example1-RPACT.R

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2026-11-06

```
# Using RPACT

# Install RPACT and GGPLOT2

library(rpact)

## Installation qualification for rpact 4.4.0 has not yet been performed.

## Please run testPackage() before using the package in GxP relevant environm
ents.

# If necessary:
#
# install.packages("ggplot2")

# Example 1: Normal responses
#
# Two-arm trial, new treatment vs control
#
# Observations distributed as
#
#   X~N(mu_c,sigma^2)  on the control arm
#
#   X~N(mu_t,sigma^2)  on the new treatment arm
#
# Treatment effect theta = mu_t - mu_c
#
# To test H_0: theta =< 0 vs theta > 0 with one-sided type I error
# probability alpha=0.025 and power 1-beta=0.9 at
#
#   theta = delta = 0.4
#
# when sigma^2 = 0.64

alpha=0.025
beta=0.1
sigma=0.8
delta=0.4
ifix=(qnorm(1-alpha)+qnorm(1-beta))^2/delta^2

# Fixed sample size design
# By default, RPACT uses the t-distribution in sample size
# calculations
# We shall assume a known variance, so give the command
```

```r
#   normalApproximation = TRUE
ss_mean <- getSampleSizeMeans(
  alpha = 0.025,
  beta = 0.1,
  sided = 1,
  alternative = 0.4,
  stDev = 0.8,
  normalApproximation = TRUE
)
summary(ss_mean)
```

Sample size calculation for a continuous endpoint

Fixed sample analysis, one-sided significance level 2.5%, power 90%. The results were calculated for a two-sample t-test (normal approximation), H0: mu(1) - mu(2) = 0, H1: effect = 0.4, standard deviation = 0.8.

Stage	Fixed
Stage level (one-sided)	0.0250
Efficacy boundary (z-value scale)	1.960
Efficacy boundary (t)	0.242
Number of subjects	168.1

Legend:

- *(t)*: treatment effect scale

```r
# Group sequential design
# Design a group sequential trial with 5 analyses
#
# Error spending design, non-binding futility boundary,
# rho-family for both spending functions, rho=2 for efficacy
# and futility boundaries
#
# In RPACT the rho-family is called the Kim and DeMets alpha
# spending function and must be specified for both the
# efficacy and the futility boundaries.
#
# Define a design object with 5 analyses and a parameter
# of 2 for the rho family
des_rho5 <- getDesignGroupSequential(
  alpha = 0.025,
  beta = 0.1,
  sided = 1,
  kMax = 5,
  typeOfDesign = "asKD",
  typeBetaSpending = "bsKD",
  gammaA = 2,
  gammaB = 2
```

```
)
# See properties of this design, including efficacy
# and futility boundaries on the Z-scale
summary(des_rho5)
```

Sequential analysis with a maximum of 5 looks (group sequential design)

Kim & DeMets alpha spending design (gammaA = 2) and Kim & DeMets beta spending (gammaB = 2), non-binding futility, one-sided overall significance level 2.5%, power 90%, undefined endpoint, inflation factor 1.1327, ASN H1 0.7062, ASN H01 0.8093, ASN H0 0.5916.

Stage	1	2	3	4	5
Planned information rate	20%	40%	60%	80%	100%
Cumulative alpha spent	0.0010	0.0040	0.0090	0.0160	0.0250
Cumulative beta spent	0.0040	0.0160	0.0360	0.0640	0.1000
Stage levels (one-sided)	0.0010	0.0033	0.0067	0.0113	0.0173
Efficacy boundary (z-value scale)	3.090	2.714	2.473	2.280	2.114
Futility boundary (z-value scale)	-1.109	-0.022	0.774	1.447	
Cumulative power	0.0609	0.3049	0.5947	0.8022	0.9000
Futility probabilities under H1	0.004	0.012	0.020	0.028	

```
# These boundaries on the Z-scale apply to cases with
# power 1-beta at the treatment effect under which type 2
# error is spent.
# The sample size and hence, the absolute information
# levels, need to be chosen to give power 1-beta
# at our specified alternative theta=delta.
# Based on this group sequential design, we find the
# sample size required (assuming known variance)
ss_gsd <- getSampleSizeMeans(
  design = des_rho5,
  alternative = delta,
  stDev = sigma,
```

```
  normalApproximation = T
)

ss_gsd$maxNumberOfSubjects

## [1] 190.4342

ss_gsd$maxNumberOfSubjects1

## [1] 95.2171

ss_gsd$maxNumberOfSubjects2

## [1] 95.2171

# Compare with fixed sample size
ss_gsd$nFixed

## [1] 168.1188

# extract design characteristics to get inflation factor
# (and other information)
dc_des_rho5 <- getDesignCharacteristics(des_rho5)

dc_des_rho5$inflationFactor

## [1] 1.132736

dc_des_rho5$.design$alphaSpent

## [1] 0.001 0.004 0.009 0.016 0.025

dc_des_rho5$.design$betaSpent

## [1] 0.004 0.016 0.036 0.064 0.100

# To see everything:
dc_des_rho5
```

Group sequential design characteristics

- *Number of subjects fixed*: 10.5074
- *Shift*: 11.9021
- *Inflation factor*: 1.1327
- *Informations*: 2.380, 4.761, 7.141, 9.522, 11.902
- *Power*: 0.06089, 0.30489, 0.59473, 0.80216, 0.90000
- *Rejection probabilities under H1*: 0.06089, 0.24401, 0.28984, 0.20743, 0.09784
- *Futility probabilities under H1*: 0.0040, 0.0120, 0.0200, 0.0280
- *Ratio expected vs fixed sample size under H1*: 0.7062
- *Ratio expected vs fixed sample size under a value between H0 and H1*: 0.8093

- *Ratio expected vs fixed sample size under H0*: 0.5916

```
# Information is calculated for power 1-beta at theta=1
# For information needed to give power at theta=delta, type
dc_des_rho5$information/delta^2
```

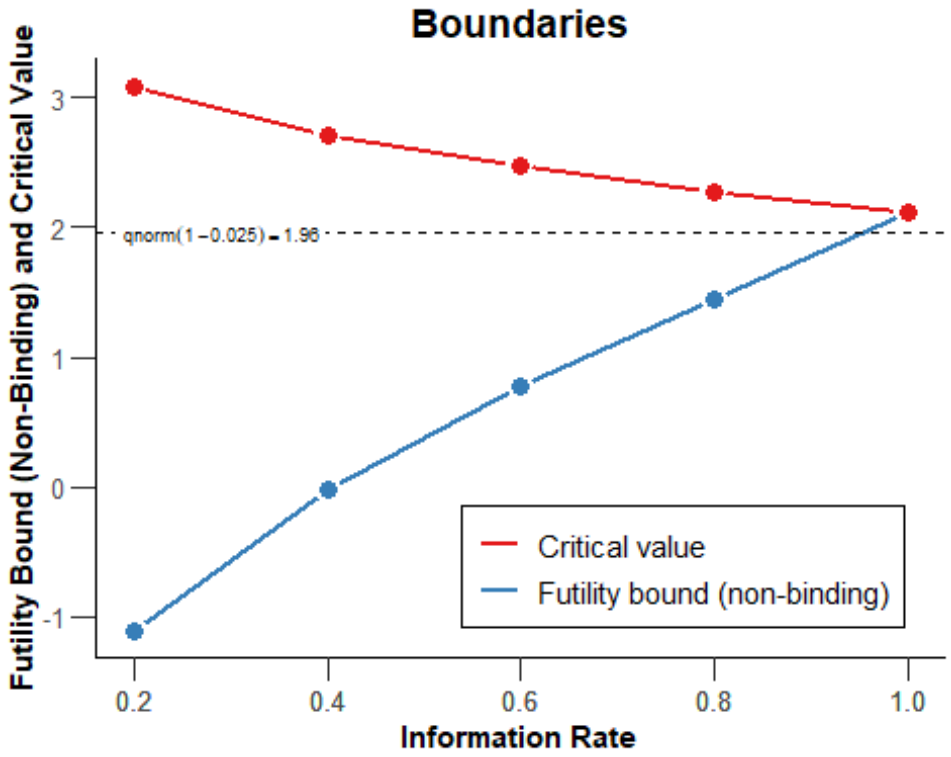
```
## [1] 14.87767 29.75534 44.63302 59.51069 74.38836
```

```
# We san also see the inflation factor as
ss_gsd$maxNumberOfSubjects/ss_gsd$nFixed
```

```
## [1] 1.132736
```

```
# We can plot the boundary

plot(des_rho5)
```




```
# Probability of stopping early under different values of theta

# store the information max from the design
iMax <- ifix * dc_des_rho5$inflationFactor
iMax
```

```
## [1] 74.38836
```

```
# get the prob. of stopping under theta = 0
asn <- getPowerAndAverageSampleNumber(
  design = des_rho5,
```

```
  theta = 0,
  nMax = iMax
)

# Focusing on sub parts we have probabilities of
#
# rejecting the null hypothesis per stage
asn$rejectPerStage

##                   [,1]
## stage = 1 0.001000000
## stage = 2 0.002999988
## stage = 3 0.004996126
## stage = 4 0.006890494
## stage = 5 0.007223386

# stopping for futility per stage
asn$futilityPerStage

##                 [,1]
## stage = 1 0.1336706
## stage = 2 0.3668944
## stage = 3 0.2920610
## stage = 4 0.1391776

# overall probability of rejecting the null hypothesis
asn$calculatedPower

## [1] 0.02310999

# probability of not rejecting the null hypothesis
1 - asn$calculatedPower

## [1] 0.97689

# expected number of patients per treatment group
asn$averageSampleNumber

## [1] 38.85233

# We can repeat this analysis for theta=delta and
# theta=delta/2
asn <- getPowerAndAverageSampleNumber(
  design = des_rho5,
  theta = c(delta, delta/2),
  nMax = iMax
)

asn$rejectPerStage

##                   [,1]       [,2]
## stage = 1 0.06088716 0.01020293
```

```
## stage = 2 0.24400678 0.04581429
## stage = 3 0.28983512 0.08496301
## stage = 4 0.20742667 0.11216731
## stage = 5 0.09784428 0.10480742

asn$futilityPerStage

##            [,1]       [,2]
## stage = 1 0.004 0.03001058
## stage = 2 0.012 0.11050370
## stage = 3 0.020 0.16730451
## stage = 4 0.028 0.18110004

asn$calculatedPower

## [1] 0.900000 0.357955

asn$averageSampleNumber

## [1] 46.37867 53.14884

# Results headed [,1] are for theta=delta
# Results headed [,2] are for theta=delta/2

# Expected sample size as a function of theta
# While there is an inflation of the maximum number of
# patients compared to a fixed sample design,
# the average sample size is reduced due to the chance
# of early stopping.

# treatment effects
theta.vec <- seq(-0.1, 0.5, by = 0.02)

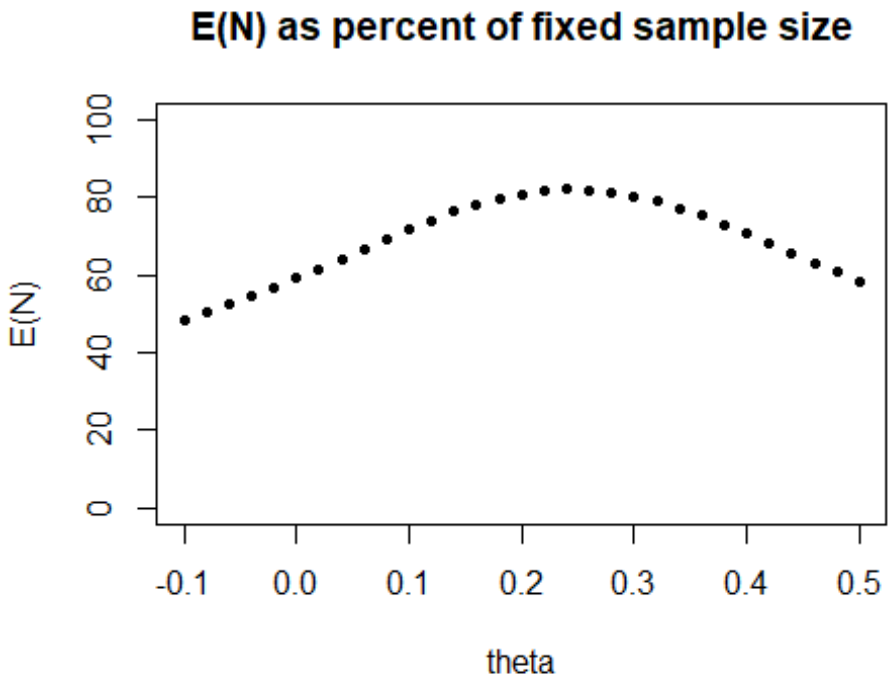
# store the information max from the design
iMax <- ifix * dc_des_rho5$inflationFactor

# expected information for each theta
asn <- getPowerAndAverageSampleNumber(
  design = des_rho5,
  theta = theta.vec,
  nMax = iMax
)

# expected information as percent of fixed design
einf.percent.vec <- 100 *
  asn$averageSampleNumber / ifix

# plot
plot(
  theta.vec,
  einf.percent.vec,
```

```
  ylim = c(0, 100),
  pch = 20,
  main = "E(N) as percent of fixed sample size",
  ylab = "E(N)",
  xlab = "theta"
)
```




```
# Example data set

# We explore the consequences of observed sample sizes and
# observed information fractions that deviate from the
# originally planned design

# Suppose we have cumulative sample sizes on treatment
# and control

nt=c(20,40,60,82,95)
nc=c(20,40,60,82,95)

iobs=1/(sigma^2/nt+sigma^2/nc)

# and treatment effect estimates

theta.hat=c(0.10,0.06,0.21,0.31)

# RPACT can calculate the error spending EFFICACY boundary
```

```r
# stage by stage

# Since the futility boundary is non-binding, we do not
# need too know what that boundary is when calculating
# the efficacy boundary.

# Analysis 1

# We have observed 40 subjects out of a target of
# ss_gsd$maxNumberOfSubjects = 190.434
# So, the observed information fraction is 40/190.434
#
# We need to state the information fractions for later
# analyses. We can just put in the values that were
# originally planned -- these will not affect the
# first boundary value
designUpdate1 <- getDesignGroupSequential(
  sided = 1,
  alpha = 0.025,
  beta = 0.1,
  informationRates = c(40/ss_gsd$maxNumberOfSubjects,0.4,0.6,0.8,1),
  typeOfDesign = "asKD",
  gammaA = 2
)
summary(designUpdate1)
```

Sequential analysis with a maximum of 5 looks (group sequential design)

Kim & DeMets alpha spending design (gammaA = 2), one-sided overall significance level 2.5%, power 90%, undefined endpoint, inflation factor 1.0584, ASN H1 0.704, ASN H01 0.9669, ASN H0 1.052.

Stage	1	2	3	4	5
Planned information rate	21%	40%	60%	80%	100%
Cumulative alpha spent	0.0011	0.0040	0.0090	0.0160	0.0250
Stage levels (one-sided)	0.0011	0.0033	0.0067	0.0113	0.0173
Efficacy boundary (z-value scale)	3.061	2.720	2.473	2.280	2.114
Cumulative power	0.0627	0.2792	0.5602	0.7752	0.9000

```r
# We see the efficacy boundary is at Z=3.061

# Continuing to the next analysis
# Now we give the observed sample sizes at analyses 1 and 2
designUpdate2 <- getDesignGroupSequential(
  sided = 1,
  alpha = 0.025,
  beta = 0.1,
  informationRates = c(c(40,80)/ss_gsd$maxNumberOfSubjects,0.6,0.8,1),
  typeOfDesign = "asKD",
  gammaA = 2
)
summary(designUpdate2)
```

Sequential analysis with a maximum of 5 looks (group sequential design)

Kim & DeMets alpha spending design (gammaA = 2), one-sided overall significance level 2.5%, power 90%, undefined endpoint, inflation factor 1.0585, ASN H1 0.7032, ASN H01 0.9666, ASN H0 1.0521.

Stage	1	2	3	4	5
Planned information rate	21%	42%	60%	80%	100%
Cumulative alpha spent	0.0011	0.0044	0.0090	0.0160	0.0250
Stage levels (one-sided)	0.0011	0.0037	0.0065	0.0113	0.0172
Efficacy boundary (z-value scale)	3.061	2.681	2.482	2.281	2.114
Cumulative power	0.0627	0.3096	0.5590	0.7751	0.9000

```r
# We see the second efficacy boundary point is at Z=2.681

# Continuing to the analysis 3
# Now we give the observed sample sizes at analyses 1, 2 and 3
designUpdate3 <- getDesignGroupSequential(
  sided = 1,
  alpha = 0.025,
  beta = 0.1,
  informationRates = c(c(40,80,120)/ss_gsd$maxNumberOfSubjects,0.8,1),
  typeOfDesign = "asKD",
  gammaA = 2
)
summary(designUpdate3)
```

Sequential analysis with a maximum of 5 looks (group sequential design)

Kim & DeMets alpha spending design (gammaA = 2), one-sided overall significance level 2.5%, power 90%, undefined endpoint, inflation factor 1.0589, ASN H1 0.7042, ASN H01 0.9666, ASN H0 1.0525.

Stage	1	2	3	4	5
Planned information rate	21%	42%	63%	80%	100%
Cumulative alpha spent	0.0011	0.0044	0.0099	0.0160	0.0250
Stage levels (one-sided)	0.0011	0.0037	0.0074	0.0109	0.0172
Efficacy boundary (z-value scale)	3.061	2.681	2.436	2.293	2.115
Cumulative power	0.0627	0.3097	0.5999	0.7742	0.9000

```
# We see the third efficacy boundary point is at Z=2.436

designUpdate4 <- getDesignGroupSequential(
  sided = 1,
  alpha = 0.025,
  beta = 0.1,
  informationRates = c(c(40,80,120,164)/ss_gsd$maxNumberOfSubjects,1),
  typeOfDesign = "asKD",
  gammaA = 2
)
summary(designUpdate4)
```

Sequential analysis with a maximum of 5 looks (group sequential design)

Kim & DeMets alpha spending design (gammaA = 2), one-sided overall significance level 2.5%, power 90%, undefined endpoint, inflation factor 1.0622, ASN H1 0.7095, ASN H01 0.9696, ASN H0 1.0558.

Stage	1	2	3	4	5
Planned information rate	21%	42%	63%	86.1%	100%
Cumulative alpha spent	0.0011	0.0044	0.0099	0.0185	0.0250
Stage levels	0.0011	0.0037	0.0074	0.0134	0.0163

Stage	1	2	3	4	5
(one-sided)					
Efficacy boundary (z-value scale)	3.061	2.681	2.436	2.213	2.137
Cumulative power	0.0630	0.3109	0.6014	0.8252	0.9000

```r
# The fourth efficacy boundary point is at Z=2.213

# The final analysis is handled differently to allow a
# final information level that differs from the target.
#
# In calculating the efficacy boundary, it is important that
# the RATIOS of information levels are correct. These ratios
# are preserved if we sample sizes by the final observed sample
# size to make the last value in informationRates equal to 1.
#
# However, we need to preserve the type I error probabilities
# already seen at earlier analyses and these depended on the
# observed sample sizes. This is achieved by adding the commands
#  typeOfDesign = "asUser",
#  userAlphaSpending = designUpdate4$alphaSpent
# Now, the remainder of alpha will be spent at the final analysis.
designUpdate5 <- getDesignGroupSequential(
  sided = 1,
  alpha = 0.025,
  beta = 0.1,
  informationRates = c(c(40,80,120,164,190)/190),
  typeOfDesign = "asUser",
  userAlphaSpending = designUpdate4$alphaSpent
)
summary(designUpdate5)
```

Sequential analysis with a maximum of 5 looks (group sequential design)

User defined alpha spending design (0.001103, 0.004412, 0.009927, 0.018541, 0.025), one-sided overall significance level 2.5%, power 90%, undefined endpoint, inflation factor 1.0616, ASN H1 0.7098, ASN H01 0.9694, ASN H0 1.0552.

Stage	1	2	3	4	5
Planned information rate	21.1%	42.1%	63.2%	86.3%	100%
Cumulative alpha spent	0.0011	0.0044	0.0099	0.0185	0.0250
Stage levels	0.0011	0.0037	0.0074	0.0134	0.0164

Stage	1	2	3	4	5
(one-sided)					
Efficacy boundary (z-value scale)	3.061	2.681	2.436	2.213	2.135
Cumulative power	0.0632	0.3115	0.6023	0.8259	0.9000

```
# The final efficacy boundary point is at Z=2.135

# For more decimal places, see
designUpdate5$criticalValues

## [1] 3.061002 2.680778 2.435903 2.213348 2.135178

# These values agree very nicely with those from CJ's code

# RPACT does not yet provide an error spending FUTILITY
# boundary. For an approximate answer, one can type the
# following.
# These calculations also give the correct efficacy boundary
# apart from at the final analysis

des_rho5_1 <- getDesignGroupSequential(
  alpha = 0.025,
  beta = 0.1,
  sided = 1,
  kMax = 5,
  informationRates = c(iobs[1]/iMax,c(0.4,0.6,0.8,1)),
  typeOfDesign = "asKD",
  typeBetaSpending = "bsKD",
  gammaA = 2,
  gammaB = 2
)
summary(des_rho5_1)
```

Sequential analysis with a maximum of 5 looks (group sequential design)

Kim & DeMets alpha spending design (gammaA = 2) and Kim & DeMets beta spending (gammaB = 2), non-binding futility, one-sided overall significance level 2.5%, power 90%, undefined endpoint, inflation factor 1.1328, ASN H1 0.7053, ASN H01 0.8089, ASN H0 0.5899.

Stage	1	2	3	4	5
Planned information rate	21%	40%	60%	80%	100%
Cumulative	0.0011	0.0040	0.0090	0.0160	0.0250

Stage	1	2	3	4	5
alpha spent					
Cumulative beta spent	0.0044	0.0160	0.0360	0.0640	0.1000
Stage levels (one-sided)	0.0011	0.0033	0.0067	0.0113	0.0173
Efficacy boundary (z-value scale)	3.061	2.720	2.473	2.280	2.114
Futility boundary (z-value scale)	-1.038	-0.027	0.774	1.447	
Cumulative power	0.0695	0.3040	0.5946	0.8021	0.9000
Futility probabilities under H1	0.004	0.012	0.020	0.028	

```
des_rho5_2 <- getDesignGroupSequential(
  alpha = 0.025,
  beta = 0.1,
  sided = 1,
  kMax = 5,
  informationRates = c(iobs[c(1,2)]/iMax,0.6,0.8,1),
  typeOfDesign = "asKD",
  typeBetaSpending = "bsKD",
  gammaA = 2,
  gammaB = 2
)
summary(des_rho5_2)
```

Sequential analysis with a maximum of 5 looks (group sequential design)

Kim & DeMets alpha spending design (gammaA = 2) and Kim & DeMets beta spending (gammaB = 2), non-binding futility, one-sided overall significance level 2.5%, power 90%, undefined endpoint, inflation factor 1.1331, ASN H1 0.7044, ASN H01 0.808, ASN H0 0.5904.

Stage	1	2	3	4	5
Planned information rate	21%	42%	60%	80%	100%
Cumulative alpha spent	0.0011	0.0044	0.0090	0.0160	0.0250

Stage	1	2	3	4	5
Cumulative beta spent	0.0044	0.0176	0.0360	0.0640	0.1000
Stage levels (one-sided)	0.0011	0.0037	0.0065	0.0113	0.0172
Efficacy boundary (z-value scale)	3.061	2.681	2.482	2.281	2.114
Futility boundary (z-value scale)	-1.037	0.072	0.766	1.447	
Cumulative power	0.0695	0.3362	0.5935	0.8021	0.9000
Futility probabilities under H1	0.004	0.013	0.018	0.028	

```r
des_rho5_3 <- getDesignGroupSequential(
  alpha = 0.025,
  beta = 0.1,
  sided = 1,
  kMax = 5,
  informationRates = c(iobs[c(1,2,3)]/iMax,0.8,1),
  typeOfDesign = "asKD",
  typeBetaSpending = "bsKD",
  gammaA = 2,
  gammaB = 2
)
summary(des_rho5_3)
```

Sequential analysis with a maximum of 5 looks (group sequential design)

Kim & DeMets alpha spending design (gammaA = 2) and Kim & DeMets beta spending (gammaB = 2), non-binding futility, one-sided overall significance level 2.5%, power 90%, undefined endpoint, inflation factor 1.1339, ASN H1 0.7058, ASN H01 0.8078, ASN H0 0.5933.

Stage	1	2	3	4	5
Planned information rate	21%	42%	63%	80%	100%
Cumulative alpha spent	0.0011	0.0044	0.0099	0.0160	0.0250
Cumulative beta spent	0.0044	0.0176	0.0397	0.0640	0.1000

Stage	1	2	3	4	5
Stage levels (one-sided)	0.0011	0.0037	0.0074	0.0109	0.0172
Efficacy boundary (z-value scale)	3.061	2.681	2.436	2.293	2.115
Futility boundary (z-value scale)	-1.037	0.073	0.888	1.438	
Cumulative power	0.0696	0.3365	0.6344	0.8015	0.9000
Futility probabilities under H1	0.004	0.013	0.022	0.024	

```
des_rho5_4 <- getDesignGroupSequential(
  alpha = 0.025,
  beta = 0.1,
  sided = 1,
  kMax = 5,
  informationRates = c(iobs[c(1,2,3,4)]/iMax,1),
  typeOfDesign = "asKD",
  typeBetaSpending = "bsKD",
  gammaA = 2,
  gammaB = 2
)
summary(des_rho5_4)
```

Sequential analysis with a maximum of 5 looks (group sequential design)

Kim & DeMets alpha spending design (gammaA = 2) and Kim & DeMets beta spending (gammaB = 2), non-binding futility, one-sided overall significance level 2.5%, power 90%, undefined endpoint, inflation factor 1.1421, ASN H1 0.7135, ASN H01 0.8146, ASN H0 0.5999.

Stage	1	2	3	4	5
Planned information rate	21%	42%	63%	86.1%	100%
Cumulative alpha spent	0.0011	0.0044	0.0099	0.0185	0.0250
Cumulative beta spent	0.0044	0.0176	0.0397	0.0742	0.1000
Stage levels (one-sided)	0.0011	0.0037	0.0074	0.0134	0.0163

Stage	1	2	3	4	5
Efficacy boundary (z-value scale)	3.061	2.681	2.436	2.213	2.137
Futility boundary (z-value scale)	-1.031	0.081	0.898	1.667	
Cumulative power	0.0703	0.3395	0.6381	0.8479	0.9000
Futility probabilities under H1	0.004	0.013	0.022	0.034	

```r
des_rho5_5 <- getDesignGroupSequential(
  alpha = 0.025,
  beta = 0.1,
  sided = 1,
  kMax = 5,
  informationRates = c(iobs[c(1,2,3,4)]/iMax,1),
  typeOfDesign = "asKD",
  typeBetaSpending = "bsKD",
  gammaA = 2,
  gammaB = 2
)
# Ignore the efficacy boundary at this analysis
summary(des_rho5_5)
```

Sequential analysis with a maximum of 5 looks (group sequential design)

Kim & DeMets alpha spending design (gammaA = 2) and Kim & DeMets beta spending (gammaB = 2), non-binding futility, one-sided overall significance level 2.5%, power 90%, undefined endpoint, inflation factor 1.1421, ASN H1 0.7135, ASN H01 0.8146, ASN H0 0.5999.

Stage	1	2	3	4	5
Planned information rate	21%	42%	63%	86.1%	100%
Cumulative alpha spent	0.0011	0.0044	0.0099	0.0185	0.0250
Cumulative beta spent	0.0044	0.0176	0.0397	0.0742	0.1000
Stage levels (one-sided)	0.0011	0.0037	0.0074	0.0134	0.0163
Efficacy	3.061	2.681	2.436	2.213	2.137

Stage	1	2	3	4	5
boundary (z-value scale)					
Futility boundary (z-value scale)	-1.031	0.081	0.898	1.667	
Cumulative power	0.0703	0.3395	0.6381	0.8479	0.9000
Futility probabilities under H1	0.004	0.013	0.022	0.034	

```r
# We could run the whole sequence of analyses as follows:

design <- getDesignGroupSequential(
  alpha = 0.025,
  beta = 0.1,
  kMax = 5,
  typeOfDesign = "asKD",
  gammaA = 2,
  typeBetaSpending = "bsKD",
  gammaB = 2,
  bindingFutility = FALSE
)
sampleSizes <- getSampleSizeMeans(
  design = design,
  alternative = 0.4,
  stDev = 0.8,
  normalApproximation = TRUE
)
power <- getPowerMeans(
  design = design,
  alternative = c(-0.1, 0.5),
  stDev = 0.8,
  maxNumberOfSubjects = sampleSizes$maxNumberOfSubjects,
  normalApproximation = TRUE
)
summary(sampleSizes)
```

Sample size calculation for a continuous endpoint

Sequential analysis with a maximum of 5 looks (group sequential design), one-sided overall significance level 2.5%, power 90%. The results were calculated for a two-sample t-test (normal approximation), H0: mu(1) - mu(2) = 0, H1: effect = 0.4, standard deviation = 0.8.

Stage	1	2	3	4	5

Stage	1	2	3	4	5
Planned information rate	20%	40%	60%	80%	100%
Cumulative alpha spent	0.0010	0.0040	0.0090	0.0160	0.0250
Cumulative beta spent	0.0040	0.0160	0.0360	0.0640	0.1000
Stage levels (one-sided)	0.0010	0.0033	0.0067	0.0113	0.0173
Efficacy boundary (z-value scale)	3.090	2.714	2.473	2.280	2.114
Futility boundary (z-value scale)	-1.109	-0.022	0.774	1.447	
Efficacy boundary (t)	0.801	0.498	0.370	0.296	0.245
Futility boundary (t)	-0.288	-0.004	0.116	0.188	
Cumulative power	0.0609	0.3049	0.5947	0.8022	0.9000
Number of subjects	38.1	76.2	114.3	152.3	190.4
Expected number of subjects under H1					118.7
Overall exit probability (under H0)	0.1347	0.3699	0.2971	0.1461	
Overall exit probability (under H1)	0.0649	0.2560	0.3098	0.2354	
Exit probability for efficacy (under H0)	0.0010	0.0030	0.0050	0.0069	
Exit probability	0.0609	0.2440	0.2898	0.2074	

Stage	1	2	3	4	5
for efficacy (under H1)					
Exit probability for futility (under H0)	0.1337	0.3669	0.2921	0.1392	
Exit probability for futility (under H1)	0.0040	0.0120	0.0200	0.0280	

Legend:

- *(t)*: treatment effect scale

```
summary(power)
```

Power calculation for a continuous endpoint

Sequential analysis with a maximum of 5 looks (group sequential design), one-sided overall significance level 2.5%. The results were calculated 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 = 0.8, maximum number of subjects = 191.

Stage	1	2	3	4	5
Planned information rate	20%	40%	60%	80%	100%
Cumulative alpha spent	0.0010	0.0040	0.0090	0.0160	0.0250
Cumulative beta spent	0.0040	0.0160	0.0360	0.0640	0.1000
Stage levels (one-sided)	0.0010	0.0033	0.0067	0.0113	0.0173
Efficacy boundary (z-value scale)	3.090	2.714	2.473	2.280	2.114
Futility boundary (z-value scale)	-1.109	-0.022	0.774	1.447	
Efficacy boundary (t)	0.801	0.498	0.370	0.296	0.245

Stage	1	2	3	4	5
Futility boundary (t)	-0.288	-0.004	0.116	0.188	
Cumulative power, alt. = -0.1	0.0003	0.0008	0.0014	0.0021	0.0028
Cumulative power, alt. = 0.5	0.1227	0.5126	0.8164	0.9462	0.9815
Number of subjects	38.1	76.2	114.3	152.3	190.4
Expected number of subjects under H1, alt. = -0.1					81.4
Expected number of subjects under H1, alt. = 0.5					98.2
Overall exit probability (under H0)	0.1347	0.3699	0.2971	0.1461	
Overall exit probability (under H1), alt. = -0.1	0.2349	0.4724	0.2244	0.0582	
Overall exit probability (under H1), alt. = 0.5	0.1239	0.3925	0.3075	0.1347	
Exit probability for efficacy (under H0)	0.0010	0.0030	0.0050	0.0069	
Exit probability for efficacy (under H1), alt. = -0.1	0.0003	0.0005	0.0006	0.0007	

Stage	1	2	3	4	5
Exit probability for efficacy (under H1), alt. = 0.5	0.1227	0.3899	0.3038	0.1299	
Exit probability for futility (under H0)	0.1337	0.3669	0.2921	0.1392	
Exit probability for futility (under H1), alt. = -0.1	0.2347	0.4719	0.2237	0.0575	
Exit probability for futility (under H1), alt. = 0.5	0.0012	0.0026	0.0037	0.0048	

Legend:

- *(t)*: treatment effect scale
- *alt.*: alternative

```
dataObserved <- getDataset(
  cumMeans1 = c(0.1, 0.06, 0.21, 0.31),
  cumMeans2= c(0, 0, 0, 0),
  cumN1 = c(20,40,60,82),
  cumN2 = c(20,40,60,82),
  cumStDev1 = 0.8*c(1, 1, 1, 1),
  cumStDev2 = 0.8*c(1, 1, 1, 1)
)
designDummy <- getDesignGroupSequential(
  alpha = 0.025,
  typeOfDesign = "asKD",
  gammaA = 2
)
getAnalysisResults(
  # informationEpsilon = 0,  #  can be entered in case of underrunning
  maxInformation = 190,
  design = designDummy,
  dataInput = dataObserved,
  normalApproximation = TRUE
) |> summary()
```

```
## The observed information rates for 'maxInformation' = 190 at stage 4 are:
0.211, 0.421, 0.632, 0.863, 1
```

Analysis results for a continuous endpoint

Sequential analysis with 5 looks (group sequential design), one-sided overall significance level 2.5%. The results were calculated using a two-sample t-test, normal approximation test, equal variances option. H0: mu(1) - mu(2) = 0 against H1: mu(1) - mu(2) > 0.

Stage	1	2	3	4	5
Planned information rate	21.1%	42.1%	63.2%	86.3%	100%
Cumulative alpha spent	0.0011	0.0044	0.0100	0.0186	0.0250
Stage levels (one-sided)	0.0011	0.0037	0.0075	0.0135	0.0163
Efficacy boundary (z-value scale)	3.060	2.679	2.434	2.211	2.137
Cumulative effect size	0.100	0.060	0.210	0.310	
Cumulative (pooled) standard deviation	0.800	0.800	0.800	0.800	
Overall test statistic	0.395	0.335	1.438	2.481	
Overall p-value	0.3463	0.3687	0.0752	0.0065	
Test action	continue	continue	continue	reject and stop	
Conditional rejection probability	0.0188	0.0070	0.0624	0.6750	
95% repeated confidence interval	[-0.674; 0.874]	[-0.419; 0.539]	[-0.146; 0.566]	[0.034; 0.586]	
Repeated p-value	>0.5	>0.5	0.2221	0.0126	
Final p-value				0.0133	

Stage	1	2	3	4	5
Final confidence interval				[0.036; 0.545]	
Median unbiased estimate				0.295	