# Package ‘bpp’

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**Type** Package  
**Title** Computations Around Bayesian Predictive Power  
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**VignetteBuilder** knitr  

**Description** Implements functions to update Bayesian Predictive Power Computations after not stopping a clinical trial at an interim analysis. Such an interim analysis can either be blinded or unblinded. Code is provided for Normally distributed endpoints with known variance, with a prominent example being the hazard ratio.

**License** GPL (>= 2)  
**LazyLoad** yes  
**NeedsCompilation** no  
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Description

Implements functions to update Bayesian Predictive Power Computations after not stopping a clinical trial at an interim analysis, whether blinded or unblinded, for a Normally distributed endpoint with known variance, with a prominent example being the hazard ratio.

Details

Package: bpp
Type: Package
Version: 1.0.0
Date: 2016-12-13
License: GPL (>=2)
LazyLoad: yes

Author(s)

Kaspar Rufibach (maintainer)
<kaspar.rufibach@roche.com>

References


Examples
basicPlot

# type bpp_interim for code of all the computations in Rufibach et al (2016a).

---

**basicPlot**

*Basic plot functions to illustrate prior and posterior densities when considering a time-to-event endpoint*

**Description**

Basic plot function, labels are specific to the hazard ratio, i.e. when looking at a time-to-event endpoint.

**Usage**

```r
basicPlot(leg = TRUE, IntEffBoundary = NA, IntFutBoundary = NA, successmean = NA, priormean = NA)
```

**Arguments**

- `leg` logical, display legend?
- `IntEffBoundary` Interim efficacy boundary.
- `IntFutBoundary` Interim futility boundary.
- `successmean` The mean that defines success at the final analysis. Typically chosen to be the minimal detectable difference, i.e. the critical on the scale of the effect size of interest corresponding to the significance level at the final analysis.
- `priormean` Mean of the prior.

**Value**

Empty generic plot.

**Author(s)**

Kaspar Rufibach (maintainer)

<kaspar.rufibach@roche.com>

**References**


**Examples**

# type bpp_interim for code of all the computations in Rufibach et al (2016a).
Bayesian Predictive Power (BPP) for Normally Distributed Endpoint

**Description**
Compute BPP for a Normally distributed endpoint, e.g. log(hazard ratio).

**Usage**
```r
bpp(prior = c("normal", "flat"), successmean, finalsigma, priormean, ...)
```

**Arguments**
- `prior`: Prior density on effect sizes.
- `successmean`: The mean that defines success at the final analysis. Typically chosen to be the minimal detectable difference, i.e. the critical on the scale of the effect size of interest corresponding to the significance level at the final analysis.
- `finalsigma`: (Known) standard deviation at which the final analysis of the study under consideration takes place.
- `priormean`: Prior mean.
- ... Further arguments specific to the chosen prior (see `bpp` for examples).

**Value**
A real number, the bpp.

**Author(s)**
Kaspar Rufibach (maintainer)
<kaspar.rufibach@roche.com>

**References**

**Examples**
```r
# type ?bpp_interim for code of all the computations in Rufibach et al (2016a).
```
Bayesian Predictive Power (BPP) for Normally Distributed Endpoint

Description

Compute BPP and posterior density for a Normally distributed endpoint, e.g. log(hazard ratio), assuming either an unblinded or blinded interim result.

Usage

```
bpp_interim(prior = c("normal", "flat"), datasigma, finalsigma, successmean,
            IntEffBoundary, IntFutBoundary, IntFix, priormean,
            propA = 0.5, thetas, ...)```

Arguments

- **prior**: Prior density on effect sizes.
- **datasigma**: (Known) standard error of estimate at interim analysis.
- **finalsigma**: (Known) standard error at which the final analysis of the study under consideration takes place.
- **successmean**: The mean that defines success at the final analysis. Typically chosen to be the minimal detectable difference, i.e. the critical on the scale of the effect size of interest corresponding to the significance level at the final analysis.
- **IntEffBoundary**: Efficacy boundary at the interim analysis.
- **IntFutBoundary**: Futility boundary at the interim analysis.
- **IntFix**: Effect sizes observed at the interim analysis, to compute BPP for an unblinded interim analysis.
- **priormean**: Prior mean.
- **propA**: Proportion of subjects randomized to arm A.
- **thetas**: Grid to compute posterior density on.
- **...**: Further arguments specific to the chosen prior (see bpp_interim for examples).

Value

A list containing the following elements:

- **initial BPP**: BPP based on the prior.
- **BPP after not stopping at interim interval**: BPP after not stopping at a blinded interim.
- **BPP after not stopping at interim exact**: BPP after not stopping at an unblinded interim.
- **posterior density interval**: The posterior density, interval knowledge.
posterior power interval
The posterior power, interval knowledge.

posterior density exact
The posterior density, exact knowledge of interim result.

Author(s)
Kaspar Rufibach (maintainer)
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References


Examples

```r
# Reproduce all the computations in Rufibach et al (2016a) for a Normal prior.
# -----------------------------

# set all parameters:
# -----------------------------

# prior mean / sd
hr0 <- 0.85
sd0 <- 0.11
priormean <- log(hr0)

# specifications for pivotal study
propA <- 0.5  # proportion of patients randomized to arm A
fac <- (propA * (1 - propA)) * (-1)
nevents <- c(0.5, 1) * 1600
finalsigma <- sqrt(fac / nevents[2])
alphas <- c(0.001, 0.049)
za <- qnorm(1 - alphas / 2)
hrMDD <- exp(- za * sqrt(fac / nevents))
successmean <- log(hrMDD[2])

# efficacy and futility interim boundary
effi <- log(hrMDD[1])
futi <- log(1.025)

# grid to compute densities on
thetas <- seq(-0.65, 0.3, by = 0.01)
```
# compare normal and flat prior density
par(las = 1, mar = c(9, 5, 2, 1), mfrow = c(1, 2))
plot(0, 0, type = "n", xlim = c(-0.6, 0.3), ylim = c(-0.1, 5), xlab = "", ylab = "density",
     main = "")
title(expression("Normal and flat prior density for $\theta$ line = 0.7))
basicPlot(leg = FALSE, IntEffBoundary = effi, IntFutBoundary = futi, successmean = successmean,
         priormean = priormean)
lines(thetas, dnorm(thetas, mean = log(hr0), sd = sd0), col = 2, lwd = 2)

# flat prior:
hr0flat <- 0.866
width1 <- 0.21
height1 <- 2.48
lines(thetas, dUniformNormalTails(thetas, mu = log(hr0flat), width = width1, height = height1),
      lwd = 2, col = 3)

# computations for Normal prior

# prior probabilities to be below 0.7 or above 1:
lims <- c(0.7, 1)
prnorm1 <- plnorm(lims[1], meanlog = log(hr0), sdlog = sd0, lower.tail = TRUE, log.p = FALSE)
prnorm2 <- plnorm(lims[2], meanlog = log(hr0), sdlog = sd0, lower.tail = FALSE, log.p = FALSE)
# 1 - prnorm(lims[2], mean = log(hr0), sd = sd0)

# initial bpp
bpp0 <- bpp(prior = "normal", successmean = successmean, finalsigma = finalsigma,
            priormean = log(hr0), priorsigma = sd0)

# update prior with first external study
hr1 <- 0.396
sd1 <- 0.837
up1 <- NormalNormalPosterior(datamean = log(hr1), datasigma = sd1, n = 1,
                              nu = log(hr0), tau = sd0)
bpp1 <- bpp(prior = "normal", successmean = successmean, finalsigma = finalsigma,
            priormean = up1$postmean, priorsigma = up1$postsigma)

# update prior with second external study (result derived from pooled analysis:
# Cox regression on patient level, stratified by study):
hr2 <- 0.287
sd2 <- 0.658
up2 <- NormalNormalPosterior(datamean = log(hr2), datasigma = sd2, n = 1, nu = log(hr0), tau = sd0)
bpp2 <- bpp(prior = "normal", successmean = successmean, finalsigma = finalsigma,
            priormean = up2$postmean, priorsigma = up2$postsigma)

# compute bpp after not stopping at interim:
# assuming both boundaries:
bpp3.tmp <- bpp_1interim(prior = "normal", datasigma = sqrt(fac / nevents[1]),
\begin{verbatim}
finalsigma = finalsigma, successmean = successmean,
IntEffBoundary = effi, IntFutBoundary = futi, IntFix = 1,
priormean = up2$postmean, propA = 0.5, thetas,
priorsigma = up2$postsigma)
bpp3 <- bpp3.tmp$"BPP after not stopping at interim interval"
post3 <- bpp3.tmp$"posterior density interval"

# assuming only efficacy boundary:
bpp3_effi_only <- bpp_linterim(prior = "normal", datasigma = sqrt(fac / nevents[1]),
finalsigma = finalsigma, successmean = successmean, IntEffBoundary = effi, IntFutBoundary = log(Inf), IntFix = 1,
priormean = up2$postmean, propA = 0.5, thetas = thetas,
priorsigma = up2$postsigma)$"BPP after not stopping at interim interval"

# assuming only futility boundary:
bpp3_futi_only <- bpp_linterim(prior = "normal", datasigma = sqrt(fac / nevents[1]),
finalsigma = finalsigma, successmean = successmean, IntEffBoundary = log(0), IntFutBoundary = futi, IntFix = 1,
priormean = up2$postmean, propA = 0.5, thetas = thetas,
priorsigma = up2$postsigma)$"BPP after not stopping at interim interval"

# assuming interim efficacy boundary:
bpp4.tmp <- bpp_linterim(prior = "normal", datasigma = sqrt(fac / nevents[1]),
finalsigma = finalsigma, successmean = successmean, IntEffBoundary = effi,
IntFutBoundary = Inf, IntFix = c(effi, futi), priormean = up2$postmean,
propA = 0.5, thetas, priorsigma = up2$postsigma)
bpp4 <- bpp4.tmp$"BPP after not stopping at interim exact"[2, 1]
post4 <- bpp4.tmp$"posterior density exact"[, 1]

# assuming interim futility boundary:
bpp5.tmp <- bpp_linterim(prior = "normal", datasigma = sqrt(fac / nevents[1]),
finalsigma = finalsigma, successmean = successmean, IntEffBoundary = effi,
IntFutBoundary = Inf, IntFix = futi, priormean = up2$postmean,
propA = 0.5, thetas, priorsigma = up2$postsigma)
bpp5 <- bpp5.tmp$"BPP after not stopping at interim exact"[2, 1]
post5 <- bpp5.tmp$"posterior density exact" # same as post4[, 2]

# reproduce plots in paper

# first two updates
par(las = 1, mar = c(9, 5, 2, 1), mfrow = c(1, 2))
plot(0, 0, type = "n", xlim = c(-0.6, 0.3), ylim = c(-0.1, 5), xlab = "", ylab = "density",
main = "")
title(expression("Normal prior density and corresponding posteriors for \"*theta\"", line = 0.7))
basicPlot(leg = FALSE, IntEffBoundary = effi, IntFutBoundary = futi, successmean = successmean,
priormean = priormean)
lines(thetas, dnorm(thetas, mean = log(hr0), sd = sd0), col = 2, lwd = 2)
lines(thetas, dnorm(thetas, mean = up1$postmean, sd = up1$postsigma), col = 3, lwd = 2)
lines(thetas, dnorm(thetas, mean = up2$postmean, sd = up2$postsigma), col = 4, lwd = 2)
\end{verbatim}
```r
lines(thetas, post3, col = 1, lwd = 2)
legend(-0.64, 5.2, c("prior", "posterior after Sub1", "posterior after Sub1 & Sub2", "posterior after Sub1 & Sub2 and not stopping at interim"), lty = 1, col = c(2:4, 1), bty = "n", lwd = 2)

# posterior densities for interval knowledge and thetahat equal to boundaries:
plot(0, 0, type = "n", xlab = expression("\theta_{prior}\)), ylim = c(-0.1, 8), xlab = "", ylab = "density", main = "")
title(expression("Posteriors for \theta after not stopping at interim, for Normal prior"), line = 0.7)

basicPlot(leg = FALSE, IntEffBoundary = effi, IntFutBoundary = futi, successmean = successmean, priormean = priormean)
lines(thetas, post3, col = 1, lwd = 2)
lines(thetas, post4, col = 2, lwd = 2)
lines(thetas, post5, col = 3, lwd = 2)

leg2 <- c("interval knowledge",
               expression(hat(theta)*" = efficacy boundary"),
               expression(hat(theta)*" = futility boundary")
)
legend(-0.62, 8.2, leg2, lty = 1, col = 1:3, lwd = 2, bty = "n", title = "posterior after not stopping at interim,")

# Reproduce all the computations in Rufibach et al (2016a) for flat prior.

# set all parameters first:

# parameters of flat prior:
priormean <- log(hr0flat)

# computations for flat prior

# prior probabilities to be below 0.7 or above 1:
lims <- c(0.7, 1)
flat1 <- pUniformNormalTails(x = log(lims[1]), mu = priormean, width = width1, height = height1)
flat2 <- 1 - pUniformNormalTails(x = log(lims[2]), mu = priormean, width = width1, height = height1)

# prior
bpp0_1 <- bpp(prior = "flat", successmean = successmean, finalsigma = finalsigma, priormean = priormean, width = width1, height = height1)

# update with first external study
hr1 <- 0.396
st1 <- 0.837
bpp1_1 <- integrate(FlatNormalPosterior, lower = -Inf, upper = Inf, successmean = successmean,
```

The above code snippet is likely part of a statistical analysis or a simulation for a Bayesian approach with prior distributions and posterior analyses.
finalsigma = finalsigma, datamean = log(hr), datasigma = s1, 
    priormean = priormean, width = width1, height = height1)$value 

# update prior (result derived from pooled analysis: Cox regression on patient level, 
# stratified by study) 
hr2 <- 0.287 
sd2 <- 0.658 
bpp2.1 <- integrate(FlatNormalPosterior, -Inf, Inf, successmean = successmean, 
    finalsigma = finalsigma, datamean = log(hr2), 
    datasigma = sd2, priormean = priormean, 
    width = width1, height = height1)$value 

# update after not stopping at interim 
# first compute synthesized prior: 
hr0 <- 0.85 
sd0 <- 0.11 
up2 <- NormalNormalPosterior(datamean = log(hr2), datasigma = sd2, n = 1, nu = log(hr0), tau = sd0) 

# assuming both boundaries: 
bpp3.1 <- bpp3.1$l"BPP after not stopping at interim interval" 
post3.1 <- bpp3.1$l"posterior density interval" 

# assuming only efficacy boundary: 
bpp3.1_effi_only <- bpp3.1$l"BPP after not stopping at interim interval" 

# assuming only futility boundary: 

# assuming interim efficacy boundary: 
bpp4.1 <- bpp4.1$l"BPP after not stopping at interim exact"[2, 1] 
post4.1 <- bpp4.1$l"posterior density exact" 

# assuming interim futility boundary:
```r
bpp5.1 <- integrate(Vectorize(estimate_toIntegrate), lower = -Inf, upper = Inf, prior = "flat", successmean = successmean, finalsigma = finalsigma, datamean = futi, datasigma = sqrt(fac / nevents[1]), priormean = up2$postmean, width = width1, height = height1)$value

bpp5.1.tmp <- bpp_linterim(prior = "flat", datasigma = sqrt(fac / nevents[1]), finalsigma = finalsigma, successmean = successmean, IntEffBoundary = log(0), IntFutBoundary = effi, IntFix = futi, priormean = up2$postmean, propA = 0.5, thetas = thetas, width = width1, height = height1)

bpp5.1 <- bpp5.1.tmp$"BPP after not stopping at interim exact"[2, 1]
post5.1 <- bpp5.1.tmp$"posterior density exact"

# plots for flat prior

# first two updates with external studies
# compute posteriors
flatpost1 <- rep(NA, length(thetas))
flatpost2 <- flatpost1
for (i in 1:length(thetas)){
  flatpost1[i] <- estimate_posterior(x = thetas[i], prior = "flat", datamean = log(hr1), datasigma = sd1, priormean = priormean, width = width1, height = height1)
  flatpost2[i] <- estimate_posterior(x = thetas[i], prior = "flat", datamean = log(hr2), datasigma = sd2, priormean = priormean, width = width1, height = height1)
}

par(las = 1, mar = c(9, 5, 2, 1), mfrow = c(1, 2))
plot(0, 0, type = "n", xlim = c(-0.6, 0.3), ylim = c(-0.10, 5), xlab = "", ylab = "density", main = "")
title(expression("Flat prior density and corresponding posteriors for \( \theta \hat{} \), line = 0.7))
basicPlot(leg = FALSE, IntEffBoundary = effi, IntFutBoundary = futi, successmean = successmean, priormean = priormean)
lines(thetas, duniformNormalTails(thetas, mu = priormean, width = width1, height = height1), lwd = 2, col = 2)
lines(thetas, flatpost1, col = 3, lwd = 2)
lines(thetas, flatpost2, col = 4, lwd = 2)
lines(thetas, postS_1, col = 1, lwd = 2)

legend(-0.64, 5.2, c("prior", "posterior after Sub1", "posterior after Sub1 & Sub2", "posterior after Sub1 & Sub2 and not stopping at interim"), lty = 1, col = c(2:4, 1), bty = "n", lwd = 2)

# posterior densities for interval knowledge and thetahat equal to boundaries:
plot(0, 0, type = "n", xlim = c(-0.6, 0.3), ylim = c(-0.10, 8), xlab = "", ylab = "density", main = "")
title(expression("Posteriors for \( \theta \hat{} \) after not stopping at interim, for Flat prior"), line = 0.7)
```
Bayesian Predictive Power (BPP) for Normally Distributed Endpoint

Description

Compute BPP and posterior density for a Normally distributed endpoint, e.g. log(hazard ratio), assuming the trial did not stop at two blinded interim analyses.

Usage

bpp_2interim(prior = "normal", datasigma, finalsigma, successmean, IntEffBoundary, IntFutBoundary, priormean, thetas, ...)

```
basicPlot(leg = FALSE, IntEffBoundary = effi, IntFutBoundary = futi, successmean = successmean, 
          priormean = priormean)
lines(thetas, post3_1, col = 1, lwd = 2)
lines(thetas, post4_1, col = 2, lwd = 2)
lines(thetas, post5_1, col = 3, lwd = 2)

leg.flat <- c("interval knowledge",
              expression(hat(theta)*" = efficacy boundary"),
              expression(hat(theta)*" = futility boundary")
)

legend(-0.62, 8.2, leg.flat, lty = 1, col = 1:3, lwd = 2, bty = "n",
       title = "posterior after not stopping at interim")

# reproduce Table 1 in Rufibach et al (2016a)
# ----------------------------------------------
mat <- matrix(NA, ncol = 2, nrow = 10)
mat[, 1] <- c(pnorm1L, pnormR, bppL, bpp1, bpp2, bpp3, bpp3_futi_only, bpp3_effi_only, 
               bpp4, bpp5)
mat[, 2] <- c(flat1, flat2, bpp0_1, bpp1_1, bpp2_1, bpp3_1, bpp3_1_futi_only, 
               bpp3_1_effi_only, bpp4_1, bpp5_1)
rownames(mat) <- c("Normal prior", "Flat prior")
colnames(mat) <- c(paste("Probability for hazard ratio to be \le\$ \", lims[1], sep = " "), 
                    paste("Probability for hazard ratio to be \ge\$ \", lims[2], sep = " "), 
                    "Pos after not stopping at interim", "Pos after not stopping at interim assuming \$int\(\theta\) \in \(\text{effi}\(\theta\), \text{futi}\(\theta\)\)$", 
                    "Pos after not stopping at interim, assuming \$int\(\theta\) \in \([-\infty, \text{futi}\(\theta\)]\)$", 
                    "Pos after not stopping at interim, assuming \$int\(\theta\) \in \(\text{effi}\(\theta\), \infty\)$", 
                    "Pos after not stopping at interim, assuming \$int\(\theta\) = \text{futi}\(\theta\)$", 
                    "Pos after not stopping at interim, assuming \$int\(\theta\) = \text{effi}\(\theta\)$")
as.data.frame(format(mat, digits = 2))
```
Arguments

prior  Prior density on effect sizes. So far, this function only accommodates a Normal prior, as opposed to bpp_1interim where also the pessimistic prior introduced in Rufibach et al (2016a) can be specified.

datasigma  (Known) standard error of estimate at interim analysis.

finalsigma  (Known) standard error at which the final analysis of the study under consideration takes place.

successmean  The mean that defines success at the final analysis. Typically chosen to be the minimal detectable difference, i.e. the critical on the scale of the effect size of interest corresponding to the significance level at the final analysis.

IntEffBoundary  2-d vector of efficacy boundaries at the interim analyses.

IntFutBoundary  2-d vector of futility boundary at the interim analyses.

priormean  Prior mean.

thetas  Grid to compute posterior density on.

...  Further arguments specific to the chosen prior (see bpp_1interim for examples).

Value

A list containing the following elements:

- initial BPP  BPP based on the prior.
- BPP after not stopping at interim interval  BPP after not stopping at a blinded interim.
- posterior density interval  The posterior density, interval knowledge.

Author(s)

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References


estimate_posterior

Examples

# ---------------------------------------------------------------
# Illustrate the update after two passed interims using the Gallium clinical trial
# ---------------------------------------------------------------

# ------------------------------
# set all parameters:
# ------------------------------
# prior mean / sd
hr0 <- 0.9288563
priormean <- log(hr0)
priorsigma <- sqrt(4 / 12)

# specifications for pivotal study
propA <- 0.5  # proportion of patients randomized to arm A
fac <- (propA * (1 - propA)) ^ (-1)
nevents <- c(111, 248, 370)
datasigma <- sqrt(fac / nevents[1:2])
finalsigma <- sqrt(fac / nevents[3])
za <- c(3.9285726330559, 2.5028231888636, 1.9936294555664)
alphas <- 2 * (1 - pnorm(za))
hrMDD <- exp(- za * sqrt(fac / nevents))
successmean <- log(hrMDD[3])

# efficacy and futility interim boundary
effi <- log(c(0, hrMDD[2]))
futi <- log(c(1, Inf))

# grid to compute densities on
thetas <- seq(-0.65, 0.3, by = 0.01)

bpp_2interim(prior = "normal", datasigma = datasigma, finalsigma = finalsigma,
successmean = successmean, IntEffBoundary = effi, IntFutBoundary = futi,
priormean = priormean, thetas = thetas, priorsigma = priorsigma)

estimate_posterior  Posterior density conditional on known interim result

Description

If we update the prior with a known estimate at an interim analysis, we get this density.

Usage

estimate_posterior(x, prior = c("normal", "flat"), datamean, datasigma, priormean, ...)
Arguments

- `x`: Value at which to evaluate the function.
- `prior`: Prior density on effect sizes.
- `datamean`: Mean of the data.
- `datasigma`: (Known) standard deviation of `datamean`.
- `priormean`: Prior mean.
- `...`: Further arguments specific to the chosen prior (see `bpp` for examples).

Value

Value of the function, a real number.

Author(s)

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References


Examples

```r
# type bpp_interim for code of all the computations in Rufibach et al (2016a).
```

Description

If we update the prior with a known estimate at an interim analysis, we get a density that is proportional to the value of this function.

Usage

```r
estimate_posterior_nominator(x, prior = c("normal", "flat"), datamean, datasigma, priormean, ...)
```
estimate_toIntegrate

Arguments

- **x**: Value at which to evaluate the function.
- **prior**: Prior density on effect sizes.
- **datamean**: Mean of the data.
- **datasigma**: (Known) standard deviation of datamean.
- **priormean**: Prior mean.
- **...**: Further arguments specific to the chosen prior (see bpp for examples).

Value

Value of the function, a real number.

Author(s)

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References


Examples

# type bpp_interim for code of all the computations in Rufibach et al (2016a).

Description

Product of posterior density and conditional power for known interim result, integrate over this function to get BPP.

Usage

```r
estimate_toIntegrate(x, prior = c("normal", "flat"), successmean,
                      finalsigma, datamean, datasigma, priormean, propA = 0.5, ...)
```
Arguments

- **x**: Value at which to evaluate the function.
- **prior**: Prior density on effect sizes.
- **successmean**: The mean that defines success at the final analysis. Typically chosen to be the minimal detectable difference, i.e. the critical on the scale of the effect size of interest corresponding to the significance level at the final analysis.
- **finalsigma**: (Known) standard deviation at which the final analysis of the study under consideration takes place.
- **datamean**: Mean of the data.
- **datasigma**: (Known) standard deviation of datamean.
- **priormean**: Prior mean.
- **propA**: Proportion of subjects randomized to arm A.
- **...**: Further arguments specific to the chosen prior (see bpp for examples).

Value

Value of the function, a real number.

Author(s)

Kaspar Rufibach (maintainer)

<kaspar.rufibach@roche.com>

References


Examples

```
# type ?bpp_interim for code of all the computations in Rufibach et al (2016a).
```

FlatNormalPosterior  Integrand to compute Bayesian Predictive Power when flat prior has been updated with likelihood

Description

Assume we have a flat prior on our effect, update it with a Normal likelihood and then want to compute Bayesian Predictive Power. This function provides the integrand for that computation, i.e. the product of the power function and the posterior.
Usage

FlatNormalPosterior(x, successmean, finalsigma, datamean, datasigma, priormean, width, height)

Arguments

x                  Value at which to evaluate the function.
successmean       The mean that defines success at the final analysis. Typically chosen to be the minimal detectable difference, i.e. the critical on the scale of the effect size of interest corresponding to the significance level at the final analysis.
finalsigma         (Known) standard deviation at which the final analysis of the study under consideration takes place.
datamean           Mean of the data.
datasigma          (Known) standard deviation of datamean.
priormean          Prior mean.
width               Width of the flat part of the prior.
height              Height of the flat part of the prior.

Value

Value of the function, a real number.

Author(s)

Kaspar Rufibach (maintainer)
<kaspar.rufibach@roche.com>

References


Examples

# type ?bpp_interim for code of all the computations in Rufibach et al (2016a).
interval_posterior_nominator

Posterior density conditional on interim result, only known as interval, is proportional to the value of this function

Description

If we update the prior with the knowledge that the interim estimate was between a futility and efficacy boundary at an interim analysis, we get a density that is proportional to the value of this function.

Usage

interval_posterior_nominator(x, prior = c("normal", "flat"), IntEffBoundary, IntFutBoundary, datasigma, priormean, ...)

Arguments

x Value at which to evaluate the function.
prior Prior density on effect sizes.
IntEffBoundary Efficacy boundary at the interim analysis.
IntFutBoundary Futility boundary at the interim analysis.
datasigma (Known) standard deviation of datamean, i.e. at interim analysis.
priormean Prior mean.
... Further arguments specific to the chosen prior (see bpp for examples).

Value

Value of the function, a real number.

Author(s)

Kaspar Rufibach (maintainer)
<kaspar.rufibach@roche.com>

References


Examples

# type ?bpp_interim for code of all the computations in Rufibach et al (2016a).
interval_posterior_nominator2

Posterior density conditional on two interim results, both only known as intervals, is proportional to the value of this function

Description

If we update the prior with the knowledge that two interim estimates were between a futility and efficacy boundary, we get a density that is proportional to the value of this function.

Usage

interval_posterior_nominator2(x, prior = "normal",
    IntEffBoundary, IntFutBoundary, datasigma, priormean, ...)

Arguments

- **x**: Value at which to evaluate the function.
- **prior**: Prior density on effect sizes.
- **IntEffBoundary**: Efficacy boundary at the interim analysis.
- **IntFutBoundary**: Futility boundary at the interim analysis.
- **datasigma**: (Known) standard deviation of datamean, i.e. at interim analysis.
- **priormean**: Prior mean.
- **...**: Further arguments specific to the chosen prior (see bpp for examples).

Value

Value of the function, a real number.

Author(s)

Kaspar Rufibach (maintainer)
<kaspar.rufibach@roche.com>

References


Examples

# type ?bpp_2interim for code of all the computations in Rufibach et al (2016a).
interval_toIntegrate  

Product of posterior density and conditional power for blinded interim result

Description

Product of posterior density and conditional power for blinded interim result, integrate over this function to get BPP.

Usage

interval_toIntegrate(x, prior = c("normal", "flat"), datasigma, finalsigma, successmean, IntEffBoundary, IntFutBoundary, priormean, ...)

Arguments

- **x**: Value at which to evaluate the function.
- **prior**: Prior density on effect sizes.
- **datasigma**: (Known) standard deviation of datamean, i.e. at interim analysis.
- **finalsigma**: (Known) standard deviation at which the final analysis of the study under consideration takes place.
- **successmean**: The mean that defines success at the final analysis. Typically chosen to be the minimal detectable difference, i.e. the critical on the scale of the effect size of interest corresponding to the significance level at the final analysis.
- **IntEffBoundary**: Efficacy boundary at the interim analysis.
- **IntFutBoundary**: Futility boundary at the interim analysis.
- **priormean**: Prior mean.
- **...**: Further arguments specific to the chosen prior (see bpp for examples).

Value

Value of the function, a real number.

Author(s)

Kaspar Rufibach (maintainer)
<kaspar.rufibach@roche.com>

References

Examples

# type bpp_interim for code of all the computations in Rufibach et al (2016a).

interval_toIntegrate2  Product of posterior density and conditional power for blinded interim result

Description

Product of posterior density and conditional power for two blinded interim results, integrate over this function to get BPP.

Usage

interval_toIntegrate2(x, prior = "normal", datasigma, finalsigma, successmean, IntEffBoundary, IntFutBoundary, priormean, ...)

Arguments

x  Value at which to evaluate the function.
prior  Prior density on effect sizes.
datasigma  (Known) standard deviation of datamean, i.e. at interim analysis.
finalsigma  (Known) standard deviation at which the final analysis of the study under consideration takes place.
successmean  The mean that defines success at the final analysis. Typically chosen to be the minimal detectable difference, i.e. the critical on the scale of the effect size of interest corresponding to the significance level at the final analysis.
IntEffBoundary  Efficacy boundary at the interim analysis.
IntFutBoundary  Futility boundary at the interim analysis.
priormean  Prior mean.
...  Further arguments specific to the chosen prior (see bpp for examples).

Value

Value of the function, a real number.

Author(s)

Kaspar Rufibach (maintainer)
<kaspar.rufibach@roche.com>
References

Examples

```r
# type ?bpp_zinterim for code of all the computations in Rufibach et al (2016a).
```

### Description
Compute the posterior distribution in a conjugate normal model for known variance: Let \(X_1, \ldots, X_n\) be a sample from a \(N(\mu, \sigma^2)\) distribution, with \(\sigma\) assumed known. We assume a prior distribution on \(\mu\), namely \(N(\nu, \tau^2)\). The posterior distribution is then \(\mu|x \sim N(\mu_p, \sigma_p^2)\) with

\[
\mu_p = \frac{1}{(\sigma^2/n) + \tau^{-2}}\left[\frac{\bar{x}}{(\sigma^2/n)} + \frac{\nu}{\tau^2}\right]
\]

and

\[
\sigma_p = \frac{1}{(\sigma^2/n) + \tau^{-2}}^{-1}.
\]

These formulas are available e.g. in Held (2008, p. 147ff).

### Usage

```r
NormalNormalPosterior(datamean, datasigma, n, nu, tau)
```

### Arguments
- `datamean`: Mean of the data.
- `datasigma`: (Known) standard deviation of `datamean`.
- `n`: Number of observations.
- `nu`: Prior mean.
- `tau`: Prior standard deviation.

### Value
A list with the entries:
- `postmean`: Posterior mean.
- `postsigma`: Posterior standard deviation.
Author(s)
Kaspar Rufibach (maintainer)
<kaspar.rufibach@roche.com>

References

Examples
```r
## data:
n <- 25
sd0 <- 3
x <- rnorm(n, mean = 2, sd = sd0)

## prior:
nu <- 0
tau <- 2

## posterior:
NormalNormalPosterior(datamean = mean(x), datasigma = sd0, n = 77, nu = nu, tau = tau)
```

---

**post_power**

*Conditional power conditioning on a blinded interim*

### Description
Conditional power conditioning on a blinded interim, i.e. the estimate after the interim is only known to lie in an interval.

### Usage
```
post_power(x, datasigma, finalsigma, successmean, IntEffBoundary, IntFutBoundary)
```

### Arguments
- **x** Value at which to evaluate the function.
- **datasigma** (Known) standard deviation of `datamean`.
- **finalsigma** (Known) standard deviation at which the final analysis of the study under consideration takes place.
- **successmean** The mean that defines success at the final analysis. Typically chosen to be the minimal detectable difference, i.e. the critical on the scale of the effect size of interest corresponding to the significance level at the final analysis.
- **IntEffBoundary** Efficacy boundary at the interim analysis.
- **IntFutBoundary** Futility boundary at the interim analysis.
Value

Value of the function, a real number.

Author(s)

Kaspar Rufibach (maintainer)
<kaspar.rufibach@roche.com>

References


Examples

```R
# type ?bpr_interim for code of all the computations in Rufibach et al (2016a).
```

<table>
<thead>
<tr>
<th>UniformNormalTails</th>
<th>Density and CDF for Uniform Distribution with Normal tails</th>
</tr>
</thead>
</table>

Description

Density function and cumulative distribution function for a Uniform density with Normal tails. Introduced in Rufibach et al (2016a) as pessimistic distribution to compute Bayesian Predictive Power.

Usage

dUniformNormalTails(x, mu, width, height)
pUniformNormalTails(x, mu, width, height)

Arguments

- `x`: Vector of quantiles.
- `mu`: Mean of the pessimistic prior.
- `width`: Width of the flat part of the prior.
- `height`: Height of the flat part of the prior.

Value

Density at x.
Author(s)

Kaspar Rufibach (maintainer)
<kaspar.rufibach@roche.com>

References


Examples

# type ?bpp_interim for code of all the computations in Rufibach et al (2016a).
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