

How to create summaries with rpact

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Last change: 01 Dezember, 2020

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Summary

This R Markdown document provides many different examples that illustrate the usage of the *R generic function* `summary` with `rpact`. This is a technical vignette and is to be considered mainly as a comprehensive overview of the possible summaries in `rpact`.

1 Global options

First, load the `rpact` package

```
library(rpact)
packageVersion("rpact")
```

```
## [1] '3.0.3'
```

The following options can be set globally:

`rpact.summary.output.size`: one of `c("small", "medium", "large")`; defines how many details will be included into the summary; default is "large", i.e., all available details are displayed.

`rpact.summary.justify`: one of `c("right", "left", "centre")`; shall the values be right-justified (the default), left-justified or centered.

`rpact.summary.intervalFormat`: defines how intervals will be displayed in the summary, default is `"[%s; %s]"`.

`rpact.summary.digits`: defines how many digits are to be used for numeric values (default is 3).

`rpact.summary.digits.probs`: defines how many digits are to be used for numeric values (default is one more than value of `rpact.summary.digits`, i.e., 4).

`rpact.summary.trim zeroes`: if TRUE (default) zeroes will always displayed as "0", e.g. "0.000" will become "0".

Examples

```
options("rpact.summary.output.size" = "small") # small, medium, large
options("rpact.summary.output.size" = "medium") # small, medium, large
options("rpact.summary.output.size" = "large") # small, medium, large

options("rpact.summary.intervalFormat" = "[%s; %s]")
options("rpact.summary.intervalFormat" = "%s - %s")
options("rpact.summary.enforceIntervalView" = TRUE)
options("rpact.summary.justify" = "left")
options("rpact.summary.justify" = "centre")
options("rpact.summary.justify" = "right")
```

2 Design summaries

```
summary(getDesignGroupSequential(beta = 0.05, typeOfDesign = "asKD", gammaA = 1,
  typeBetaSpending = "bsOF"))
```

```
## Sequential analysis with a maximum of 3 looks (group sequential design)
##
## Kim & DeMets alpha spending design, one-sided local significance level 2.5%,
## power 95%, undefined endpoint.
##
## Stage                1         2         3
## Information rate      33.3%    66.7%   100%
## Efficacy boundary (z-value scale)  2.394  2.294  2.200
## Futility boundary (z-value scale) -0.993  0.982
## Cumulative alpha spent      0.0083 0.0167 0.0250
## Overall power           0.4259 0.8092 0.9500
## One-sided local significance level 0.0083 0.0109 0.0139
```

```
summary(getDesignGroupSequential(kMax = 1))
```

```
## Fixed sample analysis
##
## O'Brien & Fleming design, one-sided local significance level 2.5%, power 80%,
## undefined endpoint.
##
## Stage                Fixed
## Efficacy boundary (z-value scale)  1.960
## One-sided local significance level 0.0250
```

```
summary(getDesignGroupSequential(kMax = 4, sided = 2))
```

```
## Sequential analysis with a maximum of 4 looks (group sequential design)
##
## O'Brien & Fleming design, two-sided local significance level 2.5%, power 80%,
## undefined endpoint.
##
## Stage                1          2          3          4
## Information rate      25%       50%       75%       100%
## Efficacy boundary (z-value scale)  4.579   3.238   2.644   2.289
## Cumulative alpha spent <0.0001  0.0012  0.0086  0.0250
## Overall power         0.0012  0.1494  0.5227  0.8000
## Two-sided local significance level <0.0001  0.0012  0.0082  0.0221
```

```
summary(getDesignGroupSequential(kMax = 4, sided = 2), digits = 0)
```

```
## Sequential analysis with a maximum of 4 looks (group sequential design)
##
## O'Brien & Fleming design, two-sided local significance level 2.5%, power 80%,
## undefined endpoint.
##
## Stage                1          2          3          4
## Information rate      25%       50%       75%       100%
## Efficacy boundary (z-value scale)  4.579   3.238   2.644   2.289
## Cumulative alpha spent 0.000004679 0.001207215 0.008644578 0.024999990
## Overall power         0.001247  0.149399  0.522709  0.800000
## Two-sided local significance level 0.000004679 0.001205239 0.008204894 0.022058711
```

```
summary(getDesignGroupSequential(kMax = 1, sided = 2))
```

```
## Fixed sample analysis
##
## O'Brien & Fleming design, two-sided local significance level 2.5%, power 80%,
## undefined endpoint.
##
## Stage                Fixed
## Efficacy boundary (z-value scale)  2.241
## Two-sided local significance level 0.0250
```

```
summary(getDesignGroupSequential(futilityBounds = c(-6, 0)))
```

```
## Sequential analysis with a maximum of 3 looks (group sequential design)
##
## O'Brien & Fleming design, one-sided local significance level 2.5%, power 80%,
## undefined endpoint.
##
## Stage                1          2          3
## Information rate      33.3%   66.7%   100%
## Efficacy boundary (z-value scale)  3.471   2.454   2.004
## Futility boundary (z-value scale) -6.000  0.000
## Cumulative alpha spent 0.0003  0.0072  0.0250
## Overall power         0.0329  0.4426  0.8000
## One-sided local significance level 0.0003  0.0071  0.0225
```

```
summary(getDesignGroupSequential(futilityBounds = c(-6, 0)), digits = 5)
```

```
## Sequential analysis with a maximum of 3 looks (group sequential design)
```

```
##
## O'Brien & Fleming design, one-sided local significance level 2.5%, power 80%,
## undefined endpoint.
##
## Stage          1          2          3
## Information rate      33.3%    66.7%    100%
## Efficacy boundary (z-value scale)  3.47109  2.45443  2.00404
## Futility boundary (z-value scale) -6.00000  0.00000
## Cumulative alpha spent      0.000259  0.007160  0.025000
## Overall power          0.032939  0.442575  0.800000
## One-sided local significance level 0.000259  0.007055  0.022533
```

```
summary(getDesignInverseNormal(kMax = 1))
```

```
## Fixed sample analysis
##
## O'Brien & Fleming design, one-sided local significance level 2.5%, power 80%,
## undefined endpoint.
##
## Stage          Fixed
## Efficacy boundary (z-value scale)  1.960
## One-sided local significance level 0.0250
```

```
summary(getDesignInverseNormal(futilityBounds = c(0, 1)))
```

```
## Sequential analysis with a maximum of 3 looks
## (inverse normal combination test design)
##
## O'Brien & Fleming design, one-sided local significance level 2.5%, power 80%,
## undefined endpoint.
##
## Stage          1          2          3
## Information rate      33.3%    66.7%    100%
## Efficacy boundary (z-value scale)  3.471  2.454  2.004
## Futility boundary (z-value scale)    0  1.000
## Cumulative alpha spent      0.0003  0.0072  0.0250
## Overall power          0.0377  0.4763  0.8000
## One-sided local significance level 0.0003  0.0071  0.0225
```

```
summary(getDesignInverseNormal(kMax = 1))
```

```
## Fixed sample analysis
##
## O'Brien & Fleming design, one-sided local significance level 2.5%, power 80%,
## undefined endpoint.
##
## Stage          Fixed
## Efficacy boundary (z-value scale)  1.960
## One-sided local significance level 0.0250
```

```
summary(getDesignInverseNormal(kMax = 4, sided = 2))
```

```
## Sequential analysis with a maximum of 4 looks
## (inverse normal combination test design)
##
## O'Brien & Fleming design, two-sided local significance level 2.5%, power 80%,
## undefined endpoint.
```

```

##
## Stage          1          2          3          4
## Information rate      25%      50%      75%      100%
## Efficacy boundary (z-value scale)  4.579  3.238  2.644  2.289
## Cumulative alpha spent      <0.0001  0.0012  0.0086  0.0250
## Overall power          0.0012  0.1494  0.5227  0.8000
## Two-sided local significance level <0.0001  0.0012  0.0082  0.0221
summary(getDesignInverseNormal(kMax = 4, sided = 2), digits = 0)

## Sequential analysis with a maximum of 4 looks
## (inverse normal combination test design)
##
## O'Brien & Fleming design, two-sided local significance level 2.5%, power 80%,
## undefined endpoint.
##
## Stage          1          2          3          4
## Information rate      25%      50%      75%      100%
## Efficacy boundary (z-value scale)  4.579  3.238  2.644  2.289
## Cumulative alpha spent  0.000004679  0.001207215  0.008644578  0.024999990
## Overall power          0.001247  0.149399  0.522709  0.800000
## Two-sided local significance level 0.000004679  0.001205239  0.008204894  0.022058711
summary(getDesignInverseNormal(kMax = 1, sided = 2))

## Fixed sample analysis
##
## O'Brien & Fleming design, two-sided local significance level 2.5%, power 80%,
## undefined endpoint.
##
## Stage          Fixed
## Efficacy boundary (z-value scale)  2.241
## Two-sided local significance level 0.0250
summary(getDesignFisher())

## Sequential analysis with a maximum of 3 looks (Fisher's combination test design)
##
## Fisher's combination test design, one-sided local significance level 2.5%,
## undefined endpoint.
##
## Stage          1          2          3
## Information rate      33.3%      66.7%      100%
## Efficacy boundary (p product scale) 0.0123085  0.0016636  0.0002911
## Cumulative alpha spent      0.0123  0.0196  0.0250
## One-sided local significance level  0.0123  0.0123  0.0123
summary(getDesignFisher(alpha0Vec = c(0.1, 0.2)))

## Sequential analysis with a maximum of 3 looks (Fisher's combination test design)
##
## Fisher's combination test design, one-sided local significance level 2.5%,
## undefined endpoint.
##
## Stage          1          2          3
## Information rate      33.3%      66.7%      100%
## Efficacy boundary (p product scale)  0.0193942  0.0028231  0.0005226

```

```
## Futility boundary (separate p-value scale)    0.100    0.200
## Cumulative alpha spent                       0.0194    0.0240    0.0250
## One-sided local significance level           0.0194    0.0194    0.0194
```

```
summary(getDesignFisher(kMax = 1))
```

```
## Fixed sample analysis
##
## Fisher's combination test design, one-sided local significance level 2.5%,
## undefined endpoint.
##
## Stage                                Fixed
## Efficacy boundary (p product scale) 0.025
## One-sided local significance level 0.0250
```

```
summary(getDesignFisher(kMax = 4, sided = 2), digits = 5)
```

```
## Sequential analysis with a maximum of 4 looks (Fisher's combination test design)
##
## Fisher's combination test design, two-sided local significance level 1.25%,
## undefined endpoint.
##
## Stage                1            2            3            4
## Information rate      25%          50%          75%          100%
## Efficacy boundary (p product scale) 0.00501771 0.00059549 0.00009426 0.00001716
## Cumulative alpha spent      0.005018    0.008171    0.010556    0.012500
## Two-sided local significance level 0.010035    0.010035    0.010035    0.010035
```

```
summary(getDesignFisher(kMax = 4, sided = 2), digits = 0)
```

```
## Sequential analysis with a maximum of 4 looks (Fisher's combination test design)
##
## Fisher's combination test design, two-sided local significance level 1.25%,
## undefined endpoint.
##
## Stage                1            2            3            4
## Information rate      25%          50%          75%          100%
## Efficacy boundary (p product scale) 0.00501771 0.00059549 0.00009426 0.00001716
## Cumulative alpha spent      0.005018    0.008171    0.010556    0.012500
## Two-sided local significance level 0.01004    0.01004    0.01004    0.01004
```

```
summary(getDesignFisher(kMax = 1, sided = 2))
```

```
## Fixed sample analysis
##
## Fisher's combination test design, two-sided local significance level 1.25%,
## undefined endpoint.
##
## Stage                                Fixed
## Efficacy boundary (p product scale) 0.0125
## Two-sided local significance level 0.0250
```

3 Design plan summaries

3.1 Design plan summaries - means

```
summary(getSampleSizeMeans(sided = 2, alternative = -0.5))

## Sample size calculation for a continuous endpoint
##
## Fixed sample analysis.
## The sample size was calculated for a two-sample t-test (two-sided),
## H0:  $\mu(1) - \mu(2) = 0$ , H1: effect = -0.5, standard deviation = 1, power 80%.
##
## Stage                               Fixed
## Efficacy boundary (z-value scale)    2.241
## Number of subjects                   154.6
## Two-sided local significance level    0.0250
## Efficacy boundary (t)                -0.364 - 0.364
##
## Legend:
## (t): treatment effect scale

summary(getSampleSizeMeans(sided = 2), alternative = -0.5) # warning expected

## Warning: Argument unknown in summary(...): 'alternative' = -0.5 will be ignored

## Sample size calculation for a continuous endpoint
##
## Fixed sample analysis.
## The sample size was calculated for a two-sample t-test (two-sided),
## H0:  $\mu(1) - \mu(2) = 0$ , H1: effect as specified, standard deviation = 1, power 80%.
##
## Stage                               Fixed
## Efficacy boundary (z-value scale)    2.241
## Number of subjects, alt. = 0.2      953.0
## Number of subjects, alt. = 0.4      240.2
## Number of subjects, alt. = 0.6      108.2
## Number of subjects, alt. = 0.8       62.0
## Number of subjects, alt. = 1        40.6
## Two-sided local significance level    0.0250
## Efficacy boundary (t), alt. = 0.2   -0.145 - 0.145
## Efficacy boundary (t), alt. = 0.4   -0.291 - 0.291
## Efficacy boundary (t), alt. = 0.6   -0.437 - 0.437
## Efficacy boundary (t), alt. = 0.8   -0.584 - 0.584
## Efficacy boundary (t), alt. = 1     -0.732 - 0.732
##
## Legend:
## alt.: alternative
## (t): treatment effect scale

summary(getPowerMeans(sided = 1, alternative = c(-0.5,-0.3),
  numberOfSubjects = 100, directionUpper = FALSE))

## Power calculation for a continuous endpoint
##
## Fixed sample analysis.
## The results were calculated for a two-sample t-test (one-sided),
```

```

## H0: mu(1) - mu(2) = 0, power directed towards smaller values,
## H1: effect as specified, standard deviation = 1.
##
## Stage                Fixed
## Efficacy boundary (z-value scale)  1.960
## Power, alt. = -0.5                0.6969
## Power, alt. = -0.3                0.3175
## Number of subjects                100.0
## One-sided local significance level 0.0250
## Efficacy boundary (t)             -0.397
##
## Legend:
##   alt.: alternative
##   (t): treatment effect scale
summary(getSampleSizeMeans(thetaH0 = 0, alternative = 0.5, sided = 1, stDev = 2.5))

## Sample size calculation for a continuous endpoint
##
## Fixed sample analysis.
## The sample size was calculated for a two-sample t-test (one-sided),
## H0: mu(1) - mu(2) = 0, H1: effect = 0.5, standard deviation = 2.5, power 80%.
##
## Stage                Fixed
## Efficacy boundary (z-value scale)  1.960
## Number of subjects                786.8
## One-sided local significance level 0.0250
## Efficacy boundary (t)             0.350
##
## Legend:
##   (t): treatment effect scale
summary(getPowerMeans(thetaH0 = 0, alternative = 0.5, sided = 1, stDev = 2.5,
  numberOfSubjects = 100, directionUpper = FALSE))

## Power calculation for a continuous endpoint
##
## Fixed sample analysis.
## The results were calculated for a two-sample t-test (one-sided),
## H0: mu(1) - mu(2) = 0, power directed towards smaller values, H1: effect = 0.5,
## standard deviation = 2.5.
##
## Stage                Fixed
## Efficacy boundary (z-value scale)  1.960
## Power                0.0016
## Number of subjects                100.0
## One-sided local significance level 0.0250
## Efficacy boundary (t)             -0.992
##
## Legend:
##   (t): treatment effect scale
summary(getSampleSizeMeans(thetaH0 = 0, alternative = 0.5, sided = 1, stDev = 1, groups = 1))

## Sample size calculation for a continuous endpoint
##

```



```
## Fixed sample analysis.
## The sample size was calculated for a one-sample t-test (one-sided), H0: mu = 0,
## H1: effect = 0.5, standard deviation = 1, power 80%.
##
## Stage                Fixed
## Efficacy boundary (z-value scale)  1.960
## Number of subjects                33.4
## One-sided local significance level 0.0250
## Efficacy boundary (t)              0.352
##
## Legend:
##   (t): treatment effect scale
```

```
summary(getSampleSizeMeans(thetaH0 = 0, sided = 2, stDev = 1, groups = 1))
```

```
## Sample size calculation for a continuous endpoint
##
## Fixed sample analysis.
## The sample size was calculated for a one-sample t-test (two-sided), H0: mu = 0,
## H1: effect as specified, standard deviation = 1, power 80%.
##
## Stage                Fixed
## Efficacy boundary (z-value scale)  2.241
## Number of subjects, alt. = 0.2    240.1
## Number of subjects, alt. = 0.4     61.9
## Number of subjects, alt. = 0.6     29.0
## Number of subjects, alt. = 0.8     17.5
## Number of subjects, alt. = 1       12.2
## Two-sided local significance level  0.0250
## Efficacy boundary (t), alt. = 0.2  -0.146 - 0.146
## Efficacy boundary (t), alt. = 0.4  -0.292 - 0.292
## Efficacy boundary (t), alt. = 0.6  -0.440 - 0.440
## Efficacy boundary (t), alt. = 0.8  -0.590 - 0.590
## Efficacy boundary (t), alt. = 1    -0.742 - 0.742
##
## Legend:
##   alt.: alternative
##   (t): treatment effect scale
```

```
summary(getSampleSizeMeans(thetaH0 = 0, alternative = 1.2, sided = 2, stDev = 5))
```

```
## Sample size calculation for a continuous endpoint
##
## Fixed sample analysis.
## The sample size was calculated for a two-sample t-test (two-sided),
## H0: mu(1) - mu(2) = 0, H1: effect = 1.2, standard deviation = 5, power 80%.
##
## Stage                Fixed
## Efficacy boundary (z-value scale)  2.241
## Number of subjects                662.6
## Two-sided local significance level  0.0250
## Efficacy boundary (t)              -0.873 - 0.873
##
## Legend:
##   (t): treatment effect scale
```

```
summary(getSampleSizeMeans(thetaH0 = 0, alternative = 1.2, sided = 2, stDev = 5,
  allocationRatioPlanned = 0))
```

```
## Sample size calculation for a continuous endpoint
##
## Fixed sample analysis.
## The sample size was calculated for a two-sample t-test (two-sided),
## H0: mu(1) - mu(2) = 0, H1: effect = 1.2, standard deviation = 5, power 80%.
##
## Stage                Fixed
## Efficacy boundary (z-value scale)    2.241
## Number of subjects                662.6
## Two-sided local significance level    0.0250
## Efficacy boundary (t)              -0.873 - 0.873
##
## Legend:
##   (t): treatment effect scale
```

```
summary(getSampleSizeMeans(thetaH0 = 0, alternative = 1.2, sided = 2, stDev = 5, groups = 1))
```

```
## Sample size calculation for a continuous endpoint
##
## Fixed sample analysis.
## The sample size was calculated for a one-sample t-test (two-sided), H0: mu = 0,
## H1: effect = 1.2, standard deviation = 5, power 80%.
##
## Stage                Fixed
## Efficacy boundary (z-value scale)    2.241
## Number of subjects                167.5
## Two-sided local significance level    0.0250
## Efficacy boundary (t)              -0.874 - 0.874
##
## Legend:
##   (t): treatment effect scale
```

```
summary(getSampleSizeMeans(getDesignGroupSequential(futilityBounds = c(1, 2))))
```

```
## Sample size calculation for a continuous endpoint
##
## Sequential analysis with a maximum of 3 looks (group sequential design).
## The sample size was calculated for a two-sample t-test (one-sided),
## H0: mu(1) - mu(2) = 0, H1: effect as specified, standard deviation = 1, power 80%.
##
## Stage                1      2      3
## Information rate          33.3% 66.7% 100%
## Efficacy boundary (z-value scale)    3.471 2.454 2.004
## Futility boundary (z-value scale)    1.000 2.000
## Overall power            0.0967 0.7030 0.8000
## Number of subjects, alt. = 0.2      472.2 944.4 1416.5
## Number of subjects, alt. = 0.4      118.9 237.8 356.8
## Number of subjects, alt. = 0.6       53.5 107.0 160.5
## Number of subjects, alt. = 0.8       30.6  61.3  91.9
## Number of subjects, alt. = 1        20.1  40.1  60.2
## Exit probability for futility        0.1209 0.0758
## Cumulative alpha spent              0.0003 0.0072 0.0250
```

```

## One-sided local significance level          0.0003 0.0071 0.0225
## Efficacy boundary (t), alt. = 0.2          0.322  0.160  0.107
## Efficacy boundary (t), alt. = 0.4          0.655  0.321  0.213
## Efficacy boundary (t), alt. = 0.6          1.013  0.483  0.319
## Efficacy boundary (t), alt. = 0.8          1.413  0.646  0.424
## Efficacy boundary (t), alt. = 1            1.882  0.812  0.528
## Futility boundary (t), alt. = 0.2          0.092  0.130
## Futility boundary (t), alt. = 0.4          0.184  0.261
## Futility boundary (t), alt. = 0.6          0.276  0.391
## Futility boundary (t), alt. = 0.8          0.368  0.522
## Futility boundary (t), alt. = 1            0.459  0.653
## Overall exit probability (under H0)         0.8416 0.1462
## Overall exit probability (under H1), alt. = 0.2 0.2176 0.6822
## Overall exit probability (under H1), alt. = 0.4 0.2176 0.6822
## Overall exit probability (under H1), alt. = 0.6 0.2176 0.6822
## Overall exit probability (under H1), alt. = 0.8 0.2176 0.6822
## Overall exit probability (under H1), alt. = 1 0.2176 0.6822
## Exit probability for efficacy (under H0)    0.0003 0.0062
## Exit probability for efficacy (under H1)    0.0967 0.6064
## Exit probability for futility (under H0)    0.8413 0.1400
## Exit probability for futility (under H1)    0.1209 0.0758
##
## Legend:
##   alt.: alternative
##   (t): treatment effect scale
summary(getSampleSizeMeans(getDesignGroupSequential(futilityBounds = c(1, 2))), digits = 0)

## Sample size calculation for a continuous endpoint
##
## Sequential analysis with a maximum of 3 looks (group sequential design).
## The sample size was calculated for a two-sample t-test (one-sided),
## H0:  $\mu(1) - \mu(2) = 0$ , H1: effect as specified, standard deviation = 1, power 80%.
##
## Stage                1          2          3
## Information rate      33.3%     66.7%     100%
## Efficacy boundary (z-value scale)  3.471     2.454     2.004
## Futility boundary (z-value scale)  1.000     2.000
## Overall power         0.09667   0.70304   0.80000
## Number of subjects, alt. = 0.2     472.2     944.4     1416.5
## Number of subjects, alt. = 0.4     118.9     237.8     356.8
## Number of subjects, alt. = 0.6      53.5     107.0     160.5
## Number of subjects, alt. = 0.8      30.6      61.3      91.9
## Number of subjects, alt. = 1        20.1      40.1      60.2
## Exit probability for futility        0.12094   0.07581
## Cumulative alpha spent              0.0002592 0.0071601 0.0250000
## One-sided local significance level    0.0002592 0.0070554 0.0225331
## Efficacy boundary (t), alt. = 0.2    0.322     0.160     0.107
## Efficacy boundary (t), alt. = 0.4    0.655     0.321     0.213
## Efficacy boundary (t), alt. = 0.6    1.013     0.483     0.319
## Efficacy boundary (t), alt. = 0.8    1.413     0.646     0.424
## Efficacy boundary (t), alt. = 1      1.882     0.812     0.528
## Futility boundary (t), alt. = 0.2     0.0921    0.1303
## Futility boundary (t), alt. = 0.4     0.184     0.261
## Futility boundary (t), alt. = 0.6     0.276     0.391

```

```
## Futility boundary (t), alt. = 0.8           0.368    0.522
## Futility boundary (t), alt. = 1           0.459    0.653
## Overall exit probability (under H0)        0.8416   0.1462
## Overall exit probability (under H1), alt. = 0.2 0.2176   0.6822
## Overall exit probability (under H1), alt. = 0.4 0.2176   0.6822
## Overall exit probability (under H1), alt. = 0.6 0.2176   0.6822
## Overall exit probability (under H1), alt. = 0.8 0.2176   0.6822
## Overall exit probability (under H1), alt. = 1 0.2176   0.6822
## Exit probability for efficacy (under H0)    0.0002592 0.0062354
## Exit probability for efficacy (under H1)    0.09667   0.60637
## Exit probability for futility (under H0)    0.8413    0.1400
## Exit probability for futility (under H1)    0.12094   0.07581
```

```
##
```

```
## Legend:
```

```
## alt.: alternative
```

```
## (t): treatment effect scale
```

```
summary(getPowerMeans(getDesignGroupSequential(futilityBounds = c(1, 2)),
  maxNumberOfSubjects = 100, alternative = 1))
```

```
## Power calculation for a continuous endpoint
```

```
##
```

```
## Sequential analysis with a maximum of 3 looks (group sequential design).
```

```
## The results were calculated for a two-sample t-test (one-sided),
```

```
## H0:  $\mu(1) - \mu(2) = 0$ , power directed towards larger values, H1: effect = 1,
```

```
## standard deviation = 1.
```

```
##
```

```
## Stage           1       2       3
## Information rate 33.3% 66.7% 100%
## Efficacy boundary (z-value scale) 3.471 2.454 2.004
## Futility boundary (z-value scale) 1.000 2.000
## Overall power    0.2700 0.9281 0.9563
## Number of subjects 33.3 66.7 100.0
## Exit probability for futility 0.0316 0.0120
## Cumulative alpha spent 0.0003 0.0072 0.0250
## One-sided local significance level 0.0003 0.0071 0.0225
## Efficacy boundary (t) 1.340 0.618 0.406
## Futility boundary (t) 0.352 0.500
## Overall exit probability (under H0) 0.8416 0.1462
## Overall exit probability (under H1) 0.3015 0.6702
## Exit probability for efficacy (under H0) 0.0003 0.0062
## Exit probability for efficacy (under H1) 0.2700 0.6582
## Exit probability for futility (under H0) 0.8413 0.1400
## Exit probability for futility (under H1) 0.0316 0.0120
```

```
##
```

```
## Legend:
```

```
## (t): treatment effect scale
```

```
summary(getSampleSizeMeans(getDesignGroupSequential(kMax = 4, sided = 2)))
```

```
## Sample size calculation for a continuous endpoint
```

```
##
```

```
## Sequential analysis with a maximum of 4 looks (group sequential design).
```

```
## The sample size was calculated for a two-sample t-test (two-sided),
```

```
## H0:  $\mu(1) - \mu(2) = 0$ , H1: effect as specified, standard deviation = 1, power 80%.
```

```

##
## Stage                1                2                3                4
## Information rate      25%              50%              75%              100%
## Efficacy boundary (z-value scale)  4.579          3.238          2.644          2.289
## Overall power        0.0012          0.1494          0.5227          0.8000
## Number of subjects, alt. = 0.2    242.3          484.6          726.9          969.2
## Number of subjects, alt. = 0.4     61.1          122.1          183.2          244.2
## Number of subjects, alt. = 0.6     27.5          55.0           82.5          110.0
## Number of subjects, alt. = 0.8     15.8          31.5           47.3           63.0
## Number of subjects, alt. = 1       10.3          20.7           31.0           41.3
## Cumulative alpha spent <0.0001          0.0012          0.0086          0.0250
## Two-sided local significance level <0.0001          0.0012          0.0082          0.0221
## Efficacy boundary (t), alt. = 0.2  -0.602 - 0.602 -0.296 - 0.296 -0.197 - 0.197 -0.147 - 0.147
## Efficacy boundary (t), alt. = 0.4  -1.290 - 1.290 -0.600 - 0.600 -0.395 - 0.395 -0.295 - 0.295
## Efficacy boundary (t), alt. = 0.6  -2.204 - 2.204 -0.923 - 0.923 -0.597 - 0.597 -0.443 - 0.443
## Efficacy boundary (t), alt. = 0.8  -3.652 - 3.652 -1.276 - 1.276 -0.804 - 0.804 -0.592 - 0.592
## Efficacy boundary (t), alt. = 1    -6.468 - 6.468 -1.678 - 1.678 -1.019 - 1.019 -0.742 - 0.742
## Exit probability for efficacy (under H0) <0.0001          0.0012          0.0074
## Exit probability for efficacy (under H1) 0.0012          0.1482          0.3733
##
## Legend:
##   alt.: alternative
##   (t): treatment effect scale

```

```

summary(getPowerMeans(getDesignGroupSequential(kMax = 4, sided = 2),
  maxNumberOfSubjects = 100))

```

```

## Power calculation for a continuous endpoint
##
## Sequential analysis with a maximum of 4 looks (group sequential design).
## The results were calculated for a two-sample t-test (two-sided),
## H0: mu(1) - mu(2) = 0, H1: effect as specified, standard deviation = 1.
##
## Stage                1                2                3
## Information rate      25%              50%              75%
## Efficacy boundary (z-value scale)  4.579          3.238          2.644
## Overall power, alt. = 0            <0.0001          0.0012          0.0086
## Overall power, alt. = 0.2          <0.0001          0.0056          0.0382
## Overall power, alt. = 0.4          0.0002          0.0328          0.1779
## Overall power, alt. = 0.6          0.0010          0.1264          0.4718
## Overall power, alt. = 0.8          0.0046          0.3280          0.7831
## Overall power, alt. = 1            0.0174          0.5996          0.9491
## Number of subjects                25.0           50.0           75.0
## Cumulative alpha spent <0.0001          0.0012          0.0086
## Two-sided local significance level <0.0001          0.0012          0.0082
## Efficacy boundary (t)             -2.376 - 2.376 -0.974 - 0.974 -0.628 - 0.628 -0
## Exit probability for efficacy (under H0) <0.0001          0.0012          0.0074
## Exit probability for efficacy (under H1), alt. = 0 <0.0001          0.0012          0.0074
## Exit probability for efficacy (under H1), alt. = 0.2 <0.0001          0.0056          0.0326
## Exit probability for efficacy (under H1), alt. = 0.4 0.0002          0.0326          0.1451
## Exit probability for efficacy (under H1), alt. = 0.6 0.0010          0.1255          0.3454
## Exit probability for efficacy (under H1), alt. = 0.8 0.0046          0.3234          0.4551
## Exit probability for efficacy (under H1), alt. = 1 0.0174          0.5822          0.3495
##
## Legend:

```

```

## alt.: alternative
## (t): treatment effect scale
summary(getPowerMeans(getDesignGroupSequential(kMax = 1, sided = 2),
  maxNumberOfSubjects = 100, directionUpper = TRUE))

## Power calculation for a continuous endpoint
##
## Fixed sample analysis.
## The results were calculated for a two-sample t-test (two-sided),
## H0:  $\mu(1) - \mu(2) = 0$ , H1: effect as specified, standard deviation = 1.
##
## Stage                               Fixed
## Efficacy boundary (z-value scale)    2.241
## Power, alt. = 0                      0.0250
## Power, alt. = 0.2                    0.1055
## Power, alt. = 0.4                    0.3947
## Power, alt. = 0.6                    0.7642
## Power, alt. = 0.8                    0.9561
## Power, alt. = 1                      0.9965
## Number of subjects                   100.0
## Two-sided local significance level    0.0250
## Efficacy boundary (t)                -0.455 - 0.455
##
## Legend:
## alt.: alternative
## (t): treatment effect scale
summary(getPowerMeans(getDesignGroupSequential(kMax = 1, sided = 1),
  maxNumberOfSubjects = 100, directionUpper = FALSE))

## Power calculation for a continuous endpoint
##
## Fixed sample analysis.
## The results were calculated for a two-sample t-test (one-sided),
## H0:  $\mu(1) - \mu(2) = 0$ , power directed towards smaller values,
## H1: effect as specified, standard deviation = 1.
##
## Stage                               Fixed
## Efficacy boundary (z-value scale)    1.960
## Power, alt. = 0                      0.0250
## Power, alt. = 0.2                    0.0016
## Power, alt. = 0.4                    <0.0001
## Power, alt. = 0.6                    <0.0001
## Power, alt. = 0.8                    <0.0001
## Power, alt. = 1                      <0.0001
## Number of subjects                   100.0
## One-sided local significance level    0.0250
## Efficacy boundary (t)                -0.397
##
## Legend:
## alt.: alternative
## (t): treatment effect scale
summary(getSampleSizeMeans(getDesignInverseNormal(futilityBounds = c(1, 2))))

```

```

## Sample size calculation for a continuous endpoint
##
## Sequential analysis with a maximum of 3 looks
## (inverse normal combination test design).
## The sample size was calculated for a two-sample t-test (one-sided),
## H0: mu(1) - mu(2) = 0, H1: effect as specified, standard deviation = 1, power 80%.
##
## Stage                1        2        3
## Information rate      33.3%   66.7%   100%
## Efficacy boundary (z-value scale)  3.471  2.454  2.004
## Futility boundary (z-value scale)  1.000  2.000
## Overall power         0.0967  0.7030  0.8000
## Number of subjects, alt. = 0.2    472.2  944.4 1416.5
## Number of subjects, alt. = 0.4    118.9  237.8  356.8
## Number of subjects, alt. = 0.6     53.5  107.0  160.5
## Number of subjects, alt. = 0.8     30.6   61.3   91.9
## Number of subjects, alt. = 1       20.1   40.1   60.2
## Exit probability for futility       0.1209  0.0758
## Cumulative alpha spent             0.0003  0.0072  0.0250
## One-sided local significance level  0.0003  0.0071  0.0225
## Efficacy boundary (t), alt. = 0.2  0.322  0.160  0.107
## Efficacy boundary (t), alt. = 0.4  0.655  0.321  0.213
## Efficacy boundary (t), alt. = 0.6  1.013  0.483  0.319
## Efficacy boundary (t), alt. = 0.8  1.413  0.646  0.424
## Efficacy boundary (t), alt. = 1    1.882  0.812  0.528
## Futility boundary (t), alt. = 0.2  0.092  0.130
## Futility boundary (t), alt. = 0.4  0.184  0.261
## Futility boundary (t), alt. = 0.6  0.276  0.391
## Futility boundary (t), alt. = 0.8  0.368  0.522
## Futility boundary (t), alt. = 1    0.459  0.653
## Overall exit probability (under H0)  0.8416  0.1462
## Overall exit probability (under H1), alt. = 0.2  0.2176  0.6822
## Overall exit probability (under H1), alt. = 0.4  0.2176  0.6822
## Overall exit probability (under H1), alt. = 0.6  0.2176  0.6822
## Overall exit probability (under H1), alt. = 0.8  0.2176  0.6822
## Overall exit probability (under H1), alt. = 1    0.2176  0.6822
## Exit probability for efficacy (under H0)  0.0003  0.0062
## Exit probability for efficacy (under H1)  0.0967  0.6064
## Exit probability for futility (under H0)  0.8413  0.1400
## Exit probability for futility (under H1)  0.1209  0.0758
##
## Legend:
##   alt.: alternative
##   (t): treatment effect scale
summary(getSampleSizeMeans(getDesignGroupSequential(futilityBounds = c(1, 2))), digits = 4)

## Sample size calculation for a continuous endpoint
##
## Sequential analysis with a maximum of 3 looks (group sequential design).
## The sample size was calculated for a two-sample t-test (one-sided),
## H0: mu(1) - mu(2) = 0, H1: effect as specified, standard deviation = 1, power 80%.
##
## Stage                1        2        3
## Information rate      33.3%   66.7%   100%

```

```

## Efficacy boundary (z-value scale)          3.4711  2.4544  2.0040
## Futility boundary (z-value scale)         1.0000  2.0000
## Overall power                             0.09667 0.70304 0.80000
## Number of subjects, alt. = 0.2           472.2   944.4  1416.5
## Number of subjects, alt. = 0.4           118.9   237.8   356.8
## Number of subjects, alt. = 0.6            53.5   107.0   160.5
## Number of subjects, alt. = 0.8            30.6    61.3    91.9
## Number of subjects, alt. = 1              20.1    40.1    60.2
## Exit probability for futility              0.12094 0.07581
## Cumulative alpha spent                    0.00026 0.00716 0.02500
## One-sided local significance level         0.00026 0.00706 0.02253
## Efficacy boundary (t), alt. = 0.2        0.3217  0.1600  0.1066
## Efficacy boundary (t), alt. = 0.4        0.6548  0.3207  0.2130
## Efficacy boundary (t), alt. = 0.6        1.0127  0.4826  0.3189
## Efficacy boundary (t), alt. = 0.8        1.4130  0.6462  0.4240
## Efficacy boundary (t), alt. = 1          1.8816  0.8123  0.5280
## Futility boundary (t), alt. = 0.2         0.0921  0.1303
## Futility boundary (t), alt. = 0.4         0.1842  0.2608
## Futility boundary (t), alt. = 0.6         0.2761  0.3913
## Futility boundary (t), alt. = 0.8         0.3678  0.5220
## Futility boundary (t), alt. = 1           0.4592  0.6529
## Overall exit probability (under H0)        0.84160 0.14622
## Overall exit probability (under H1), alt. = 0.2 0.21761 0.68219
## Overall exit probability (under H1), alt. = 0.4 0.21761 0.68219
## Overall exit probability (under H1), alt. = 0.6 0.21761 0.68219
## Overall exit probability (under H1), alt. = 0.8 0.21761 0.68219
## Overall exit probability (under H1), alt. = 1 0.21761 0.68219
## Exit probability for efficacy (under H0)   0.00026 0.00624
## Exit probability for efficacy (under H1)   0.09667 0.60637
## Exit probability for futility (under H0)   0.84134 0.13999
## Exit probability for futility (under H1)   0.12094 0.07581
##
## Legend:
##   alt.: alternative
##   (t): treatment effect scale
summary(getSampleSizeMeans(getDesignGroupSequential(futilityBounds = c(1, 2))), digits = 3)

## Sample size calculation for a continuous endpoint
##
## Sequential analysis with a maximum of 3 looks (group sequential design).
## The sample size was calculated for a two-sample t-test (one-sided),
## H0: mu(1) - mu(2) = 0, H1: effect as specified, standard deviation = 1, power 80%.
##
## Stage                1          2          3
## Information rate      33.3%    66.7%   100%
## Efficacy boundary (z-value scale)          3.471  2.454  2.004
## Futility boundary (z-value scale)          1.000  2.000
## Overall power         0.0967 0.7030 0.8000
## Number of subjects, alt. = 0.2           472.2  944.4 1416.5
## Number of subjects, alt. = 0.4           118.9  237.8  356.8
## Number of subjects, alt. = 0.6            53.5  107.0  160.5
## Number of subjects, alt. = 0.8            30.6   61.3   91.9
## Number of subjects, alt. = 1              20.1   40.1   60.2
## Exit probability for futility              0.1209 0.0758

```



```

## Cumulative alpha spent                0.0003 0.0072 0.0250
## One-sided local significance level     0.0003 0.0071 0.0225
## Efficacy boundary (t), alt. = 0.2     0.322  0.160  0.107
## Efficacy boundary (t), alt. = 0.4     0.655  0.321  0.213
## Efficacy boundary (t), alt. = 0.6     1.013  0.483  0.319
## Efficacy boundary (t), alt. = 0.8     1.413  0.646  0.424
## Efficacy boundary (t), alt. = 1       1.882  0.812  0.528
## Futility boundary (t), alt. = 0.2     0.092  0.130
## Futility boundary (t), alt. = 0.4     0.184  0.261
## Futility boundary (t), alt. = 0.6     0.276  0.391
## Futility boundary (t), alt. = 0.8     0.368  0.522
## Futility boundary (t), alt. = 1       0.459  0.653
## Overall exit probability (under H0)    0.8416 0.1462
## Overall exit probability (under H1), alt. = 0.2 0.2176 0.6822
## Overall exit probability (under H1), alt. = 0.4 0.2176 0.6822
## Overall exit probability (under H1), alt. = 0.6 0.2176 0.6822
## Overall exit probability (under H1), alt. = 0.8 0.2176 0.6822
## Overall exit probability (under H1), alt. = 1 0.2176 0.6822
## Exit probability for efficacy (under H0) 0.0003 0.0062
## Exit probability for efficacy (under H1) 0.0967 0.6064
## Exit probability for futility (under H0) 0.8413 0.1400
## Exit probability for futility (under H1) 0.1209 0.0758
##
## Legend:
##   alt.: alternative
##   (t): treatment effect scale
summary(getSampleSizeMeans(getDesignGroupSequential(futilityBounds = c(1, 2))), digits = 2)

## Sample size calculation for a continuous endpoint
##
## Sequential analysis with a maximum of 3 looks (group sequential design).
## The sample size was calculated for a two-sample t-test (one-sided),
## H0: mu(1) - mu(2) = 0, H1: effect as specified, standard deviation = 1, power 80%.
##
## Stage                1          2          3
## Information rate     33.3%   66.7%   100%
## Efficacy boundary (z-value scale)    3.47    2.45    2.00
## Futility boundary (z-value scale)     1.00    2.00
## Overall power        0.097   0.703   0.800
## Number of subjects, alt. = 0.2     472.2  944.4 1416.5
## Number of subjects, alt. = 0.4     118.9  237.8  356.8
## Number of subjects, alt. = 0.6      53.5  107.0  160.5
## Number of subjects, alt. = 0.8      30.6   61.3   91.9
## Number of subjects, alt. = 1        20.1   40.1   60.2
## Exit probability for futility         0.121  0.076
## Cumulative alpha spent               <0.001  0.007  0.025
## One-sided local significance level    <0.001  0.007  0.023
## Efficacy boundary (t), alt. = 0.2    0.32   0.16   0.11
## Efficacy boundary (t), alt. = 0.4    0.65   0.32   0.21
## Efficacy boundary (t), alt. = 0.6    1.01   0.48   0.32
## Efficacy boundary (t), alt. = 0.8    1.41   0.65   0.42
## Efficacy boundary (t), alt. = 1      1.88   0.81   0.53
## Futility boundary (t), alt. = 0.2    0.09   0.13
## Futility boundary (t), alt. = 0.4    0.18   0.26

```

```

## Futility boundary (t), alt. = 0.6           0.28  0.39
## Futility boundary (t), alt. = 0.8           0.37  0.52
## Futility boundary (t), alt. = 1             0.46  0.65
## Overall exit probability (under H0)          0.842  0.146
## Overall exit probability (under H1), alt. = 0.2 0.218  0.682
## Overall exit probability (under H1), alt. = 0.4 0.218  0.682
## Overall exit probability (under H1), alt. = 0.6 0.218  0.682
## Overall exit probability (under H1), alt. = 0.8 0.218  0.682
## Overall exit probability (under H1), alt. = 1   0.218  0.682
## Exit probability for efficacy (under H0)      <0.001  0.006
## Exit probability for efficacy (under H1)       0.097  0.606
## Exit probability for futility (under H0)       0.841  0.140
## Exit probability for futility (under H1)       0.121  0.076
##
## Legend:
##   alt.: alternative
##   (t): treatment effect scale
summary(getSampleSizeMeans(getDesignGroupSequential(futilityBounds = c(1, 2))), digits = 0)

## Sample size calculation for a continuous endpoint
##
## Sequential analysis with a maximum of 3 looks (group sequential design).
## The sample size was calculated for a two-sample t-test (one-sided),
## H0: mu(1) - mu(2) = 0, H1: effect as specified, standard deviation = 1, power 80%.
##
## Stage                1          2          3
## Information rate      33.3%     66.7%     100%
## Efficacy boundary (z-value scale)  3.471     2.454     2.004
## Futility boundary (z-value scale)  1.000     2.000
## Overall power         0.09667    0.70304    0.80000
## Number of subjects, alt. = 0.2    472.2     944.4     1416.5
## Number of subjects, alt. = 0.4    118.9     237.8     356.8
## Number of subjects, alt. = 0.6     53.5     107.0     160.5
## Number of subjects, alt. = 0.8     30.6     61.3     91.9
## Number of subjects, alt. = 1       20.1     40.1     60.2
## Exit probability for futility       0.12094    0.07581
## Cumulative alpha spent             0.0002592  0.0071601  0.0250000
## One-sided local significance level  0.0002592  0.0070554  0.0225331
## Efficacy boundary (t), alt. = 0.2    0.322     0.160     0.107
## Efficacy boundary (t), alt. = 0.4    0.655     0.321     0.213
## Efficacy boundary (t), alt. = 0.6    1.013     0.483     0.319
## Efficacy boundary (t), alt. = 0.8    1.413     0.646     0.424
## Efficacy boundary (t), alt. = 1     1.882     0.812     0.528
## Futility boundary (t), alt. = 0.2    0.0921    0.1303
## Futility boundary (t), alt. = 0.4    0.184     0.261
## Futility boundary (t), alt. = 0.6    0.276     0.391
## Futility boundary (t), alt. = 0.8    0.368     0.522
## Futility boundary (t), alt. = 1     0.459     0.653
## Overall exit probability (under H0)    0.8416    0.1462
## Overall exit probability (under H1), alt. = 0.2 0.2176    0.6822
## Overall exit probability (under H1), alt. = 0.4 0.2176    0.6822
## Overall exit probability (under H1), alt. = 0.6 0.2176    0.6822
## Overall exit probability (under H1), alt. = 0.8 0.2176    0.6822
## Overall exit probability (under H1), alt. = 1   0.2176    0.6822

```

```

## Exit probability for efficacy (under H0)          0.0002592 0.0062354
## Exit probability for efficacy (under H1)          0.09667  0.60637
## Exit probability for futility (under H0)          0.8413   0.1400
## Exit probability for futility (under H1)          0.12094  0.07581
##
## Legend:
##   alt.: alternative
##   (t): treatment effect scale
summary(getSampleSizeMeans(getDesignGroupSequential(futilityBounds = c(1, 2))), digits = -1)

## Sample size calculation for a continuous endpoint
##
## Sequential analysis with a maximum of 3 looks (group sequential design).
## The sample size was calculated for a two-sample t-test (one-sided),
## H0: mu(1) - mu(2) = 0, H1: effect as specified, standard deviation = 1, power 80%.
##
## Stage                                     1                               2
## Information rate                          33.3%                            66.7%
## Efficacy boundary (z-value scale)          3.4710914446541                2.45443229863352        2.0040
## Futility boundary (z-value scale)          1                               2
## Overall power                             0.0966650610605351            0.70304005701407        0.8000
## Number of subjects, alt. = 0.2            472.175971190466              944.351942380932        1416.
## Number of subjects, alt. = 0.4            118.918820873684              237.837641747368        356.75
## Number of subjects, alt. = 0.6            53.5130463596028              107.026092719206        160.53
## Number of subjects, alt. = 0.8            30.6352725529709              61.2705451059418        91.905
## Number of subjects, alt. = 1              20.0614501594328              40.1229003188657        60.184
## Exit probability for futility              0.120939971783343            0.0758116678791493
## Cumulative alpha spent                    0.000259173723496486          0.00716005940148245
## One-sided local significance level         0.000259173723496486          0.00705536161371023    0.022533
## Efficacy boundary (t), alt. = 0.2         0.321710839190332            0.16003836007769        0.10658
## Efficacy boundary (t), alt. = 0.4         0.654823493383795            0.320689953155161        0.21295
## Efficacy boundary (t), alt. = 0.6         1.01268266453838              0.482561132966479        0.31885
## Efficacy boundary (t), alt. = 0.8         1.41302933799472              0.646240615813088        0.42399
## Efficacy boundary (t), alt. = 1           1.88164819392793              0.812280944461675        0.52802
## Futility boundary (t), alt. = 0.2          0.09213829                    0.13033753
## Futility boundary (t), alt. = 0.4          0.18418994                    0.26075187
## Futility boundary (t), alt. = 0.6          0.27608063                    0.39130341
## Futility boundary (t), alt. = 0.8          0.36776309                    0.52201903
## Futility boundary (t), alt. = 1            0.45923643                    0.65287366
## Overall exit probability (under H0)         0.841603919792039            0.146222739762505
## Overall exit probability (under H1), alt. = 0.2 0.217605032843878            0.682186663832684
## Overall exit probability (under H1), alt. = 0.4 0.217605032843878            0.682186663832684
## Overall exit probability (under H1), alt. = 0.6 0.217605032843878            0.682186663832684
## Overall exit probability (under H1), alt. = 0.8 0.217605032843878            0.682186663832684
## Overall exit probability (under H1), alt. = 1 0.217605032843878            0.682186663832684
## Exit probability for efficacy (under H0)     0.000259173723496486          0.00623541950983228
## Exit probability for efficacy (under H1)     0.0966650610605351            0.606374995953535
## Exit probability for futility (under H0)     0.841344746068543            0.139987320252672
## Exit probability for futility (under H1)     0.120939971783343            0.0758116678791493
##
## Legend:
##   alt.: alternative
##   (t): treatment effect scale

```

3.2 Design plan summaries - rates

```
summary(getSampleSizeRates(pi2 = 0.3))
```

```
## Sample size calculation for a binary endpoint
##
## Fixed sample analysis.
## The sample size was calculated for a two-sample test for rates (one-sided),
## H0: pi(1) - pi(2) = 0, H1: treatment rate pi(1) as specified,
## control rate pi(2) = 0.3, power 80%.
##
## Stage                               Fixed
## Efficacy boundary (z-value scale)    1.960
## Number of subjects, pi(1) = 0.4     711.9
## Number of subjects, pi(1) = 0.5     186.0
## Number of subjects, pi(1) = 0.6      83.9
## One-sided local significance level 0.0250
## Efficacy boundary (t), pi(1) = 0.4  0.069
## Efficacy boundary (t), pi(1) = 0.5  0.139
## Efficacy boundary (t), pi(1) = 0.6  0.210
##
## Legend:
## (t): approximate treatment effect scale
```

```
summary(getSampleSizeRates(groups = 1, thetaH0 = 0.3))
```

```
## Sample size calculation for a binary endpoint
##
## Fixed sample analysis.
## The sample size was calculated for a one-sample test for rates (one-sided),
## H0: pi = 0.3, H1: treatment rate pi as specified, power 80%.
##
## Stage                               Fixed
## Efficacy boundary (z-value scale)    1.960
## Number of subjects, pi(1) = 0.4     171.7
## Number of subjects, pi(1) = 0.5      43.5
## Number of subjects, pi(1) = 0.6      19.1
## One-sided local significance level 0.0250
## Efficacy boundary (t), pi(1) = 0.4  0.369
## Efficacy boundary (t), pi(1) = 0.5  0.436
## Efficacy boundary (t), pi(1) = 0.6  0.506
##
## Legend:
## (t): approximate treatment effect scale
```

```
summary(getSampleSizeRates(groups = 1, thetaH0 = 0.45))
```

```
## Sample size calculation for a binary endpoint
##
## Fixed sample analysis.
## The sample size was calculated for a one-sample test for rates (one-sided),
## H0: pi = 0.45, H1: treatment rate pi as specified, power 80%.
##
## Stage                               Fixed
## Efficacy boundary (z-value scale)    1.960
## Number of subjects, pi(1) = 0.4     769.9
```

```

## Number of subjects, pi(1) = 0.5      779.4
## Number of subjects, pi(1) = 0.6      85.5
## One-sided local significance level 0.0250
## Efficacy boundary (t), pi(1) = 0.4  0.415
## Efficacy boundary (t), pi(1) = 0.5  0.485
## Efficacy boundary (t), pi(1) = 0.6  0.555
##
## Legend:
##   (t): approximate treatment effect scale
summary(getSampleSizeRates(groups = 2, thetaH0 = 0.45, allocationRatioPlanned = 0))

```

```

## Sample size calculation for a binary endpoint
##
## Fixed sample analysis.
## The sample size was calculated for a two-sample test for rates (one-sided),
## H0: pi(1) - pi(2) = 0.45, H1: treatment rate pi(1) as specified,
## control rate pi(2) = 0.2, optimum planned allocation ratio, power 80%.
##
## Stage                                Fixed
## Efficacy boundary (z-value scale)    1.960
## Number of subjects, pi(1) = 0.4      86.8
## Number of subjects, pi(1) = 0.5     255.9
## Number of subjects, pi(1) = 0.6    2393.1
## Optimum allocation ratio, pi(1) = 0.4 1.778
## Optimum allocation ratio, pi(1) = 0.5 1.501
## Optimum allocation ratio, pi(1) = 0.6 1.280
## One-sided local significance level    0.0250
## Efficacy boundary (t), pi(1) = 0.4    0.276
## Efficacy boundary (t), pi(1) = 0.5    0.346
## Efficacy boundary (t), pi(1) = 0.6    0.415
##
## Legend:
##   (t): approximate treatment effect scale

```

```
summary(getSampleSizeRates(getDesignGroupSequential(futilityBounds = c(1, 2))))
```

```

## Sample size calculation for a binary endpoint
##
## Sequential analysis with a maximum of 3 looks (group sequential design).
## The sample size was calculated for a two-sample test for rates (one-sided),
## H0: pi(1) - pi(2) = 0, H1: treatment rate pi(1) as specified,
## control rate pi(2) = 0.2, power 80%.
##
## Stage                                1      2      3
## Information rate                      33.3% 66.7% 100%
## Efficacy boundary (z-value scale)      3.471 2.454 2.004
## Futility boundary (z-value scale)      1.000 2.000
## Overall power                          0.0967 0.7030 0.8000
## Number of subjects, pi(1) = 0.4       97.5 195.0 292.5
## Number of subjects, pi(1) = 0.5       46.2  92.4 138.6
## Number of subjects, pi(1) = 0.6       26.8  53.6  80.4
## Exit probability for futility          0.1209 0.0758
## Cumulative alpha spent                  0.0003 0.0072 0.0250
## One-sided local significance level      0.0003 0.0071 0.0225

```

```

## Efficacy boundary (t), pi(1) = 0.4          0.339  0.158  0.102
## Efficacy boundary (t), pi(1) = 0.5          0.509  0.238  0.152
## Efficacy boundary (t), pi(1) = 0.6          0.669  0.322  0.205
## Futility boundary (t), pi(1) = 0.4          0.087  0.126
## Futility boundary (t), pi(1) = 0.5          0.130  0.190
## Futility boundary (t), pi(1) = 0.6          0.175  0.257
## Overall exit probability (under H0)          0.8416 0.1462
## Overall exit probability (under H1), pi(1) = 0.4 0.2176 0.6822
## Overall exit probability (under H1), pi(1) = 0.5 0.2176 0.6822
## Overall exit probability (under H1), pi(1) = 0.6 0.2176 0.6822
## Exit probability for efficacy (under H0)      0.0003 0.0062
## Exit probability for efficacy (under H1)      0.0967 0.6064
## Exit probability for futility (under H0)      0.8413 0.1400
## Exit probability for futility (under H1)      0.1209 0.0758

```

```
##
```

```
## Legend:
```

```
## (t): approximate treatment effect scale
```

```
summary(getPowerRates(getDesignGroupSequential(futilityBounds = c(1, 2)),
  maxNumberOfSubjects = 100))
```

```
## Power calculation for a binary endpoint
```

```
##
```

```
## Sequential analysis with a maximum of 3 looks (group sequential design).
```

```
## The results were calculated for a two-sample test for rates (one-sided),
```

```
## H0: pi(1) - pi(2) = 0, power directed towards larger values,
```

```
## H1: treatment rate pi(1) as specified, control rate pi(2) = 0.2.
```

```
##
```

```

## Stage                1         2         3
## Information rate      33.3%    66.7%   100%
## Efficacy boundary (z-value scale)  3.471  2.454  2.004
## Futility boundary (z-value scale)  1.000  2.000
## Overall power, pi(1) = 0.2        0.0003 0.0065 0.0109
## Overall power, pi(1) = 0.3        0.0025 0.0599 0.0985
## Overall power, pi(1) = 0.4        0.0136 0.2358 0.3411
## Overall power, pi(1) = 0.5        0.0527 0.5384 0.6613
## Number of subjects              33.3    66.7   100.0
## Exit probability for futility, pi(1) = 0.2  0.8413 0.1400
## Exit probability for futility, pi(1) = 0.3  0.6317 0.2464
## Exit probability for futility, pi(1) = 0.4  0.3963 0.2399
## Exit probability for futility, pi(1) = 0.5  0.1970 0.1333
## Cumulative alpha spent          0.0003 0.0072 0.0250
## One-sided local significance level  0.0003 0.0071 0.0225
## Efficacy boundary (t)           0.601  0.285  0.182
## Futility boundary (t)           0.155  0.227
## Overall exit probability (under H0)      0.8416 0.1462
## Overall exit probability (under H1), pi(1) = 0.2  0.8416 0.1462
## Overall exit probability (under H1), pi(1) = 0.3  0.6342 0.3038
## Overall exit probability (under H1), pi(1) = 0.4  0.4099 0.4621
## Overall exit probability (under H1), pi(1) = 0.5  0.2498 0.6189
## Exit probability for efficacy (under H0)      0.0003 0.0062
## Exit probability for efficacy (under H1), pi(1) = 0.2  0.0003 0.0062
## Exit probability for efficacy (under H1), pi(1) = 0.3  0.0025 0.0574
## Exit probability for efficacy (under H1), pi(1) = 0.4  0.0136 0.2222
## Exit probability for efficacy (under H1), pi(1) = 0.5  0.0527 0.4856

```

```
## Exit probability for futility (under H0)          0.8413 0.1400
## Exit probability for futility (under H1), pi(1) = 0.2 0.8413 0.1400
## Exit probability for futility (under H1), pi(1) = 0.3 0.6317 0.2464
## Exit probability for futility (under H1), pi(1) = 0.4 0.3963 0.2399
## Exit probability for futility (under H1), pi(1) = 0.5 0.1970 0.1333
##
```

```
## Legend:
```

```
## (t): approximate treatment effect scale
```

```
summary(getSampleSizeRates(getDesignGroupSequential(kMax = 4, sided = 2)))
```

```
## Sample size calculation for a binary endpoint
```

```
##
```

```
## Sequential analysis with a maximum of 4 looks (group sequential design).
```

```
## The sample size was calculated for a two-sample test for rates (two-sided),
```

```
## H0: pi(1) - pi(2) = 0, H1: treatment rate pi(1) as specified,
```

```
## control rate pi(2) = 0.2, power 80%.
```

```
##
```

## Stage	1	2	3	4
## Information rate	25%	50%	75%	100%
## Efficacy boundary (z-value scale)	4.579	3.238	2.644	2.289
## Overall power	0.0012	0.1494	0.5227	0.8000
## Number of subjects, pi(1) = 0.4	50.1	100.2	150.2	200.3
## Number of subjects, pi(1) = 0.5	23.8	47.5	71.3	95.0
## Number of subjects, pi(1) = 0.6	13.8	27.6	41.5	55.3
## Cumulative alpha spent	<0.0001	0.0012	0.0086	0.0250
## Two-sided local significance level	<0.0001	0.0012	0.0082	0.0221
## Efficacy boundary (t), pi(1) = 0.4	- 0.646 -0.196	- 0.310 -0.144	- 0.197 -0.113	- 0.144
## Efficacy boundary (t), pi(1) = 0.5		- 0.465 -0.191	- 0.299 -0.154	- 0.217
## Efficacy boundary (t), pi(1) = 0.6		- 0.616	- 0.402 -0.189	- 0.293
## Exit probability for efficacy (under H0)	<0.0001	0.0012	0.0074	
## Exit probability for efficacy (under H1)	0.0012	0.1482	0.3733	

```
##
```

```
## Legend:
```

```
## (t): approximate treatment effect scale
```

```
summary(getSampleSizeRates(getDesignGroupSequential(kMax = 4, sided = 2),
  groups = 1, thetaH0 = 0.3))
```

```
## Sample size calculation for a binary endpoint
```

```
##
```

```
## Sequential analysis with a maximum of 4 looks (group sequential design).
```

```
## The sample size was calculated for a one-sample test for rates (two-sided),
```

```
## H0: pi = 0.3, H1: treatment rate pi as specified, power 80%.
```

```
##
```

## Stage	1	2	3	4
## Information rate	25%	50%	75%	100%
## Efficacy boundary (z-value scale)	4.579	3.238	2.644	2.289
## Overall power	0.0012	0.1494	0.5227	0.8000
## Number of subjects, pi(1) = 0.4	52.7	105.4	158.0	210.7
## Number of subjects, pi(1) = 0.5	13.3	26.7	40.0	53.3
## Number of subjects, pi(1) = 0.6	5.9	11.7	17.6	23.4
## Cumulative alpha spent	<0.0001	0.0012	0.0086	0.0250
## Two-sided local significance level	<0.0001	0.0012	0.0082	0.0221
## Efficacy boundary (t), pi(1) = 0.4	0.011 - 0.589	0.155 - 0.445	0.204 - 0.396	0.228 - 0.372

```
## Efficacy boundary (t), pi(1) = 0.5      -0.275 - 0.875 0.013 - 0.587 0.108 - 0.492 0.156 - 0.444
## Efficacy boundary (t), pi(1) = 0.6      -0.567 - 1.167 -0.134 - 0.734 0.011 - 0.589 0.083 - 0.517
## Exit probability for efficacy (under H0)    <0.0001          0.0012          0.0074
## Exit probability for efficacy (under H1)     0.0012          0.1482          0.3733
##
```

```
## Legend:
```

```
## (t): approximate treatment effect scale
```

```
summary(getSampleSizeRates(getDesignGroupSequential(kMax = 1, sided = 2),
  groups = 1, thetaH0 = 0.2, pi1 = c(0.4,0.5)))
```

```
## Sample size calculation for a binary endpoint
```

```
##
```

```
## Fixed sample analysis.
```

```
## The sample size was calculated for a one-sample test for rates (two-sided),
```

```
## H0: pi = 0.2, H1: treatment rate pi as specified, power 80%.
```

```
##
```

```
## Stage                               Fixed
```

```
## Efficacy boundary (z-value scale)     2.241
```

```
## Number of subjects, pi(1) = 0.4      42.8
```

```
## Number of subjects, pi(1) = 0.5      19.3
```

```
## Two-sided local significance level     0.0250
```

```
## Efficacy boundary (t), pi(1) = 0.4   0.063 - 0.337
```

```
## Efficacy boundary (t), pi(1) = 0.5  -0.004 - 0.404
```

```
##
```

```
## Legend:
```

```
## (t): approximate treatment effect scale
```

```
summary(getSampleSizeRates(getDesignGroupSequential(kMax = 1, sided = 2),
  groups = 1, thetaH0 = 0.2, pi1 = 0.4))
```

```
## Sample size calculation for a binary endpoint
```

```
##
```

```
## Fixed sample analysis.
```

```
## The sample size was calculated for a one-sample test for rates (two-sided),
```

```
## H0: pi = 0.2, H1: treatment rate pi = 0.4, power 80%.
```

```
##
```

```
## Stage                               Fixed
```

```
## Efficacy boundary (z-value scale)     2.241
```

```
## Number of subjects                    42.8
```

```
## Two-sided local significance level     0.0250
```

```
## Efficacy boundary (t)                  0.063 - 0.337
```

```
##
```

```
## Legend:
```

```
## (t): approximate treatment effect scale
```

```
summary(getSampleSizeRates(getDesignGroupSequential(kMax = 1, sided = 2),
  groups = 2, thetaH0 = 0, pi1 = 0.25))
```

```
## Sample size calculation for a binary endpoint
```

```
##
```

```
## Fixed sample analysis.
```

```
## The sample size was calculated for a two-sample test for rates (two-sided),
```

```
## H0: pi(1) - pi(2) = 0, H1; treatment rate pi(1) = 0.25, control rate pi(2) = 0.2,
```

```
## power 80%.
```

```
##
```



```
## Stage Fixed
## Efficacy boundary (z-value scale) 2.241
## Number of subjects 2649.3
## Two-sided local significance level 0.0250
## Efficacy boundary (t) -0.034 - 0.036
```

```
##
```

```
## Legend:
```

```
## (t): approximate treatment effect scale
```

```
summary(getPowerRates(getDesignGroupSequential(kMax = 4, sided = 2),
  maxNumberOfSubjects = 100))
```

```
## Power calculation for a binary endpoint
```

```
##
```

```
## Sequential analysis with a maximum of 4 looks (group sequential design).
```

```
## The results were calculated for a two-sample test for rates (two-sided),
```

```
## H0:  $\pi(1) - \pi(2) = 0$ , H1: treatment rate  $\pi(1)$  as specified,
```

```
## control rate  $\pi(2) = 0.2$ .
```

```
##
```

## Stage	1	2	3
## Information rate	25%	50%	75%
## Efficacy boundary (z-value scale)	4.579	3.238	2.644
## Overall power, $\pi(1) = 0.2$	<0.0001	0.0012	0.0086
## Overall power, $\pi(1) = 0.3$	<0.0001	0.0077	0.0509
## Overall power, $\pi(1) = 0.4$	0.0002	0.0450	0.2280
## Overall power, $\pi(1) = 0.5$	0.0014	0.1637	0.5516
## Number of subjects	25.0	50.0	75.0
## Cumulative alpha spent	<0.0001	0.0012	0.0086
## Two-sided local significance level	<0.0001	0.0012	0.0082
## Efficacy boundary (t)		- 0.453	-0.188 - 0.290 -
## Exit probability for efficacy (under H0)	<0.0001	0.0012	0.0074
## Exit probability for efficacy (under H1), $\pi(1) = 0.2$	<0.0001	0.0012	0.0074
## Exit probability for efficacy (under H1), $\pi(1) = 0.3$	<0.0001	0.0076	0.0433
## Exit probability for efficacy (under H1), $\pi(1) = 0.4$	0.0002	0.0448	0.1830
## Exit probability for efficacy (under H1), $\pi(1) = 0.5$	0.0014	0.1622	0.3879

```
##
```

```
## Legend:
```

```
## (t): approximate treatment effect scale
```

3.3 Design plan summaries - survival

```
summary(getSampleSizeSurvival())
```

```
## Sample size calculation for a survival endpoint
```

```
##
```

```
## Fixed sample analysis.
```

```
## The sample size was calculated for a two-sample logrank test (one-sided),
```

```
## H0: hazard ratio = 1, H1: treatment  $\pi(1)$  as specified, control  $\pi(2) = 0.2$ ,
```

```
## power 80%.
```

```
##
```

```
## Stage Fixed
## Efficacy boundary (z-value scale) 1.960
## Number of subjects,  $\pi(1) = 0.4$  154.7
## Number of subjects,  $\pi(1) = 0.5$  71.0
## Number of subjects,  $\pi(1) = 0.6$  40.1
```

```
## Number of events, pi(1) = 0.4      46
## Number of events, pi(1) = 0.5      25
## Number of events, pi(1) = 0.6      16
## Analysis time                       18.0
## Expected study duration, pi(1) = 0.4 18.0
## Expected study duration, pi(1) = 0.5 18.0
## Expected study duration, pi(1) = 0.6 18.0
## One-sided local significance level  0.0250
## Efficacy boundary (t), pi(1) = 0.4  1.785
## Efficacy boundary (t), pi(1) = 0.5  2.210
## Efficacy boundary (t), pi(1) = 0.6  2.686
```

```
##
```

```
## Legend:
```

```
## (t): approximate treatment effect scale
```

```
summary(getSampleSizeSurvival(lambda2 = 0.3, hazardRatio = 1.2))
```

```
## Sample size calculation for a survival endpoint
```

```
##
```

```
## Fixed sample analysis.
```

```
## The sample size was calculated for a two-sample logrank test (one-sided),
```

```
## H0: hazard ratio = 1, H1: hazard ratio = 1.2, control lambda(2) = 0.3, power 80%.
```

```
##
```

```
## Stage                               Fixed
```

```
## Efficacy boundary (z-value scale)    1.960
```

```
## Number of subjects                   979.2
```

```
## Number of events                     945
```

```
## Analysis time                        18.0
```

```
## Expected study duration              18.0
```

```
## One-sided local significance level  0.0250
```

```
## Efficacy boundary (t)                1.136
```

```
##
```

```
## Legend:
```

```
## (t): approximate treatment effect scale
```

```
summary(getSampleSizeSurvival(median2 = 2.3, hazardRatio = 1.2))
```

```
## Sample size calculation for a survival endpoint
```

```
##
```

```
## Fixed sample analysis.
```

```
## The sample size was calculated for a two-sample logrank test (one-sided),
```

```
## H0: hazard ratio = 1, H1: hazard ratio = 1.2, control median(2) = 2.3, power 80%.
```

```
##
```

```
## Stage                               Fixed
```

```
## Efficacy boundary (z-value scale)    1.960
```

```
## Number of subjects                   978.8
```

```
## Number of events                     945
```

```
## Analysis time                        18.0
```

```
## Expected study duration              18.0
```

```
## One-sided local significance level  0.0250
```

```
## Efficacy boundary (t)                1.136
```

```
##
```

```
## Legend:
```

```
## (t): approximate treatment effect scale
```

```
summary(getSampleSizeSurvival(median1 = 3.2, median2 = 2.3))
```

```
## Sample size calculation for a survival endpoint
##
## Fixed sample analysis.
## The sample size was calculated for a two-sample logrank test (one-sided),
## H0: hazard ratio = 1, H1: treatment median(1) = 3.2, control median(2) = 2.3,
## power 80%.
##
## Stage                               Fixed
## Efficacy boundary (z-value scale)    1.960
## Number of subjects                   309.7
## Number of events                      288
## Analysis time                        18.0
## Expected study duration              18.0
## One-sided local significance level    0.0250
## Efficacy boundary (t)                 0.794
##
## Legend:
## (t): approximate treatment effect scale
```

```
summary(getSampleSizeSurvival(median1 = c(3.1, 3.2), median2 = 2.3))
```

```
## Sample size calculation for a survival endpoint
##
## Fixed sample analysis.
## The sample size was calculated for a two-sample logrank test (one-sided),
## H0: hazard ratio = 1, H1: treatment median(1) as specified, control median(2) = 2.3,
## power 80%.
##
## Stage                               Fixed
## Efficacy boundary (z-value scale)    1.960
## Number of subjects, median(1) = 3.1  377.9
## Number of subjects, median(1) = 3.2  309.7
## Number of events, median(1) = 3.1    353
## Number of events, median(1) = 3.2    288
## Analysis time                        18.0
## Expected study duration, median(1) = 3.1 18.0
## Expected study duration, median(1) = 3.2 18.0
## One-sided local significance level    0.0250
## Efficacy boundary (t), median(1) = 3.1 0.812
## Efficacy boundary (t), median(1) = 3.2 0.794
##
## Legend:
## (t): approximate treatment effect scale
```

```
summary(getSampleSizeSurvival(lambda2 = 0.3, hazardRatio = c(1.2, 2)))
```

```
## Sample size calculation for a survival endpoint
##
## Fixed sample analysis.
## The sample size was calculated for a two-sample logrank test (one-sided),
## H0: hazard ratio = 1, H1: hazard ratio as specified, control lambda(2) = 0.3,
## power 80%.
##
```

```
## Stage Fixed
## Efficacy boundary (z-value scale) 1.960
## Number of subjects, HR = 1.2 979.2
## Number of subjects, HR = 2 67.0
## Number of events, HR = 1.2 945
## Number of events, HR = 2 66
## Analysis time 18.0
## Expected study duration, HR = 1.2 18.0
## Expected study duration, HR = 2 18.0
## One-sided local significance level 0.0250
## Efficacy boundary (t), HR = 1.2 1.136
## Efficacy boundary (t), HR = 2 1.624
```

```
##
```

```
## Legend:
```

```
## HR: hazard ratio
```

```
## (t): approximate treatment effect scale
```

```
summary(getSampleSizeSurvival(pi2 = 0.3, hazardRatio = 1.2))
```

```
## Sample size calculation for a survival endpoint
```

```
##
```

```
## Fixed sample analysis.
```

```
## The sample size was calculated for a two-sample logrank test (one-sided),
```

```
## H0: hazard ratio = 1, H1: hazard ratio = 1.2, control pi(2) = 0.3, power 80%.
```

```
##
```

```
## Stage Fixed
## Efficacy boundary (z-value scale) 1.960
## Number of subjects 2953.8
## Number of events 945
## Analysis time 18.0
## Expected study duration 18.0
## One-sided local significance level 0.0250
## Efficacy boundary (t) 1.136
```

```
##
```

```
## Legend:
```

```
## (t): approximate treatment effect scale
```

```
summary(getSampleSizeSurvival(pi1 = 0.1, pi2 = 0.3))
```

```
## Sample size calculation for a survival endpoint
```

```
##
```

```
## Fixed sample analysis.
```

```
## The sample size was calculated for a two-sample logrank test (one-sided),
```

```
## H0: hazard ratio = 1, H1: treatment pi(1) = 0.1, control pi(2) = 0.3, power 80%.
```

```
##
```

```
## Stage Fixed
## Efficacy boundary (z-value scale) 1.960
## Number of subjects 106.7
## Number of events 22
## Analysis time 18.0
## Expected study duration 18.0
## One-sided local significance level 0.0250
## Efficacy boundary (t) 0.426
```

```
##
```

```
## Legend:
```

```

## (t): approximate treatment effect scale
summary(getSampleSizeSurvival(lambda2 = 0.03, lambda1 = c(0.040)))

## Sample size calculation for a survival endpoint
##
## Fixed sample analysis.
## The sample size was calculated for a two-sample logrank test (one-sided),
## H0: hazard ratio = 1, H1: treatment lambda(1) = 0.04, control lambda(2) = 0.03,
## power 80%.
##
## Stage                               Fixed
## Efficacy boundary (z-value scale)    1.960
## Number of subjects                   1126.0
## Number of events                      380
## Analysis time                        18.0
## Expected study duration              18.0
## One-sided local significance level    0.0250
## Efficacy boundary (t)                1.223
##
## Legend:
## (t): approximate treatment effect scale

piecewiseSurvivalTime <- list(
  "0 - <6" = 0.025,
  "6 - <9" = 0.04,
  "9 - <15" = 0.015,
  "15 - <21" = 0.01,
  ">= 21" = 0.007)
summary(getSampleSizeSurvival(piecewiseSurvivalTime = piecewiseSurvivalTime,
  hazardRatio = 1.2))

## Sample size calculation for a survival endpoint
##
## Fixed sample analysis.
## The sample size was calculated for a two-sample logrank test (one-sided),
## H0: hazard ratio = 1, H1: hazard ratio = 1.2, piecewise survival distribution,
## power 80%.
##
## Stage                               Fixed
## Efficacy boundary (z-value scale)    1.960
## Number of subjects                   3350.9
## Number of events                      945
## Analysis time                        18.0
## Expected study duration              18.0
## One-sided local significance level    0.0250
## Efficacy boundary (t)                1.136
##
## Legend:
## (t): approximate treatment effect scale

summary(getSampleSizeSurvival(getDesignGroupSequential(futilityBounds = c(1, 2))))

## Sample size calculation for a survival endpoint
##
## Sequential analysis with a maximum of 3 looks (group sequential design).

```

```

## The sample size was calculated for a two-sample logrank test (one-sided),
## H0: hazard ratio = 1, H1: treatment pi(1) as specified, control pi(2) = 0.2,
## power 80%.
##
## Stage                1        2        3
## Information rate      33.3%   66.7%   100%
## Efficacy boundary (z-value scale)  3.471  2.454  2.004
## Futility boundary (z-value scale)  1.000  2.000
## Overall power         0.0967  0.7030  0.8000
## Number of subjects, pi(1) = 0.4   215.2  278.5  278.5
## Number of subjects, pi(1) = 0.5    97.0  127.9  127.9
## Number of subjects, pi(1) = 0.6    53.6   72.2   72.2
## Exit probability for futility       0.1209  0.0758
## Cumulative number of events, pi(1) = 0.4    28    55    83
## Cumulative number of events, pi(1) = 0.5    15    30    44
## Cumulative number of events, pi(1) = 0.6    10    19    29
## Analysis time, pi(1) = 0.4             9.3   13.5   18.0
## Analysis time, pi(1) = 0.5             9.1   13.4   18.0
## Analysis time, pi(1) = 0.6             8.9   13.1   18.0
## Expected study duration, pi(1) = 0.4      13.0
## Expected study duration, pi(1) = 0.5      12.9
## Expected study duration, pi(1) = 0.6      12.7
## Cumulative alpha spent                  0.0003  0.0072  0.0250
## One-sided local significance level        0.0003  0.0071  0.0225
## Efficacy boundary (t), pi(1) = 0.4       3.761  1.939  1.555
## Efficacy boundary (t), pi(1) = 0.5       6.127  2.475  1.830
## Efficacy boundary (t), pi(1) = 0.6       9.575  3.094  2.123
## Futility boundary (t), pi(1) = 0.4       1.465  1.715
## Futility boundary (t), pi(1) = 0.5       1.686  2.093
## Futility boundary (t), pi(1) = 0.6       1.917  2.510
## Overall exit probability (under H0)       0.8416  0.1462
## Overall exit probability (under H1), pi(1) = 0.4  0.2176  0.6822
## Overall exit probability (under H1), pi(1) = 0.5  0.2176  0.6822
## Overall exit probability (under H1), pi(1) = 0.6  0.2176  0.6822
## Exit probability for efficacy (under H0)  0.0003  0.0062
## Exit probability for efficacy (under H1)  0.0967  0.6064
## Exit probability for futility (under H0)  0.8413  0.1400
## Exit probability for futility (under H1)  0.1209  0.0758
##
## Legend:
## (t): approximate treatment effect scale
summary(getPowerSurvival(getDesignGroupSequential(futilityBounds = c(1, 2)),
  median1 = 37, median2 = 32, maxNumberOfSubjects = 100, maxNumberOfEvents = 60))

## Power calculation for a survival endpoint
##
## Sequential analysis with a maximum of 3 looks (group sequential design).
## The results were calculated for a two-sample logrank test (one-sided),
## H0: hazard ratio = 1, power directed towards larger values,
## H1: treatment median(1) = 37, control median(2) = 32.
##
## Stage                1        2        3
## Information rate      33.3%   66.7%   100%
## Efficacy boundary (z-value scale)  3.471  2.454  2.004

```

```

## Futility boundary (z-value scale)          1.000  2.000
## Overall power                             <0.0001  0.0016  0.0026
## Number of subjects                         100.0  100.0  100.0
## Exit probability for futility              0.9074  0.0870
## Expected number of events                  21.9
## Cumulative number of events                20      40      60
## Analysis time                             17.2    31.4    51.6
## Expected study duration                   18.6
## Cumulative alpha spent                    0.0003  0.0072  0.0250
## One-sided local significance level         0.0003  0.0071  0.0225
## Efficacy boundary (t)                     4.722   2.173   1.678
## Futility boundary (t)                     1.564   1.882
## Overall exit probability (under H0)        0.8416  0.1462
## Overall exit probability (under H1)        0.9074  0.0886
## Exit probability for efficacy (under H0)   0.0003  0.0062
## Exit probability for efficacy (under H1) <0.0001  0.0016
## Exit probability for futility (under H0)   0.8413  0.1400
## Exit probability for futility (under H1)   0.9074  0.0870
##
## Legend:
## (t): approximate treatment effect scale

```

```

summary(getPowerSurvival(getDesignGroupSequential(futilityBounds = c(1, 2)),
  maxNumberOfSubjects = 100, maxNumberOfEvents = 60))

```

```

## Power calculation for a survival endpoint
##
## Sequential analysis with a maximum of 3 looks (group sequential design).
## The results were calculated for a two-sample logrank test (one-sided),
## H0: hazard ratio = 1, power directed towards larger values,
## H1: treatment pi(1) as specified, control pi(2) = 0.2.
##
## Stage                                1      2      3
## Information rate                      33.3%  66.7%  100%
## Efficacy boundary (z-value scale)     3.471  2.454  2.004
## Futility boundary (z-value scale)     1.000  2.000
## Overall power, pi(1) = 0.2            0.0003  0.0065  0.0109
## Overall power, pi(1) = 0.3            0.0077  0.1543  0.2357
## Overall power, pi(1) = 0.4            0.0527  0.5382  0.6611
## Overall power, pi(1) = 0.5            0.1745  0.8481  0.9049
## Number of subjects, pi(1) = 0.2       100.0  100.0  100.0
## Number of subjects, pi(1) = 0.3       100.0  100.0  100.0
## Number of subjects, pi(1) = 0.4       100.0  100.0  100.0
## Number of subjects, pi(1) = 0.5       100.0  100.0  100.0
## Exit probability for futility, pi(1) = 0.2  0.8413  0.1400
## Exit probability for futility, pi(1) = 0.3  0.4806  0.2580
## Exit probability for futility, pi(1) = 0.4  0.1971  0.1334
## Exit probability for futility, pi(1) = 0.5  0.0625  0.0318
## Expected number of events, pi(1) = 0.2   23.4
## Expected number of events, pi(1) = 0.3   32.4
## Expected number of events, pi(1) = 0.4   37.6
## Expected number of events, pi(1) = 0.5   36.4
## Cumulative number of events              20      40      60
## Analysis time, pi(1) = 0.2             18.1    33.6    55.4
## Analysis time, pi(1) = 0.3             15.4    27.6    45.0

```

```

## Analysis time, pi(1) = 0.4          13.6   23.6   38.5
## Analysis time, pi(1) = 0.5          12.3   20.7   33.9
## Expected study duration, pi(1) = 0.2  20.8
## Expected study duration, pi(1) = 0.3  23.5
## Expected study duration, pi(1) = 0.4  23.1
## Expected study duration, pi(1) = 0.5  19.5
## Cumulative alpha spent              0.0003 0.0072 0.0250
## One-sided local significance level    0.0003 0.0071 0.0225
## Efficacy boundary (t)                4.722  2.173  1.678
## Futility boundary (t)                1.564  1.882
## Overall exit probability (under H0)    0.8416 0.1462
## Overall exit probability (under H1), pi(1) = 0.2  0.8416 0.1462
## Overall exit probability (under H1), pi(1) = 0.3  0.4883 0.4046
## Overall exit probability (under H1), pi(1) = 0.4  0.2498 0.6189
## Overall exit probability (under H1), pi(1) = 0.5  0.2369 0.7055
## Exit probability for efficacy (under H0) 0.0003 0.0062
## Exit probability for efficacy (under H1), pi(1) = 0.2 0.0003 0.0062
## Exit probability for efficacy (under H1), pi(1) = 0.3 0.0077 0.1466
## Exit probability for efficacy (under H1), pi(1) = 0.4 0.0527 0.4855
## Exit probability for efficacy (under H1), pi(1) = 0.5 0.1745 0.6736
## Exit probability for futility (under H0) 0.8413 0.1400
## Exit probability for futility (under H1), pi(1) = 0.2 0.8413 0.1400
## Exit probability for futility (under H1), pi(1) = 0.3 0.4806 0.2580
## Exit probability for futility (under H1), pi(1) = 0.4 0.1971 0.1334
## Exit probability for futility (under H1), pi(1) = 0.5 0.0625 0.0318

```

```
##
```

```
## Legend:
```

```
## (t): approximate treatment effect scale
```

```
summary(getSampleSizeSurvival(getDesignGroupSequential(kMax = 4, sided = 2)))
```

```
## Sample size calculation for a survival endpoint
```

```
##
```

```
## Sequential analysis with a maximum of 4 looks (group sequential design).
```

```
## The sample size was calculated for a two-sample logrank test (two-sided),
```

```
## H0: hazard ratio = 1, H1: treatment pi(1) as specified, control pi(2) = 0.2,
```

```
## power 80%.
```

```
##
```

## Stage	1	2	3	4
## Information rate	25%	50%	75%	100%
## Efficacy boundary (z-value scale)	4.579	3.238	2.644	2.289
## Overall power	0.0012	0.1494	0.5227	0.8000
## Number of subjects, pi(1) = 0.4	126.6	182.5	190.5	190.5
## Number of subjects, pi(1) = 0.5	56.9	82.6	87.5	87.5
## Number of subjects, pi(1) = 0.6	31.3	45.8	49.4	49.4
## Cumulative number of events, pi(1) = 0.4	15	29	43	57
## Cumulative number of events, pi(1) = 0.5	8	16	23	31
## Cumulative number of events, pi(1) = 0.6	5	10	15	20
## Analysis time, pi(1) = 0.4	8.0	11.5	14.6	18.0
## Analysis time, pi(1) = 0.5	7.8	11.3	14.4	18.0
## Analysis time, pi(1) = 0.6	7.6	11.1	14.2	18.0
## Expected study duration, pi(1) = 0.4	15.7			
## Expected study duration, pi(1) = 0.5	15.7			
## Expected study duration, pi(1) = 0.6	15.6			
## Cumulative alpha spent	<0.0001	0.0012	0.0086	0.0250


```

## Two-sided local significance level          <0.0001          0.0012          0.0082          0.0221
## Efficacy boundary (t), pi(1) = 0.4        0.087 - 11.467  0.295 - 3.386  0.443 - 2.255  0.543 - 1.840
## Efficacy boundary (t), pi(1) = 0.5        0.035 - 28.174  0.188 - 5.308  0.329 - 3.043  0.434 - 2.304
## Efficacy boundary (t), pi(1) = 0.6        0.016 - 64.101  0.125 - 8.006  0.250 - 4.002  0.353 - 2.830
## Exit probability for efficacy (under H0)    <0.0001          0.0012          0.0074
## Exit probability for efficacy (under H1)    0.0012          0.1482          0.3733
##
## Legend:
## (t): approximate treatment effect scale
summary(getPowerSurvival(getDesignGroupSequential(kMax = 4, sided = 2),
  maxNumberOfSubjects = 100, maxNumberOfEvents = 60))

## Power calculation for a survival endpoint
##
## Sequential analysis with a maximum of 4 looks (group sequential design).
## The results were calculated for a two-sample logrank test (two-sided),
## H0: hazard ratio = 1, H1: treatment pi(1) as specified, control pi(2) = 0.2.
##
## Stage                1                2                3
## Information rate      25%             50%             75%
## Efficacy boundary (z-value scale)          4.579           3.238           2.644
## Overall power, pi(1) = 0.2                 <0.0001         0.0012         0.0086
## Overall power, pi(1) = 0.3                 0.0001         0.0254         0.1446
## Overall power, pi(1) = 0.4                 0.0015         0.1662         0.5565
## Overall power, pi(1) = 0.5                 0.0086         0.4469         0.8779
## Number of subjects, pi(1) = 0.2            100.0           100.0           100.0
## Number of subjects, pi(1) = 0.3            100.0           100.0           100.0
## Number of subjects, pi(1) = 0.4            96.5            100.0           100.0
## Number of subjects, pi(1) = 0.5            87.6            100.0           100.0
## Expected number of events, pi(1) = 0.2     59.9
## Expected number of events, pi(1) = 0.3     57.4
## Expected number of events, pi(1) = 0.4     49.1
## Expected number of events, pi(1) = 0.5     40.0
## Cumulative number of events                15              30              45
## Analysis time, pi(1) = 0.2                 14.9            25.3            38.3
## Analysis time, pi(1) = 0.3                 12.9            21.1            31.3
## Analysis time, pi(1) = 0.4                 11.6            18.2            26.7
## Analysis time, pi(1) = 0.5                 10.5            16.1            23.4
## Expected study duration, pi(1) = 0.2       55.2
## Expected study duration, pi(1) = 0.3       42.8
## Expected study duration, pi(1) = 0.4       30.5
## Expected study duration, pi(1) = 0.5       21.4
## Cumulative alpha spent                     <0.0001         0.0012         0.0086
## Two-sided local significance level          <0.0001         0.0012         0.0082
## Efficacy boundary (t)                      0.094 - 10.638  0.307 - 3.262  0.455 - 2.199
## Exit probability for efficacy (under H0)    <0.0001         0.0012         0.0074
## Exit probability for efficacy (under H1), pi(1) = 0.2 <0.0001         0.0012         0.0074
## Exit probability for efficacy (under H1), pi(1) = 0.3 0.0001         0.0253         0.1192
## Exit probability for efficacy (under H1), pi(1) = 0.4 0.0015         0.1647         0.3903
## Exit probability for efficacy (under H1), pi(1) = 0.5 0.0086         0.4383         0.4310
##
## Legend:
## (t): approximate treatment effect scale

```

```
summary(getSampleSizeSurvival(sided = 2, lambda2 = log(2)/6, lambda1 = log(2)/8))
```

```
## Sample size calculation for a survival endpoint
##
## Fixed sample analysis.
## The sample size was calculated for a two-sample logrank test (two-sided),
## H0: hazard ratio = 1, H1: treatment lambda(1) = 0.087, control lambda(2) = 0.116,
## power 80%.
##
## Stage                               Fixed
## Efficacy boundary (z-value scale)    2.241
## Number of subjects                   675.7
## Number of events                      460
## Analysis time                        18.0
## Expected study duration              18.0
## Two-sided local significance level    0.0250
## Efficacy boundary (t)                0.811 - 1.233
##
## Legend:
## (t): approximate treatment effect scale
```

```
summary(getPowerSurvival(sided = 2, maxNumberOfSubjects = 200, maxNumberOfEvents = 40,
  lambda2 = log(2)/6, lambda1 = log(2)/8))
```

```
## Power calculation for a survival endpoint
##
## Fixed sample analysis.
## The results were calculated for a two-sample logrank test (two-sided),
## H0: hazard ratio = 1, H1: treatment lambda(1) = 0.087, control lambda(2) = 0.116.
##
## Stage                               Fixed
## Efficacy boundary (z-value scale)    2.241
## Power                                0.0923
## Number of subjects                   130.2
## Number of events                     40
## Analysis time                        7.8
## Expected study duration              7.8
## Two-sided local significance level    0.0250
## Efficacy boundary (t)                0.492 - 2.032
##
## Legend:
## (t): approximate treatment effect scale
```

```
summary(getSampleSizeSurvival(getDesignGroupSequential(sided = 2),
  lambda2 = log(2)/6, hazardRatio = c(0.55),
  accrualTime = c(0,10), accrualIntensity = 60))
```

```
## Warning: Accrual duration longer than maximal study duration (time to maximal number of events); fol
```

```
## Sample size calculation for a survival endpoint
##
## Sequential analysis with a maximum of 3 looks (group sequential design).
## The sample size was calculated for a two-sample logrank test (two-sided),
## H0: hazard ratio = 1, H1: hazard ratio = 0.55, control lambda(2) = 0.116, power 80%.
##
## Stage                               1                2                3
```

## Information rate	33.3%	66.7%	100%
## Efficacy boundary (z-value scale)	3.935	2.783	2.272
## Overall power	0.0160	0.4013	0.8000
## Number of subjects	232.9	338.1	422.5
## Cumulative number of events	36	72	108
## Analysis time	3.9	5.6	7.0
## Expected study duration	6.4		
## Cumulative alpha spent	<0.0001	0.0054	0.0250
## Two-sided local significance level	<0.0001	0.0054	0.0231
## Efficacy boundary (t)	0.269 - 3.721	0.518 - 1.929	0.645 - 1.550
## Exit probability for efficacy (under H0)	<0.0001	0.0053	
## Exit probability for efficacy (under H1)	0.0160	0.3853	

##

Legend:

(t): approximate treatment effect scale

```
summary(getPowerSurvival(getDesignGroupSequential(kMax = 2), maxNumberOfEvents = 200,
  maxNumberOfSubjects = 400, lambda2 = log(2) / 60, lambda1 = log(2) / 50,
  dropoutRate1 = 0.025, dropoutRate2 = 0.025, dropoutTime = 12,
  accrualTime = 0, accrualIntensity = 30))
```

Power calculation for a survival endpoint

##

Sequential analysis with a maximum of 2 looks (group sequential design).

The results were calculated for a two-sample logrank test (one-sided),

H0: hazard ratio = 1, power directed towards larger values,

H1: treatment $\lambda(1) = 0.014$, control $\lambda(2) = 0.012$.

##

## Stage	1	2
## Information rate	50%	100%
## Efficacy boundary (z-value scale)	2.797	1.977
## Overall power	0.0297	0.2489
## Number of subjects	400.0	400.0
## Expected number of events	197.0	
## Cumulative number of events	100	200
## Analysis time	30.1	66.0
## Expected study duration	64.9	
## Cumulative alpha spent	0.0026	0.0250
## One-sided local significance level	0.0026	0.0240
## Efficacy boundary (t)	1.749	1.323
## Exit probability for efficacy (under H0)	0.0026	
## Exit probability for efficacy (under H1)	0.0297	

##

Legend:

(t): approximate treatment effect scale

```
summary(getPowerSurvival(getDesignGroupSequential(kMax = 3), maxNumberOfEvents = 200,
  maxNumberOfSubjects = 400, lambda2 = log(2) / 60,
  lambda1 = c(log(2) / 50, log(2) / 60),
  dropoutRate1 = 0.025, dropoutRate2 = 0.025, dropoutTime = 12,
  accrualTime = 0, accrualIntensity = 30))
```

Power calculation for a survival endpoint

##

Sequential analysis with a maximum of 3 looks (group sequential design).

```

## The results were calculated for a two-sample logrank test (one-sided),
## H0: hazard ratio = 1, power directed towards larger values,
## H1: treatment lambda(1) as specified, control lambda(2) = 0.012.
##
## Stage                1      2      3
## Information rate      33.3%  66.7%  100%
## Efficacy boundary (z-value scale)  3.471  2.454  2.004
## Overall power, lambda(1) = 0.014  0.0032  0.0810  0.2464
## Overall power, lambda(1) = 0.012  0.0003  0.0072  0.0250
## Number of subjects, lambda(1) = 0.014  400.0  400.0  400.0
## Number of subjects, lambda(1) = 0.012  400.0  400.0  400.0
## Expected number of events, lambda(1) = 0.014  194.4
## Expected number of events, lambda(1) = 0.012  199.5
## Cumulative number of events                67    134    200
## Analysis time, lambda(1) = 0.014          21.4   40.0   66.0
## Analysis time, lambda(1) = 0.012          22.8   43.5   72.3
## Expected study duration, lambda(1) = 0.014  63.8
## Expected study duration, lambda(1) = 0.012  72.1
## Cumulative alpha spent                    0.0003  0.0072  0.0250
## One-sided local significance level          0.0003  0.0071  0.0225
## Efficacy boundary (t)                     2.340   1.530   1.328
## Exit probability for efficacy (under H0)    0.0003  0.0069
## Exit probability for efficacy (under H1), lambda(1) = 0.014  0.0032  0.0778
## Exit probability for efficacy (under H1), lambda(1) = 0.012  0.0003  0.0069
##
## Legend:
## (t): approximate treatment effect scale

```

```

summary(getPowerSurvival(getDesignGroupSequential(kMax = 3), maxNumberOfEvents = 200,
  maxNumberOfSubjects = 400, lambda2 = log(2) / 60, hazardRatio = c(0.7, 0.8),
  directionUpper = FALSE, dropoutRate1 = 0.025, dropoutRate2 = 0.025,
  dropoutTime = 12, accrualTime = 0, accrualIntensity = 30))

```

```

## Power calculation for a survival endpoint
##
## Sequential analysis with a maximum of 3 looks (group sequential design).
## The results were calculated for a two-sample logrank test (one-sided),
## H0: hazard ratio = 1, power directed towards smaller values,
## H1: hazard ratio as specified, control lambda(2) = 0.012.
##
## Stage                1      2      3
## Information rate      33.3%  66.7%  100%
## Efficacy boundary (z-value scale)  3.471  2.454  2.004
## Overall power, HR = 0.7  0.0220  0.3472  0.7051
## Overall power, HR = 0.8  0.0052  0.1224  0.3448
## Number of subjects, HR = 0.7  400.0  400.0  400.0
## Number of subjects, HR = 0.8  400.0  400.0  400.0
## Expected number of events, HR = 0.7  175.4
## Expected number of events, HR = 0.8  191.5
## Cumulative number of events                67    134    200
## Analysis time, HR = 0.7          25.8   50.6   86.2
## Analysis time, HR = 0.8          24.7   47.8   80.7
## Expected study duration, HR = 0.7  73.3
## Expected study duration, HR = 0.8  76.5
## Cumulative alpha spent                    0.0003  0.0072  0.0250

```

```

## One-sided local significance level          0.0003 0.0071 0.0225
## Efficacy boundary (t)                     0.427  0.654  0.753
## Exit probability for efficacy (under H0)    0.0003 0.0069
## Exit probability for efficacy (under H1), HR = 0.7 0.0220 0.3253
## Exit probability for efficacy (under H1), HR = 0.8 0.0052 0.1172
##
## Legend:
##   HR: hazard ratio
##   (t): approximate treatment effect scale
design <- getDesignGroupSequential(sided = 2, alpha = 0.05, beta = 0.2,
  informationRates = c(0.6, 1), typeOfDesign = "asOF", twoSidedPower = FALSE)

summary(getSampleSizeSurvival(design,
  lambda2 = log(2) / 60, hazardRatio = 0.74,
  dropoutRate1 = 0.025, dropoutRate2 = 0.025, dropoutTime = 12,
  accrualTime = 0, accrualIntensity = 30,
  followUpTime = 12))

## Sample size calculation for a survival endpoint
##
## Sequential analysis with a maximum of 2 looks (group sequential design).
## The sample size was calculated for a two-sample logrank test (two-sided),
## H0: hazard ratio = 1, H1: hazard ratio = 0.74, control lambda(2) = 0.012, power 80%.
##
## Stage                1                2
## Information rate      60%              100%
## Efficacy boundary (z-value scale)      2.669              1.981
## Overall power         0.3123           0.8000
## Number of subjects    1211.4          1294.4
## Cumulative number of events            210              350
## Analysis time         40.4             55.1
## Expected study duration                50.5
## Cumulative alpha spent                 0.0076           0.0500
## Two-sided local significance level      0.0076           0.0476
## Efficacy boundary (t)                  0.692 - 1.446  0.809 - 1.236
## Exit probability for efficacy (under H0) 0.0076
## Exit probability for efficacy (under H1) 0.3123
##
## Legend:
##   (t): approximate treatment effect scale
summary(getSampleSizeSurvival(design,
  lambda2 = log(2) / 60, lambda1 = log(2) / 50,
  dropoutRate1 = 0.025, dropoutRate2 = 0.025, dropoutTime = 12,
  accrualTime = 0, accrualIntensity = 30,
  followUpTime = 12))

## Sample size calculation for a survival endpoint
##
## Sequential analysis with a maximum of 2 looks (group sequential design).
## The sample size was calculated for a two-sample logrank test (two-sided),
## H0: hazard ratio = 1, H1: treatment lambda(1) = 0.014, control lambda(2) = 0.012,
## power 80%.
##

```

```
## Stage                1                2
## Information rate      60%             100%
## Efficacy boundary (z-value scale)  2.669         1.981
## Overall power        0.3123         0.8000
## Number of subjects   1899.9         2249.7
## Cumulative number of events      572           953
## Analysis time        63.3           87.0
## Expected study duration      79.6
## Cumulative alpha spent      0.0076         0.0500
## Two-sided local significance level  0.0076         0.0476
## Efficacy boundary (t)      0.800 - 1.250  0.880 - 1.137
## Exit probability for efficacy (under H0)  0.0076
## Exit probability for efficacy (under H1)  0.3123
```

```
##
```

```
## Legend:
```

```
## (t): approximate treatment effect scale
```

```
summary(getSampleSizeSurvival(getDesignGroupSequential(kMax = 4, sided = 2)))
```

```
## Sample size calculation for a survival endpoint
```

```
##
```

```
## Sequential analysis with a maximum of 4 looks (group sequential design).
```

```
## The sample size was calculated for a two-sample logrank test (two-sided),
```

```
## H0: hazard ratio = 1, H1: treatment pi(1) as specified, control pi(2) = 0.2,
```

```
## power 80%.
```

```
##
```

```
## Stage                1                2                3                4
## Information rate      25%             50%             75%             100%
## Efficacy boundary (z-value scale)  4.579         3.238         2.644         2.289
## Overall power        0.0012         0.1494         0.5227         0.8000
## Number of subjects, pi(1) = 0.4   126.6         182.5         190.5         190.5
## Number of subjects, pi(1) = 0.5    56.9          82.6          87.5          87.5
## Number of subjects, pi(1) = 0.6    31.3          45.8          49.4          49.4
## Cumulative number of events, pi(1) = 0.4    15            29            43            57
## Cumulative number of events, pi(1) = 0.5     8            16            23            31
## Cumulative number of events, pi(1) = 0.6     5            10            15            20
## Analysis time, pi(1) = 0.4           8.0          11.5          14.6          18.0
## Analysis time, pi(1) = 0.5           7.8          11.3          14.4          18.0
## Analysis time, pi(1) = 0.6           7.6          11.1          14.2          18.0
## Expected study duration, pi(1) = 0.4    15.7
## Expected study duration, pi(1) = 0.5    15.7
## Expected study duration, pi(1) = 0.6    15.6
## Cumulative alpha spent      <0.0001         0.0012         0.0086         0.0250
## Two-sided local significance level  <0.0001         0.0012         0.0082         0.0221
## Efficacy boundary (t), pi(1) = 0.4   0.087 - 11.467  0.295 - 3.386  0.443 - 2.255  0.543 - 1.840
## Efficacy boundary (t), pi(1) = 0.5   0.035 - 28.174  0.188 - 5.308  0.329 - 3.043  0.434 - 2.304
## Efficacy boundary (t), pi(1) = 0.6   0.016 - 64.101  0.125 - 8.006  0.250 - 4.002  0.353 - 2.830
## Exit probability for efficacy (under H0)  <0.0001         0.0012         0.0074
## Exit probability for efficacy (under H1)  0.0012         0.1482         0.3733
```

```
##
```

```
## Legend:
```

```
## (t): approximate treatment effect scale
```

4 Simulation results summaries

4.1 Create two typical designs

```
design <- getDesignInverseNormal(kMax = 3, alpha = 0.025,
  futilityBounds = c(-0.5, 0), bindingFutility = FALSE,
  typeOfDesign = "WT", deltaWT = 0.25,
  informationRates = c(0.4, 0.7, 1))

designF <- getDesignFisher(kMax = 3, alpha = 0.025,
  alphaOVec = c(0.5, 0.4), bindingFutility = FALSE,
  informationRates = c(0.4, 0.7, 1))
```

4.2 Simulation results base

4.2.1 Simulation results base - means

```
summary(getSimulationMeans(design = design, plannedSubjects = c(40, 70, 100),
  groups = 1,
  alternative = seq(0,0.4,0.1),
  stDev = 1.2,
  maxNumberOfIterations = 1000,
  seed = 1234))
```

```
## Simulation of a continuous endpoint
##
## Sequential analysis with a maximum of 3 looks
## (inverse normal combination test design).
## The results were simulated for a one-sample t-test (normal approximation),
## H0: mu = 0, power directed towards larger values, H1: effect as specified,
## standard deviation = 1.2, planned cumulative sample size = c(40, 70, 100),
## simulation runs = 1000, seed = 1234.
##
## Stage                1      2      3
## Fixed weight          0.632  0.548  0.548
## Efficacy boundary (z-value scale)  2.631  2.287  2.092
## Futility boundary (z-value scale) -0.500  0.000
## Overall power, alt. = 0          0.0040  0.0110  0.0270
## Overall power, alt. = 0.1        0.0160  0.0690  0.1240
## Overall power, alt. = 0.2        0.0530  0.2030  0.3570
## Overall power, alt. = 0.3        0.1510  0.4700  0.7160
## Overall power, alt. = 0.4        0.2630  0.6960  0.9090
## Expected number of subjects, alt. = 0          73.8
## Expected number of subjects, alt. = 0.1        84.8
## Expected number of subjects, alt. = 0.2        86.9
## Expected number of subjects, alt. = 0.3        80.0
## Expected number of subjects, alt. = 0.4        71.0
## Stagewise number of subjects, alt. = 0          40.0  30.0  30.0
## Stagewise number of subjects, alt. = 0.1        40.0  30.0  30.0
## Stagewise number of subjects, alt. = 0.2        40.0  30.0  30.0
## Stagewise number of subjects, alt. = 0.3        40.0  30.0  30.0
## Stagewise number of subjects, alt. = 0.4        40.0  30.0  30.0
## Exit probability for futility, alt. = 0          0.3200  0.2170
## Exit probability for futility, alt. = 0.1        0.1490  0.1220
```

```

## Exit probability for futility, alt. = 0.2 0.0700 0.0420
## Exit probability for futility, alt. = 0.3 0.0160 0.0120
## Exit probability for futility, alt. = 0.4 0.0030 0.0010
## Conditional power (achieved), alt. = 0          0.0839 0.0958
## Conditional power (achieved), alt. = 0.1        0.1438 0.1542
## Conditional power (achieved), alt. = 0.2        0.2534 0.2595
## Conditional power (achieved), alt. = 0.3        0.3835 0.3894
## Conditional power (achieved), alt. = 0.4        0.4744 0.4814
##
## Legend:
## alt.: alternative
summary(getSimulationMeans(design = design, plannedSubjects = c(40,70,100),
  alternative = seq(0,0.8,0.2),
  stDev = 1.2,
  allocationRatioPlanned = 2,
  maxNumberOfIterations = 1000,
  seed = 1234))

## Simulation of a continuous endpoint
##
## Sequential analysis with a maximum of 3 looks
## (inverse normal combination test design).
## The results were simulated for a two-sample t-test (normal approximation),
## H0:  $\mu(1) - \mu(2) = 0$ , power directed towards larger values,
## H1: effect as specified, standard deviation = 1.2,
## planned cumulative sample size = c(40, 70, 100), planned allocation ratio = 2,
## simulation runs = 1000, seed = 1234.
##
## Stage                1          2          3
## Fixed weight          0.632    0.548    0.548
## Efficacy boundary (z-value scale)  2.631    2.287    2.092
## Futility boundary (z-value scale) -0.500    0.000
## Overall power, alt. = 0          0.0040 0.0110 0.0270
## Overall power, alt. = 0.2        0.0140 0.0630 0.1190
## Overall power, alt. = 0.4        0.0420 0.1840 0.3290
## Overall power, alt. = 0.6        0.1310 0.4030 0.6500
## Overall power, alt. = 0.8        0.2310 0.6520 0.8660
## Expected number of subjects, alt. = 0          73.8
## Expected number of subjects, alt. = 0.2        84.8
## Expected number of subjects, alt. = 0.4        87.4
## Expected number of subjects, alt. = 0.6        82.2
## Expected number of subjects, alt. = 0.8        73.1
## Stagewise number of subjects, alt. = 0          40.0    30.0    30.0
## Stagewise number of subjects, alt. = 0.2        40.0    30.0    30.0
## Stagewise number of subjects, alt. = 0.4        40.0    30.0    30.0
## Stagewise number of subjects, alt. = 0.6        40.0    30.0    30.0
## Stagewise number of subjects, alt. = 0.8        40.0    30.0    30.0
## Exit probability for futility, alt. = 0    0.3200 0.2170
## Exit probability for futility, alt. = 0.2    0.1470 0.1370
## Exit probability for futility, alt. = 0.4    0.0720 0.0500
## Exit probability for futility, alt. = 0.6    0.0220 0.0140
## Exit probability for futility, alt. = 0.8    0.0060 0.0020
## Conditional power (achieved), alt. = 0          0.0839 0.0958
## Conditional power (achieved), alt. = 0.2        0.1366 0.1441

```



```

## Conditional power (achieved), alt. = 0.4          0.2398 0.2430
## Conditional power (achieved), alt. = 0.6          0.3535 0.3723
## Conditional power (achieved), alt. = 0.8          0.4506 0.4427
##
## Legend:
## alt.: alternative
summary(getSimulationMeans(design = design, plannedSubjects = c(40,70,100),
  alternative = seq(0,0.8,0.2),
  stDev = 1.2,
  conditionalPower = 0.8,
  minNumberOfSubjectsPerStage = c(40,20,20),
  maxNumberOfSubjectsPerStage = c(40,100,100),
  maxNumberOfIterations = 1000,
  seed = 1234))

## Simulation of a continuous endpoint
##
## Sequential analysis with a maximum of 3 looks
## (inverse normal combination test design).
## The results were simulated for a two-sample t-test (normal approximation),
## H0:  $\mu(1) - \mu(2) = 0$ , power directed towards larger values,
## H1: effect as specified, standard deviation = 1.2,
## planned cumulative sample size = c(40, 70, 100),
## sample size reassessment: conditional power = 0.8,
## minimum subjects per stage = c(40, 20, 20),
## maximum subjects per stage = c(40, 100, 100), simulation runs = 1000, seed = 1234.
##
## Stage                1          2          3
## Fixed weight                0.632  0.548  0.548
## Efficacy boundary (z-value scale)  2.631  2.287  2.092
## Futility boundary (z-value scale) -0.500  0.000
## Overall power, alt. = 0          0.0040 0.0110 0.0270
## Overall power, alt. = 0.2        0.0200 0.0890 0.2120
## Overall power, alt. = 0.4        0.0420 0.2760 0.6120
## Overall power, alt. = 0.6        0.1340 0.6420 0.9150
## Overall power, alt. = 0.8        0.2780 0.8780 0.9870
## Expected number of subjects, alt. = 0    149.5
## Expected number of subjects, alt. = 0.2  183.7
## Expected number of subjects, alt. = 0.4  172.7
## Expected number of subjects, alt. = 0.6  128.1
## Expected number of subjects, alt. = 0.8   94.7
## Stagewise number of subjects, alt. = 0    40.0  96.3  98.3
## Stagewise number of subjects, alt. = 0.2  40.0  93.5  96.4
## Stagewise number of subjects, alt. = 0.4  40.0  85.2  87.4
## Stagewise number of subjects, alt. = 0.6  40.0  74.8  74.0
## Stagewise number of subjects, alt. = 0.8  40.0  65.6  64.0
## Exit probability for futility, alt. = 0   0.3200 0.2170
## Exit probability for futility, alt. = 0.2 0.1470 0.0810
## Exit probability for futility, alt. = 0.4 0.0650 0.0110
## Exit probability for futility, alt. = 0.6 0.0210 0
## Exit probability for futility, alt. = 0.8 0.0040 0
## Conditional power (achieved), alt. = 0          0.1486 0.1281
## Conditional power (achieved), alt. = 0.2        0.2464 0.2557
## Conditional power (achieved), alt. = 0.4        0.3542 0.4626

```

```

## Conditional power (achieved), alt. = 0.6          0.5218 0.6472
## Conditional power (achieved), alt. = 0.8          0.6118 0.7064
##
## Legend:
## alt.: alternative

summary(getSimulationMeans(design = design, plannedSubjects = c(40,70,100),
  alternative = seq(0,0.8,0.2),
  stDev = 1.2,
  conditionalPower = 0.8,
  minNumberOfSubjectsPerStage = c(40,20,20),
  maxNumberOfSubjectsPerStage = c(40,100,100),
  thetaH1 = 0.6, stDevH1 = 1.5,
  maxNumberOfIterations = 1000,
  seed = 1234))

## Simulation of a continuous endpoint
##
## Sequential analysis with a maximum of 3 looks
## (inverse normal combination test design).
## The results were simulated for a two-sample t-test (normal approximation),
## H0:  $\mu(1) - \mu(2) = 0$ , power directed towards larger values,
## H1: effect as specified, standard deviation = 1.2,
## planned cumulative sample size = c(40, 70, 100),
## sample size reassessment: conditional power = 0.8,
## minimum subjects per stage = c(40, 20, 20),
## maximum subjects per stage = c(40, 100, 100), theta H1 = 0.6,
## standard deviation H1 = 1.5, simulation runs = 1000, seed = 1234.
##
## Stage                1          2          3
## Fixed weight          0.632    0.548    0.548
## Efficacy boundary (z-value scale)  2.631    2.287    2.092
## Futility boundary (z-value scale) -0.500    0.000
## Overall power, alt. = 0          0.0040    0.0110    0.0270
## Overall power, alt. = 0.2        0.0190    0.0960    0.2090
## Overall power, alt. = 0.4        0.0390    0.3250    0.6260
## Overall power, alt. = 0.6        0.1330    0.7100    0.9300
## Overall power, alt. = 0.8        0.2830    0.9320    0.9930
## Expected number of subjects, alt. = 0      151.5
## Expected number of subjects, alt. = 0.2    186.1
## Expected number of subjects, alt. = 0.4    179.3
## Expected number of subjects, alt. = 0.6    139.1
## Expected number of subjects, alt. = 0.8    108.2
## Stagewise number of subjects, alt. = 0     40.0    99.3    98.1
## Stagewise number of subjects, alt. = 0.2   40.0    98.6    95.0
## Stagewise number of subjects, alt. = 0.4   40.0    96.8    86.6
## Stagewise number of subjects, alt. = 0.6   40.0    93.5    75.7
## Stagewise number of subjects, alt. = 0.8   40.0    88.9    73.3
## Exit probability for futility, alt. = 0    0.3200    0.2170
## Exit probability for futility, alt. = 0.2  0.1500    0.0790
## Exit probability for futility, alt. = 0.4  0.0610    0.0110
## Exit probability for futility, alt. = 0.6  0.0230     0
## Exit probability for futility, alt. = 0.8  0.0030     0
## Conditional power (achieved), alt. = 0          0.2206    0.3011
## Conditional power (achieved), alt. = 0.2        0.3112    0.4507

```

```
## Conditional power (achieved), alt. = 0.4      0.4009 0.5970
## Conditional power (achieved), alt. = 0.6      0.5292 0.7151
## Conditional power (achieved), alt. = 0.8      0.6066 0.7396
##
## Legend:
## alt.: alternative
```

4.2.2 Simulation results base - rates

```
summary(getSimulationRates(design = designF, plannedSubjects = c(40,70,100),
  groups = 1,
  thetaH0 = 0.2,
  pi1 = seq(0.05,0.2,0.05),
  directionUpper = FALSE,
  maxNumberOfIterations = 1000,
  seed = 1234))
```

```
## Simulation of a binary endpoint
##
## Sequential analysis with a maximum of 3 looks (Fisher's combination test design).
## The results were simulated for a one-sample test for rates (normal approximation),
## H0: pi = 0.2, power directed towards smaller values,
## H1: treatment rate pi as specified, simulation runs = 1000, seed = 1234.
##
## Stage                1      2      3
## Fixed weight          1    0.866  0.866
## Efficacy boundary (p product scale)  0.013187 0.002705 0.000641
## Futility boundary (separate p-value scale)  0.500    0.400
## Overall power, pi(1) = 0.05      0.6790  0.9040  0.9780
## Overall power, pi(1) = 0.1       0.2150  0.3760  0.5540
## Overall power, pi(1) = 0.15      0.0390  0.0670  0.1070
## Overall power, pi(1) = 0.2       0.0090  0.0100  0.0110
## Expected number of subjects, pi(1) = 0.05    52.4
## Expected number of subjects, pi(1) = 0.1     78.0
## Expected number of subjects, pi(1) = 0.15    76.9
## Expected number of subjects, pi(1) = 0.2     58.0
## Stagewise number of subjects, pi(1) = 0.05   40.0    30.0    30.0
## Stagewise number of subjects, pi(1) = 0.1   40.0    30.0    30.0
## Stagewise number of subjects, pi(1) = 0.15  40.0    30.0    30.0
## Stagewise number of subjects, pi(1) = 0.2   40.0    30.0    30.0
## Exit probability for futility, pi(1) = 0.05  0.0010  0.0020
## Exit probability for futility, pi(1) = 0.1   0.0410  0.0600
## Exit probability for futility, pi(1) = 0.15  0.2250  0.2150
## Exit probability for futility, pi(1) = 0.2   0.5680  0.2440
## Conditional power (achieved), pi(1) = 0.05      0.4489  0.5698
## Conditional power (achieved), pi(1) = 0.1       0.2752  0.3434
## Conditional power (achieved), pi(1) = 0.15      0.1405  0.1871
## Conditional power (achieved), pi(1) = 0.2       0.0820  0.0932
```

```
summary(getSimulationRates(design = designF, plannedSubjects = c(40,70,100),
  thetaH0 = -0.2,
  pi1 = seq(0.05,0.2,0.05),
  pi2 = 0.4,
  allocationRatioPlanned = 2,
```

```
directionUpper = FALSE,
maxNumberOfIterations = 1000,
seed = 1234))
```

```
## Simulation of a binary endpoint
##
## Sequential analysis with a maximum of 3 looks (Fisher's combination test design).
## The results were simulated for a two-sample test for rates (normal approximation),
## H0:  $\pi(1) - \pi(2) = -0.2$ , power directed towards smaller values,
## H1: treatment rate  $\pi(1)$  as specified, control rate  $\pi(2) = 0.4$ ,
## planned cumulative sample size = c(40, 70, 100), planned allocation ratio = 2,
## simulation runs = 1000, seed = 1234.
##
## Stage                1          2          3
## Fixed weight                1    0.866    0.866
## Efficacy boundary (p product scale)    0.013187 0.002705 0.000641
## Futility boundary (separate p-value scale)    0.500    0.400
## Overall power,  $\pi(1) = 0.05$             0.1780    0.2890    0.3760
## Overall power,  $\pi(1) = 0.1$              0.0810    0.1270    0.1740
## Overall power,  $\pi(1) = 0.15$            0.0320    0.0570    0.0710
## Overall power,  $\pi(1) = 0.2$             0.0110    0.0150    0.0180
## Expected number of subjects,  $\pi(1) = 0.05$     71.2
## Expected number of subjects,  $\pi(1) = 0.1$     70.6
## Expected number of subjects,  $\pi(1) = 0.15$     66.2
## Expected number of subjects,  $\pi(1) = 0.2$     61.2
## Stagewise number of subjects,  $\pi(1) = 0.05$     40.0    30.0    30.0
## Stagewise number of subjects,  $\pi(1) = 0.1$     40.0    30.0    30.0
## Stagewise number of subjects,  $\pi(1) = 0.15$     40.0    30.0    30.0
## Stagewise number of subjects,  $\pi(1) = 0.2$     40.0    30.0    30.0
## Exit probability for futility,  $\pi(1) = 0.05$     0.1720    0.1490
## Exit probability for futility,  $\pi(1) = 0.1$     0.2670    0.2370
## Exit probability for futility,  $\pi(1) = 0.15$     0.4000    0.2370
## Exit probability for futility,  $\pi(1) = 0.2$     0.4910    0.2860
## Conditional power (achieved),  $\pi(1) = 0.05$                 0.2199    0.2413
## Conditional power (achieved),  $\pi(1) = 0.1$                 0.1698    0.1753
## Conditional power (achieved),  $\pi(1) = 0.15$                 0.1274    0.1280
## Conditional power (achieved),  $\pi(1) = 0.2$                 0.0988    0.1051
```

```
summary(getSimulationRates(design = designF, plannedSubjects = c(40,70,100),
  thetaH0 = -0.2,
  pi1 = seq(0.05,0.2,0.05),
  pi2 = 0.4,
  allocationRatioPlanned = 2,
  directionUpper = FALSE,
  conditionalPower = 0.8,
  minNumberOfSubjectsPerStage = c(40,20,20),
  maxNumberOfSubjectsPerStage = c(40,100,100),
  maxNumberOfIterations = 1000,
  seed = 1234))
```

```
## Simulation of a binary endpoint
##
## Sequential analysis with a maximum of 3 looks (Fisher's combination test design).
## The results were simulated for a two-sample test for rates (normal approximation),
## H0:  $\pi(1) - \pi(2) = -0.2$ , power directed towards smaller values,
```

```

## H1: treatment rate pi(1) as specified, control rate pi(2) = 0.4,
## planned cumulative sample size = c(40, 70, 100), planned allocation ratio = 2,
## sample size reassessment: conditional power = 0.8,
## minimum subjects per stage = c(40, 20, 20),
## maximum subjects per stage = c(40, 100, 100), simulation runs = 1000, seed = 1234.
##
## Stage                1          2          3
## Fixed weight                1    0.866    0.866
## Efficacy boundary (p product scale)    0.013187 0.002705 0.000641
## Futility boundary (separate p-value scale)    0.500    0.400
## Overall power, pi(1) = 0.05            0.1750    0.4100    0.5860
## Overall power, pi(1) = 0.1            0.0760    0.1590    0.2500
## Overall power, pi(1) = 0.15          0.0340    0.0640    0.0820
## Overall power, pi(1) = 0.2            0.0110    0.0140    0.0160
## Expected number of subjects, pi(1) = 0.05    136.0
## Expected number of subjects, pi(1) = 0.1    138.2
## Expected number of subjects, pi(1) = 0.15    127.2
## Expected number of subjects, pi(1) = 0.2    106.7
## Stagewise number of subjects, pi(1) = 0.05    40.0    92.5    98.4
## Stagewise number of subjects, pi(1) = 0.1    40.0    93.4    97.8
## Stagewise number of subjects, pi(1) = 0.15    40.0    96.1    99.5
## Stagewise number of subjects, pi(1) = 0.2    40.0    96.8    99.7
## Exit probability for futility, pi(1) = 0.05    0.1760    0.0490
## Exit probability for futility, pi(1) = 0.1    0.2850    0.1620
## Exit probability for futility, pi(1) = 0.15    0.4010    0.2050
## Exit probability for futility, pi(1) = 0.2    0.4960    0.3000
## Conditional power (achieved), pi(1) = 0.05                0.4075    0.3830
## Conditional power (achieved), pi(1) = 0.1                0.3286    0.2884
## Conditional power (achieved), pi(1) = 0.15              0.2713    0.2133
## Conditional power (achieved), pi(1) = 0.2                0.2090    0.1542

```

```

summary(getSimulationRates(design = designF, plannedSubjects = c(40,70,100),
  thetaH0 = -0.2,
  pi1 = seq(0.05,0.2,0.05),
  pi2 = 0.4,
  allocationRatioPlanned = 2,
  directionUpper = FALSE,
  conditionalPower = 0.8,
  minNumberOfSubjectsPerStage = c(40,20,20),
  maxNumberOfSubjectsPerStage = c(40,100,100),
  pi1H1 = 0.1, pi2H1 = 0.4,
  maxNumberOfIterations = 1000,
  seed = 1234))

```

```

## Simulation of a binary endpoint
##
## Sequential analysis with a maximum of 3 looks (Fisher's combination test design).
## The results were simulated for a two-sample test for rates (normal approximation),
## H0: pi(1) - pi(2) = -0.2, power directed towards smaller values,
## H1: treatment rate pi(1) as specified, control rate pi(2) = 0.4,
## planned cumulative sample size = c(40, 70, 100), planned allocation ratio = 2,
## sample size reassessment: conditional power = 0.8,
## minimum subjects per stage = c(40, 20, 20),
## maximum subjects per stage = c(40, 100, 100), pi(treatment)H1 = 0.1,
## pi(control)H1 = 0.4, simulation runs = 1000, seed = 1234.

```

```

##
## Stage                1          2          3
## Fixed weight         1      0.866    0.866
## Efficacy boundary (p product scale) 0.013187 0.002705 0.000641
## Futility boundary (separate p-value scale) 0.500    0.400
## Overall power, pi(1) = 0.05      0.1730    0.4190    0.5920
## Overall power, pi(1) = 0.1      0.0770    0.1750    0.2690
## Overall power, pi(1) = 0.15     0.0320    0.0620    0.0820
## Overall power, pi(1) = 0.2      0.0110    0.0150    0.0170
## Expected number of subjects, pi(1) = 0.05 141.1
## Expected number of subjects, pi(1) = 0.1 141.7
## Expected number of subjects, pi(1) = 0.15 130.9
## Expected number of subjects, pi(1) = 0.2 108.6
## Stagewise number of subjects, pi(1) = 0.05 40.0    100.0    100.0
## Stagewise number of subjects, pi(1) = 0.1 40.0    100.0    100.0
## Stagewise number of subjects, pi(1) = 0.15 40.0    100.0    100.0
## Stagewise number of subjects, pi(1) = 0.2 40.0    100.0    100.0
## Exit probability for futility, pi(1) = 0.05 0.1760    0.0450
## Exit probability for futility, pi(1) = 0.1 0.2950    0.1410
## Exit probability for futility, pi(1) = 0.15 0.3970    0.2030
## Exit probability for futility, pi(1) = 0.2 0.4940    0.3000
## Conditional power (achieved), pi(1) = 0.05      0.1821    0.2480
## Conditional power (achieved), pi(1) = 0.1      0.1563    0.2001
## Conditional power (achieved), pi(1) = 0.15     0.1330    0.1666
## Conditional power (achieved), pi(1) = 0.2      0.1162    0.1309

```

4.2.3 Simulation results base - survival

```

design <- getDesignInverseNormal(alpha = 0.05, kMax = 4, futilityBounds = c(0,0,0),
  sided = 1, typeOfDesign = "WT", deltaWT = 0.1)

summary(getSimulationSurvival(design,
  lambda2 = log(2) / 60, lambda1 = c(log(2) / 80),
  plannedEvents = c(50, 100, 150, 200),
  maxNumberOfSubjects = 400,
  directionUpper = FALSE,
  maxNumberOfIterations = 1000,
  seed = 1234), digits = 0)

## Simulation of a survival endpoint
##
## Sequential analysis with a maximum of 4 looks
## (inverse normal combination test design).
## The results were simulated for a two-sample logrank test,
## H0: hazard ratio = 1, power directed towards smaller values,
## H1: treatment lambda(1) = 0.009, control lambda(2) = 0.012,
## planned cumulative events = c(50, 100, 150, 200), maximum number of subjects = 400,
## simulation runs = 1000, seed = 1234.
##
## Stage                1          2          3          4
## Fixed weight         0.5      0.5      0.5      0.5
## Efficacy boundary (z-value scale) 3.069    2.326    1.978    1.763
## Futility boundary (z-value scale) 0.000    0.000    0.000
## Overall power        0.0240    0.2260    0.4550    0.6190

```

```
## Expected number of subjects      400.0
## Number of subjects               400.0 400.0 400.0 400.0
## Exit probability for futility     0.1230 0.0210 0.0070
## Expected number of events        143.9
## Cumulative number of events       50    100    150    200
## Analysis time                     19.30 34.51 52.73 74.94
## Expected study duration           52.52
## Conditional power (achieved)      0.3355 0.3758 0.3823
```

```
summary(getSimulationSurvival(design,
  median2 = 60, median1 = 80,
  plannedEvents = c(50, 100, 150, 200),
  maxNumberOfSubjects = 400,
  directionUpper = FALSE,
  maxNumberOfIterations = 1000,
  seed = 1234))
```

```
## Simulation of a survival endpoint
##
## Sequential analysis with a maximum of 4 looks
## (inverse normal combination test design).
## The results were simulated for a two-sample logrank test,
## H0: hazard ratio = 1, power directed towards smaller values,
## H1: treatment median(1) = 80, control median(2) = 60,
## planned cumulative events = c(50, 100, 150, 200), maximum number of subjects = 400,
## simulation runs = 1000, seed = 1234.
```

```
##
## Stage                1        2        3        4
## Fixed weight          0.5      0.5      0.5      0.5
## Efficacy boundary (z-value scale) 3.069 2.326 1.978 1.763
## Futility boundary (z-value scale) 0      0      0
## Overall power         0.0240 0.2260 0.4550 0.6190
## Expected number of subjects      400.0
## Number of subjects             400.0 400.0 400.0 400.0
## Exit probability for futility     0.1230 0.0210 0.0070
## Expected number of events        143.9
## Cumulative number of events       50    100    150    200
## Analysis time               19.3    34.5    52.7    74.9
## Expected study duration         52.5
## Conditional power (achieved)      0.3355 0.3758 0.3823
```

```
summary(getSimulationSurvival(design,
  median2 = 60, median1 = c(50, 80),
  plannedEvents = c(50, 100, 150, 200),
  maxNumberOfSubjects = 400,
  directionUpper = FALSE,
  maxNumberOfIterations = 1000,
  seed = 1234))
```

```
## Simulation of a survival endpoint
##
## Sequential analysis with a maximum of 4 looks
## (inverse normal combination test design).
## The results were simulated for a two-sample logrank test,
## H0: hazard ratio = 1, power directed towards smaller values,
## H1: treatment median(1) as specified, control median(2) = 60,
```

```

## planned cumulative events = c(50, 100, 150, 200), maximum number of subjects = 400,
## simulation runs = 1000, seed = 1234.
##
## Stage                1      2      3      4
## Fixed weight        0.5    0.5    0.5    0.5
## Efficacy boundary (z-value scale)  3.069  2.326  1.978  1.763
## Futility boundary (z-value scale)  0      0      0
## Overall power, median(1) = 50      0 0.0020 0.0030 0.0040
## Overall power, median(1) = 80      0.0180 0.1770 0.4000 0.5810
## Expected number of subjects, median(1) = 50  400.0
## Expected number of subjects, median(1) = 80  400.0
## Number of subjects, median(1) = 50      400.0  400.0  400.0  400.0
## Number of subjects, median(1) = 80      400.0  400.0  400.0  400.0
## Exit probability for futility, median(1) = 50 0.7130 0.1380 0.0640
## Exit probability for futility, median(1) = 80 0.1480 0.0280 0.0060
## Expected number of events, median(1) = 50   75.8
## Expected number of events, median(1) = 80  145.0
## Cumulative number of events, median(1) = 50   50    100   150   200
## Cumulative number of events, median(1) = 80   50    100   150   200
## Analysis time, median(1) = 50      16.6   28.7   43.3   60.1
## Analysis time, median(1) = 80      19.3   34.6   52.8   74.6
## Expected study duration, median(1) = 50     23.6
## Expected study duration, median(1) = 80     53.0
## Conditional power (achieved), median(1) = 50      0.0734 0.0778 0.0476
## Conditional power (achieved), median(1) = 80      0.3216 0.3587 0.3803

```

```

summary(getSimulationSurvival(design,
  lambda2 = log(2) / 60, hazardRatio = c(1.2, 1.4),
  plannedEvents = c(50, 100, 150, 200),
  maxNumberOfSubjects = 400,
  directionUpper = FALSE,
  maxNumberOfIterations = 1000,
  seed = 1234))

```

```

## Simulation of a survival endpoint
##
## Sequential analysis with a maximum of 4 looks
## (inverse normal combination test design).
## The results were simulated for a two-sample logrank test,
## H0: hazard ratio = 1, power directed towards smaller values,
## H1: hazard ratio as specified, control lambda(2) = 0.012,
## planned cumulative events = c(50, 100, 150, 200), maximum number of subjects = 400,
## simulation runs = 1000, seed = 1234.
##
## Stage                1      2      3      4
## Fixed weight        0.5    0.5    0.5    0.5
## Efficacy boundary (z-value scale)  3.069  2.326  1.978  1.763
## Futility boundary (z-value scale)  0      0      0
## Overall power, HR = 1.2      0 0.0020 0.0030 0.0040
## Overall power, HR = 1.4      0      0      0      0
## Expected number of subjects, HR = 1.2  400.0
## Expected number of subjects, HR = 1.4  400.0
## Number of subjects, HR = 1.2      400.0  400.0  400.0  400.0
## Number of subjects, HR = 1.4      400.0  400.0  400.0  400.0
## Exit probability for futility, HR = 1.2 0.7130 0.1380 0.0640

```



```

## Exit probability for futility, HR = 1.4 0.8820 0.0850 0.0250
## Expected number of events, HR = 1.2      75.8
## Expected number of events, HR = 1.4      58.0
## Cumulative number of events, HR = 1.2     50    100    150    200
## Cumulative number of events, HR = 1.4     50    100    150    200
## Analysis time, HR = 1.2                   16.6   28.7   43.3   60.1
## Analysis time, HR = 1.4                   15.8   26.7   40.0   56.5
## Expected study duration, HR = 1.2         23.6
## Expected study duration, HR = 1.4         17.6
## Conditional power (achieved), HR = 1.2    0.0734 0.0778 0.0476
## Conditional power (achieved), HR = 1.4    0.0326 0.0315 0.0102

```

```
##
```

```
## Legend:
```

```
## HR: hazard ratio
```

```

summary(getSimulationSurvival(design,
  lambda2 = log(2) / 60, hazardRatio = c(1.2, 1.4),
  plannedEvents = c(50, 100, 150, 200),
  maxNumberOfSubjects = 400,
  directionUpper = FALSE,
  allocation1 = 1, allocation2 = 2,
  maxNumberOfIterations = 1000,
  seed = 1234))

```

```
## Simulation of a survival endpoint
```

```
##
```

```
## Sequential analysis with a maximum of 4 looks
```

```
## (inverse normal combination test design).
```

```
## The results were simulated for a two-sample logrank test,
```

```
## H0: hazard ratio = 1, power directed towards smaller values,
```

```
## H1: hazard ratio as specified, control lambda(2) = 0.012,
```

```
## planned cumulative events = c(50, 100, 150, 200), planned allocation ratio = 0.5,
```

```
## maximum number of subjects = 400, simulation runs = 1000, seed = 1234.
```

```
##
```

```

## Stage          1      2      3      4
## Fixed weight    0.5    0.5    0.5    0.5
## Efficacy boundary (z-value scale)  3.069  2.326  1.978  1.763
## Futility boundary (z-value scale)    0      0      0
## Overall power, HR = 1.2              0      0      0  0.0010
## Overall power, HR = 1.4              0      0      0      0
## Expected number of subjects, HR = 1.2  400.0
## Expected number of subjects, HR = 1.4  400.0
## Number of subjects, HR = 1.2          400.0  400.0  400.0  400.0
## Number of subjects, HR = 1.4          400.0  400.0  400.0  400.0
## Exit probability for futility, HR = 1.2 0.7500 0.1330 0.0440
## Exit probability for futility, HR = 1.4 0.8910 0.0740 0.0240
## Expected number of events, HR = 1.2    72.0
## Expected number of events, HR = 1.4    57.8
## Cumulative number of events, HR = 1.2   50    100    150    200
## Cumulative number of events, HR = 1.4   50    100    150    200
## Analysis time, HR = 1.2                 16.9   29.3   44.2   62.1
## Analysis time, HR = 1.4                 16.3   27.8   41.8   58.6
## Expected study duration, HR = 1.2       23.0
## Expected study duration, HR = 1.4       18.3
## Conditional power (achieved), HR = 1.2  0.0840 0.1031 0.0860

```

```
## Conditional power (achieved), HR = 1.4          0.0682 0.0395 0.0297
##
## Legend:
##   HR: hazard ratio
```

```
summary(getSimulationSurvival(design = design,
  plannedEvents = c(40,70,100,150),
  maxNumberOfSubjects = 400,
  thetaH0 = 1.2,
  pi1 = seq(0.1,0.25,0.05),
  pi2 = 0.2,
  allocation1 = 2,
  directionUpper = FALSE,
  maxNumberOfIterations = 1000,
  seed = 1234))
```

```
## Simulation of a survival endpoint
##
## Sequential analysis with a maximum of 4 looks
## (inverse normal combination test design).
## The results were simulated for a two-sample logrank test,
## H0: hazard ratio = 1.2, power directed towards smaller values,
## H1: treatment pi(1) as specified, control pi(2) = 0.2,
## planned cumulative events = c(40, 70, 100, 150), planned allocation ratio = 2,
## maximum number of subjects = 400, simulation runs = 1000, seed = 1234.
##
## Stage                1         2         3         4
## Fixed weight          0.5       0.5       0.5       0.5
## Efficacy boundary (z-value scale)  3.069  2.326  1.978  1.763
## Futility boundary (z-value scale)    0         0         0
## Overall power, pi(1) = 0.1          0.4690 0.9460 0.9940 0.9990
## Overall power, pi(1) = 0.15         0.0740 0.4420 0.7090 0.8610
## Overall power, pi(1) = 0.2          0.0060 0.0620 0.1560 0.2520
## Overall power, pi(1) = 0.25         0 0.0080 0.0200 0.0250
## Expected number of subjects, pi(1) = 0.1    399.9
## Expected number of subjects, pi(1) = 0.15    399.7
## Expected number of subjects, pi(1) = 0.2    395.2
## Expected number of subjects, pi(1) = 0.25    377.4
## Number of subjects, pi(1) = 0.1          399.8  400.0  400.0  400.0
## Number of subjects, pi(1) = 0.15         397.2  400.0  400.0  400.0
## Number of subjects, pi(1) = 0.2          383.0  400.0  400.0  400.0
## Number of subjects, pi(1) = 0.25         359.2  400.0  400.0  400.0
## Exit probability for futility, pi(1) = 0.1  0.0010    0    0
## Exit probability for futility, pi(1) = 0.15 0.0420 0.0070 0.0020
## Exit probability for futility, pi(1) = 0.2  0.2750 0.0790 0.0330
## Exit probability for futility, pi(1) = 0.25 0.5540 0.1320 0.0750
## Expected number of events, pi(1) = 0.1     57.7
## Expected number of events, pi(1) = 0.15    93.8
## Expected number of events, pi(1) = 0.2    101.9
## Expected number of events, pi(1) = 0.25    73.5
## Cumulative number of events, pi(1) = 0.1    40     70    100    150
## Cumulative number of events, pi(1) = 0.15    40     70    100    150
## Cumulative number of events, pi(1) = 0.2    40     70    100    150
## Cumulative number of events, pi(1) = 0.25    40     70    100    150
## Analysis time, pi(1) = 0.1          14.9   22.1   30.0   46.5
```

```
## Analysis time, pi(1) = 0.15      13.1  18.8  25.0  37.1
## Analysis time, pi(1) = 0.2      11.7  16.4  21.5  31.4
## Analysis time, pi(1) = 0.25     10.8  14.9  19.2  27.6
## Expected study duration, pi(1) = 0.1      19.2
## Expected study duration, pi(1) = 0.15     24.2
## Expected study duration, pi(1) = 0.2      22.6
## Expected study duration, pi(1) = 0.25     15.7
## Conditional power (achieved), pi(1) = 0.1      0.7311 0.6144 0.6388
## Conditional power (achieved), pi(1) = 0.15     0.4014 0.4159 0.4513
## Conditional power (achieved), pi(1) = 0.2      0.1930 0.2203 0.3010
## Conditional power (achieved), pi(1) = 0.25     0.0997 0.1140 0.1443
```

```
summary(getSimulationSurvival(design = design,
  plannedEvents = c(40,70,100,150),
  maxNumberOfSubjects = 600,
  thetaH0 = 1.2,
  pi1 = seq(0.1,0.25,0.05),
  pi2 = 0.2,
  allocation1 = 2,
  directionUpper = FALSE,
  conditionalPower = 0.8,
  minNumberOfEventsPerStage = c(40,20,20,20),
  maxNumberOfEventsPerStage = c(40,100,100,100),
  maxNumberOfIterations = 1000,
  seed = 1234))
```

```
## Simulation of a survival endpoint
##
## Sequential analysis with a maximum of 4 looks
## (inverse normal combination test design).
## The results were simulated for a two-sample logrank test,
## H0: hazard ratio = 1.2, power directed towards smaller values,
## H1: treatment pi(1) as specified, control pi(2) = 0.2,
## planned cumulative events = c(40, 70, 100, 150), planned allocation ratio = 2,
## sample size reassessment: conditional power = 0.8,
## minimum events per stage = c(40, 20, 20, 20),
## maximum events per stage = c(40, 100, 100, 100), maximum number of subjects = 600,
## simulation runs = 1000, seed = 1234.
##
## Stage          1      2      3      4
## Fixed weight      0.5    0.5    0.5    0.5
## Efficacy boundary (z-value scale)  3.069  2.326  1.978  1.763
## Futility boundary (z-value scale)    0      0      0
## Overall power, pi(1) = 0.1      0.4490 0.9760 0.9980 0.9980
## Overall power, pi(1) = 0.15     0.0720 0.5670 0.8670 0.9290
## Overall power, pi(1) = 0.2      0.0110 0.0830 0.2190 0.3670
## Overall power, pi(1) = 0.25     0.0010 0.0010 0.0090 0.0210
## Expected number of subjects, pi(1) = 0.1      589.6
## Expected number of subjects, pi(1) = 0.15     589.5
## Expected number of subjects, pi(1) = 0.2      564.3
## Expected number of subjects, pi(1) = 0.25     508.1
## Number of subjects, pi(1) = 0.1      576.9  600.0  600.0
## Number of subjects, pi(1) = 0.15     522.5  599.6  600.0  600.0
## Number of subjects, pi(1) = 0.2      474.5  598.5  600.0  600.0
## Number of subjects, pi(1) = 0.25     434.7  598.3  600.0  600.0
```

```

## Exit probability for futility, pi(1) = 0.1 0.0020      0      0
## Exit probability for futility, pi(1) = 0.15 0.0610 0.0010      0
## Exit probability for futility, pi(1) = 0.2 0.2720 0.0520 0.0080
## Exit probability for futility, pi(1) = 0.25 0.5530 0.1760 0.0780
## Expected number of events, pi(1) = 0.1      65.6
## Expected number of events, pi(1) = 0.15     132.8
## Expected number of events, pi(1) = 0.2     200.6
## Expected number of events, pi(1) = 0.25     126.9
## Cumulative number of events, pi(1) = 0.1      40      85      125      125
## Cumulative number of events, pi(1) = 0.15     40      111     181     261
## Cumulative number of events, pi(1) = 0.2     40      129     219     316
## Cumulative number of events, pi(1) = 0.25     40      136     233     331
## Analysis time, pi(1) = 0.1      11.8    19.1    22.4
## Analysis time, pi(1) = 0.15     10.5    19.7    30.7    45.2
## Analysis time, pi(1) = 0.2       9.5    19.1    30.8    47.8
## Analysis time, pi(1) = 0.25      8.7    17.6    28.0    41.9
## Expected study duration, pi(1) = 0.1      16.0
## Expected study duration, pi(1) = 0.15     23.4
## Expected study duration, pi(1) = 0.2     30.6
## Expected study duration, pi(1) = 0.25     18.2
## Conditional power (achieved), pi(1) = 0.1      0.7901 0.8140
## Conditional power (achieved), pi(1) = 0.15     0.5511 0.6627 0.6403
## Conditional power (achieved), pi(1) = 0.2     0.3192 0.3477 0.3627
## Conditional power (achieved), pi(1) = 0.25     0.2115 0.1616 0.1329

```

```

summary(getSimulationSurvival(design = design,
  plannedEvents = c(40,70,100,150),
  maxNumberOfSubjects = 600,
  thetaH0 = 1.2,
  pi1 = seq(0.1,0.25,0.05),
  pi2 = 0.2,
  allocation1 = 2,
  directionUpper = FALSE,
  conditionalPower = 0.8,
  minNumberOfEventsPerStage = c(40,20,20,20),
  maxNumberOfEventsPerStage = c(40,100,100,100),
  thetaH1 = 1,
  maxNumberOfIterations = 1000,
  seed = 1234))

```

```

## Simulation of a survival endpoint
##
## Sequential analysis with a maximum of 4 looks
## (inverse normal combination test design).
## The results were simulated for a two-sample logrank test,
## H0: hazard ratio = 1.2, power directed towards smaller values,
## H1: treatment pi(1) as specified, control pi(2) = 0.2,
## planned cumulative events = c(40, 70, 100, 150), planned allocation ratio = 2,
## sample size reassessment: conditional power = 0.8,
## minimum events per stage = c(40, 20, 20, 20),
## maximum events per stage = c(40, 100, 100, 100), thetaH1 = 0.833,
## maximum number of subjects = 600, simulation runs = 1000, seed = 1234.
##
## Stage          1      2      3      4
## Fixed weight   0.5    0.5    0.5    0.5

```

## Efficacy boundary (z-value scale)	3.069	2.326	1.978	1.763
## Futility boundary (z-value scale)	0	0	0	
## Overall power, pi(1) = 0.1	0.4490	0.9970	0.9980	0.9980
## Overall power, pi(1) = 0.15	0.0720	0.6740	0.9060	0.9350
## Overall power, pi(1) = 0.2	0.0110	0.1030	0.2520	0.3910
## Overall power, pi(1) = 0.25	0.0010	0.0030	0.0110	0.0220
## Expected number of subjects, pi(1) = 0.1	589.6			
## Expected number of subjects, pi(1) = 0.15	589.7			
## Expected number of subjects, pi(1) = 0.2	564.5			
## Expected number of subjects, pi(1) = 0.25	508.4			
## Number of subjects, pi(1) = 0.1	576.9	600.0	600.0	
## Number of subjects, pi(1) = 0.15	522.5	600.0	600.0	600.0
## Number of subjects, pi(1) = 0.2	474.5	600.0	600.0	600.0
## Number of subjects, pi(1) = 0.25	434.7	600.0	600.0	600.0
## Exit probability for futility, pi(1) = 0.1	0.0020	0	0	
## Exit probability for futility, pi(1) = 0.15	0.0610	0.0010	0	
## Exit probability for futility, pi(1) = 0.2	0.2720	0.0520	0.0080	
## Exit probability for futility, pi(1) = 0.25	0.5530	0.1760	0.0810	
## Expected number of events, pi(1) = 0.1	95.0			
## Expected number of events, pi(1) = 0.15	156.3			
## Expected number of events, pi(1) = 0.2	210.6			
## Expected number of events, pi(1) = 0.25	129.3			
## Cumulative number of events, pi(1) = 0.1	40	140	240	240
## Cumulative number of events, pi(1) = 0.15	40	140	240	340
## Cumulative number of events, pi(1) = 0.2	40	140	240	340
## Cumulative number of events, pi(1) = 0.25	40	140	240	340
## Analysis time, pi(1) = 0.1	11.8	28.5	52.1	
## Analysis time, pi(1) = 0.15	10.5	23.6	39.7	61.5
## Analysis time, pi(1) = 0.2	9.5	20.4	33.5	51.1
## Analysis time, pi(1) = 0.25	8.7	18.0	29.1	43.8
## Expected study duration, pi(1) = 0.1	21.0			
## Expected study duration, pi(1) = 0.15	26.8			
## Expected study duration, pi(1) = 0.2	32.1			
## Expected study duration, pi(1) = 0.25	18.5			
## Conditional power (achieved), pi(1) = 0.1		0.4405	0.6022	
## Conditional power (achieved), pi(1) = 0.15		0.2556	0.4813	0.5406
## Conditional power (achieved), pi(1) = 0.2		0.1305	0.2567	0.3413
## Conditional power (achieved), pi(1) = 0.25		0.0794	0.1206	0.1487

4.3 Simulation results multi-arm

4.3.1 Simulation results multi-arm - means

```
options("rpact.summary.output.size" = "medium") # small, medium, large

design <- getDesignFisher(alpha = 0.05, kMax = 3)

summary(getSimulationMultiArmMeans(design = design,
  plannedSubjects = c(40,70,100),
  activeArms = 3,
  typeOfShape = "linear",
  typeOfSelection = "rBest",
  rValue = 2,
  stDev = 1.2,
```

```
maxNumberOfIterations = 100,
seed = 1234))
```

```
## Simulation of a continuous endpoint (multi-arm design)
##
## Sequential analysis with a maximum of 3 looks (Fisher's combination test design).
## The results were simulated for a multi-arm comparisons for means
## (3 treatments vs. control), H0: mu(i) - mu(control) = 0, H1: effect as specified,
## standard deviation = 1.2, planned cumulative sample size = c(40, 70, 100),
## intersection test = Dunnett, effect shape = linear, selection = r best, r = 2,
## effect measure based on effect estimate, success criterion: all,
## simulation runs = 100, seed = 1234.
##
## Stage                1          2          3
## Fixed weight         1          1          1
## Efficacy boundary (p product scale)  0.0255136 0.0038966 0.0007481
## Reject at least one, mu_max = 0      0.0500
## Reject at least one, mu_max = 0.2    0.2100
## Reject at least one, mu_max = 0.4    0.5400
## Reject at least one, mu_max = 0.6    0.8500
## Reject at least one, mu_max = 0.8    1.0000
## Reject at least one, mu_max = 1      1.0000
## Success per stage, mu_max = 0         0      0.0200      0
## Success per stage, mu_max = 0.2       0      0.0200     0.0300
## Success per stage, mu_max = 0.4       0.0200  0.1400     0.0400
## Success per stage, mu_max = 0.6       0.0900  0.2900     0.1200
## Success per stage, mu_max = 0.8       0.1700  0.4800     0.1900
## Success per stage, mu_max = 1         0.2800  0.5800     0.1200
## Expected number of subjects, mu_max = 0  338.2
## Expected number of subjects, mu_max = 0.2  338.2
## Expected number of subjects, mu_max = 0.4  323.8
## Expected number of subjects, mu_max = 0.6  297.7
## Expected number of subjects, mu_max = 0.8  266.2
## Expected number of subjects, mu_max = 1   237.4
## Overall exit probability, mu_max = 0      0      0.0200
## Overall exit probability, mu_max = 0.2    0      0.0200
## Overall exit probability, mu_max = 0.4    0.0200  0.1400
## Overall exit probability, mu_max = 0.6    0.0900  0.2900
## Overall exit probability, mu_max = 0.8    0.1700  0.4800
## Overall exit probability, mu_max = 1     0.2800  0.5800
## Stagewise number of subjects, mu_max = 0
## treatment arm 1      40.0      19.2      19.3
## treatment arm 2      40.0      18.9      19.0
## treatment arm 3      40.0      21.9      21.7
## control arm          40.0      30.0      30.0
## Stagewise number of subjects, mu_max = 0.2
## treatment arm 1      40.0      15.9      16.2
## treatment arm 2      40.0      19.2      19.0
## treatment arm 3      40.0      24.9      24.8
## control arm          40.0      30.0      30.0
## Stagewise number of subjects, mu_max = 0.4
## treatment arm 1      40.0      12.6      13.9
## treatment arm 2      40.0      20.8      20.0
## treatment arm 3      40.0      26.6      26.1
```

```

## control arm 40.0 30.0 30.0
## Stagewise number of subjects, mu_max = 0.6
## treatment arm 1 40.0 9.6 11.1
## treatment arm 2 40.0 22.4 21.3
## treatment arm 3 40.0 28.0 27.6
## control arm 40.0 30.0 30.0
## Stagewise number of subjects, mu_max = 0.8
## treatment arm 1 40.0 4.3 6.0
## treatment arm 2 40.0 26.0 24.0
## treatment arm 3 40.0 29.6 30.0
## control arm 40.0 30.0 30.0
## Stagewise number of subjects, mu_max = 1
## treatment arm 1 40.0 2.1 6.4
## treatment arm 2 40.0 27.9 23.6
## treatment arm 3 40.0 30.0 30.0
## control arm 40.0 30.0 30.0
## Selected arms, mu_max = 0
## treatment arm 1 1.0000 0.6400 0.6300
## treatment arm 2 1.0000 0.6300 0.6200
## treatment arm 3 1.0000 0.7300 0.7100
## Selected arms, mu_max = 0.2
## treatment arm 1 1.0000 0.5300 0.5300
## treatment arm 2 1.0000 0.6400 0.6200
## treatment arm 3 1.0000 0.8300 0.8100
## Selected arms, mu_max = 0.4
## treatment arm 1 1.0000 0.4100 0.3900
## treatment arm 2 1.0000 0.6800 0.5600
## treatment arm 3 1.0000 0.8700 0.7300
## Selected arms, mu_max = 0.6
## treatment arm 1 1.0000 0.2900 0.2300
## treatment arm 2 1.0000 0.6800 0.4400
## treatment arm 3 1.0000 0.8500 0.5700
## Selected arms, mu_max = 0.8
## treatment arm 1 1.0000 0.1200 0.0700
## treatment arm 2 1.0000 0.7200 0.2800
## treatment arm 3 1.0000 0.8200 0.3500
## Selected arms, mu_max = 1
## treatment arm 1 1.0000 0.0500 0.0300
## treatment arm 2 1.0000 0.6700 0.1100
## treatment arm 3 1.0000 0.7200 0.1400
## Number of active arms, mu_max = 0 3.000 2.000 2.000
## Number of active arms, mu_max = 0.2 3.000 2.000 2.000
## Number of active arms, mu_max = 0.4 3.000 2.000 2.000
## Number of active arms, mu_max = 0.6 3.000 2.000 2.000
## Number of active arms, mu_max = 0.8 3.000 2.000 2.000
## Number of active arms, mu_max = 1 3.000 2.000 2.000
##
## Legend:
## (i): treatment arm i

```

```

summary(getSimulationMultiArmMeans(design = design,
  plannedSubjects = c(40,70,100),
  activeArms = 3,
  typeOfShape = "sigmoidEmax",

```

```

gED50 = 2,
typeOfSelection = "rBest",
rValue = 2,
stDev = 1.2,
maxNumberOfIterations = 100,
seed = 1234))

## Simulation of a continuous endpoint (multi-arm design)
##
## Sequential analysis with a maximum of 3 looks (Fisher's combination test design).
## The results were simulated for a multi-arm comparisons for means
## (3 treatments vs. control), H0:  $\mu(i) - \mu(\text{control}) = 0$ , H1: effect as specified,
## standard deviation = 1.2, planned cumulative sample size = c(40, 70, 100),
## intersection test = Dunnett, effect shape = sigmoid emax, slope = 1, ED50 = 2,
## selection = r best, r = 2, effect measure based on effect estimate,
## success criterion: all, simulation runs = 100, seed = 1234.
##
## Stage                1          2          3
## Fixed weight          1          1          1
## Efficacy boundary (p product scale)    0.0255136 0.0038966 0.0007481
## Reject at least one, mu_max = 0        0.0500
## Reject at least one, mu_max = 0.2      0.1400
## Reject at least one, mu_max = 0.4      0.2900
## Reject at least one, mu_max = 0.6      0.4800
## Reject at least one, mu_max = 0.8      0.7100
## Reject at least one, mu_max = 1        0.9100
## Success per stage, mu_max = 0           0    0.0200    0
## Success per stage, mu_max = 0.2         0    0.0200    0.0100
## Success per stage, mu_max = 0.4        0.0200 0.0400    0.0400
## Success per stage, mu_max = 0.6        0.0400 0.1600    0.0500
## Success per stage, mu_max = 0.8        0.0700 0.2400    0.1100
## Success per stage, mu_max = 1          0.2000 0.4000    0.0900
## Expected number of subjects, mu_max = 0  338.2
## Expected number of subjects, mu_max = 0.2 338.2
## Expected number of subjects, mu_max = 0.4 332.8
## Expected number of subjects, mu_max = 0.6 318.4
## Expected number of subjects, mu_max = 0.8 305.8
## Expected number of subjects, mu_max = 1  268.0
## Overall exit probability, mu_max = 0     0    0.0200
## Overall exit probability, mu_max = 0.2   0    0.0200
## Overall exit probability, mu_max = 0.4   0.0200 0.0400
## Overall exit probability, mu_max = 0.6   0.0400 0.1600
## Overall exit probability, mu_max = 0.8   0.0700 0.2400
## Overall exit probability, mu_max = 1     0.2000 0.4000
## Stagewise number of subjects, mu_max = 0
## treatment arm 1          40.0    19.2    19.3
## treatment arm 2          40.0    18.9    19.0
## treatment arm 3          40.0    21.9    21.7
## control arm              40.0    30.0    30.0
## Stagewise number of subjects, mu_max = 0.2
## treatment arm 1          40.0    17.4    17.8
## treatment arm 2          40.0    20.1    19.9
## treatment arm 3          40.0    22.5    22.3
## control arm              40.0    30.0    30.0

```



```

## Stagewise number of subjects, mu_max = 0.4
## treatment arm 1          40.0      17.1      17.6
## treatment arm 2          40.0      20.8      20.7
## treatment arm 3          40.0      22.0      21.7
## control arm              40.0      30.0      30.0
## Stagewise number of subjects, mu_max = 0.6
## treatment arm 1          40.0      15.9      16.5
## treatment arm 2          40.0      18.8      19.1
## treatment arm 3          40.0      25.3      24.4
## control arm              40.0      30.0      30.0
## Stagewise number of subjects, mu_max = 0.8
## treatment arm 1          40.0      12.6      12.2
## treatment arm 2          40.0      22.9      23.5
## treatment arm 3          40.0      24.5      24.3
## control arm              40.0      30.0      30.0
## Stagewise number of subjects, mu_max = 1
## treatment arm 1          40.0      12.4      16.5
## treatment arm 2          40.0      20.2      18.0
## treatment arm 3          40.0      27.4      25.5
## control arm              40.0      30.0      30.0
## Selected arms, mu_max = 0
## treatment arm 1          1.0000    0.6400    0.6300
## treatment arm 2          1.0000    0.6300    0.6200
## treatment arm 3          1.0000    0.7300    0.7100
## Selected arms, mu_max = 0.2
## treatment arm 1          1.0000    0.5800    0.5800
## treatment arm 2          1.0000    0.6700    0.6500
## treatment arm 3          1.0000    0.7500    0.7300
## Selected arms, mu_max = 0.4
## treatment arm 1          1.0000    0.5600    0.5500
## treatment arm 2          1.0000    0.6800    0.6500
## treatment arm 3          1.0000    0.7200    0.6800
## Selected arms, mu_max = 0.6
## treatment arm 1          1.0000    0.5100    0.4400
## treatment arm 2          1.0000    0.6000    0.5100
## treatment arm 3          1.0000    0.8100    0.6500
## Selected arms, mu_max = 0.8
## treatment arm 1          1.0000    0.3900    0.2800
## treatment arm 2          1.0000    0.7100    0.5400
## treatment arm 3          1.0000    0.7600    0.5600
## Selected arms, mu_max = 1
## treatment arm 1          1.0000    0.3300    0.2200
## treatment arm 2          1.0000    0.5400    0.2400
## treatment arm 3          1.0000    0.7300    0.3400
## Number of active arms, mu_max = 0          3.000    2.000    2.000
## Number of active arms, mu_max = 0.2      3.000    2.000    2.000
## Number of active arms, mu_max = 0.4      3.000    2.000    2.000
## Number of active arms, mu_max = 0.6      3.000    2.000    2.000
## Number of active arms, mu_max = 0.8      3.000    2.000    2.000
## Number of active arms, mu_max = 1        3.000    2.000    2.000
##
## Legend:
## (i): treatment arm i

```

```

summary(getSimulationMultiArmMeans(design = design,
  plannedSubjects = c(40,70,100),
  activeArms = 3,
  typeOfShape = "linear",
  typeOfSelection = "rBest",
  rValue = 2,
  stDev = 1.2,
  conditionalPower = 0.8,
  minNumberOfSubjectsPerStage = c(40,20,20),
  maxNumberOfSubjectsPerStage = c(40,100,100),
  maxNumberOfIterations = 100,
  seed = 1234))

## Simulation of a continuous endpoint (multi-arm design)
##
## Sequential analysis with a maximum of 3 looks (Fisher's combination test design).
## The results were simulated for a multi-arm comparisons for means
## (3 treatments vs. control), H0:  $\mu(i) - \mu(\text{control}) = 0$ , H1: effect as specified,
## standard deviation = 1.2, planned cumulative sample size = c(40, 70, 100),
## intersection test = Dunnett, effect shape = linear, selection = r best, r = 2,
## effect measure based on effect estimate, success criterion: all,
## sample size reassessment: conditional power = 0.8,
## minimum subjects per stage = c(40, 20, 20),
## maximum subjects per stage = c(40, 100, 100), simulation runs = 100, seed = 1234.
##
## Stage                1          2          3
## Fixed weight          1          1          1
## Efficacy boundary (p product scale)    0.0255136 0.0038966 0.0007481
## Reject at least one, mu_max = 0        0.0500
## Reject at least one, mu_max = 0.2      0.3800
## Reject at least one, mu_max = 0.4      0.8800
## Reject at least one, mu_max = 0.6      0.9900
## Reject at least one, mu_max = 0.8      1.0000
## Reject at least one, mu_max = 1        1.0000
## Success per stage, mu_max = 0           0    0.0200    0
## Success per stage, mu_max = 0.2         0    0.0200    0.0800
## Success per stage, mu_max = 0.4         0.0200 0.2000    0.1000
## Success per stage, mu_max = 0.6         0.0900 0.4800    0.1200
## Success per stage, mu_max = 0.8         0.1700 0.5500    0.1500
## Success per stage, mu_max = 1           0.2800 0.5900    0.0600
## Expected number of subjects, mu_max = 0  749.3
## Expected number of subjects, mu_max = 0.2 705.9
## Expected number of subjects, mu_max = 0.4 563.2
## Expected number of subjects, mu_max = 0.6 392.4
## Expected number of subjects, mu_max = 0.8 288.9
## Expected number of subjects, mu_max = 1  232.8
## Overall exit probability, mu_max = 0     0    0.0200
## Overall exit probability, mu_max = 0.2   0    0.0200
## Overall exit probability, mu_max = 0.4   0.0200 0.2000
## Overall exit probability, mu_max = 0.6   0.0900 0.4800
## Overall exit probability, mu_max = 0.8   0.1700 0.5500
## Overall exit probability, mu_max = 1     0.2800 0.5900
## Stagewise number of subjects, mu_max = 0
## treatment arm 1                40.0    63.4    64.3

```

## treatment arm 2	40.0	62.0	63.3
## treatment arm 3	40.0	71.4	72.4
## control arm	40.0	98.4	100.0
## Stagewise number of subjects, mu_max = 0.2			
## treatment arm 1	40.0	47.8	50.4
## treatment arm 2	40.0	57.0	56.9
## treatment arm 3	40.0	79.1	76.5
## control arm	40.0	91.9	91.9
## Stagewise number of subjects, mu_max = 0.4			
## treatment arm 1	40.0	37.3	38.3
## treatment arm 2	40.0	51.9	48.4
## treatment arm 3	40.0	67.2	61.5
## control arm	40.0	78.2	74.1
## Stagewise number of subjects, mu_max = 0.6			
## treatment arm 1	40.0	24.6	20.0
## treatment arm 2	40.0	47.0	28.0
## treatment arm 3	40.0	60.8	32.1
## control arm	40.0	66.2	40.1
## Stagewise number of subjects, mu_max = 0.8			
## treatment arm 1	40.0	5.4	5.7
## treatment arm 2	40.0	39.6	17.1
## treatment arm 3	40.0	43.2	22.9
## control arm	40.0	44.1	22.9
## Stagewise number of subjects, mu_max = 1			
## treatment arm 1	40.0	2.0	4.6
## treatment arm 2	40.0	28.1	15.4
## treatment arm 3	40.0	30.1	20.0
## control arm	40.0	30.1	20.0
## Selected arms, mu_max = 0			
## treatment arm 1	1.0000	0.6400	0.6300
## treatment arm 2	1.0000	0.6300	0.6200
## treatment arm 3	1.0000	0.7300	0.7100
## Selected arms, mu_max = 0.2			
## treatment arm 1	1.0000	0.5300	0.5300
## treatment arm 2	1.0000	0.6400	0.6200
## treatment arm 3	1.0000	0.8300	0.8100
## Selected arms, mu_max = 0.4			
## treatment arm 1	1.0000	0.4100	0.3800
## treatment arm 2	1.0000	0.6800	0.5100
## treatment arm 3	1.0000	0.8700	0.6700
## Selected arms, mu_max = 0.6			
## treatment arm 1	1.0000	0.2900	0.1900
## treatment arm 2	1.0000	0.6800	0.2900
## treatment arm 3	1.0000	0.8500	0.3800
## Selected arms, mu_max = 0.8			
## treatment arm 1	1.0000	0.1200	0.0800
## treatment arm 2	1.0000	0.7200	0.2000
## treatment arm 3	1.0000	0.8200	0.2800
## Selected arms, mu_max = 1			
## treatment arm 1	1.0000	0.0500	0.0300
## treatment arm 2	1.0000	0.6700	0.1000
## treatment arm 3	1.0000	0.7200	0.1300
## Number of active arms, mu_max = 0	3.000	2.000	2.000
## Number of active arms, mu_max = 0.2	3.000	2.000	2.000

```
## Number of active arms, mu_max = 0.4          3.000    2.000    2.000
## Number of active arms, mu_max = 0.6          3.000    2.000    2.000
## Number of active arms, mu_max = 0.8          3.000    2.000    2.000
## Number of active arms, mu_max = 1            3.000    2.000    2.000
```

```
##
```

```
## Legend:
```

```
## (i): treatment arm i
```

```
summary(getSimulationMultiArmMeans(design = design,
  plannedSubjects = c(40, 70, 100),
  activeArms = 3,
  typeOfShape = "linear",
  typeOfSelection = "rBest",
  rValue = 2,
  stDev = 1.2,
  conditionalPower = 0.8,
  minNumberOfSubjectsPerStage = c(40,20,20),
  maxNumberOfSubjectsPerStage = c(40,100,100),
  thetaH1 = 0.6, stDevH1 = 1.5,
  maxNumberOfIterations = 100,
  seed = 1234))
```

```
## Simulation of a continuous endpoint (multi-arm design)
```

```
##
```

```
## Sequential analysis with a maximum of 3 looks (Fisher's combination test design).
```

```
## The results were simulated for a multi-arm comparisons for means
```

```
## (3 treatments vs. control), H0:  $\mu(i) - \mu(\text{control}) = 0$ , H1: effect as specified,
```

```
## standard deviation = 1.2, planned cumulative sample size = c(40, 70, 100),
```

```
## intersection test = Dunnett, effect shape = linear, selection = r best, r = 2,
```

```
## effect measure based on effect estimate, success criterion: all,
```

```
## sample size reassessment: conditional power = 0.8,
```

```
## minimum subjects per stage = c(40, 20, 20),
```

```
## maximum subjects per stage = c(40, 100, 100), theta H1 = 0.6,
```

```
## standard deviation H1 = 1.5, simulation runs = 100, seed = 1234.
```

```
##
```

## Stage	1	2	3
## Fixed weight	1	1	1
## Efficacy boundary (p product scale)	0.0255136	0.0038966	0.0007481
## Reject at least one, mu_max = 0	0.0500		
## Reject at least one, mu_max = 0.2	0.3700		
## Reject at least one, mu_max = 0.4	0.8700		
## Reject at least one, mu_max = 0.6	0.9800		
## Reject at least one, mu_max = 0.8	1.0000		
## Reject at least one, mu_max = 1	1.0000		
## Success per stage, mu_max = 0	0	0.0200	0
## Success per stage, mu_max = 0.2	0	0.0200	0.0800
## Success per stage, mu_max = 0.4	0.0200	0.1700	0.0900
## Success per stage, mu_max = 0.6	0.0900	0.4500	0.0900
## Success per stage, mu_max = 0.8	0.1700	0.5300	0.1400
## Success per stage, mu_max = 1	0.2800	0.5800	0.0700
## Expected number of subjects, mu_max = 0	736.6		
## Expected number of subjects, mu_max = 0.2	661.4		
## Expected number of subjects, mu_max = 0.4	496.8		
## Expected number of subjects, mu_max = 0.6	362.1		
## Expected number of subjects, mu_max = 0.8	273.0		

```

## Expected number of subjects, mu_max = 1          227.7
## Overall exit probability, mu_max = 0              0    0.0200
## Overall exit probability, mu_max = 0.2            0    0.0200
## Overall exit probability, mu_max = 0.4           0.0200  0.1700
## Overall exit probability, mu_max = 0.6           0.0900  0.4500
## Overall exit probability, mu_max = 0.8           0.1700  0.5300
## Overall exit probability, mu_max = 1             0.2800  0.5800
## Stagewise number of subjects, mu_max = 0
## treatment arm 1                                40.0    63.1    62.7
## treatment arm 2                                40.0    60.7    61.4
## treatment arm 3                                40.0    69.8    70.6
## control arm                                     40.0    96.8    97.3
## Stagewise number of subjects, mu_max = 0.2
## treatment arm 1                                40.0    45.9    43.7
## treatment arm 2                                40.0    55.4    49.2
## treatment arm 3                                40.0    76.3    67.0
## control arm                                     40.0    88.8    79.9
## Stagewise number of subjects, mu_max = 0.4
## treatment arm 1                                40.0    34.8    25.4
## treatment arm 2                                40.0    48.8    32.5
## treatment arm 3                                40.0    62.1    42.9
## control arm                                     40.0    72.9    50.4
## Stagewise number of subjects, mu_max = 0.6
## treatment arm 1                                40.0    20.7    15.2
## treatment arm 2                                40.0    42.3    22.8
## treatment arm 3                                40.0    52.8    25.9
## control arm                                     40.0    57.9    31.9
## Stagewise number of subjects, mu_max = 0.8
## treatment arm 1                                40.0     4.3     5.3
## treatment arm 2                                40.0    34.2    15.5
## treatment arm 3                                40.0    37.2    20.8
## control arm                                     40.0    37.9    20.8
## Stagewise number of subjects, mu_max = 1
## treatment arm 1                                40.0     1.6     5.7
## treatment arm 2                                40.0    25.8    14.3
## treatment arm 3                                40.0    27.5    20.0
## control arm                                     40.0    27.5    20.0
## Selected arms, mu_max = 0
## treatment arm 1                                1.0000  0.6400  0.6300
## treatment arm 2                                1.0000  0.6300  0.6200
## treatment arm 3                                1.0000  0.7300  0.7100
## Selected arms, mu_max = 0.2
## treatment arm 1                                1.0000  0.5300  0.5300
## treatment arm 2                                1.0000  0.6400  0.6200
## treatment arm 3                                1.0000  0.8300  0.8100
## Selected arms, mu_max = 0.4
## treatment arm 1                                1.0000  0.4100  0.3900
## treatment arm 2                                1.0000  0.6800  0.5300
## treatment arm 3                                1.0000  0.8700  0.7000
## Selected arms, mu_max = 0.6
## treatment arm 1                                1.0000  0.2900  0.2100
## treatment arm 2                                1.0000  0.6800  0.3000
## treatment arm 3                                1.0000  0.8500  0.4100
## Selected arms, mu_max = 0.8

```

```

## treatment arm 1          1.0000    0.1200    0.0800
## treatment arm 2          1.0000    0.7200    0.2200
## treatment arm 3          1.0000    0.8200    0.3000
## Selected arms, mu_max = 1
## treatment arm 1          1.0000    0.0500    0.0400
## treatment arm 2          1.0000    0.6700    0.1000
## treatment arm 3          1.0000    0.7200    0.1400
## Number of active arms, mu_max = 0          3.000    2.000    2.000
## Number of active arms, mu_max = 0.2        3.000    2.000    2.000
## Number of active arms, mu_max = 0.4        3.000    2.000    2.000
## Number of active arms, mu_max = 0.6        3.000    2.000    2.000
## Number of active arms, mu_max = 0.8        3.000    2.000    2.000
## Number of active arms, mu_max = 1          3.000    2.000    2.000
##
## Legend:
## (i): treatment arm i

```

```

summary(getSimulationMultiArmMeans(seed = 1234,
  getDesignFisher(informationRates = c(0.2, 0.6, 1)),
  typeOfShape = "linear", activeArms = 4,
  plannedSubjects = c(10, 30, 50), stDev = 1.2,
  muMaxVector = seq(0.3, 0.6, 0.1), adaptations = rep(TRUE, 2),
  minNumberOfSubjectsPerStage = c(10, 4, 4),
  maxNumberOfSubjectsPerStage = c(10, 100, 100),
  maxNumberOfIterations = 10,
  calcSubjectsFunction = function(..., stage, minNumberOfSubjectsPerStage) {
    return(ifelse(stage == 3, 33, minNumberOfSubjectsPerStage[stage]))
  })

```

```

## Simulation of a continuous endpoint (multi-arm design)
##
## Sequential analysis with a maximum of 3 looks (Fisher's combination test design).
## The results were simulated for a multi-arm comparisons for means
## (4 treatments vs. control), H0: mu(i) - mu(control) = 0, H1: effect as specified,
## standard deviation = 1.2, planned cumulative sample size = c(10, 30, 50),
## intersection test = Dunnett, effect shape = linear, selection = best,
## effect measure based on effect estimate, success criterion: all,
## sample size reassessment: user defined 'calcSubjectsFunction',
## minimum subjects per stage = c(10, 4, 4),
## maximum subjects per stage = c(10, 100, 100), simulation runs = 10, seed = 1234.
##
## Stage          1          2          3
## Fixed weight          1      1.414      1.414
## Efficacy boundary (p product scale)    0.01083295 0.00032301 0.00002196
## Reject at least one, mu_max = 0.3          0.1000
## Reject at least one, mu_max = 0.4          0.1000
## Reject at least one, mu_max = 0.5          0.3000
## Reject at least one, mu_max = 0.6          0.4000
## Success per stage, mu_max = 0.3          0      0.1000          0
## Success per stage, mu_max = 0.4          0      0.1000          0
## Success per stage, mu_max = 0.5          0      0.2000      0.1000
## Success per stage, mu_max = 0.6          0      0.2000      0.2000
## Expected number of subjects, mu_max = 0.3    117.4
## Expected number of subjects, mu_max = 0.4    117.4
## Expected number of subjects, mu_max = 0.5    110.8

```

```

## Expected number of subjects, mu_max = 0.6      110.8
## Overall exit probability, mu_max = 0.3          0      0.1000
## Overall exit probability, mu_max = 0.4          0      0.1000
## Overall exit probability, mu_max = 0.5          0      0.2000
## Overall exit probability, mu_max = 0.6          0      0.2000
## Stagewise number of subjects, mu_max = 0.3
## treatment arm 1                               10.0      0.4      3.7
## treatment arm 2                               10.0      1.2     11.0
## treatment arm 3                               10.0      0.4      3.7
## treatment arm 4                               10.0      2.0     14.7
## control arm                                   10.0      4.0     33.0
## Stagewise number of subjects, mu_max = 0.4
## treatment arm 1                               10.0      0.4      3.7
## treatment arm 2                               10.0      1.6     14.7
## treatment arm 3                               10.0      1.2      7.3
## treatment arm 4                               10.0      0.8      7.3
## control arm                                   10.0      4.0     33.0
## Stagewise number of subjects, mu_max = 0.5
## treatment arm 1                               10.0      0.4      0.0
## treatment arm 2                               10.0      0.0      0.0
## treatment arm 3                               10.0      1.6     16.5
## treatment arm 4                               10.0      2.0     16.5
## control arm                                   10.0      4.0     33.0
## Stagewise number of subjects, mu_max = 0.6
## treatment arm 1                               10.0      0.0      0.0
## treatment arm 2                               10.0      1.2      8.2
## treatment arm 3                               10.0      0.4      4.1
## treatment arm 4                               10.0      2.4     20.6
## control arm                                   10.0      4.0     33.0
## Selected arms, mu_max = 0.3
## treatment arm 1                               1.0000    0.1000    0.1000
## treatment arm 2                               1.0000    0.3000    0.3000
## treatment arm 3                               1.0000    0.1000    0.1000
## treatment arm 4                               1.0000    0.5000    0.4000
## Selected arms, mu_max = 0.4
## treatment arm 1                               1.0000    0.1000    0.1000
## treatment arm 2                               1.0000    0.4000    0.4000
## treatment arm 3                               1.0000    0.3000    0.2000
## treatment arm 4                               1.0000    0.2000    0.2000
## Selected arms, mu_max = 0.5
## treatment arm 1                               1.0000    0.1000     0
## treatment arm 2                               1.0000     0         0
## treatment arm 3                               1.0000    0.4000    0.4000
## treatment arm 4                               1.0000    0.5000    0.4000
## Selected arms, mu_max = 0.6
## treatment arm 1                               1.0000     0         0
## treatment arm 2                               1.0000    0.3000    0.2000
## treatment arm 3                               1.0000    0.1000    0.1000
## treatment arm 4                               1.0000    0.6000    0.5000
## Number of active arms, mu_max = 0.3           4.000    1.000    1.000
## Number of active arms, mu_max = 0.4           4.000    1.000    1.000
## Number of active arms, mu_max = 0.5           4.000    1.000    1.000
## Number of active arms, mu_max = 0.6           4.000    1.000    1.000
##

```

```
## Legend:
```

```
## (i): treatment arm i
```

```
summary(getSimulationMultiArmMeans(seed = 1234,
  getDesignFisher(informationRates = c(0.2, 0.6, 1)),
  typeOfShape = "linear", activeArms = 4,
  plannedSubjects = c(10, 30, 50), stDev = 1.2,
  muMaxVector = seq(0.3, 0.6, 0.1), adaptations = rep(TRUE, 2),
  typeOfSelection = "userDefined",
  maxNumberOfIterations = 10,
  selectArmsFunction = function(effectSizes) {
    return(c(TRUE, FALSE, FALSE, FALSE))
  })
```

```
## Simulation of a continuous endpoint (multi-arm design)
```

```
##
```

```
## Sequential analysis with a maximum of 3 looks (Fisher's combination test design).
```

```
## The results were simulated for a multi-arm comparisons for means
```

```
## (4 treatments vs. control), H0:  $\mu(i) - \mu(\text{control}) = 0$ , H1: effect as specified,
```

```
## standard deviation = 1.2, planned cumulative sample size = c(10, 30, 50),
```

```
## intersection test = Dunnett, effect shape = linear, selection = user defined,
```

```
## effect measure based on effect estimate, success criterion: all,
```

```
## simulation runs = 10, seed = 1234.
```

```
##
```

## Stage	1	2	3
## Fixed weight	1	1.414	1.414
## Efficacy boundary (p product scale)	0.01083295	0.00032301	0.00002196
## Reject at least one, $\mu_{\max} = 0.3$	0.1000		
## Reject at least one, $\mu_{\max} = 0.4$	0.1000		
## Reject at least one, $\mu_{\max} = 0.5$	0.2000		
## Reject at least one, $\mu_{\max} = 0.6$	0.1000		
## Success per stage, $\mu_{\max} = 0.3$	0	0	0
## Success per stage, $\mu_{\max} = 0.4$	0	0.1000	0
## Success per stage, $\mu_{\max} = 0.5$	0	0.1000	0
## Success per stage, $\mu_{\max} = 0.6$	0	0	0
## Expected number of subjects, $\mu_{\max} = 0.3$	130.0		
## Expected number of subjects, $\mu_{\max} = 0.4$	126.0		
## Expected number of subjects, $\mu_{\max} = 0.5$	126.0		
## Expected number of subjects, $\mu_{\max} = 0.6$	130.0		
## Overall exit probability, $\mu_{\max} = 0.3$	0	0	
## Overall exit probability, $\mu_{\max} = 0.4$	0	0.1000	
## Overall exit probability, $\mu_{\max} = 0.5$	0	0.1000	
## Overall exit probability, $\mu_{\max} = 0.6$	0	0	
## Stagewise number of subjects, $\mu_{\max} = 0.3$			
## treatment arm 1	10.0	20.0	20.0
## treatment arm 2	10.0	0.0	0.0
## treatment arm 3	10.0	0.0	0.0
## treatment arm 4	10.0	0.0	0.0
## control arm	10.0	20.0	20.0
## Stagewise number of subjects, $\mu_{\max} = 0.4$			
## treatment arm 1	10.0	20.0	20.0
## treatment arm 2	10.0	0.0	0.0
## treatment arm 3	10.0	0.0	0.0
## treatment arm 4	10.0	0.0	0.0
## control arm	10.0	20.0	20.0


```

## Stagewise number of subjects, mu_max = 0.5
## treatment arm 1           10.0      20.0      20.0
## treatment arm 2           10.0       0.0       0.0
## treatment arm 3           10.0       0.0       0.0
## treatment arm 4           10.0       0.0       0.0
## control arm               10.0      20.0      20.0
## Stagewise number of subjects, mu_max = 0.6
## treatment arm 1           10.0      20.0      20.0
## treatment arm 2           10.0       0.0       0.0
## treatment arm 3           10.0       0.0       0.0
## treatment arm 4           10.0       0.0       0.0
## control arm               10.0      20.0      20.0
## Selected arms, mu_max = 0.3
## treatment arm 1           1.0000     1.0000     1.0000
## treatment arm 2           1.0000       0         0
## treatment arm 3           1.0000       0         0
## treatment arm 4           1.0000       0         0
## Selected arms, mu_max = 0.4
## treatment arm 1           1.0000     1.0000     0.9000
## treatment arm 2           1.0000       0         0
## treatment arm 3           1.0000       0         0
## treatment arm 4           1.0000       0         0
## Selected arms, mu_max = 0.5
## treatment arm 1           1.0000     1.0000     0.9000
## treatment arm 2           1.0000       0         0
## treatment arm 3           1.0000       0         0
## treatment arm 4           1.0000       0         0
## Selected arms, mu_max = 0.6
## treatment arm 1           1.0000     1.0000     1.0000
## treatment arm 2           1.0000       0         0
## treatment arm 3           1.0000       0         0
## treatment arm 4           1.0000       0         0
## Number of active arms, mu_max = 0.3      4.000     1.000     1.000
## Number of active arms, mu_max = 0.4      4.000     1.000     1.000
## Number of active arms, mu_max = 0.5      4.000     1.000     1.000
## Number of active arms, mu_max = 0.6      4.000     1.000     1.000
##
## Legend:
## (i): treatment arm i

```

4.3.2 Simulation results multi-arm - rates

```

options("rpact.summary.output.size" = "medium") # small, medium, large

summary(getSimulationMultiArmRates(design = design,
  plannedSubjects = c(40, 70, 100),
  activeArms = 3,
  typeOfShape = "linear",
  typeOfSelection = "rBest",
  rValue = 2,
  piControl = 0.4,
  maxNumberOfIterations = 100,
  seed = 1234))

```

```

## Simulation of a binary endpoint (multi-arm design)
##
## Sequential analysis with a maximum of 3 looks (Fisher's combination test design).
## The results were simulated for a multi-arm comparisons for rates
## (3 treatments vs. control),
## H0:  $\pi(i) - \pi(\text{control}) = 0$ , power directed towards larger values,
## H1: treatment rate  $\pi_{\text{max}}$  as specified, control rate  $\pi(\text{control}) = 0.4$ ,
## planned cumulative sample size = c(40, 70, 100), intersection test = Dunnett,
## effect shape = linear, selection = r best, r = 2,
## effect measure based on effect estimate, success criterion: all,
## simulation runs = 100, seed = 1234.
##
## Stage                1          2          3
## Fixed weight          1          1          1
## Efficacy boundary (p product scale) 0.0255136 0.0038966 0.0007481
## Reject at least one,  $\pi_{\text{max}} = 0.2$           0
## Reject at least one,  $\pi_{\text{max}} = 0.3$           0.0100
## Reject at least one,  $\pi_{\text{max}} = 0.4$           0.0600
## Reject at least one,  $\pi_{\text{max}} = 0.5$           0.2400
## Success per stage,  $\pi_{\text{max}} = 0.2$           0          0          0
## Success per stage,  $\pi_{\text{max}} = 0.3$           0          0          0
## Success per stage,  $\pi_{\text{max}} = 0.4$           0          0.0200          0
## Success per stage,  $\pi_{\text{max}} = 0.5$           0.0100          0.0300          0.0400
## Expected number of subjects,  $\pi_{\text{max}} = 0.2$           340.0
## Expected number of subjects,  $\pi_{\text{max}} = 0.3$           340.0
## Expected number of subjects,  $\pi_{\text{max}} = 0.4$           338.2
## Expected number of subjects,  $\pi_{\text{max}} = 0.5$           335.5
## Overall exit probability,  $\pi_{\text{max}} = 0.2$           0          0
## Overall exit probability,  $\pi_{\text{max}} = 0.3$           0          0
## Overall exit probability,  $\pi_{\text{max}} = 0.4$           0          0.0200
## Overall exit probability,  $\pi_{\text{max}} = 0.5$           0.0100          0.0300
## Stagewise number of subjects,  $\pi_{\text{max}} = 0.2$ 
## treatment arm 1          40.0          28.2          28.2
## treatment arm 2          40.0          23.7          23.7
## treatment arm 3          40.0          8.1          8.1
## control arm              40.0          30.0          30.0
## Stagewise number of subjects,  $\pi_{\text{max}} = 0.3$ 
## treatment arm 1          40.0          24.3          24.3
## treatment arm 2          40.0          20.7          20.7
## treatment arm 3          40.0          15.0          15.0
## control arm              40.0          30.0          30.0
## Stagewise number of subjects,  $\pi_{\text{max}} = 0.4$ 
## treatment arm 1          40.0          18.3          18.4
## treatment arm 2          40.0          21.9          21.7
## treatment arm 3          40.0          19.8          19.9
## control arm              40.0          30.0          30.0
## Stagewise number of subjects,  $\pi_{\text{max}} = 0.5$ 
## treatment arm 1          40.0          14.2          13.8
## treatment arm 2          40.0          20.3          20.6
## treatment arm 3          40.0          25.5          25.6
## control arm              40.0          30.0          30.0
## Selected arms,  $\pi_{\text{max}} = 0.2$ 
## treatment arm 1          1.0000          0.9400          0.9400
## treatment arm 2          1.0000          0.7900          0.7900

```

```

## treatment arm 3                1.0000    0.2700    0.2700
## Selected arms, pi_max = 0.3
## treatment arm 1                1.0000    0.8100    0.8100
## treatment arm 2                1.0000    0.6900    0.6900
## treatment arm 3                1.0000    0.5000    0.5000
## Selected arms, pi_max = 0.4
## treatment arm 1                1.0000    0.6100    0.6000
## treatment arm 2                1.0000    0.7300    0.7100
## treatment arm 3                1.0000    0.6600    0.6500
## Selected arms, pi_max = 0.5
## treatment arm 1                1.0000    0.4700    0.4400
## treatment arm 2                1.0000    0.6700    0.6600
## treatment arm 3                1.0000    0.8400    0.8200
## Number of active arms, pi_max = 0.2        3.000    2.000    2.000
## Number of active arms, pi_max = 0.3        3.000    2.000    2.000
## Number of active arms, pi_max = 0.4        3.000    2.000    2.000
## Number of active arms, pi_max = 0.5        3.000    2.000    2.000

```

```

##
## Legend:
## (i): treatment arm i

```

```

summary(getSimulationMultiArmRates(design = design,
  plannedSubjects = c(40, 70, 100),
  activeArms = 3,
  typeOfShape = "sigmoidEmax",
  gED50 = 2,
  typeOfSelection = "rBest",
  rValue = 2,
  maxNumberOfIterations = 100,
  seed = 1234))

```

```

## Simulation of a binary endpoint (multi-arm design)
##
## Sequential analysis with a maximum of 3 looks (Fisher's combination test design).
## The results were simulated for a multi-arm comparisons for rates
## (3 treatments vs. control),
## H0: pi(i) - pi(control) = 0, power directed towards larger values,
## H1: treatment rate pi_max as specified, control rate pi(control) = 0.2,
## planned cumulative sample size = c(40, 70, 100), intersection test = Dunnett,
## effect shape = sigmoid emax, slope = 1, ED50 = 2, selection = r best, r = 2,
## effect measure based on effect estimate, success criterion: all,
## simulation runs = 100, seed = 1234.
##
## Stage                1            2            3
## Fixed weight                1            1            1
## Efficacy boundary (p product scale)    0.0255136 0.0038966 0.0007481
## Reject at least one, pi_max = 0.2                0
## Reject at least one, pi_max = 0.3            0.0100
## Reject at least one, pi_max = 0.4            0.1400
## Reject at least one, pi_max = 0.5            0.2400
## Success per stage, pi_max = 0.2                0            0            0
## Success per stage, pi_max = 0.3                0            0            0
## Success per stage, pi_max = 0.4                0            0.0500    0.0200
## Success per stage, pi_max = 0.5                0            0.0400    0.0200
## Expected number of subjects, pi_max = 0.2    340.0

```

```

## Expected number of subjects, pi_max = 0.3      340.0
## Expected number of subjects, pi_max = 0.4      335.5
## Expected number of subjects, pi_max = 0.5      336.4
## Overall exit probability, pi_max = 0.2          0          0
## Overall exit probability, pi_max = 0.3          0          0
## Overall exit probability, pi_max = 0.4          0      0.0500
## Overall exit probability, pi_max = 0.5          0      0.0400
## Stagewise number of subjects, pi_max = 0.2
## treatment arm 1          40.0      11.4      11.4
## treatment arm 2          40.0      22.5      22.5
## treatment arm 3          40.0      26.1      26.1
## control arm              40.0      30.0      30.0
## Stagewise number of subjects, pi_max = 0.3
## treatment arm 1          40.0      10.2      10.2
## treatment arm 2          40.0      21.9      21.9
## treatment arm 3          40.0      27.9      27.9
## control arm              40.0      30.0      30.0
## Stagewise number of subjects, pi_max = 0.4
## treatment arm 1          40.0       5.7       6.0
## treatment arm 2          40.0      25.8      25.6
## treatment arm 3          40.0      28.5      28.4
## control arm              40.0      30.0      30.0
## Stagewise number of subjects, pi_max = 0.5
## treatment arm 1          40.0       5.7       5.6
## treatment arm 2          40.0      25.2      25.3
## treatment arm 3          40.0      29.1      29.1
## control arm              40.0      30.0      30.0
## Selected arms, pi_max = 0.2
## treatment arm 1          1.0000   0.3800   0.3800
## treatment arm 2          1.0000   0.7500   0.7500
## treatment arm 3          1.0000   0.8700   0.8700
## Selected arms, pi_max = 0.3
## treatment arm 1          1.0000   0.3400   0.3400
## treatment arm 2          1.0000   0.7300   0.7300
## treatment arm 3          1.0000   0.9300   0.9300
## Selected arms, pi_max = 0.4
## treatment arm 1          1.0000   0.1900   0.1900
## treatment arm 2          1.0000   0.8600   0.8100
## treatment arm 3          1.0000   0.9500   0.9000
## Selected arms, pi_max = 0.5
## treatment arm 1          1.0000   0.1900   0.1800
## treatment arm 2          1.0000   0.8400   0.8100
## treatment arm 3          1.0000   0.9700   0.9300
## Number of active arms, pi_max = 0.2            3.000    2.000    2.000
## Number of active arms, pi_max = 0.3            3.000    2.000    2.000
## Number of active arms, pi_max = 0.4            3.000    2.000    2.000
## Number of active arms, pi_max = 0.5            3.000    2.000    2.000

```

```
##
```

```
## Legend:
```

```
## (i): treatment arm i
```

```
summary(getSimulationMultiArmRates(design = design,
  plannedSubjects = c(40, 70, 100),
  activeArms = 3,
```

```

typeOfShape = "linear",
typeOfSelection = "rBest",
rValue = 2,
piControl = 0.4,
conditionalPower = 0.8,
minNumberOfSubjectsPerStage = c(40,20,20),
maxNumberOfSubjectsPerStage = c(40,100,100),
maxNumberOfIterations = 100,
seed = 1234))

```

```

## Simulation of a binary endpoint (multi-arm design)
##
## Sequential analysis with a maximum of 3 looks (Fisher's combination test design).
## The results were simulated for a multi-arm comparisons for rates
## (3 treatments vs. control),
## H0: pi(i) - pi(control) = 0, power directed towards larger values,
## H1: treatment rate pi_max as specified, control rate pi(control) = 0.4,
## planned cumulative sample size = c(40, 70, 100), intersection test = Dunnett,
## effect shape = linear, selection = r best, r = 2,
## effect measure based on effect estimate, success criterion: all,
## sample size reassessment: conditional power = 0.8,
## minimum subjects per stage = c(40, 20, 20),
## maximum subjects per stage = c(40, 100, 100), simulation runs = 100, seed = 1234.
##
## Stage                1          2          3
## Fixed weight          1          1          1
## Efficacy boundary (p product scale)    0.0255136 0.0038966 0.0007481
## Reject at least one, pi_max = 0.2      0.0100
## Reject at least one, pi_max = 0.3      0.0100
## Reject at least one, pi_max = 0.4      0.0700
## Reject at least one, pi_max = 0.5      0.4400
## Success per stage, pi_max = 0.2         0          0          0
## Success per stage, pi_max = 0.3      0.0100         0          0
## Success per stage, pi_max = 0.4         0      0.0100         0
## Success per stage, pi_max = 0.5         0      0.0500      0.0400
## Expected number of subjects, pi_max = 0.2    760.0
## Expected number of subjects, pi_max = 0.3    754.0
## Expected number of subjects, pi_max = 0.4    753.8
## Expected number of subjects, pi_max = 0.5    698.0
## Overall exit probability, pi_max = 0.2         0          0
## Overall exit probability, pi_max = 0.3      0.0100         0
## Overall exit probability, pi_max = 0.4         0      0.0100
## Overall exit probability, pi_max = 0.5         0      0.0500
## Stagewise number of subjects, pi_max = 0.2
## treatment arm 1          40.0      94.0      94.0
## treatment arm 2          40.0      84.0      84.0
## treatment arm 3          40.0      22.0      22.0
## control arm              40.0     100.0     100.0
## Stagewise number of subjects, pi_max = 0.3
## treatment arm 1          40.0      77.8      77.8
## treatment arm 2          40.0      66.7      66.7
## treatment arm 3          40.0      55.6      55.6
## control arm              40.0     100.0     100.0
## Stagewise number of subjects, pi_max = 0.4

```

```

## treatment arm 1          40.0      72.0      72.7
## treatment arm 2          40.0      54.9      55.6
## treatment arm 3          40.0      70.9      71.7
## control arm              40.0      98.9     100.0
## Stagewise number of subjects, pi_max = 0.5
## treatment arm 1          40.0      46.5      47.8
## treatment arm 2          40.0      58.1      57.6
## treatment arm 3          40.0      78.1      79.7
## control arm              40.0      91.4      92.6
## Selected arms, pi_max = 0.2
## treatment arm 1          1.0000    0.9400    0.9400
## treatment arm 2          1.0000    0.8400    0.8400
## treatment arm 3          1.0000    0.2200    0.2200
## Selected arms, pi_max = 0.3
## treatment arm 1          1.0000    0.7700    0.7700
## treatment arm 2          1.0000    0.6600    0.6600
## treatment arm 3          1.0000    0.5500    0.5500
## Selected arms, pi_max = 0.4
## treatment arm 1          1.0000    0.7200    0.7200
## treatment arm 2          1.0000    0.5600    0.5500
## treatment arm 3          1.0000    0.7200    0.7100
## Selected arms, pi_max = 0.5
## treatment arm 1          1.0000    0.4900    0.4800
## treatment arm 2          1.0000    0.6500    0.6000
## treatment arm 3          1.0000    0.8600    0.8200
## Number of active arms, pi_max = 0.2          3.000    2.000    2.000
## Number of active arms, pi_max = 0.3          3.000    2.000    2.000
## Number of active arms, pi_max = 0.4          3.000    2.000    2.000
## Number of active arms, pi_max = 0.5          3.000    2.000    2.000
##
## Legend:
## (i): treatment arm i

```

```

summary(getSimulationMultiArmRates(design = design,
  plannedSubjects = c(40, 70, 100),
  activeArms = 3,
  typeOfShape = "userDefined",
  effectMatrix = matrix(c(0.1,0.2,0.3,
    0.2,0.3,0.4,
    0.2,0.4,0.4), nrow = 3),
  typeOfSelection = "rBest",
  rValue = 2,
  directionUpper = FALSE,
  allocationRatioPlanned = 2,
  piControl = 0.4,
  conditionalPower = 0.8,
  minNumberOfSubjectsPerStage = c(40,20,20),
  maxNumberOfSubjectsPerStage = c(40,100,100),
  piH1 = 0.6, piControlH1 = 0.4,
  maxNumberOfIterations = 100,
  seed = 1234))

```

```

## Simulation of a binary endpoint (multi-arm design)
##
## Sequential analysis with a maximum of 3 looks (Fisher's combination test design).

```

```

## The results were simulated for a multi-arm comparisons for rates
## (3 treatments vs. control),
## H0:  $\pi(i) - \pi(\text{control}) = 0$ , power directed towards smaller values,
## H1: treatment rate  $\pi_{\text{max}}$  as specified, control rate  $\pi(\text{control}) = 0.4$ ,
## planned cumulative sample size = c(40, 70, 100), planned allocation ratio = 2,
## intersection test = Dunnett, effect shape = user defined, selection = r best, r = 2,
## effect measure based on effect estimate, success criterion: all,
## sample size reassessment: conditional power = 0.8,
## minimum subjects per stage = c(40, 20, 20),
## maximum subjects per stage = c(40, 100, 100),  $\pi(\text{treatment})_{H1} = 0.6$ ,
##  $\pi(\text{control})_{H1} = 0.4$ , simulation runs = 100, seed = 1234.
##
## Stage                1          2          3
## Fixed weight         1          1          1
## Efficacy boundary (p product scale) 0.0255136 0.0038966 0.0007481
## Reject at least one [1]          1.0000
## Reject at least one [2]          0.9200
## Reject at least one [3]          0.4300
## Success per stage [1]          0.1800          0.5500          0.1000
## Success per stage [2]              0          0.1600          0.0900
## Success per stage [3]          0.0100          0.0200              0
## Expected number of subjects [1]          304.5
## Expected number of subjects [2]          504.0
## Expected number of subjects [3]          616.0
## Overall exit probability [1]          0.1800          0.5500
## Overall exit probability [2]              0          0.1600
## Overall exit probability [3]          0.0100          0.0200
## Stagewise number of subjects [1]
##   treatment arm 1          40.0          69.3          22.2
##   treatment arm 2          40.0          39.8          16.3
##   treatment arm 3          40.0          34.4          13.3
##   control arm            20.0          35.9          13.0
## Stagewise number of subjects [2]
##   treatment arm 1          40.0          91.0          62.6
##   treatment arm 2          40.0          78.6          54.8
##   treatment arm 3          40.0          14.4          10.2
##   control arm            20.0          46.0          31.9
## Stagewise number of subjects [3]
##   treatment arm 1          40.0          93.9          88.0
##   treatment arm 2          40.0          45.5          41.0
##   treatment arm 3          40.0          60.6          59.4
##   control arm            20.0          50.0          47.1
## Selected arms [1]
##   treatment arm 1          1.0000          0.8000          0.2600
##   treatment arm 2          1.0000          0.4300          0.1400
##   treatment arm 3          1.0000          0.4100          0.1400
## Selected arms [2]
##   treatment arm 1          1.0000          0.9900          0.8300
##   treatment arm 2          1.0000          0.8500          0.7000
##   treatment arm 3          1.0000          0.1600          0.1500
## Selected arms [3]
##   treatment arm 1          1.0000          0.9300          0.9100
##   treatment arm 2          1.0000          0.4500          0.4300
##   treatment arm 3          1.0000          0.6000          0.6000

```

```
## Number of active arms [1]          3.000    2.000    2.000
## Number of active arms [2]          3.000    2.000    2.000
## Number of active arms [3]          3.000    2.000    2.000
```

```
##
```

```
## Legend:
```

```
## (i): treatment arm i
```

```
## [j]: effect matrix row j (situation to consider)
```

```
summary(getSimulationMultiArmRates(seed = 1234,
  getDesignFisher(informationRates = c(0.2, 0.6, 1)),
  typeOfShape = "linear", activeArms = 4,
  plannedSubjects = c(10, 30, 50),
  piMaxVector = seq(0.3, 0.6, 0.1), adaptations = rep(TRUE, 2),
  typeOfSelection = "userDefined",
  maxNumberOfIterations = 10, selectArmsFunction = function(effectSizes) {
    return(c(TRUE, FALSE, FALSE, FALSE))
  }))
```

```
## Simulation of a binary endpoint (multi-arm design)
```

```
##
```

```
## Sequential analysis with a maximum of 3 looks (Fisher's combination test design).
```

```
## The results were simulated for a multi-arm comparisons for rates
```

```
## (4 treatments vs. control),
```

```
## H0:  $\pi(i) - \pi(\text{control}) = 0$ , power directed towards larger values,
```

```
## H1: treatment rate  $\pi_{\text{max}}$  as specified, control rate  $\pi(\text{control}) = 0.2$ ,
```

```
## planned cumulative sample size = c(10, 30, 50), intersection test = Dunnett,
```

```
## effect shape = linear, selection = user defined,
```

```
## effect measure based on effect estimate, success criterion: all,
```

```
## simulation runs = 10, seed = 1234.
```

```
##
```

## Stage	1	2	3
## Fixed weight	1	1.414	1.414
## Efficacy boundary (p product scale)	0.01083295	0.00032301	0.00002196
## Reject at least one, $\pi_{\text{max}} = 0.3$	0		
## Reject at least one, $\pi_{\text{max}} = 0.4$	0		
## Reject at least one, $\pi_{\text{max}} = 0.5$	0.1000		
## Reject at least one, $\pi_{\text{max}} = 0.6$	0.4000		
## Success per stage, $\pi_{\text{max}} = 0.3$	0	0	0
## Success per stage, $\pi_{\text{max}} = 0.4$	0	0	0
## Success per stage, $\pi_{\text{max}} = 0.5$	0	0	0.1000
## Success per stage, $\pi_{\text{max}} = 0.6$	0	0.1000	0
## Expected number of subjects, $\pi_{\text{max}} = 0.3$	130.0		
## Expected number of subjects, $\pi_{\text{max}} = 0.4$	130.0		
## Expected number of subjects, $\pi_{\text{max}} = 0.5$	130.0		
## Expected number of subjects, $\pi_{\text{max}} = 0.6$	126.0		
## Overall exit probability, $\pi_{\text{max}} = 0.3$	0	0	
## Overall exit probability, $\pi_{\text{max}} = 0.4$	0	0	
## Overall exit probability, $\pi_{\text{max}} = 0.5$	0	0	
## Overall exit probability, $\pi_{\text{max}} = 0.6$	0	0.1000	
## Stagewise number of subjects, $\pi_{\text{max}} = 0.3$			
## treatment arm 1	10.0	20.0	20.0
## treatment arm 2	10.0	0.0	0.0
## treatment arm 3	10.0	0.0	0.0
## treatment arm 4	10.0	0.0	0.0
## control arm	10.0	20.0	20.0


```

## Stagewise number of subjects, pi_max = 0.4
## treatment arm 1          10.0      20.0      20.0
## treatment arm 2          10.0       0.0       0.0
## treatment arm 3          10.0       0.0       0.0
## treatment arm 4          10.0       0.0       0.0
## control arm              10.0      20.0      20.0
## Stagewise number of subjects, pi_max = 0.5
## treatment arm 1          10.0      20.0      20.0
## treatment arm 2          10.0       0.0       0.0
## treatment arm 3          10.0       0.0       0.0
## treatment arm 4          10.0       0.0       0.0
## control arm              10.0      20.0      20.0
## Stagewise number of subjects, pi_max = 0.6
## treatment arm 1          10.0      20.0      20.0
## treatment arm 2          10.0       0.0       0.0
## treatment arm 3          10.0       0.0       0.0
## treatment arm 4          10.0       0.0       0.0
## control arm              10.0      20.0      20.0
## Selected arms, pi_max = 0.3
## treatment arm 1          1.0000    1.0000    1.0000
## treatment arm 2          1.0000     0         0
## treatment arm 3          1.0000     0         0
## treatment arm 4          1.0000     0         0
## Selected arms, pi_max = 0.4
## treatment arm 1          1.0000    1.0000    1.0000
## treatment arm 2          1.0000     0         0
## treatment arm 3          1.0000     0         0
## treatment arm 4          1.0000     0         0
## Selected arms, pi_max = 0.5
## treatment arm 1          1.0000    1.0000    1.0000
## treatment arm 2          1.0000     0         0
## treatment arm 3          1.0000     0         0
## treatment arm 4          1.0000     0         0
## Selected arms, pi_max = 0.6
## treatment arm 1          1.0000    1.0000    0.9000
## treatment arm 2          1.0000     0         0
## treatment arm 3          1.0000     0         0
## treatment arm 4          1.0000     0         0
## Number of active arms, pi_max = 0.3      4.000    1.000    1.000
## Number of active arms, pi_max = 0.4      4.000    1.000    1.000
## Number of active arms, pi_max = 0.5      4.000    1.000    1.000
## Number of active arms, pi_max = 0.6      4.000    1.000    1.000
##
## Legend:
## (i): treatment arm i

```

```

summary(getSimulationMultiArmRates(seed = 1234,
  getDesignFisher(informationRates = c(0.2, 0.6, 1)),
  typeOfShape = "linear", activeArms = 4,
  plannedSubjects = c(10, 30, 50), piControl = 0.3,
  piMaxVector = seq(0.3, 0.6, 0.1), adaptations = rep(TRUE, 2),
  minNumberOfSubjectsPerStage = c(10, 4, 4), maxNumberOfSubjectsPerStage = c(10, 100, 100),
  maxNumberOfIterations = 10,
  calcSubjectsFunction = function(..., stage, minNumberOfSubjectsPerStage) {

```

```

return(ifelse(stage == 3, 33, minNumberOfSubjectsPerStage[stage]))
}))

```

```

## Simulation of a binary endpoint (multi-arm design)
##
## Sequential analysis with a maximum of 3 looks (Fisher's combination test design).
## The results were simulated for a multi-arm comparisons for rates
## (4 treatments vs. control),
## H0:  $\pi(i) - \pi(\text{control}) = 0$ , power directed towards larger values,
## H1: treatment rate  $\pi_{\text{max}}$  as specified, control rate  $\pi(\text{control}) = 0.3$ ,
## planned cumulative sample size = c(10, 30, 50), intersection test = Dunnett,
## effect shape = linear, selection = best, effect measure based on effect estimate,
## success criterion: all,
## sample size reassessment: user defined 'calcSubjectsFunction',
## minimum subjects per stage = c(10, 4, 4),
## maximum subjects per stage = c(10, 100, 100), simulation runs = 10, seed = 1234.
##
## Stage                1          2          3
## Fixed weight          1      1.414      1.414
## Efficacy boundary (p product scale)  0.01083295  0.00032301  0.00002196
## Reject at least one,  $\pi_{\text{max}} = 0.3$           0
## Reject at least one,  $\pi_{\text{max}} = 0.4$           0
## Reject at least one,  $\pi_{\text{max}} = 0.5$         0.2000
## Reject at least one,  $\pi_{\text{max}} = 0.6$         0.4000
## Success per stage,  $\pi_{\text{max}} = 0.3$           0          0          0
## Success per stage,  $\pi_{\text{max}} = 0.4$           0          0          0
## Success per stage,  $\pi_{\text{max}} = 0.5$           0          0      0.2000
## Success per stage,  $\pi_{\text{max}} = 0.6$           0      0.1000      0.3000
## Expected number of subjects,  $\pi_{\text{max}} = 0.3$     124.0
## Expected number of subjects,  $\pi_{\text{max}} = 0.4$     124.0
## Expected number of subjects,  $\pi_{\text{max}} = 0.5$     124.0
## Expected number of subjects,  $\pi_{\text{max}} = 0.6$     117.4
## Overall exit probability,  $\pi_{\text{max}} = 0.3$           0          0
## Overall exit probability,  $\pi_{\text{max}} = 0.4$           0          0
## Overall exit probability,  $\pi_{\text{max}} = 0.5$           0          0
## Overall exit probability,  $\pi_{\text{max}} = 0.6$           0      0.1000
## Stagewise number of subjects,  $\pi_{\text{max}} = 0.3$ 
## treatment arm 1          10.0          0.4          3.3
## treatment arm 2          10.0          0.0          0.0
## treatment arm 3          10.0          1.2          9.9
## treatment arm 4          10.0          2.4          19.8
## control arm              10.0          4.0          33.0
## Stagewise number of subjects,  $\pi_{\text{max}} = 0.4$ 
## treatment arm 1          10.0          1.6          13.2
## treatment arm 2          10.0          0.4          3.3
## treatment arm 3          10.0          0.8          6.6
## treatment arm 4          10.0          1.2          9.9
## control arm              10.0          4.0          33.0
## Stagewise number of subjects,  $\pi_{\text{max}} = 0.5$ 
## treatment arm 1          10.0          0.0          0.0
## treatment arm 2          10.0          1.6          13.2
## treatment arm 3          10.0          0.8          6.6
## treatment arm 4          10.0          1.6          13.2
## control arm              10.0          4.0          33.0

```

```

## Stagewise number of subjects, pi_max = 0.6
## treatment arm 1           10.0      0.4      3.7
## treatment arm 2           10.0      0.8      7.3
## treatment arm 3           10.0      0.4      3.7
## treatment arm 4           10.0      2.4     18.3
## control arm               10.0      4.0     33.0
## Selected arms, pi_max = 0.3
## treatment arm 1           1.0000    0.1000    0.1000
## treatment arm 2           1.0000     0         0
## treatment arm 3           1.0000    0.3000    0.3000
## treatment arm 4           1.0000    0.6000    0.6000
## Selected arms, pi_max = 0.4
## treatment arm 1           1.0000    0.4000    0.4000
## treatment arm 2           1.0000    0.1000    0.1000
## treatment arm 3           1.0000    0.2000    0.2000
## treatment arm 4           1.0000    0.3000    0.3000
## Selected arms, pi_max = 0.5
## treatment arm 1           1.0000     0         0
## treatment arm 2           1.0000    0.4000    0.4000
## treatment arm 3           1.0000    0.2000    0.2000
## treatment arm 4           1.0000    0.4000    0.4000
## Selected arms, pi_max = 0.6
## treatment arm 1           1.0000    0.1000    0.1000
## treatment arm 2           1.0000    0.2000    0.2000
## treatment arm 3           1.0000    0.1000    0.1000
## treatment arm 4           1.0000    0.6000    0.5000
## Number of active arms, pi_max = 0.3      4.000    1.000    1.000
## Number of active arms, pi_max = 0.4      4.000    1.000    1.000
## Number of active arms, pi_max = 0.5      4.000    1.000    1.000
## Number of active arms, pi_max = 0.6      4.000    1.000    1.000
##
## Legend:
## (i): treatment arm i

```

4.3.3 Simulation results multi-arm - survival

```
options("rpact.summary.output.size" = "medium") # small, medium, large
```

```
summary(getSimulationMultiArmSurvival(design = design,
  plannedEvents = c(40, 70, 100),
  activeArms = 3,
  typeOfShape = "linear",
  typeOfSelection = "rBest",
  rValue = 2,
  maxNumberOfIterations = 100,
  seed = 1234))
```

```

## Simulation of a survival endpoint (multi-arm design)
##
## Sequential analysis with a maximum of 3 looks (Fisher's combination test design).
## The results were simulated for a multi-arm logrank test (3 treatments vs. control),
## H0: hazard ratio(i) = 1, power directed towards larger values,
## H1: omega_max as specified, planned cumulative events = c(40, 70, 100),
## intersection test = Dunnett, effect shape = linear, selection = r best, r = 2,

```

```

## effect measure based on effect estimate, success criterion: all,
## simulation runs = 100, seed = 1234.
##
## Stage                1          2          3
## Fixed weight         1          1          1
## Efficacy boundary (p product scale)    0.0255136 0.0038966 0.0007481
## Reject at least one, omega_max = 1      0.0400
## Reject at least one, omega_max = 1.4    0.1800
## Reject at least one, omega_max = 1.8    0.5000
## Reject at least one, omega_max = 2.2    0.8000
## Reject at least one, omega_max = 2.6    0.9100
## Success per stage, omega_max = 1         0          0          0
## Success per stage, omega_max = 1.4      0.0100    0.0500    0.0100
## Success per stage, omega_max = 1.8      0.0400    0.1500    0.0600
## Success per stage, omega_max = 2.2      0.1000    0.2400    0.1300
## Success per stage, omega_max = 2.6      0.1300    0.4000    0.1900
## Expected number of events, omega_max = 1 100.0
## Expected number of events, omega_max = 1.4 97.9
## Expected number of events, omega_max = 1.8 93.1
## Expected number of events, omega_max = 2.2 86.8
## Expected number of events, omega_max = 2.6 80.2
## Overall exit probability, omega_max = 1   0          0
## Overall exit probability, omega_max = 1.4 0.0100    0.0500
## Overall exit probability, omega_max = 1.8 0.0400    0.1500
## Overall exit probability, omega_max = 2.2 0.1000    0.2400
## Overall exit probability, omega_max = 2.6 0.1300    0.4000
## Cumulative number of events, omega_max = 1
## treatment arm 1 vs. control             20.0       35.0       50.0
## treatment arm 2 vs. control             20.0       35.0       50.0
## treatment arm 3 vs. control             20.0       35.0       50.0
## Cumulative number of events, omega_max = 1.4
## treatment arm 1 vs. control             17.8       31.1       44.4
## treatment arm 2 vs. control             18.9       33.1       47.2
## treatment arm 3 vs. control             20.0       35.0       50.0
## Cumulative number of events, omega_max = 1.8
## treatment arm 1 vs. control             16.2       28.3       40.5
## treatment arm 2 vs. control             18.1       31.7       45.2
## treatment arm 3 vs. control             20.0       35.0       50.0
## Cumulative number of events, omega_max = 2.2
## treatment arm 1 vs. control             15.0       26.2       37.5
## treatment arm 2 vs. control             17.5       30.6       43.8
## treatment arm 3 vs. control             20.0       35.0       50.0
## Cumulative number of events, omega_max = 2.6
## treatment arm 1 vs. control             14.1       24.6       35.2
## treatment arm 2 vs. control             17.0       29.8       42.6
## treatment arm 3 vs. control             20.0       35.0       50.0
## Selected arms, omega_max = 1
## treatment arm 1 vs. control             1.0000     0.6000     0.6000
## treatment arm 2 vs. control             1.0000     0.6500     0.6500
## treatment arm 3 vs. control             1.0000     0.7500     0.7500
## Selected arms, omega_max = 1.4
## treatment arm 1 vs. control             1.0000     0.4400     0.4300
## treatment arm 2 vs. control             1.0000     0.7000     0.6600
## treatment arm 3 vs. control             1.0000     0.8400     0.7900

```

```

## Selected arms, omega_max = 1.8
## treatment arm 1 vs. control          1.0000    0.3600    0.3000
## treatment arm 2 vs. control          1.0000    0.7400    0.6400
## treatment arm 3 vs. control          1.0000    0.8200    0.6800
## Selected arms, omega_max = 2.2
## treatment arm 1 vs. control          1.0000    0.2900    0.2500
## treatment arm 2 vs. control          1.0000    0.6600    0.4500
## treatment arm 3 vs. control          1.0000    0.8500    0.6200
## Selected arms, omega_max = 2.6
## treatment arm 1 vs. control          1.0000    0.2400    0.1900
## treatment arm 2 vs. control          1.0000    0.6800    0.3200
## treatment arm 3 vs. control          1.0000    0.8200    0.4300
## Number of active arms, omega_max = 1          3.000    2.000    2.000
## Number of active arms, omega_max = 1.4        3.000    2.000    2.000
## Number of active arms, omega_max = 1.8        3.000    2.000    2.000
## Number of active arms, omega_max = 2.2        3.000    2.000    2.000
## Number of active arms, omega_max = 2.6        3.000    2.000    2.000

```

```
##
```

```
## Legend:
```

```
## (i): results of treatment arm i vs. control arm
```

```

summary(getSimulationMultiArmSurvival(design = design,
  plannedEvents = c(40, 70, 100),
  activeArms = 3,
  typeOfShape = "sigmoidEmax",
  gED50 = 2,
  typeOfSelection = "epsilon",
  epsilonValue = 0.1,
  maxNumberOfIterations = 100,
  seed = 1234))

```

```
## Simulation of a survival endpoint (multi-arm design)
```

```
##
```

```

## Sequential analysis with a maximum of 3 looks (Fisher's combination test design).
## The results were simulated for a multi-arm logrank test (3 treatments vs. control),
## H0: hazard ratio(i) = 1, power directed towards larger values,
## H1: omega_max as specified, planned cumulative events = c(40, 70, 100),
## intersection test = Dunnett, effect shape = sigmoid emax, slope = 1, ED50 = 2,
## selection = epsilon rule, eps = 0.1, effect measure based on effect estimate,
## success criterion: all, simulation runs = 100, seed = 1234.

```

```
##
```

```

## Stage          1          2          3
## Fixed weight          1          1          1
## Efficacy boundary (p product scale)    0.0255136 0.0038966 0.0007481
## Reject at least one, omega_max = 1          0.0600
## Reject at least one, omega_max = 1.4        0.1100
## Reject at least one, omega_max = 1.8        0.2800
## Reject at least one, omega_max = 2.2        0.6400
## Reject at least one, omega_max = 2.6        0.7200
## Success per stage, omega_max = 1          0    0.0200    0.0400
## Success per stage, omega_max = 1.4        0    0.0700    0.0400
## Success per stage, omega_max = 1.8        0.0100    0.1400    0.1200
## Success per stage, omega_max = 2.2        0.0400    0.3700    0.2300
## Success per stage, omega_max = 2.6        0.1300    0.4200    0.1700
## Expected number of events, omega_max = 1          99.4

```

## Expected number of events, omega_max = 1.4	97.9		
## Expected number of events, omega_max = 1.8	95.2		
## Expected number of events, omega_max = 2.2	86.5		
## Expected number of events, omega_max = 2.6	79.6		
## Overall exit probability, omega_max = 1	0	0.0200	
## Overall exit probability, omega_max = 1.4	0	0.0700	
## Overall exit probability, omega_max = 1.8	0.0100	0.1400	
## Overall exit probability, omega_max = 2.2	0.0400	0.3700	
## Overall exit probability, omega_max = 2.6	0.1300	0.4200	
## Cumulative number of events, omega_max = 1			
## treatment arm 1 vs. control	20.0	35.0	50.0
## treatment arm 2 vs. control	20.0	35.0	50.0
## treatment arm 3 vs. control	20.0	35.0	50.0
## Cumulative number of events, omega_max = 1.4			
## treatment arm 1 vs. control	18.7	32.7	46.6
## treatment arm 2 vs. control	19.2	33.7	48.1
## treatment arm 3 vs. control	19.6	34.3	49.0
## Cumulative number of events, omega_max = 1.8			
## treatment arm 1 vs. control	17.6	30.8	44.0
## treatment arm 2 vs. control	18.7	32.6	46.6
## treatment arm 3 vs. control	19.3	33.7	48.2
## Cumulative number of events, omega_max = 2.2			
## treatment arm 1 vs. control	16.8	29.4	42.0
## treatment arm 2 vs. control	18.2	31.8	45.5
## treatment arm 3 vs. control	19.0	33.3	47.6
## Cumulative number of events, omega_max = 2.6			
## treatment arm 1 vs. control	16.1	28.2	40.3
## treatment arm 2 vs. control	17.8	31.1	44.5
## treatment arm 3 vs. control	18.8	32.9	47.0
## Selected arms, omega_max = 1			
## treatment arm 1 vs. control	1.0000	0.4400	0.4000
## treatment arm 2 vs. control	1.0000	0.4200	0.4100
## treatment arm 3 vs. control	1.0000	0.3400	0.2400
## Selected arms, omega_max = 1.4			
## treatment arm 1 vs. control	1.0000	0.4400	0.3200
## treatment arm 2 vs. control	1.0000	0.4000	0.3500
## treatment arm 3 vs. control	1.0000	0.4200	0.3100
## Selected arms, omega_max = 1.8			
## treatment arm 1 vs. control	1.0000	0.2500	0.2300
## treatment arm 2 vs. control	1.0000	0.3700	0.2800
## treatment arm 3 vs. control	1.0000	0.5400	0.3600
## Selected arms, omega_max = 2.2			
## treatment arm 1 vs. control	1.0000	0.2800	0.1300
## treatment arm 2 vs. control	1.0000	0.3400	0.2600
## treatment arm 3 vs. control	1.0000	0.5200	0.2300
## Selected arms, omega_max = 2.6			
## treatment arm 1 vs. control	1.0000	0.2400	0.1500
## treatment arm 2 vs. control	1.0000	0.3600	0.1600
## treatment arm 3 vs. control	1.0000	0.4800	0.1700
## Number of active arms, omega_max = 1	3.000	1.200	1.071
## Number of active arms, omega_max = 1.4	3.000	1.260	1.054
## Number of active arms, omega_max = 1.8	3.000	1.172	1.024
## Number of active arms, omega_max = 2.2	3.000	1.188	1.051
## Number of active arms, omega_max = 2.6	3.000	1.241	1.067

```

##
## Legend:
## (i): results of treatment arm i vs. control arm
summary(getSimulationMultiArmSurvival(design = design,
  plannedEvents = c(40, 70, 100),
  activeArms = 3,
  typeOfShape = "userDefined",
  effectMatrix = matrix(c(1.1,1.2,1.3,
    1.2,1.3,1.4,
    1.2,1.4,1.4), nrow = 3),
  typeOfSelection = "rBest",
  rValue = 2,
  allocationRatioPlanned = 2,
  conditionalPower = 0.8,
  minNumberOfEventsPerStage = c(40,20,20),
  maxNumberOfEventsPerStage = c(40,100,100),
  thetaH1 = 1.6,
  maxNumberOfIterations = 100,
  seed = 1234))

## Simulation of a survival endpoint (multi-arm design)
##
## Sequential analysis with a maximum of 3 looks (Fisher's combination test design).
## The results were simulated for a multi-arm logrank test (3 treatments vs. control),
## H0: hazard ratio(i) = 1, power directed towards larger values,
## H1: omega_max as specified, planned cumulative events = c(40, 70, 100),
## planned allocation ratio = 2, intersection test = Dunnett,
## effect shape = user defined, selection = r best, r = 2,
## effect measure based on effect estimate, success criterion: all,
## sample size reassessment: conditional power = 0.8,
## minimum events per stage = c(40, 20, 20),
## maximum events per stage = c(40, 100, 100), thetaH1 = 1.6, simulation runs = 100,
## seed = 1234.
##
## Stage                1          2          3
## Fixed weight          1          1          1
## Efficacy boundary (p product scale) 0.0255136 0.0038966 0.0007481
## Reject at least one [1]          0.1200
## Reject at least one [2]          0.3500
## Reject at least one [3]          0.3700
## Success per stage [1]           0      0.0400      0.0300
## Success per stage [2]          0.0200      0.0900      0.0600
## Success per stage [3]          0.0300      0.1000      0.1000
## Expected number of events [1]        231.4
## Expected number of events [2]        217.8
## Expected number of events [3]        213.4
## Overall exit probability [1]           0      0.0400
## Overall exit probability [2]          0.0200      0.0900
## Overall exit probability [3]          0.0300      0.1000
## Cumulative number of events [1]
## treatment arm 1 vs. control          16.0          54.9          94.1
## treatment arm 2 vs. control          17.0          58.3          100.0
## treatment arm 3 vs. control          17.0          58.3          100.0
## Cumulative number of events [2]

```

```

## treatment arm 1 vs. control      15.5      52.2      88.9
## treatment arm 2 vs. control      16.4      55.2      94.2
## treatment arm 3 vs. control      17.3      58.3      99.4
## Cumulative number of events [3]
## treatment arm 1 vs. control      15.7      53.3      89.3
## treatment arm 2 vs. control      16.5      56.3      94.3
## treatment arm 3 vs. control      16.5      56.3      94.3
## Selected arms [1]
## treatment arm 1 vs. control      1.0000    0.4900    0.4800
## treatment arm 2 vs. control      1.0000    0.7200    0.6800
## treatment arm 3 vs. control      1.0000    0.7900    0.7600
## Selected arms [2]
## treatment arm 1 vs. control      1.0000    0.4700    0.4400
## treatment arm 2 vs. control      1.0000    0.6800    0.6000
## treatment arm 3 vs. control      1.0000    0.8100    0.7400
## Selected arms [3]
## treatment arm 1 vs. control      1.0000    0.5800    0.5000
## treatment arm 2 vs. control      1.0000    0.7300    0.6600
## treatment arm 3 vs. control      1.0000    0.6300    0.5800
## Number of active arms [1]        3.000    2.000    2.000
## Number of active arms [2]        3.000    2.000    2.000
## Number of active arms [3]        3.000    2.000    2.000
##
## Legend:
## (i): results of treatment arm i vs. control arm
## [j]: effect matrix row j (situation to consider)

```

```

summary(getSimulationMultiArmSurvival(seed = 1234,
  getDesignInverseNormal(informationRates = c(0.2, 0.6, 1)),
  typeOfShape = "linear", activeArms = 4,
  plannedEvents = c(10, 30, 50), omegaMaxVector = seq(0.3, 0.6, 0.1),
  adaptations = rep(TRUE, 2), directionUpper = FALSE,
  minNumberOfEventsPerStage = c(10, 4, 4), maxNumberOfEventsPerStage = c(10, 100, 100),
  maxNumberOfIterations = 10,
  calcEventsFunction = function(..., stage, minNumberOfEventsPerStage) {
    return(ifelse(stage == 3, 33, minNumberOfEventsPerStage[stage]))
  })

```

```

## Simulation of a survival endpoint (multi-arm design)
##
## Sequential analysis with a maximum of 3 looks
## (inverse normal combination test design).
## The results were simulated for a multi-arm logrank test (4 treatments vs. control),
## H0: hazard ratio(i) = 1, power directed towards smaller values,
## H1: omega_max as specified, planned cumulative events = c(10, 30, 50),
## intersection test = Dunnett, effect shape = linear, selection = best,
## effect measure based on effect estimate, success criterion: all,
## sample size reassessment: user defined 'calcEventsFunction',
## minimum events per stage = c(10, 4, 4), maximum events per stage = c(10, 100, 100),
## simulation runs = 10, seed = 1234.
##
## Stage                1      2      3
## Fixed weight          0.447  0.632  0.632
## Efficacy boundary (z-value scale)  4.455  2.572  1.992
## Reject at least one, omega_max = 0.3  0.3000

```



```

## Reject at least one, omega_max = 0.4      0.4000
## Reject at least one, omega_max = 0.5      0.7000
## Reject at least one, omega_max = 0.6      0.3000
## Success per stage, omega_max = 0.3        0 0.1000 0.2000
## Success per stage, omega_max = 0.4        0  0 0.4000
## Success per stage, omega_max = 0.5        0 0.2000 0.5000
## Success per stage, omega_max = 0.6        0 0.1000 0.2000
## Expected number of events, omega_max = 0.3  43.7
## Expected number of events, omega_max = 0.4  47.0
## Expected number of events, omega_max = 0.5  40.4
## Expected number of events, omega_max = 0.6  43.7
## Overall exit probability, omega_max = 0.3   0 0.1000
## Overall exit probability, omega_max = 0.4   0  0
## Overall exit probability, omega_max = 0.5   0 0.2000
## Overall exit probability, omega_max = 0.6   0 0.1000
## Cumulative number of events, omega_max = 0.3
## treatment arm 1 vs. control                5.6  7.9  26.4
## treatment arm 2 vs. control                5.1  7.1  23.9
## treatment arm 3 vs. control                4.5  6.4  21.3
## treatment arm 4 vs. control                4.0  5.6  18.8
## Cumulative number of events, omega_max = 0.4
## treatment arm 1 vs. control                5.3  7.4  24.8
## treatment arm 2 vs. control                4.9  6.8  22.8
## treatment arm 3 vs. control                4.4  6.2  20.8
## treatment arm 4 vs. control                4.0  5.6  18.8
## Cumulative number of events, omega_max = 0.5
## treatment arm 1 vs. control                5.0  7.0  23.5
## treatment arm 2 vs. control                4.7  6.5  21.9
## treatment arm 3 vs. control                4.3  6.1  20.4
## treatment arm 4 vs. control                4.0  5.6  18.8
## Cumulative number of events, omega_max = 0.6
## treatment arm 1 vs. control                4.8  6.7  22.3
## treatment arm 2 vs. control                4.5  6.3  21.1
## treatment arm 3 vs. control                4.2  6.0  20.0
## treatment arm 4 vs. control                4.0  5.6  18.8
## Selected arms, omega_max = 0.3
## treatment arm 1 vs. control                1.0000 0.1000 0.1000
## treatment arm 2 vs. control                1.0000 0.2000 0.2000
## treatment arm 3 vs. control                1.0000 0.4000 0.3000
## treatment arm 4 vs. control                1.0000 0.3000 0.3000
## Selected arms, omega_max = 0.4
## treatment arm 1 vs. control                1.0000  0  0
## treatment arm 2 vs. control                1.0000 0.1000 0.1000
## treatment arm 3 vs. control                1.0000 0.4000 0.4000
## treatment arm 4 vs. control                1.0000 0.5000 0.5000
## Selected arms, omega_max = 0.5
## treatment arm 1 vs. control                1.0000 0.1000 0.1000
## treatment arm 2 vs. control                1.0000 0.1000 0.1000
## treatment arm 3 vs. control                1.0000 0.4000 0.3000
## treatment arm 4 vs. control                1.0000 0.4000 0.3000
## Selected arms, omega_max = 0.6
## treatment arm 1 vs. control                1.0000 0.2000 0.1000
## treatment arm 2 vs. control                1.0000 0.1000 0.1000
## treatment arm 3 vs. control                1.0000 0.5000 0.5000

```

```

## treatment arm 4 vs. control          1.0000 0.2000 0.2000
## Number of active arms, omega_max = 0.3    4.000  1.000  1.000
## Number of active arms, omega_max = 0.4    4.000  1.000  1.000
## Number of active arms, omega_max = 0.5    4.000  1.000  1.000
## Number of active arms, omega_max = 0.6    4.000  1.000  1.000
##
## Legend:
## (i): results of treatment arm i vs. control arm
summary(getSimulationMultiArmSurvival(seed = 1234,
  getDesignInverseNormal(informationRates = c(0.2, 0.6, 1)),
  typeOfShape = "linear", activeArms = 4,
  plannedEvents = c(10, 30, 50), omegaMaxVector = seq(0.3, 0.6, 0.1),
  adaptations = rep(TRUE, 2), directionUpper = FALSE,
  typeOfSelection = "userDefined",
  maxNumberOfIterations = 10,
  selectArmsFunction = function(effectSizes) {
    return(c(TRUE, FALSE, FALSE, FALSE))
  })
## Simulation of a survival endpoint (multi-arm design)
##
## Sequential analysis with a maximum of 3 looks
## (inverse normal combination test design).
## The results were simulated for a multi-arm logrank test (4 treatments vs. control),
## H0: hazard ratio(i) = 1, power directed towards smaller values,
## H1: omega_max as specified, planned cumulative events = c(10, 30, 50),
## intersection test = Dunnett, effect shape = linear, selection = user defined,
## effect measure based on effect estimate, success criterion: all,
## simulation runs = 10, seed = 1234.
##
## Stage                1      2      3
## Fixed weight          0.447  0.632  0.632
## Efficacy boundary (z-value scale)  4.455  2.572  1.992
## Reject at least one, omega_max = 0.3      0
## Reject at least one, omega_max = 0.4      0
## Reject at least one, omega_max = 0.5      0
## Reject at least one, omega_max = 0.6    0.1000
## Success per stage, omega_max = 0.3        0      0      0
## Success per stage, omega_max = 0.4        0      0      0
## Success per stage, omega_max = 0.5        0      0      0
## Success per stage, omega_max = 0.6        0 0.1000      0
## Expected number of events, omega_max = 0.3  50.0
## Expected number of events, omega_max = 0.4  50.0
## Expected number of events, omega_max = 0.5  50.0
## Expected number of events, omega_max = 0.6  48.0
## Overall exit probability, omega_max = 0.3   0      0
## Overall exit probability, omega_max = 0.4   0      0
## Overall exit probability, omega_max = 0.5   0      0
## Overall exit probability, omega_max = 0.6   0 0.1000
## Cumulative number of events, omega_max = 0.3
## treatment arm 1 vs. control          5.6  16.8  28.1
## treatment arm 2 vs. control          5.1  15.2  25.4
## treatment arm 3 vs. control          4.5  13.6  22.7
## treatment arm 4 vs. control          4.0  12.0  20.0

```

```

## Cumulative number of events, omega_max = 0.4
## treatment arm 1 vs. control          5.3  15.9  26.4
## treatment arm 2 vs. control          4.9  14.6  24.3
## treatment arm 3 vs. control          4.4  13.3  22.1
## treatment arm 4 vs. control          4.0  12.0  20.0
## Cumulative number of events, omega_max = 0.5
## treatment arm 1 vs. control          5.0  15.0  25.0
## treatment arm 2 vs. control          4.7  14.0  23.3
## treatment arm 3 vs. control          4.3  13.0  21.7
## treatment arm 4 vs. control          4.0  12.0  20.0
## Cumulative number of events, omega_max = 0.6
## treatment arm 1 vs. control          4.8  14.2  23.8
## treatment arm 2 vs. control          4.5  13.5  22.5
## treatment arm 3 vs. control          4.2  12.8  21.2
## treatment arm 4 vs. control          4.0  12.0  20.0
## Selected arms, omega_max = 0.3
## treatment arm 1 vs. control          1.0000 1.0000 1.0000
## treatment arm 2 vs. control          1.0000 0 0
## treatment arm 3 vs. control          1.0000 0 0
## treatment arm 4 vs. control          1.0000 0 0
## Selected arms, omega_max = 0.4
## treatment arm 1 vs. control          1.0000 1.0000 1.0000
## treatment arm 2 vs. control          1.0000 0 0
## treatment arm 3 vs. control          1.0000 0 0
## treatment arm 4 vs. control          1.0000 0 0
## Selected arms, omega_max = 0.5
## treatment arm 1 vs. control          1.0000 1.0000 1.0000
## treatment arm 2 vs. control          1.0000 0 0
## treatment arm 3 vs. control          1.0000 0 0
## treatment arm 4 vs. control          1.0000 0 0
## Selected arms, omega_max = 0.6
## treatment arm 1 vs. control          1.0000 1.0000 0.9000
## treatment arm 2 vs. control          1.0000 0 0
## treatment arm 3 vs. control          1.0000 0 0
## treatment arm 4 vs. control          1.0000 0 0
## Number of active arms, omega_max = 0.3    4.000 1.000 1.000
## Number of active arms, omega_max = 0.4    4.000 1.000 1.000
## Number of active arms, omega_max = 0.5    4.000 1.000 1.000
## Number of active arms, omega_max = 0.6    4.000 1.000 1.000
##
## Legend:
## (i): results of treatment arm i vs. control arm

```

5 Analysis results summaries

5.1 Create three different designs

```

design1 <- getDesignInverseNormal(kMax = 4, alpha = 0.02,
  futilityBounds = c(-0.5, 0, 0.5), bindingFutility = FALSE,
  typeOfDesign = "asKD", gammaA = 1.2,
  informationRates = c(0.15, 0.4, 0.7, 1))

design2 <- getDesignFisher(kMax = 4, alpha = 0.02,

```

```
alpha0Vec = c(0.7, 0.5, 0.3), method = "equalAlpha",
bindingFutility = TRUE, informationRates = c(0.15, 0.4, 0.7, 1))

design3 <- getDesignConditionalDunnett(alpha = 0.02,
informationAtInterim = 0.4, secondStageConditioning = TRUE)
```

5.2 Analysis results base

5.2.1 Analysis results base - means

```
simpleDataExampleMeans1 <- getDataset(
  n = c(120, 130, 130),
  means = c(0.45, 0.51, 0.45) * 100,
  stDevs = c(1.3, 1.4, 1.2) * 100
)

summary(getAnalysisResults(design = design1, dataInput = simpleDataExampleMeans1,
  nPlanned = 130, thetaH0 = 30, thetaH1 = 60, assumedStDev = 100))
```

Calculation of final confidence interval performed for kMax = 4 (for kMax > 2, it is theoretically s

Analysis results for a continuous endpoint

##

Sequential analysis with 4 looks (inverse normal combination test design).

The results were calculated using a one-sample t-test (one-sided).

H0: $\mu = 30$ against H1: $\mu > 30$, assumed effect = 60,

assumed standard deviation = 100.

##

## Stage	1	2	3	4
## Fixed weight	0.387	0.5	0.548	0.548
## Efficacy boundary (z-value scale)	2.870	2.572	2.391	2.272
## Futility boundary (z-value scale)	-0.500	0.000	0.500	
## Cumulative alpha spent	0.0021	0.0067	0.0130	0.0200
## Stage level	0.0021	0.0050	0.0084	0.0116
## Overall effect size	45.000	48.120	47.053	
## Overall standard deviation	130.000	135.055	129.950	
## Test statistics	1.264	1.710	1.425	
## p-value	0.1044	0.0448	0.0783	
## Inverse normal combination	1.257	2.112	2.524	
## Test action	continue	continue	reject and stop	
## Conditional rejection probability	0.0433	0.1706	0.3851	
## Planned sample size				130
## Conditional power				0.9991
## Repeated confidence interval	10.269 - 79.731	25.952 - 70.719	30.900 - 63.004	
## Repeated p-value	0.5000	0.0662	0.0141	
## Final p-value			0.0108	
## Final confidence interval			31.784 - 60.146	
## Median unbiased estimate			46.183	

```
summary(getAnalysisResults(design = design1, dataInput = simpleDataExampleMeans1,
  nPlanned = 130, thetaH0 = 35, thetaH1 = 60), digits = 0)
```

Analysis results for a continuous endpoint

##

Sequential analysis with 4 looks (inverse normal combination test design).

```

## The results were calculated using a one-sample t-test (one-sided).
## H0: mu = 35 against H1: mu > 35, assumed effect = 60.
##
## Stage          1          2          3          4
## Fixed weight   0.387     0.5      0.548     0.548
## Efficacy boundary (z-value scale) 2.870     2.572     2.391     2.272
## Futility boundary (z-value scale) -0.500     0.000     0.500
## Cumulative alpha spent 0.002053  0.006660  0.013036  0.020000
## Stage level    0.002053  0.005050  0.008402  0.011555
## Overall effect size 45.00     48.12     47.05
## Overall standard deviation 130.0     135.1     130.0
## Test statistics 0.843     1.303     0.950
## p-value        0.20056   0.09744   0.17191
## Inverse normal combination 0.840     1.539     1.783
## Test action    continue   continue   continue
## Conditional rejection probability 0.02622   0.06339   0.07727
## Planned sample size                                130
## Assumed standard deviation                          130
## Conditional power                                0.7793
## Repeated confidence interval 10.27 - 79.73 25.95 - 70.72 30.90 - 63.00
## Repeated p-value >0.5     0.22335   0.08044
## Final p-value
## Final confidence interval
## Median unbiased estimate

```

```

summary(getAnalysisResults(design = design1, dataInput = simpleDataExampleMeans1,
  nPlanned = 130, thetaH0 = 35))

```

```

## Analysis results for a continuous endpoint
##
## Sequential analysis with 4 looks (inverse normal combination test design).
## The results were calculated using a one-sample t-test (one-sided).
## H0: mu = 35 against H1: mu > 35.
##
## Stage          1          2          3          4
## Fixed weight   0.387     0.5      0.548     0.548
## Efficacy boundary (z-value scale) 2.870     2.572     2.391     2.272
## Futility boundary (z-value scale) -0.500     0.000     0.500
## Cumulative alpha spent 0.0021     0.0067     0.0130     0.0200
## Stage level    0.0021     0.0050     0.0084     0.0116
## Overall effect size 45.000     48.120     47.053
## Overall standard deviation 130.000     135.055     129.950
## Test statistics 0.843     1.303     0.950
## p-value        0.2006     0.0974     0.1719
## Inverse normal combination 0.840     1.539     1.783
## Test action    continue   continue   continue
## Conditional rejection probability 0.0262     0.0634     0.0773
## Planned sample size                                130
## Assumed effect                                47.053
## Assumed standard deviation                      129.950
## Conditional power                                0.3571
## Repeated confidence interval 10.269 - 79.731 25.952 - 70.719 30.900 - 63.004
## Repeated p-value 0.5000     0.2234     0.0804
## Final p-value
## Final confidence interval

```

```
## Median unbiased estimate
```

```
summary(getAnalysisResults(design = design2, dataInput = simpleDataExampleMeans1,
  nPlanned = 130, thetaH1 = 50, assumedStDev = 100, thetaH0 = 35))
```

```
## Analysis results for a continuous endpoint
```

```
##
```

```
## Sequential analysis with 4 looks (Fisher's combination test design).
```

```
## The results were calculated using a one-sample t-test (one-sided).
```

```
## H0: mu = 35 against H1: mu > 35, assumed effect = 50,
```

```
## assumed standard deviation = 100.
```

```
##
```

## Stage	1	2	3	
## Fixed weight	1	1.291	1.414	
## Efficacy boundary (p product scale)	0.008926256	0.000396949	0.000023125	0.000
## Futility boundary (separate p-value scale)	0.7000	0.5000	0.3000	
## Cumulative alpha spent	0.0089	0.0149	0.0184	
## Stage level	0.0089	0.0089	0.0089	
## Overall effect size	45.000	48.120	47.053	
## Overall standard deviation	130.000	135.055	129.950	
## Test statistics	0.843	1.303	0.950	
## p-value	0.2006	0.0974	0.1719	
## Fisher combination	0.2005573	0.0099241	0.0008227	
## Test action	continue	continue	continue	
## Conditional rejection probability	0.0160	0.0210	0.0137	
## Planned sample size				
## Conditional power				
## Repeated confidence interval	16.495 - 73.505	25.961 - 70.640	28.714 - 65.004	
## Repeated p-value	0.3009	0.1574	0.1349	
## Final p-value				
## Final confidence interval				
## Median unbiased estimate				

```
simpleDataExampleMeans2 <- getDataset(
  n1 = c(23, 13, 22, 13),
  n2 = c(22, 11, 22, 11),
  means1 = c(2.7, 2.5, 4.5, 2.5) * 100,
  means2 = c(1, 1.1, 1.3, 1) * 100,
  stds1 = c(1.3, 2.4, 2.2, 1.3) * 100,
  stds2 = c(1.2, 2.2, 2.1, 1.3) * 100
)
```

```
summary(getAnalysisResults(design = design1, dataInput = simpleDataExampleMeans2,
  equalVariances = TRUE, directionUpper = TRUE))
```

```
## Analysis results for a continuous endpoint
```

```
##
```

```
## Sequential analysis with 4 looks (inverse normal combination test design).
```

```
## The results were calculated using a two-sample t-test (one-sided),
```

```
## equal variances option.
```

```
## H0: mu(1) - mu(2) = 0 against H1: mu(1) - mu(2) > 0.
```

```
##
```

## Stage	1	2	3	
## Fixed weight	0.387	0.5	0.548	
## Efficacy boundary (z-value scale)	2.870	2.572	2.391	

```

## Futility boundary (z-value scale)          -0.500          0.000          0.500
## Cumulative alpha spent                    0.0021          0.0067          0.0130
## Stage level                              0.0021          0.0050          0.0084
## Overall effect size                      170.000         159.444         219.793
## Overall standard deviation                125.216         166.324         196.455
## Test statistics                          4.553           1.479           4.935
## p-value                                  <0.0001         0.0767          <0.0001
## Inverse normal combination                4.090           3.633           5.599
## Test action                               reject and stop reject and stop reject and stop
## Conditional rejection probability          0.5469          0.7525          1.0000
## Planned sample size
## Assumed effect
## Assumed standard deviation
## Conditional power
## Repeated confidence interval              56.780 - 283.220 50.708 - 267.898 129.271 - 304.606 127.414 - 266.114
## Repeated p-value                        0.0002          0.0006          <0.0001
## Final p-value                           <0.0001
## Final confidence interval                 93.310 - 246.690
## Median unbiased estimate                 170.000

summary(getAnalysisResults(design = design2, dataInput = simpleDataExampleMeans2,
  thetaH0 = 110, equalVariances = FALSE, directionUpper = TRUE, seed = 4343))

## Final p-value cannot be calculated for kMax = 4 because the function for Fisher's design is implemented
## Calculation of final confidence interval for Fisher's design not implemented yet
## Analysis results for a continuous endpoint
##
## Sequential analysis with 4 looks (Fisher's combination test design).
## The results were calculated using a two-sample t-test (one-sided),
## unequal variances option.
## H0: mu(1) - mu(2) = 110 against H1: mu(1) - mu(2) > 110.
##
## Stage                                1                2                3
## Fixed weight                          1                1.291            1.414
## Efficacy boundary (p product scale)    0.008926256     0.000396949     0.000023125
## Futility boundary (separate p-value scale) 0.7000          0.5000          0.3000
## Cumulative alpha spent                 0.0089          0.0149          0.0184
## Stage level                            0.0089          0.0089          0.0089
## Overall effect size                    170.000         159.444         219.793
## Overall standard deviation              125.216         166.324         196.455
## Test statistics                         1.610           0.319           3.239
## p-value                                 0.0574          0.3763          0.0012
## Fisher combination                      0.0573934199    0.0162503095    0.0000011693
## Test action                             continue         continue         reject and stop
## Conditional rejection probability        0.0357          0.0154          1.0000
## Planned sample size
## Assumed effect
## Assumed standard deviation
## Conditional power
## Repeated confidence interval            78.186 - 261.814 62.257 - 264.009 135.651 - 288.520 127.414 - 266.114
## Repeated p-value                       0.1067          0.2083          0.0033
## Final p-value
## Final confidence interval
## Median unbiased estimate

```

5.2.2 Analysis results base - rates

```
simpleDataExampleRates1 <- getDataset(
  n = c(8, 10, 9, 11),
  events = c(4, 5, 5, 6)
)

summary(getAnalysisResults(design = design1, dataInput = simpleDataExampleRates1,
  stage = 3, thetaH0 = 0.75, normalApproximation = TRUE, directionUpper = FALSE,
  nPlanned = 10))
```

```
## Calculation of final confidence interval performed for kMax = 4 (for kMax > 2, it is theoretically s
```

```
## Analysis results for a binary endpoint
```

```
##
```

```
## Sequential analysis with 4 looks (inverse normal combination test design).
```

```
## The results were calculated using a one-sample test for rates (one-sided),
```

```
## normal approximation.
```

```
## H0: pi = 0.75 against H1: pi < 0.75.
```

```
##
```

## Stage	1	2	3	4
## Fixed weight	0.387	0.5	0.548	0.548
## Efficacy boundary (z-value scale)	2.870	2.572	2.391	2.272
## Futility boundary (z-value scale)	-0.500	0.000	0.500	
## Cumulative alpha spent	0.0021	0.0067	0.0130	0.0200
## Stage level	0.0021	0.0050	0.0084	0.0116
## Overall effect size	0.500	0.500	0.519	
## Test statistics	-1.633	-1.826	-1.347	
## p-value	0.0512	0.0339	0.0890	
## Inverse normal combination	1.633	2.443	2.729	
## Test action	continue	continue	reject	and stop
## Conditional rejection probability	0.0669	0.2722	0.5084	
## Planned sample size				10
## Assumed treatment rate			0.519	
## Conditional power				0.9310
## Repeated confidence interval	0.144 - 0.856	0.240 - 0.760	0.307 - 0.727	
## Repeated p-value	0.4992	0.0285	0.0079	
## Final p-value			0.0087	
## Final confidence interval			0.300 - 0.714	
## Median unbiased estimate			0.502	

```
summary(getAnalysisResults(design = design1, dataInput = simpleDataExampleRates1,
  stage = 3, thetaH0 = 0.75, normalApproximation = FALSE, directionUpper = FALSE))
```

```
## Analysis results for a binary endpoint
```

```
##
```

```
## Sequential analysis with 4 looks (inverse normal combination test design).
```

```
## The results were calculated using a one-sample test for rates (one-sided).
```

```
## H0: pi = 0.75 against H1: pi < 0.75.
```

```
##
```

## Stage	1	2	3	4
## Fixed weight	0.387	0.5	0.548	0.548
## Efficacy boundary (z-value scale)	2.870	2.572	2.391	2.272
## Futility boundary (z-value scale)	-0.500	0.000	0.500	
## Cumulative alpha spent	0.0021	0.0067	0.0130	0.0200


```
## Stage level                0.0021      0.0050      0.0084      0.0116
## Overall effect size        0.500      0.500      0.519
## Test statistics
## p-value                    0.1138      0.0781      0.1657
## Inverse normal combination 1.206      1.860      2.042
## Test action                 continue    continue    continue
## Conditional rejection probability 0.0408    0.1134    0.1518
## Planned sample size
## Assumed treatment rate                                0.519
## Conditional power
## Repeated confidence interval 0.078 - 0.922 0.188 - 0.812 0.258 - 0.776
## Repeated p-value          0.5000      0.1172      0.0464
## Final p-value
## Final confidence interval
## Median unbiased estimate
```

```
summary(getAnalysisResults(design = design2, dataInput = simpleDataExampleRates1,
  stage = 3, thetaH0 = 0.7986, normalApproximation = FALSE, directionUpper = FALSE))
```

```
## Final p-value cannot be calculated for kMax = 4 because the function for Fisher's design is implemented
```

```
## Calculation of final confidence interval for Fisher's design not implemented yet
```

```
## Analysis results for a binary endpoint
```

```
##
```

```
## Sequential analysis with 4 looks (Fisher's combination test design).
```

```
## The results were calculated using a one-sample test for rates (one-sided).
```

```
## H0:  $\pi = 0.799$  against H1:  $\pi < 0.799$ .
```

```
##
```

```
## Stage                1                2                3
## Fixed weight          1                1.291            1.414
## Efficacy boundary (p product scale) 0.008926256    0.000396949    0.000023125    0.000
## Futility boundary (separate p-value scale) 0.7000        0.5000          0.3000
## Cumulative alpha spent 0.0089        0.0149          0.0184
## Stage level          0.0089        0.0089          0.0089
## Overall effect size  0.500        0.500          0.519
## Test statistics
## p-value              0.0576        0.0337          0.0875
## Fisher combination   0.0575751    0.0007242      0.0000231
## Test action          continue      continue reject and stop
## Conditional rejection probability 0.0356      0.1061          1.0000
## Planned sample size
## Assumed treatment rate                                0.519
## Conditional power
## Repeated confidence interval 0.117 - 0.883 0.188 - 0.812 0.233 - 0.799
## Repeated p-value          0.1070      0.0301          0.0200
## Final p-value
## Final confidence interval
## Median unbiased estimate
```

```
simpleDataExampleRates2 <- getDataset(
  n1 = c(17, 23, 22),
  n2 = c(18, 20, 19),
  events1 = c(11, 12, 17),
  events2 = c(5, 10, 7)
)
```

```
summary(getAnalysisResults(design1, simpleDataExampleRates2, thetaH0 = 0, stage = 2, directionUpper = TRUE,
  normalApproximation = FALSE, pi1 = 0.9, pi2 = 0.3, nPlanned = c(20,20)))
```

```
## Repeated confidence intervals will be calculated under the normal approximation
```

```
## Analysis results for a binary endpoint
```

```
##
```

```
## Sequential analysis with 4 looks (inverse normal combination test design).
```

```
## The results were calculated using a two-sample test for rates (one-sided).
```

```
## H0:  $\pi(1) - \pi(2) = 0$  against H1:  $\pi(1) - \pi(2) > 0$ , assumed treatment rate = 0.9,
```

```
## assumed control rate = 0.3.
```

```
##
```

## Stage	1	2	3	4
## Fixed weight	0.387	0.5	0.548	0.548
## Efficacy boundary (z-value scale)	2.870	2.572	2.391	2.272
## Futility boundary (z-value scale)	-0.500	0.000	0.500	
## Cumulative alpha spent	0.0021	0.0067	0.0130	0.0200
## Stage level	0.0021	0.0050	0.0084	0.0116
## Overall effect size	0.369	0.180		
## Test statistics				
## p-value	0.0313	0.5648		
## Inverse normal combination	1.862	1.011		
## Test action	continue	continue		
## Conditional rejection probability	0.0863	0.0213		
## Planned sample size			20	20
## Conditional power			0.7257	0.9884
## Repeated confidence interval	-0.111 - 0.711	-0.125 - 0.429		
## Repeated p-value	0.3048	0.5000		
## Final p-value				
## Final confidence interval				
## Median unbiased estimate				

```
summary(getAnalysisResults(design2, simpleDataExampleRates2, thetaH0 = 0, stage = 2, directionUpper = TRUE,
  normalApproximation = TRUE, pi1 = 0.9, pi2 = 0.3, nPlanned = c(20,20)))
```

```
## Analysis results for a binary endpoint
```

```
##
```

```
## Sequential analysis with 4 looks (Fisher's combination test design).
```

```
## The results were calculated using a two-sample test for rates (one-sided),
```

```
## normal approximation.
```

```
## H0:  $\pi(1) - \pi(2) = 0$  against H1:  $\pi(1) - \pi(2) > 0$ .
```

```
##
```

## Stage	1	2	3	4
## Fixed weight	1	1.291	1.414	1.414
## Efficacy boundary (p product scale)	0.008926256	0.000396949	0.000023125	0.0000019
## Futility boundary (separate p-value scale)	0.7000	0.5000	0.3000	
## Cumulative alpha spent	0.0089	0.0149	0.0184	0.0200
## Stage level	0.0089	0.0089	0.0089	0.0089
## Overall effect size	0.369	0.180		
## Test statistics	2.192	0.142		
## p-value	0.0142	0.4434		
## Fisher combination	0.014194	0.004968		
## Test action	continue	continue		
## Conditional rejection probability	0.0876	0.0324		
## Planned sample size				

```
## Assumed treatment rate                0.575
## Assumed control rate                  0.395
## Conditional power
## Repeated confidence interval          -0.030 - 0.668 -0.095 - 0.391
## Repeated p-value                      0.0306      0.1041
## Final p-value
## Final confidence interval
## Median unbiased estimate

summary(getAnalysisResults(design2, simpleDataExampleRates2, thetaH0 = 0, stage = 2, directionUpper = TRUE,
  normalApproximation = TRUE))
```

```
## Analysis results for a binary endpoint
##
## Sequential analysis with 4 looks (Fisher's combination test design).
## The results were calculated using a two-sample test for rates (one-sided),
## normal approximation.
## H0: pi(1) - pi(2) = 0 against H1: pi(1) - pi(2) > 0.
##
## Stage                1                2                3
## Fixed weight        1                1.291            1.414            1.4
## Efficacy boundary (p product scale)  0.008926256    0.000396949    0.000023125    0.0000019
## Futility boundary (separate p-value scale)  0.7000        0.5000        0.3000
## Cumulative alpha spent  0.0089        0.0149        0.0184        0.02
## Stage level         0.0089        0.0089        0.0089        0.00
## Overall effect size  0.369        0.180
## Test statistics     2.192        0.142
## p-value             0.0142        0.4434
## Fisher combination  0.014194     0.004968
## Test action         continue      continue
## Conditional rejection probability  0.0876        0.0324
## Planned sample size
## Assumed treatment rate                0.575
## Assumed control rate                  0.395
## Conditional power
## Repeated confidence interval          -0.030 - 0.668 -0.095 - 0.391
## Repeated p-value                      0.0306      0.1041
## Final p-value
## Final confidence interval
## Median unbiased estimate
```

5.2.3 Analysis results base - survival

```
simpleDataExampleSurvival <- getDataset(
  overallEvents = c(8, 15, 29),
  overallAllocationRatios = c(1, 1, 1),
  overallLogRanks = c(1.52, 1.38, 2.9)
)

simpleDataExampleSurvival$getNumberOfGroups()

## [1] 2

summary(getAnalysisResults(design1, simpleDataExampleSurvival, directionUpper = TRUE))
```

```

## Calculation of final confidence interval performed for kMax = 4 (for kMax > 2, it is theoretically s
## Analysis results for a survival endpoint
##
## Sequential analysis with 4 looks (inverse normal combination test design).
## The results were calculated using a two-sample logrank test (one-sided).
## H0: hazard ratio = 1 against H1: hazard ratio > 1.
##
## Stage          1          2          3          4
## Fixed weight      0.387      0.5      0.548      0.548
## Efficacy boundary (z-value scale)  2.870      2.572      2.391      2.272
## Futility boundary (z-value scale) -0.500      0.000      0.500
## Cumulative alpha spent  0.0021      0.0067      0.0130      0.0200
## Stage level      0.0021      0.0050      0.0084      0.0116
## Overall effect size  2.929      2.039      2.936
## Test statistics   1.520      0.395      2.745
## p-value          0.0643      0.3464      0.0030
## Inverse normal combination  1.520      1.243      2.737
## Test action              continue      continue reject and stop
## Conditional rejection probability  0.0588      0.0350      0.5134
## Planned sample size
## Assumed effect              2.936
## Conditional power
## Repeated confidence interval  0.385 - 22.290  0.499 - 7.358  1.138 - 6.825
## Repeated p-value          0.5000      0.3740      0.0077
## Final p-value              0.0087
## Final confidence interval              1.160 - 5.900
## Median unbiased estimate              2.686
summary(getAnalysisResults(design2, simpleDataExampleSurvival, thetaH0 = 1.1, stage = 2,
  nPlanned = c(20, 40), allocationRatioPlanned = 0.5, thetaH1 = 0.5, directionUpper = FALSE))

```

```

## Calculation of final confidence interval for Fisher's design not implemented yet
## Analysis results for a survival endpoint
##
## Sequential analysis with 4 looks (Fisher's combination test design).
## The results were calculated using a two-sample logrank test (one-sided).
## H0: hazard ratio = 1.1 against H1: hazard ratio < 1.1,
## planned allocation ratio = 0.5, assumed effect = 0.5.
##
## Stage          1          2          3
## Fixed weight      1      1.291      1.414
## Efficacy boundary (p product scale)  0.008926256  0.000396949  0.000023125  0.000
## Futility boundary (separate p-value scale)  0.7000      0.5000      0.3000
## Cumulative alpha spent  0.0089      0.0149      0.0184
## Stage level      0.0089      0.0089      0.0089
## Overall effect size  2.929      2.039
## Test statistics   1.385      0.269
## p-value          0.9170      0.6061
## Fisher combination  0.9170      0.4804
## Test action              accept and stop accept and stop
## Conditional rejection probability  0      0
## Planned sample size              20
## Conditional power              0
## Repeated confidence interval  0.549 - 15.638  0.522 - 7.171

```

```
## Repeated p-value           0.5000           0.5000
## Final p-value              0.9170
## Final confidence interval
## Median unbiased estimate
```

5.3 Analysis results multi-arm

5.3.1 Analysis results multi-arm - means

```
dataExampleMeans <- getDataset(
  n1 = c(13, 25),
  n2 = c(15, NA),
  n3 = c(14, 27),
  n4 = c(12, 29),
  means1 = c(242, 222),
  means2 = c(188, NA),
  means3 = c(267, 277),
  means4 = c(92, 122),
  stDevs1 = c(244, 221),
  stDevs2 = c(212, NA),
  stDevs3 = c(256, 232),
  stDevs4 = c(215, 227))

summary(getAnalysisResults(design = design1, dataInput = dataExampleMeans,
  intersectionTest = "Simes", directionUpper = TRUE, varianceOption = "notPooled"))
```

```
## Multi-arm analysis results for a continuous endpoint
##
## Sequential analysis with 4 looks (inverse normal combination test design).
## The results were calculated using a multi-arm t-test (one-sided),
## Simes intersection test, not pooled variances option.
## H0:  $\mu(i) - \mu(\text{control}) = 0$  against H1:  $\mu(i) - \mu(\text{control}) > 0$ .
##
## Stage                1                2                3                4
## Fixed weight          0.387            0.5            0.548
## Efficacy boundary (z-value scale)  2.870            2.572            2.391
## Futility boundary (z-value scale) -0.500            0.000            0.500
## Cumulative alpha spent  0.0021            0.0067            0.0130
## Stage level           0.0021            0.0050            0.0084
## Overall effect size (1)  150.000           115.623
## Overall effect size (2)   96.000
## Overall effect size (3)  175.000           160.366
## Overall standard deviation (1)  230.586           223.577
## Overall standard deviation (2)  213.325
## Overall standard deviation (3)  238.086           229.435
## Test statistics (1)       1.634            1.637
## Test statistics (2)       1.160
## Test statistics (3)       1.894            2.524
## p-value (1)              0.0580           0.0539
## p-value (2)              0.1288
## p-value (3)              0.0351           0.0073
## Adjusted stage-wise p-value (1, 2, 3)  0.0870           0.0146
## Overall adjusted test statistics (1, 2, 3)  1.359            2.557
## Test action: reject (1)   FALSE            FALSE
```

```

## Test action: reject (2)                FALSE                FALSE
## Test action: reject (3)                FALSE                FALSE
## Conditional rejection probability (1)    0.0401                0.1440
## Conditional rejection probability (2)    0.0372                0.0372
## Conditional rejection probability (3)    0.0487                0.3133
## Planned sample size
## Assumed effect (1)                    115.623
## Assumed effect (2)
## Assumed effect (3)                    160.366
## Assumed standard deviation (1)         223.577
## Assumed standard deviation (2)
## Assumed standard deviation (3)         229.435
## Conditional power (1)
## Conditional power (2)
## Conditional power (3)
## Repeated confidence interval (1)        -184.337 - 484.337 -47.642 - 285.844
## Repeated confidence interval (2)        -204.267 - 396.267
## Repeated confidence interval (3)        -159.388 - 509.388 -4.033 - 329.274
## Repeated p-value (1)                   0.5000                0.0852
## Repeated p-value (2)                   0.5000
## Repeated p-value (3)                   0.5000                0.0209
##

```

```
## Legend:
```

```
## (i): results of treatment arm i vs. control arm
```

```
## (i, j, ...): comparison of treatment arms 'i, j, ...' vs. control arm
```

```
summary(getAnalysisResults(design = design1, dataInput = dataExampleMeans,
  intersectionTest = "Hierarchical", nPlanned = c(20, 20), thetaH0 = 1, directionUpper = TRUE, thetaH
```

```
## Warning: Repeated confidence intervals not available for 'intersectionTest' = "Hierarchical"
```

```
## Multi-arm analysis results for a continuous endpoint
```

```
##
```

```
## Sequential analysis with 4 looks (inverse normal combination test design).
```

```
## The results were calculated using a multi-arm t-test (one-sided),
```

```
## Hierarchical intersection test, overall pooled variances option.
```

```
## H0:  $\mu(i) - \mu(\text{control}) = 1$  against H1:  $\mu(i) - \mu(\text{control}) > 1$ , assumed effect = 5.
```

```
##
```

```
## Stage                1          2          3          4
## Fixed weight          0.387        0.5        0.548        0.548
## Efficacy boundary (z-value scale)  2.870        2.572        2.391        2.272
## Futility boundary (z-value scale) -0.500        0.000        0.500
## Cumulative alpha spent  0.0021        0.0067        0.0130        0.0200
## Stage level          0.0021        0.0050        0.0084        0.0116
## Overall effect size (1) 150.000      115.623
## Overall effect size (2)  96.000
## Overall effect size (3) 175.000      160.366
## Overall standard deviation (1) 230.586      223.577
## Overall standard deviation (2) 213.325
## Overall standard deviation (3) 238.086      229.435
## Test statistics (1)      1.600        1.599
## Test statistics (2)      1.055
## Test statistics (3)      1.902        2.538
## p-value (1)              0.0579        0.0569
## p-value (2)              0.1483

```

```

## p-value (3)                0.0315  0.0066
## Adjusted stage-wise p-value (1, 2, 3)    0.0579  0.0569
## Overall adjusted test statistics (1, 2, 3)  1.573  2.213
## Test action: reject (1)                FALSE  FALSE
## Test action: reject (2)                FALSE  FALSE
## Test action: reject (3)                FALSE  FALSE
## Conditional rejection probability (1)      0.0624  0.1985
## Conditional rejection probability (2)      0.0334
## Conditional rejection probability (3)      0.0334    0
## Planned sample size                                20    20
## Assumed standard deviation (1)            223.577
## Assumed standard deviation (2)
## Assumed standard deviation (3)            229.435
## Conditional power (1)                                0.1453  0.2128
## Conditional power (2)
## Conditional power (3)                                0    0
## Repeated confidence interval (1)
## Repeated confidence interval (2)
## Repeated confidence interval (3)
## Repeated p-value (1)                0.5000  0.0518
## Repeated p-value (2)                0.5000
## Repeated p-value (3)                0.5000  0.5000
##
## Legend:
## (i): results of treatment arm i vs. control arm
## (i, j, ...): comparison of treatment arms 'i, j, ...' vs. control arm
summary(getAnalysisResults(design = design1, dataInput = dataExampleMeans,
  intersectionTest = "Dunnnett", nPlanned = c(20, 20), directionUpper = TRUE, assumedStDevs = 5))

## Multi-arm analysis results for a continuous endpoint
##
## Sequential analysis with 4 looks (inverse normal combination test design).
## The results were calculated using a multi-arm t-test (one-sided),
## Dunnnett intersection test, overall pooled variances option.
## H0:  $\mu(i) - \mu(\text{control}) = 0$  against  $H1: \mu(i) - \mu(\text{control}) > 0$ ,
## assumed standard deviation = 5.
##
## Stage                1                2                3
## Fixed weight                0.387                0.5                0.548
## Efficacy boundary (z-value scale)                2.870                2.572                2.391
## Futility boundary (z-value scale)                -0.500                0.000                0.500
## Cumulative alpha spent                0.0021                0.0067                0.0130
## Stage level                0.0021                0.0050                0.0084
## Overall effect size (1)                150.000                115.623
## Overall effect size (2)                96.000
## Overall effect size (3)                175.000                160.366
## Overall standard deviation (1)                230.586                223.577
## Overall standard deviation (2)                213.325
## Overall standard deviation (3)                238.086                229.435
## Test statistics (1)                1.611                1.615
## Test statistics (2)                1.066
## Test statistics (3)                1.913                2.555
## p-value (1)                0.0567                0.0552
## p-value (2)                0.1458

```

```

## p-value (3)                0.0308                0.0063
## Adjusted stage-wise p-value (1, 2, 3)    0.0736                0.0119
## Overall adjusted test statistics (1, 2, 3) 1.449                  2.674
## Test action: reject (1)                FALSE                FALSE
## Test action: reject (2)                FALSE                FALSE
## Test action: reject (3)                FALSE                TRUE
## Conditional rejection probability (1)     0.0453                0.1568
## Conditional rejection probability (2)     0.0339                0.0339
## Conditional rejection probability (3)     0.0541                0.3588
## Planned sample size                                20
## Assumed effect (1)                                115.623
## Assumed effect (2)                                160.366
## Assumed effect (3)
## Conditional power (1)                                1.0000
## Conditional power (2)
## Conditional power (3)                                1.0000
## Repeated confidence interval (1)          -163.321 - 463.321 -42.557 - 277.863
## Repeated confidence interval (2)          -207.129 - 399.129
## Repeated confidence interval (3)          -132.903 - 482.903 5.095 - 319.007
## Repeated p-value (1)                    0.5000                0.0753
## Repeated p-value (2)                    0.5000
## Repeated p-value (3)                    0.5000                0.0149

```

```

##
## Legend:
## (i): results of treatment arm i vs. control arm
## (i, j, ...): comparison of treatment arms 'i, j, ...' vs. control arm
summary(getAnalysisResults(design = design2, dataInput = dataExampleMeans,
  intersectionTest = "Sidak", nPlanned = c(20, 20), directionUpper = TRUE))

```

```

## Multi-arm analysis results for a continuous endpoint
##
## Sequential analysis with 4 looks (Fisher's combination test design).
## The results were calculated using a multi-arm t-test (one-sided),
## Sidak intersection test, overall pooled variances option.
## H0:  $\mu(i) - \mu(\text{control}) = 0$  against H1:  $\mu(i) - \mu(\text{control}) > 0$ .
##
## Stage                1                2                3
## Fixed weight                1                1.291                1.414
## Efficacy boundary (p product scale)    0.008926256    0.000396949    0.000023125
## Futility boundary (separate p-value scale)    0.7000                0.5000                0.3000
## Cumulative alpha spent                0.0089                0.0149                0.0184
## Stage level                0.0089                0.0089                0.0089
## Overall effect size (1)                150.000                115.623
## Overall effect size (2)                96.000
## Overall effect size (3)                175.000                160.366
## Overall standard deviation (1)                230.586                223.577
## Overall standard deviation (2)                213.325
## Overall standard deviation (3)                238.086                229.435
## Test statistics (1)                1.611                1.615
## Test statistics (2)                1.066
## Test statistics (3)                1.913                2.555
## p-value (1)                0.0567                0.0552
## p-value (2)                0.1458
## p-value (3)                0.0308                0.0063

```



```

## Adjusted stage-wise p-value (1, 2, 3)                0.0894                0.0125
## Overall adjusted test statistics (1, 2, 3)           0.0894473            0.0003134
## Test action: reject (1)                            FALSE                 FALSE
## Test action: reject (2)                            FALSE                 FALSE
## Test action: reject (3)                            FALSE                 TRUE
## Conditional rejection probability (1)                0.0235                0.0483
## Conditional rejection probability (2)                0.0196                0.0196
## Conditional rejection probability (3)                0.0268                1.0000
## Planned sample size                                20
## Assumed effect (1)                                115.623
## Assumed effect (2)                                160.366
## Assumed effect (3)                                223.577
## Assumed standard deviation (1)                     229.435
## Assumed standard deviation (2)
## Assumed standard deviation (3)
## Conditional power (1)                              0.2340
## Conditional power (2)
## Conditional power (3)                              1.0000
## Repeated confidence interval (1)                   -117.375 - 417.375 -46.050 - 272.958
## Repeated confidence interval (2)                   -162.677 - 354.677
## Repeated confidence interval (3)                    -87.751 - 437.751  3.022 - 317.728
## Repeated p-value (1)                              0.1857                0.0697
## Repeated p-value (2)                              0.2336
## Repeated p-value (3)                              0.1560                0.0170

```

```

##
## Legend:
## (i): results of treatment arm i vs. control arm
## (i, j, ...): comparison of treatment arms 'i, j, ...' vs. control arm

```

```

summary(getAnalysisResults(design = design3, dataInput = dataExampleMeans, stage = 2, thetaH0 = 120,
  directionUpper = TRUE, normalApproximation = TRUE,
  assumedStDevs = c(24, 25, 23)))

```

```

## Multi-arm analysis results for a continuous endpoint
##
## Sequential analysis with 2 looks (conditional Dunnett test design).
## The results were calculated using a multi-arm t-test (one-sided),
## overall pooled variances option, conditional second stage p-values.
## H0:  $\mu(1) = 120$  against  $H1: \mu(1) > 120$ ,
## assumed standard deviation:  $sd(1) = 24, sd(2) = 25, sd(3) = 23$ .
##
## Stage                1                2
## Fixed information at interim                0.4
## Overall effect size (1)                   150.000                115.623
## Overall effect size (2)                    96.000
## Overall effect size (3)                   175.000                160.366
## Overall standard deviation (1)            230.586                223.577
## Overall standard deviation (2)            213.325
## Overall standard deviation (3)            238.086                229.435
## Test statistics (1)                       0.322                 -0.323
## Test statistics (2)                       -0.266
## Test statistics (3)                       0.601                 0.577
## p-value (1)                               0.3736                0.6267
## p-value (2)                               0.6051
## p-value (3)                               0.2739                0.2820

```

```

## Conditional error rate (1, 2, 3)          0.0062
## Second stage p-value (1, 2, 3)          0.3810
## Test action: reject (1)                 FALSE
## Test action: reject (2)                 FALSE
## Test action: reject (3)                 FALSE
## Planned sample size
## Assumed effect (1)                      115.623
## Assumed effect (2)
## Assumed effect (3)                      160.366
## Conditional power (1)
## Conditional power (2)
## Conditional power (3)
## Repeated confidence interval (1)        -7.244 - 225.387
## Repeated confidence interval (2)
## Repeated confidence interval (3)        39.389 - 267.535
## Repeated p-value (1)                    0.5000
## Repeated p-value (2)
## Repeated p-value (3)                    0.3768
##
## Legend:
## (i): results of treatment arm i vs. control arm
## (i, j, ...): comparison of treatment arms 'i, j, ...' vs. control arm

```

5.3.2 Analysis results multi-arm - rates

```

dataExampleRates <- getDataset(
  n1 = c(23, 25),
  n2 = c(25, NA),
  n3 = c(24, 27),
  n4 = c(22, 29),
  events1 = c(15, 12),
  events2 = c(19, NA),
  events3 = c(18, 22),
  events4 = c(12, 13))

summary(getAnalysisResults(design = design1, dataInput = dataExampleRates,
  intersectionTest = "Simes", nPlanned = c(20, 20), directionUpper = TRUE))

```

```

## Multi-arm analysis results for a binary endpoint
##
## Sequential analysis with 4 looks (inverse normal combination test design).
## The results were calculated using a multi-arm test for rates (one-sided),
## Simes intersection test, normal approximation.
## H0:  $\pi(i) - \pi(\text{control}) = 0$  against H1:  $\pi(i) - \pi(\text{control}) > 0$ .
##
## Stage          1          2          3
## Fixed weight    0.387    0.5      0.548    0.5
## Efficacy boundary (z-value scale)  2.870    2.572    2.391    2.2
## Futility boundary (z-value scale) -0.500    0.000    0.500
## Cumulative alpha spent  0.0021    0.0067    0.0130    0.02
## Stage level     0.0021    0.0050    0.0084    0.01
## Control rate    0.545
## Overall effect size (1)  0.107    0.072
## Overall effect size (2)  0.215

```

```

## Overall effect size (3)                0.205          0.294
## Test statistics (1)                    0.730          0.233
## Test statistics (2)                    1.549
## Test statistics (3)                    1.455          2.831
## p-value (1)                           0.2325         0.4078
## p-value (2)                           0.0607
## p-value (3)                           0.0728         0.0023
## Adjusted stage-wise p-value (1, 2, 3) 0.1093         0.0046
## Overall adjusted test statistics (1, 2, 3) 1.231          2.810
## Test action: reject (1)                FALSE          FALSE
## Test action: reject (2)                FALSE          FALSE
## Test action: reject (3)                FALSE          TRUE
## Conditional rejection probability (1)    0.0227         0.0088
## Conditional rejection probability (2)    0.0388
## Conditional rejection probability (3)    0.0339         0.3704
## Planned sample size                    20
## Assumed rate of treatment 1            0.562
## Assumed rate of treatment 2
## Assumed rate of treatment 3            0.784
## Assumed control rate                   0.490
## Conditional power (1)                  0.0046         0.02
## Conditional power (2)
## Conditional power (3)                  0.8143         0.93
## Repeated confidence interval (1)        -0.336 - 0.513 -0.236 - 0.356
## Repeated confidence interval (2)        -0.222 - 0.588
## Repeated confidence interval (3)        -0.237 - 0.583 -0.003 - 0.549
## Repeated p-value (1)                   0.5000         0.5000
## Repeated p-value (2)                   0.5000
## Repeated p-value (3)                   0.5000         0.0137
##
## Legend:
## (i): results of treatment arm i vs. control arm
## (i, j, ...): comparison of treatment arms 'i, j, ...' vs. control arm
summary(getAnalysisResults(design = design1, dataInput = dataExampleRates,
  intersectionTest = "Bonferroni", nPlanned = c(20, 20), directionUpper = TRUE, piTreatments = 0.6))

## Multi-arm analysis results for a binary endpoint
##
## Sequential analysis with 4 looks (inverse normal combination test design).
## The results were calculated using a multi-arm test for rates (one-sided),
## Bonferroni intersection test, normal approximation.
## H0: pi(i) - pi(control) = 0 against H1: pi(i) - pi(control) > 0,
## assumed treatment rate = 0.6.
##
## Stage                1                2                3
## Fixed weight          0.387                0.5                0.548                0.5
## Efficacy boundary (z-value scale) 2.870                2.572                2.391                2.2
## Futility boundary (z-value scale) -0.500                0.000                0.500
## Cumulative alpha spent 0.0021                0.0067                0.0130                0.02
## Stage level          0.0021                0.0050                0.0084                0.01
## Control rate         0.545
## Overall effect size (1) 0.107                0.072
## Overall effect size (2) 0.215
## Overall effect size (3) 0.205                0.294

```

```

## Test statistics (1)                0.730          0.233
## Test statistics (2)                1.549
## Test statistics (3)                1.455          2.831
## p-value (1)                       0.2325         0.4078
## p-value (2)                       0.0607
## p-value (3)                       0.0728         0.0023
## Adjusted stage-wise p-value (1, 2, 3) 0.1821         0.0046
## Overall adjusted test statistics (1, 2, 3) 0.907          2.612
## Test action: reject (1)           FALSE          FALSE
## Test action: reject (2)           FALSE          FALSE
## Test action: reject (3)           FALSE          TRUE
## Conditional rejection probability (1) 0.0227         0.0088
## Conditional rejection probability (2) 0.0283
## Conditional rejection probability (3) 0.0283         0.3346
## Planned sample size                                     20
## Assumed control rate                                     0.490
## Conditional power (1)                                     0.0074         0.04
## Conditional power (2)
## Conditional power (3)                                     0.4437         0.57
## Repeated confidence interval (1)    -0.336 - 0.513 -0.236 - 0.356
## Repeated confidence interval (2)    -0.222 - 0.588
## Repeated confidence interval (3)    -0.237 - 0.583 -0.003 - 0.549
## Repeated p-value (1)                0.5000         0.5000
## Repeated p-value (2)                0.5000
## Repeated p-value (3)                0.5000         0.0179
##
## Legend:
## (i): results of treatment arm i vs. control arm
## (i, j, ...): comparison of treatment arms 'i, j, ...' vs. control arm
summary(getAnalysisResults(design = design1, dataInput = dataExampleRates,
  intersectionTest = "Bonferroni", nPlanned = c(20, 20), directionUpper = TRUE, piTreatments = c(0.4,
## Multi-arm analysis results for a binary endpoint
##
## Sequential analysis with 4 looks (inverse normal combination test design).
## The results were calculated using a multi-arm test for rates (one-sided),
## Bonferroni intersection test, normal approximation.
## H0: pi(i) - pi(control) = 0 against H1: pi(i) - pi(control) > 0,
## assumed treatment rate: pi(1) = 0.4, pi(2) = 0.6, pi(3) = 0.5.
##
## Stage                1                2                3
## Fixed weight         0.387            0.5            0.548            0.5
## Efficacy boundary (z-value scale) 2.870            2.572            2.391            2.2
## Futility boundary (z-value scale) -0.500            0.000            0.500
## Cumulative alpha spent 0.0021            0.0067            0.0130            0.02
## Stage level         0.0021            0.0050            0.0084            0.01
## Control rate        0.545
## Overall effect size (1) 0.107            0.072
## Overall effect size (2) 0.215
## Overall effect size (3) 0.205            0.294
## Test statistics (1)  0.730            0.233
## Test statistics (2)  1.549
## Test statistics (3)  1.455            2.831
## p-value (1)         0.2325         0.4078

```

```

## p-value (2)                0.0607
## p-value (3)                0.0728      0.0023
## Adjusted stage-wise p-value (1, 2, 3) 0.1821      0.0046
## Overall adjusted test statistics (1, 2, 3) 0.907      2.612
## Test action: reject (1)      FALSE      FALSE
## Test action: reject (2)      FALSE      FALSE
## Test action: reject (3)      FALSE      TRUE
## Conditional rejection probability (1) 0.0227      0.0088
## Conditional rejection probability (2) 0.0283
## Conditional rejection probability (3) 0.0283      0.3346
## Planned sample size                20
## Assumed control rate                0.490
## Conditional power (1)                0.0004      0.00
## Conditional power (2)
## Conditional power (3)                0.2769      0.35
## Repeated confidence interval (1)    -0.336 - 0.513 -0.236 - 0.356
## Repeated confidence interval (2)    -0.222 - 0.588
## Repeated confidence interval (3)    -0.237 - 0.583 -0.003 - 0.549
## Repeated p-value (1)                0.5000      0.5000
## Repeated p-value (2)                0.5000
## Repeated p-value (3)                0.5000      0.0179
##
## Legend:
## (i): results of treatment arm i vs. control arm
## (i, j, ...): comparison of treatment arms 'i, j, ...' vs. control arm
summary(getAnalysisResults(design = design1, dataInput = dataExampleRates,
  intersectionTest = "Dunnnett", nPlanned = c(20, 20), directionUpper = TRUE, piControl = 0.6))

## Multi-arm analysis results for a binary endpoint
##
## Sequential analysis with 4 looks (inverse normal combination test design).
## The results were calculated using a multi-arm test for rates (one-sided),
## Dunnnett intersection test, normal approximation.
## H0: pi(i) - pi(control) = 0 against H1: pi(i) - pi(control) > 0,
## assumed control rate = 0.6.
##
## Stage                1                2                3
## Fixed weight          0.387            0.5            0.548      0.5
## Efficacy boundary (z-value scale)  2.870            2.572            2.391      2.2
## Futility boundary (z-value scale) -0.500            0.000            0.500
## Cumulative alpha spent 0.0021            0.0067            0.0130      0.02
## Stage level          0.0021            0.0050            0.0084      0.01
## Control rate          0.545
## Overall effect size (1) 0.107            0.072
## Overall effect size (2) 0.215
## Overall effect size (3) 0.205            0.294
## Test statistics (1)    0.730            0.233
## Test statistics (2)    1.549
## Test statistics (3)    1.455            2.831
## p-value (1)            0.2325            0.4078
## p-value (2)            0.0607
## p-value (3)            0.0728      0.0023
## Adjusted stage-wise p-value (1, 2, 3) 0.1391      0.0045
## Overall adjusted test statistics (1, 2, 3) 1.084      2.730

```

```

## Test action: reject (1)                FALSE          FALSE
## Test action: reject (2)                FALSE          FALSE
## Test action: reject (3)                FALSE          TRUE
## Conditional rejection probability (1)    0.0227          0.0088
## Conditional rejection probability (2)    0.0351
## Conditional rejection probability (3)    0.0351          0.3812
## Planned sample size                    20
## Assumed rate of treatment 1            0.562
## Assumed rate of treatment 2
## Assumed rate of treatment 3            0.784
## Conditional power (1)                  0.0010          0.00
## Conditional power (2)
## Conditional power (3)                  0.6578          0.80
## Repeated confidence interval (1)       -0.334 - 0.512 -0.231 - 0.349
## Repeated confidence interval (2)       -0.220 - 0.587
## Repeated confidence interval (3)       -0.235 - 0.581 0.008 - 0.545
## Repeated p-value (1)                   0.5000          0.5000
## Repeated p-value (2)                   0.5000
## Repeated p-value (3)                   0.5000          0.0127
##
## Legend:
## (i): results of treatment arm i vs. control arm
## (i, j, ...): comparison of treatment arms 'i, j, ...' vs. control arm
summary(getAnalysisResults(design = design2, dataInput = dataExampleRates,
  intersectionTest = "Sidak", nPlanned = c(20, 20), directionUpper = TRUE))

## Multi-arm analysis results for a binary endpoint
##
## Sequential analysis with 4 looks (Fisher's combination test design).
## The results were calculated using a multi-arm test for rates (one-sided),
## Sidak intersection test, normal approximation.
## H0:  $\pi(i) - \pi(\text{control}) = 0$  against H1:  $\pi(i) - \pi(\text{control}) > 0$ .
##
## Stage                1                2                3
## Fixed weight         1                1.291            1.414            1.4
## Efficacy boundary (p product scale)    0.008926256    0.000396949    0.000023125    0.0000019
## Futility boundary (separate p-value scale) 0.7000            0.5000            0.3000
## Cumulative alpha spent 0.0089            0.0149            0.0184            0.02
## Stage level          0.0089            0.0089            0.0089            0.00
## Control rate         0.545
## Overall effect size (1) 0.107            0.072
## Overall effect size (2) 0.215
## Overall effect size (3) 0.205            0.294
## Test statistics (1)  0.730            0.233
## Test statistics (2)  1.549
## Test statistics (3)  1.455            2.831
## p-value (1)          0.2325            0.4078
## p-value (2)          0.0607
## p-value (3)          0.0728            0.0023
## Adjusted stage-wise p-value (1, 2, 3) 0.1713            0.0046
## Overall adjusted test statistics (1, 2, 3) 0.1712944    0.0001661
## Test action: reject (1)                FALSE          FALSE
## Test action: reject (2)                FALSE          FALSE
## Test action: reject (3)                FALSE          TRUE

```

```

## Conditional rejection probability (1)          0.0145      0.0059
## Conditional rejection probability (2)          0.0177
## Conditional rejection probability (3)          0.0177      1.0000
## Planned sample size                                20
## Assumed rate of treatment 1                    0.562
## Assumed rate of treatment 2
## Assumed rate of treatment 3                    0.784
## Assumed control rate                          0.490
## Conditional power (1)                          0.0100      0.0100
## Conditional power (2)
## Conditional power (3)                          1.0000      1.0000
## Repeated confidence interval (1)      -0.280 - 0.466 -0.236 - 0.350
## Repeated confidence interval (2)      -0.163 - 0.546
## Repeated confidence interval (3)      -0.178 - 0.540 0.017 - 0.544
## Repeated p-value (1)                  0.3373      0.3373
## Repeated p-value (2)                  0.2658
## Repeated p-value (3)                  0.2658      0.0109
##
## Legend:
## (i): results of treatment arm i vs. control arm
## (i, j, ...): comparison of treatment arms 'i, j, ...' vs. control arm
summary(getAnalysisResults(design = design3, dataInput = dataExampleRates, normalApproximation = FALSE,
  intersectionTest = "Dunnnett", directionUpper = TRUE))

## Multi-arm analysis results for a binary endpoint
##
## Sequential analysis with 2 looks (conditional Dunnnett test design).
## The results were calculated using a multi-arm test for rates (one-sided),
## conditional second stage p-values.
## H0: pi(1) = 0 against H1: pi(1) > 0.
##
## Stage          1          2
## Fixed information at interim          0.4
## Control rate          0.545
## Overall effect size (1)          0.107          0.072
## Overall effect size (2)          0.215
## Overall effect size (3)          0.205          0.294
## Test statistics (1)          0.730          0.233
## Test statistics (2)          1.549
## Test statistics (3)          1.455          2.831
## p-value (1)          0.2325          0.4078
## p-value (2)          0.0607
## p-value (3)          0.0728          0.0023
## Conditional error rate (1, 2, 3)          0.0531
## Second stage p-value (1, 2, 3)          0.0026
## Test action: reject (1)          FALSE          FALSE
## Test action: reject (2)          FALSE          FALSE
## Test action: reject (3)          FALSE          TRUE
## Planned sample size
## Assumed rate of treatment 1                    0.562
## Assumed rate of treatment 2
## Assumed rate of treatment 3                    0.784
## Assumed control rate                          0.490
## Conditional power (1)

```

```

## Conditional power (2)
## Conditional power (3)
## Repeated confidence interval (1)           -0.153 - 0.294
## Repeated confidence interval (2)
## Repeated confidence interval (3)           0.084 - 0.497
## Repeated p-value (1)                       0.2603
## Repeated p-value (2)
## Repeated p-value (3)                       0.0018
##
## Legend:
##   (i): results of treatment arm i vs. control arm
##   (i, j, ...): comparison of treatment arms 'i, j, ...' vs. control arm

```

5.3.3 Analysis results multi-arm - survival

```

dataExampleSurvival <- getDataset(
  events1 = c(25, 32),
  events2 = c(18, NA),
  events3 = c(22, 36),
  logRanks1 = c(2.2, 1.8),
  logRanks2 = c(1.99, NA),
  logRanks3 = c(2.32, 2.11)
)

summary(getAnalysisResults(design = design1, dataInput = dataExampleSurvival,
  intersectionTest = "Simes", nPlanned = c(20, 20), directionUpper = TRUE))

```

```

## Multi-arm analysis results for a survival endpoint
##
## Sequential analysis with 4 looks (inverse normal combination test design).
## The results were calculated using a multi-arm logrank test (one-sided),
## Simes intersection test.
## H0: hazard ratio(i) = 1 against H1: hazard ratio(i) > 1.
##
## Stage                1                2                3
## Fixed weight          0.387            0.5              0.548            0.5
## Efficacy boundary (z-value scale)  2.870            2.572            2.391            2.2
## Futility boundary (z-value scale) -0.500            0.000            0.500
## Cumulative alpha spent  0.0021           0.0067           0.0130           0.02
## Stage level           0.0021           0.0050           0.0084           0.01
## Overall effect size (1)  2.411            2.103
## Overall effect size (2)  2.555
## Overall effect size (3)  2.689            2.252
## Test statistics (1)     2.200            1.800
## Test statistics (2)     1.990
## Test statistics (3)     2.320            2.110
## p-value (1)             0.0139           0.0359
## p-value (2)             0.0233
## p-value (3)             0.0102           0.0174
## Adjusted stage-wise p-value (1, 2, 3)  0.0209           0.0349
## Overall adjusted test statistics (1, 2, 3)  2.036            2.681
## Test action: reject (1)  FALSE            TRUE
## Test action: reject (2)  FALSE            FALSE
## Test action: reject (3)  FALSE            TRUE

```



```

## Conditional rejection probability (1)          0.0991          0.3460
## Conditional rejection probability (2)          0.0991
## Conditional rejection probability (3)          0.1041          0.3616
## Planned sample size                                20
## Assumed effect (1)                                2.103
## Assumed effect (2)
## Assumed effect (3)                                2.252
## Conditional power (1)                                0.8554          0.96
## Conditional power (2)
## Conditional power (3)                                0.8959          0.97
## Repeated confidence interval (1)          0.670 - 8.675  0.921 - 4.783
## Repeated confidence interval (2)          0.565 - 11.555
## Repeated confidence interval (3)          0.687 - 10.530  1.002 - 5.152
## Repeated p-value (1)                        0.2270          0.0164
## Repeated p-value (2)                        0.2270
## Repeated p-value (3)                        0.2032          0.0147
##
## Legend:
## (i): results of treatment arm i vs. control arm
## (i, j, ...): comparison of treatment arms 'i, j, ...' vs. control arm
summary(getAnalysisResults(design = design2, dataInput = dataExampleSurvival,
  intersectionTest = "Sidak", nPlanned = c(20, 20), directionUpper = TRUE))

## Multi-arm analysis results for a survival endpoint
##
## Sequential analysis with 4 looks (Fisher's combination test design).
## The results were calculated using a multi-arm logrank test (one-sided),
## Sidak intersection test.
## H0: hazard ratio(i) = 1 against H1: hazard ratio(i) > 1.
##
## Stage          1          2          3          4
## Fixed weight          1          1.291          1.414          1.414
## Efficacy boundary (p product scale)          0.008926256  0.000396949  0.000023125  0.000001911
## Futility boundary (separate p-value scale)          0.7000          0.5000          0.3000
## Cumulative alpha spent          0.0089          0.0149          0.0184          0.0200
## Stage level          0.0089          0.0089          0.0089          0.0089
## Overall effect size (1)          2.411          2.103
## Overall effect size (2)          2.555
## Overall effect size (3)          2.689          2.252
## Test statistics (1)          2.200          1.800
## Test statistics (2)          1.990
## Test statistics (3)          2.320          2.110
## p-value (1)          0.0139          0.0359
## p-value (2)          0.0233
## p-value (3)          0.0102          0.0174
## Adjusted stage-wise p-value (1, 2, 3)          0.0302          0.0346
## Overall adjusted test statistics (1, 2, 3)          0.030202  0.000392
## Test action: reject (1)          FALSE          TRUE
## Test action: reject (2)          FALSE          FALSE
## Test action: reject (3)          FALSE          TRUE
## Conditional rejection probability (1)          0.0539          1.0000
## Conditional rejection probability (2)          0.0539
## Conditional rejection probability (3)          0.0539          1.0000
## Planned sample size                                20                                20

```

```

## Assumed effect (1)                2.103
## Assumed effect (2)
## Assumed effect (3)                2.252
## Conditional power (1)              1.0000    1.0000
## Conditional power (2)
## Conditional power (3)              1.0000    1.0000
## Repeated confidence interval (1)   0.803 - 7.241 0.921 - 4.665
## Repeated confidence interval (2)   0.699 - 9.339
## Repeated confidence interval (3)   0.833 - 8.685 1.001 - 4.920
## Repeated p-value (1)               0.0606    0.0198
## Repeated p-value (2)               0.0606
## Repeated p-value (3)               0.0606    0.0198
##

```

```
## Legend:
```

```
## (i): results of treatment arm i vs. control arm
```

```
## (i, j, ...): comparison of treatment arms 'i, j, ...' vs. control arm
```

```
summary(getAnalysisResults(design = design3, dataInput = dataExampleSurvival,
  intersectionTest = "Dunnnett", directionUpper = TRUE, thetaH0 = 2))
```

```
## Multi-arm analysis results for a survival endpoint
```

```
##
```

```
## Sequential analysis with 2 looks (conditional Dunnnett test design).
```

```
## The results were calculated using a multi-arm logrank test (one-sided),
```

```
## conditional second stage p-values.
```

```
## H0: hazard ratio = 2 against H1: hazard ratio > 2.
```

```
##
```

```
## Stage                1                2
## Fixed information at interim        0.4
## Overall effect size (1)            2.411            2.103
## Overall effect size (2)            2.555
## Overall effect size (3)            2.689            2.252
## Test statistics (1)                 0.467           -0.161
## Test statistics (2)                 0.520
## Test statistics (3)                 0.694            0.031
## p-value (1)                        0.3202           0.5638
## p-value (2)                        0.3017
## p-value (3)                        0.2437           0.4878
## Conditional error rate (1, 2, 3)    0.0103
## Second stage p-value (1, 2, 3)      0.6188
## Test action: reject (1)             FALSE           FALSE
## Test action: reject (2)             FALSE           FALSE
## Test action: reject (3)             FALSE           FALSE
## Planned sample size
## Assumed effect (1)                  2.103
## Assumed effect (2)
## Assumed effect (3)                  2.252
## Conditional power (1)
## Conditional power (2)
## Conditional power (3)
## Repeated confidence interval (1)    1.122 - 3.911
## Repeated confidence interval (2)
## Repeated confidence interval (3)    1.217 - 4.197
## Repeated p-value (1)                0.4913
## Repeated p-value (2)

```

```
## Repeated p-value (3)                0.4913
##
## Legend:
##   (i): results of treatment arm i vs. control arm
##   (i, j, ...): comparison of treatment arms 'i, j, ...' vs. control arm
```

System: rpact 3.0.3, R version 4.0.3 (2020-10-10), platform: x86_64-w64-mingw32

To cite R in publications use:

R Core Team (2020). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <https://www.R-project.org/>.

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Gernot Wassmer and Friedrich Pahlke (2020). rpact: Confirmatory Adaptive Clinical Trial Design and Analysis. R package version 3.0.3. <https://www.rpact.org>

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