025$. Weighted alpha allocations to H_1 and H_2 are $\frac{1}{3}\alpha = 0.0083$ and $\frac{2}{3}\alpha = 0.0167$ respectively. By the graphical approach without considering the correlation between H_1 and H_2, the transitions $g_{12} = g_{21} = 1$ mean that when one hypothesis is rejected at the allocated level $\alpha_1(I) = \frac{1}{3}\alpha$ or $\alpha_2(I) = \frac{2}{3}\alpha$, then the remaining hypothesis will be tested at α level. When the correlation is considered, we follow the closed testing procedure (CTP): First, determine the rejection boundaries $(\alpha_1^*(I), \alpha_2^*(I))$ for $H_{12} = H_1 \cap H_2$ according to the proposed framework. If $p_1 \leq \alpha_1^*(I)$ or $p_2 \leq \alpha_2^*(I)$, then H_{12} is rejected. Then go to the next step: H_i is rejected if $p_i < \alpha$ for $i = 1, 2$.

Without loss of generality, consider the logrank test for overall population is stratified by the subgroup S and the correlation is 0.79 based on Theorem 1. With the proposed parametric testing framework, three efficiency allocation strategies are considered: (1) Equal efficiency for both hypotheses, i.e., $\epsilon_1(I) = \epsilon_2(I)$; (2) Maximize the power for H_2, i.e., $\epsilon_1(I) = 1$; (3) Maximize the power for H_1, i.e., $\epsilon_2(I) = 1$. The rejection boundaries for H_{12}, H_1 and H_2 are summarized in Table 1. It can be seen that the rejection boundaries are improved according to the efficiency allocation strategy compared to those with the correlation ignored. The improvement can be considerable when all efficiency is allocated to a single hypothesis test.

```
library(corrTests)
```

```
##########################
# Event Ratio = 250/400
##########################
#(a) w = (1/3, 2/3) Equal split of alpha
Ex1a = corrBounds(sf=list(sfuA=gsDesign::sfLDOF, sfuB=gsDesign::sfLDOF),
                  eAandB = 250, eAnotB = 0, eBnotA = 150,
                  r=list(AandB = 1/2, AnotB=0, BnotA=1/2),
                  rA=1/2, rB=1/2, gamma = NA, strat.ana="Y",
                  alpha=0.025, w=c(1/3, 2/3), epsA = NA, epsB=NA,
                  method="Balanced Allocation")
Ex1a
```

```
## $overall.alpha
##   FW.alpha      alphaA     alphaB side
## 1    0.025 0.008333333 0.01666667    1
##
## $bd
##   timingA incr.alphaA   cum.alphaA      bd.pA0  bd.zA0     epsA      bd.pA
## 1       1 0.008333333 0.008333333 0.008333333 2.39398 1.213742 0.01011451
```

```
##      bd.zA timingB incr.alphaB cum.alphaB     bd.pB0   bd.zB0     epsB
## 1 2.322073       1  0.01666667 0.01666667 0.01666667 2.128045 1.213742
##        bd.pB    bd.zB
## 1 0.02022903 2.049041
##
## $max.eps
##   max.epsA max.epsB
## 1  1.72982 1.287279
##
## $corr
##           [,1]      [,2]
## [1,] 1.0000000 0.7905694
## [2,] 0.7905694 1.0000000
##
## $cov
##      [,1]  [,2]
## [1,] 62.5  62.5
## [2,] 62.5 100.0
##
## $method
## [1] "Balanced Allocation"
##
## $strat
## [1] "Y"
```

```
#(b) w = (1/3, 2/3) espA=1
Ex1b = corrBounds(sf=list(sfuA=gsDesign::sfLDOF, sfuB=gsDesign::sfLDOF),
                  eAandB = 250, eAnotB = 0, eBnotA = 150,
                  r=list(AandB = 1/2, AnotB=0, BnotA=1/2),
                  rA=1/2, rB=1/2, gamma = NA, strat.ana="Y",
                  alpha=0.025, w=c(1/3, 2/3), epsA = 1, epsB=NA,
                  method="Customized Allocation")
Ex1b
```

```
## $overall.alpha
##   FW.alpha      alphaA     alphaB side
## 1    0.025 0.008333333 0.01666667    1
##
## $bd
##   timingA incr.alphaA  cum.alphaA      bd.pA0  bd.zA0 epsA       bd.pA   bd.zA
## 1       1 0.008333333 0.008333333 0.008333333 2.39398    1 0.008333333 2.39398
##   timingB incr.alphaB cum.alphaB     bd.pB0   bd.zB0     epsB      bd.pB
## 1       1  0.01666667 0.01666667 0.01666667 2.128045 1.287279 0.02145464
##      bd.zB
## 1 2.024592
##
## $max.eps
##   max.epsA max.epsB
## 1  1.72982 1.287279
##
## $corr
##           [,1]      [,2]
## [1,] 1.0000000 0.7905694
## [2,] 0.7905694 1.0000000
```

```
##
## $cov
##      [,1]  [,2]
## [1,] 62.5  62.5
## [2,] 62.5 100.0
##
## $method
## [1] "Customized Allocation"
##
## $strat
## [1] "Y"
```

```
#(c) w = (1/3, 2/3) espB=1
Ex1c = corrBounds(sf=list(sfuA=gsDesign::sfLDOF, sfuB=gsDesign::sfLDOF),
                  eAandB = 250, eAnotB = 0, eBnotA = 150,
                  r=list(AandB = 1/2, AnotB=0, BnotA=1/2),
                  rA=1/2, rB=1/2, gamma = NA, strat.ana="Y",
                  alpha=0.025, w=c(1/3, 2/3), epsA = NA, epsB=1,
                  method="Customized Allocation")
Ex1c
```

```
## $overall.alpha
##   FW.alpha      alphaA     alphaB side
## 1    0.025 0.008333333 0.01666667    1
##
## $bd
##   timingA incr.alphaA  cum.alphaA      bd.pA0  bd.zA0    epsA      bd.pA
## 1       1 0.008333333 0.008333333 0.008333333 2.39398 1.72982 0.01441517
##      bd.zA timingB incr.alphaB cum.alphaB     bd.pB0   bd.zB0 epsB      bd.pB
## 1 2.185799       1  0.01666667 0.01666667 0.01666667 2.128045    1 0.01666667
##      bd.zB
## 1 2.128045
##
## $max.eps
##   max.epsA max.epsB
## 1  1.72982 1.287279
##
## $corr
##           [,1]      [,2]
## [1,] 1.0000000 0.7905694
## [2,] 0.7905694 1.0000000
##
## $cov
##      [,1]  [,2]
## [1,] 62.5  62.5
## [2,] 62.5 100.0
##
## $method
## [1] "Customized Allocation"
##
## $strat
## [1] "Y"
```