Package 'ssMRCT'

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Description Calculate conditional regional consistency probabilities and sample sizes for multi-regional clinical trials under fixed-effects and random-effects models. Supports two independent trials, regional fraction selection under symmetric designs, and doubly robust regional treatment-effect estimation. Methods include Qing et al. (2025) <doi:10.1002/sim.70306> and Ren and Xu (2026) <doi:10.1002/pst.70090>.

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Contents

ssMRCT-package 2
conProb 3
conProb2 4
conProbII 6

conProbII2 8
CPlbd 10
regATE_dr 12
regFrac 14
regFrac2 15
ssCPbinary 16
ssCPnorm 17
ssCPsurvNPH 19
ssCPsurvPH 21

Index **23**

`ssMRCT-package` *Regional consistency and sample size for MRCTs*

Description

Tools for multi-regional clinical trial (MRCT) design and regional treatment-effect estimation. CP denotes a consistency probability conditional on overall trial significance, not overall power or interval coverage.

Choosing a function

conProb, **conProb2** Fixed-effects Method I CP for one or two trials.

regFrac, **regFrac2** Regional fraction for a target Method I CP. The two-trial solver requires a symmetric design.

conProbII, **conProbII2** Probability that all regional effects are nonnegative, for one or two trials.

ssCPnorm, **ssCPbinary** Random-effects design for normal or binary endpoints.

ssCPsurvPH, **ssCPsurvNPH** Random-effects design for survival endpoints.

CPlbd Lower bound on random-effects Method I CP.

regATE_dr Covariate-adjusted regional ATE from participant-level data.

Conventions

`alpha` is one-sided. Fixed-effects functions take `power`; random-effects functions take `beta = 1 - power`. Allocation ratios are treatment/control. Higher treatment effects indicate benefit; PH effects are negative log hazard ratios.

Analytical CP uses the continuous design. Returned integer sample sizes are recommendations, not a re-evaluation of CP after regional rounding. Binary Method II simulation instead uses the returned actual regional arm counts.

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References

Qing, Kunhai, Xinru Ren, Shuping Jiang, Ping Yang, Menggang Yu, and Jin Xu. 2025. "Regional Consistency Evaluation and Sample Size Calculation under Two MRCTs." *Statistics in Medicine* 44 (25–27): e70306. doi:10.1002/sim.70306.

Ren, Xinru, and Jin Xu. 2026. "Consistency Assessment and Regional Sample Size Calculation for MRCT under Random Effects Model." *Pharmaceutical Statistics* 25 (3): e70090. doi:10.1002/pst.70090.

`conProb` *Consistency probability for one MRCT: Method I*

Description

Calculate the probability that a regional treatment effect preserves a specified fraction of the overall effect, conditional on overall significance, under a fixed-effects model.

Usage

```
conProb(
  alpha,
  power,
  pi = 0.5,
  rF,
  d,
  sigmaTrt,
  sigmaCtrl = sigmaTrt,
  randRatio = 1
)
```

Arguments

`alpha`	One-sided significance level, between 0 and 0.5.
`power`	Target overall power, with `alpha < power < 1`.
`pi`	Fraction of the overall effect to preserve; `0 <= pi < 1`.
`rF`	Fraction of participants in the region of interest, in `(0, 1]`.
`d`	Positive treatment-minus-control mean difference.
`sigmaTrt`	Positive outcome standard deviation in the treatment arm.
`sigmaCtrl`	Positive outcome standard deviation in the control arm.
`randRatio`	Treatment-to-control allocation ratio, strictly positive.

Details

With regional effect estimate D_r and overall estimate D,

$$\mathrm{CP} = \Pr(D_r \geq \pi D \mid T > z_{1-\alpha}).$$

The normal approximation is integrated numerically. CP depends on `alpha`, `power`, `pi` and `rF`; the other inputs determine sample size.

Value

A list with `CP` (conditional consistency probability) and `N` (recommended total sample size).

Sample sizes

CP uses the continuous design at the requested power. The recommended control count is rounded up first, followed by the treatment count. Returned counts do not re-evaluate CP after integer regional allocation.

References

Qing, Kunhai, Xinru Ren, Shuping Jiang, Ping Yang, Menggang Yu, and Jin Xu. 2025. "Regional Consistency Evaluation and Sample Size Calculation under Two MRCTs." *Statistics in Medicine* 44 (25–27): e70306. doi:10.1002/sim.70306.

See Also

`regFrac()` to solve for a regional fraction; `conProb2()` for two trials.

Examples

```
conProb(alpha = 0.05, power = 0.8, rF = 0.271,
        d = 1, sigmaTrt = 4)
```

---

conProb2 *Pooled consistency probability for two MRCTs: Method I*

Description

Calculate Method I consistency probability from pooled data, conditional on both independent trials being significant.

Usage

```
conProb2(
  alpha,
  power1,
  power2 = power1,
  pi = 0.5,
  rF1,
  rF2 = rF1,
  d1,
  d2 = d1,
  muCtrl1 = 0,
  muCtrl2 = muCtrl1,
  sigmaTrt1,
  sigmaCtrl1 = sigmaTrt1,
```

```
  sigmaTrt2 = sigmaTrt1,
  sigmaCtrl2 = sigmaTrt2,
  randRatio1 = 1,
  randRatio2 = randRatio1
)
```

Arguments

`alpha`	One-sided significance level, between 0 and 0.5.
`power1`, `power2`	Overall power in studies 1 and 2; each lies in `(alpha, 1)`.
`pi`	Fraction of the overall effect to preserve; `0 <= pi < 1`.
`rF1`, `rF2`	Fractions in the target region in studies 1 and 2, in `(0, 1]`.
`d1`, `d2`	Positive treatment-minus-control mean differences.
`muCtrl1`, `muCtrl2`	Control-arm means; needed when pooling weights differ.
`sigmaTrt1`, `sigmaTrt2`	Positive treatment-arm outcome standard deviations.
`sigmaCtrl1`, `sigmaCtrl2`	Positive control-arm outcome standard deviations.
`randRatio1`, `randRatio2`	Positive treatment-to-control allocation ratios.

Details

Treatment and control outcomes are pooled separately using their sample sizes. Overall and regional pooling weights can differ.

$$\Pr(D_{r,\text{pool}} \geq \pi D_{\text{pool}} \mid T_1 > z_{1-\alpha}, T_2 > z_{1-\alpha}).$$

The conditional normal probability is integrated over both significant study results. Study 2 defaults to the corresponding study 1 inputs.

Value

A list with `CP`, `N1` and `N2`: the conditional consistency probability and recommended total sample sizes in studies 1 and 2.

Sample sizes

CP uses the continuous design at the requested power. The recommended control count is rounded up first, followed by the treatment count. Returned counts do not re-evaluate CP after integer regional allocation.

References

Qing, Kunhai, Xinru Ren, Shuping Jiang, Ping Yang, Menggang Yu, and Jin Xu. 2025. "Regional Consistency Evaluation and Sample Size Calculation under Two MRCTs." *Statistics in Medicine* 44 (25–27): e70306. doi:10.1002/sim.70306.

See Also

conProb(), regFrac2().

Examples

```
conProb2(alpha = 0.05, power1 = 0.8, power2 = 0.9,
         rF1 = 0.141, d1 = 1, sigmaTrt1 = 4)
```

---

conProbII *Consistency probability for one MRCT: Method II*

Description

Calculate Method II consistency probability: all regional effect estimates are nonnegative, conditional on overall significance.

Usage

```
conProbII(
  alpha,
  power,
  rF,
  d,
  sigmaTrt,
  sigmaCtrl = sigmaTrt,
  pTrt,
  pCtrl,
  randRatio = 1,
  responseType = c("continuous", "binary"),
  B = 1e+05
)
```

Arguments

alpha	One-sided significance level, between 0 and 0.5.
power	Target overall power, with alpha < power < 1.
rF	Positive fractions for all regions, summing to one.
d, sigmaTrt, sigmaCtrl	Continuous-endpoint effect and standard deviations; see conProb(). Ignored for binary endpoints.
pTrt, pCtrl	Treatment and control response probabilities for a binary endpoint, strictly between zero and one, with pTrt > pCtrl.
randRatio	Treatment-to-control allocation ratio, strictly positive.
responseType	Endpoint type: "continuous" or "binary".
B	Positive integer number of replicates; used only for binary endpoints.

Details

$$\mathrm{CP} = \Pr(D_r \geq 0 \text{ for all } r \mid T > z_{1-\alpha}).$$

Continuous endpoints use a joint normal probability, retaining dependence between regional and overall effects. Numerical integration can vary slightly with the random seed.

Value

A list with `CP` and total sample size `N`. For binary endpoints, `N` is the actual simulated total and the list also contains:

nTrt, nCtrl Actual overall treatment and control counts.

nTrtReg, nCtrlReg Actual regional treatment and control counts.

achievedPower Simulated probability of the conditioning event.

MCSE Monte Carlo standard error of CP.

successes Number of replicates meeting the conditioning event.

consistentSsuccesses Number also meeting regional consistency.

B Number of simulation replicates.

Sample sizes

CP uses the continuous design at the requested power. The recommended control count is rounded up first, followed by the treatment count. Returned counts do not re-evaluate CP after integer regional allocation.

Binary calculation

The function simulates regional binomial counts with separately rounded arm sizes. CP is the number of consistent overall successes divided by the number of overall successes. Zero regional effects count as consistent. Wald tests use the actual arm counts. With zero estimated variance, only a positive estimated effect rejects the null.

No overall successes gives `NA` for CP and its Monte Carlo standard error, with a warning. Set the random seed for reproducibility.

References

Qing, Kunhai, Xinru Ren, Shuping Jiang, Ping Yang, Menggang Yu, and Jin Xu. 2025. "Regional Consistency Evaluation and Sample Size Calculation under Two MRCTs." *Statistics in Medicine* 44 (25–27): e70306. doi:10.1002/sim.70306.

See Also

`conProbII2()`, `conProb()`.

Examples

```
set.seed(42)
conProbII(alpha = 0.05, power = 0.8, rF = rep(1/3, 3),
          d = 1, sigmaTrt = 4)
conProbII(alpha = 0.05, power = 0.8, rF = rep(1/3, 3),
          pTrt = 0.8, pCtrl = 0.7, responseType = "binary", B = 10000)
```

`conProbII2` *Pooled consistency probability for two MRCTs: Method II*

Description

Calculate Method II consistency probability from pooled regional data, conditional on both independent trials being significant.

Usage

```
conProbII2(
  alpha,
  power1,
  power2 = power1,
  rF1,
  rF2 = rF1,
  d1,
  d2 = d1,
  sigmaTrt1,
  sigmaCtrl1 = sigmaTrt1,
  sigmaTrt2 = sigmaTrt1,
  sigmaCtrl2 = sigmaTrt2,
  pTrt1,
  pCtrl1,
  pTrt2 = pTrt1,
  pCtrl2 = pCtrl1,
  randRatio1 = 1,
  randRatio2 = randRatio1,
  responseType = c("continuous", "binary"),
  B = 1e+05,
  muCtrl1 = 0,
  muCtrl2 = muCtrl1
)
```

Arguments

`alpha`	One-sided significance level, between 0 and 0.5.
`power1`, `power2`	Overall power in studies 1 and 2; each lies in `(alpha, 1)`.
`rF1`, `rF2`	Positive regional fraction vectors, each summing to one and listing the same regions in the same order.

`d1`, `d2` Positive continuous-endpoint effects; ignored for binary endpoints.

`sigmaTrt1`, `sigmaTrt2`
Positive treatment-arm outcome standard deviations.

`sigmaCtrl1`, `sigmaCtrl2`
Positive control-arm outcome standard deviations.

`pTrt1`, `pTrt2` Treatment response probabilities for binary endpoints, strictly between zero and one.

`pCtrl1`, `pCtrl2` Control response probabilities for binary endpoints, strictly between zero and the corresponding treatment probability.

`randRatio1`, `randRatio2`
Positive treatment-to-control allocation ratios.

`responseType` Endpoint type: `"continuous"` or `"binary"`.

`B` Positive integer number of replicates; used only for binary endpoints.

`muCtrl1`, `muCtrl2`
Control means for continuous endpoints only.

Details

Consistency requires every pooled regional effect to be nonnegative. Treatment and control outcomes are pooled separately. The conditioning event is significance in both trials, not in a single pooled test. For continuous endpoints, a joint normal calculation accounts for regional/overall dependence and different control means. Set the seed for reproducible numerical integration or simulation.

Value

A list with `CP`, `N1` and `N2`. For binary endpoints, `N1` and `N2` are the actual simulated totals and additional entries are:

nTrtReg1, nCtrlReg1 Regional arm counts in study 1.

nTrtReg2, nCtrlReg2 Regional arm counts in study 2.

achievedPower Simulated probability of the conditioning event.

MCSE Monte Carlo standard error of CP.

successes Number of replicates meeting the conditioning event.

consistentSuccesses Number also meeting regional consistency.

B Number of simulation replicates.

Here `achievedPower` is the simulated probability that both studies succeed.

Sample sizes

CP uses the continuous design at the requested power. The recommended control count is rounded up first, followed by the treatment count. Returned counts do not re-evaluate CP after integer regional allocation.

Binary calculation

The function simulates regional binomial counts with separately rounded arm sizes. CP is the number of consistent overall successes divided by the number of overall successes. Zero regional effects count as consistent. Wald tests use the actual arm counts. With zero estimated variance, only a positive estimated effect rejects the null.

No overall successes gives `NA` for CP and its Monte Carlo standard error, with a warning. Set the random seed for reproducibility.

References

Qing, Kunhai, Xinru Ren, Shuping Jiang, Ping Yang, Menggang Yu, and Jin Xu. 2025. "Regional Consistency Evaluation and Sample Size Calculation under Two MRCTs." *Statistics in Medicine* 44 (25–27): e70306. doi:10.1002/sim.70306.

See Also

`conProbII()`, `conProb2()`.

Examples

```
set.seed(42)
conProbII2(alpha = 0.05, power1 = 0.8, rF1 = rep(1/3, 3),
           d1 = 1, sigmaTrt1 = 4)
```

CPlbd *Random-effects consistency bound: Method I*

Description

Calculate the Method I CP lower bound from Ren and Xu (2026) and the regional normal-endpoint counts at its equality condition.

Usage

```
CPlbd(
  alpha,
  beta,
  tau_delta_r,
  delta,
  sigma0r,
  sigma1r,
  fr,
  pi = 0.5,
  randRatio = 1
)
```

Arguments

`alpha`	One-sided significance level, between 0 and 0.5.
`beta`	Type II error probability; `alpha < 1 - beta < 1`.
`tau_delta_r`	Positive ratio `tau / delta`.
`delta`	Positive mean of the regional treatment-effect distribution.
`sigma0r`, `sigma1r`	Positive control and treatment outcome standard deviations; scalars or vectors of length `length(fr)`.
`fr`	Fractions of the regions of interest, each in `(0, 1]`. Retained for compatibility and output sizing; counts are regional and are not divided by these fractions. The entries need not sum to one.
`pi`	Fraction of the overall effect to preserve; `0 <= pi < 1`.
`randRatio`	Treatment-to-control allocation ratio, strictly positive.

Details

Let $z = z_{1-\alpha} + z_{1-\beta}$ and $a = (\tau/\delta)^2 z^2/2$. If $a < 1$, the function uses the bound in equation (13), with regional control count at equality

$$n_{0r} = \frac{\Omega_r}{(1/a - 1)\tau^2}.$$

If $a \geq 1$, it uses equation (14), and equality counts are `NA`. These counts describe the regional equality condition, not a complete multi-region allocation satisfying the overall design equation.

Value

A list with:

CPlbd Scalar CP lower bound, without rounding.

n0r, n1r Rounded regional control and treatment counts.

nr Regional total, `n0r + n1r`.

Sample-size entries are numeric `NA` when the equality condition fails.

References

Ren, Xinru, and Jin Xu. 2026. "Consistency Assessment and Regional Sample Size Calculation for MRCT under Random Effects Model." *Pharmaceutical Statistics* 25 (3): e70090. doi:10.1002/pst.70090.

See Also

`ssCPnorm()`.

Examples

```
CPlbd(alpha = 0.05, beta = 0.2, tau_delta_r = 0.4, delta = 0.25,
      sigma0r = 1, sigma1r = 1, fr = c(0.1, 0.5))
```

regATE_dr *Doubly robust estimation of a regional treatment effect*

Description

Estimate the average treatment effect (ATE) in a target region using covariate information from other regions. Optionally screen source regions before borrowing information.

Usage

```
regATE_dr(
  dat,
  target_region = 1,
  compute_se = TRUE,
  region_wise = FALSE,
  p1 = NULL,
  p0 = NULL,
  pi = NULL,
  v1 = "const",
  v0 = "const",
  config = list()
)
```

Arguments

dat	A data frame with numeric outcome `y`, binary treatment `trt` (1 = treatment), region label `region`, and at least one numeric covariate. All other numeric columns are covariates. Values must be complete and finite; every region must contain both arms. Use valid R covariate names; `D`, `D_src` and `resid_sq` are reserved for internal use.
target_region	A single label identifying the target region in `dat`.
compute_se	Calculate the influence-function standard error and 95% interval.
region_wise	Screen each source region using separate treatment-arm and control-arm ANCOVA tests before refitting.
p1, p0	Treatment assignment probabilities in the target and source populations. Supply `NULL` to fit logistic models, a scalar constant, or a vector aligned with all rows of `dat`. Supplied values must be in `(0, 1)`.
pi	Probability of membership in the target region, given covariates. Accepts `NULL`, a scalar or a row-aligned vector, as for `p1`. This is a selection probability, not the CP preservation fraction.
v1, v0	Target-to-source variance ratios in the treatment and control arms. Use a positive scalar, `"const"` for a marginal variance ratio, or `"log_linear"` for a model based on log squared residuals.
config	A named list with optional `check_p_threshold` in `(0, 1)` (default 0.05). Other entries are not supported.

Details

Let D_i indicate target-region membership and $\widehat{q} = n^{-1}\sum_i D_i$. The estimator is

$$\widehat{\tau} = \frac{1}{n\widehat{q}} \sum_{i=1}^{n} \left[D_i \widehat{\Delta}(X_i) + \widehat{W}_{1i}\widehat{U}_{1i} - \widehat{W}_{0i}\widehat{U}_{0i} \right].$$

Here $\widehat{\Delta} = \widehat{m}_1 - \widehat{m}_0$, $\widehat{U}_t = Y - \widehat{m}_t(X)$, and the residual weights combine selection scores, treatment assignment and variance ratios. Outcome models are linear; estimated probability models are logistic.

Borrowing assumes conditional outcome-mean exchangeability across the regions retained. Double robustness concerns correct specification of either outcome models or both selection and treatment-assignment models; it does not remove the exchangeability assumption.

Value

A list of class `regATE_dr` with:

estimate ATE using all candidate source regions.

se_eif, ci Standard error and 95% Wald interval, or `NULL` if disabled.

remaining_regions All candidate source-region labels.

config Screening settings used.

With `region_wise = TRUE`, the list also contains:

check_results Source labels, arm-specific p-values and pass indicators.

excluded_by_check Excluded source labels.

region_wise_estimate ATE after source screening.

region_wise_se, region_wise_ci Its standard error and 95% interval.

region_wise_remaining_regions Retained source labels.

Source screening

Each arm compares `y ~ X` with `y ~ X + D_src + X:D_src`. A source is excluded if either p-value is below `check_p_threshold`. Treatment probability vectors are subset with the retained rows. Selection probabilities are re-estimated after exclusions, because the population changes. If no sources remain, the estimator uses only the target region. The reported influence-function interval does not account for uncertainty from selecting the source regions.

Examples

```
set.seed(42)
dat <- data.frame(region = rep(1:3, each = 100),
                  trt = rep(c(0, 1), 150), x = rnorm(300))
dat$y <- dat$x + dat$trt + rnorm(300)
regATE_dr(dat, target_region = 1, p1 = 0.5, p0 = 0.5)
```

regFrac *Regional fraction for one MRCT: Method I*

Description

Find the smallest continuous regional fraction attaining a target consistency probability under the fixed-effects model.

Usage

```
regFrac(
  alpha,
  power,
  pi = 0.5,
  CP = 0.8,
  d = 1,
  sigmaTrt = 4,
  sigmaCtrl = sigmaTrt,
  randRatio = 1
)
```

Arguments

alpha	One-sided significance level, between 0 and 0.5.
power	Target overall power, with `alpha < power < 1`.
pi	Fraction of the overall effect to preserve; `0 <= pi < 1`.
CP	Target consistency probability, in `(0.5, 1]`.
d	Positive treatment-minus-control mean difference.
sigmaTrt	Positive outcome standard deviation in the treatment arm.
sigmaCtrl	Positive outcome standard deviation in the control arm.
randRatio	Treatment-to-control allocation ratio, strictly positive.

Details

Solves `conProb(...)$CP = CP` for `rF`. A target of one returns `rF = 1`. Fractions are not converted to integer regional arm counts.

Value

A list with `rF` (regional fraction) and `N` (recommended total count).

Sample sizes

CP uses the continuous design at the requested power. The recommended control count is rounded up first, followed by the treatment count. Returned counts do not re-evaluate CP after integer regional allocation.

See Also

conProb(), regFrac2().

Examples

```
regFrac(alpha = 0.05, power = 0.8, CP = 0.8)
```

---

regFrac2 *Regional fraction for two symmetric MRCTs: Method I*

Description

Solve for a common regional fraction attaining the target Method I consistency probability in two independent, symmetric trials.

Usage

```
regFrac2(alpha, power, pi = 0.5, CP = 0.8)
```

Arguments

alpha	One-sided significance level, between 0 and 0.5.
power	Common overall power for both trials, with alpha < power < 1.
pi	Fraction of the overall effect to preserve; 0 <= pi < 1.
CP	Target consistency probability, in (0.5, 1].

Details

Both trials must have the same treatment effect, arm-specific variances, randomization ratio, power and regional fraction. The function solves for that common fraction. It does not optimize two unequal regional fractions. A target of one returns the full-region boundary.

Value

A numeric scalar: the common regional fraction for both trials.

References

Qing, Kunhai, Xinru Ren, Shuping Jiang, Ping Yang, Menggang Yu, and Jin Xu. 2025. "Regional Consistency Evaluation and Sample Size Calculation under Two MRCTs." *Statistics in Medicine* 44 (25–27): e70306. doi:10.1002/sim.70306.

See Also

conProb2() for a general two-trial CP calculation.

Examples

```
fraction <- regFrac2(alpha = 0.05, power = 0.8)
conProb2(alpha = 0.05, power1 = 0.8, rF1 = fraction,
         d1 = 1, sigmaTrt1 = 4)
```

`ssCPbinary` *Random-effects design for a binary endpoint: Method I*

Description

Calculate overall sample size and shrinkage-based Method I consistency probability from regional response probabilities.

Usage

```
ssCPbinary(alpha, beta, p0r, p1r, pi = 0.5, randRatio = 1, target, f)
```

Arguments

`alpha`	One-sided significance level, between 0 and 0.5.
`beta`	Type II error probability; `alpha < 1 - beta < 1`.
`p0r`, `p1r`	Control and treatment response probabilities, strictly in `(0, 1)`, as scalars or vectors with one value per region.
`pi`	Fraction of the overall effect to preserve; `0 <= pi < 1`.
`randRatio`	Treatment-to-control allocation ratio, strictly positive.
`target`	Index of the region of interest in `f`.
`f`	Positive regional fractions summing to one. At least two regions are required.

Details

Regional effects are `p1r - p0r`. Their unweighted mean and sample standard deviation define `delta` and `tau`; the mean must be positive. The sampling variance component is

$$\Omega_r = p_{1r}(1 - p_{1r})/\ell + p_{0r}(1 - p_{0r}).$$

This function uses a normal random-effects approximation, not binomial simulation. For fixed-effects Method II simulation, use `conProbII()`.

Value

A list with:

n0, n1 Recommended overall control and treatment counts.

n Total count, `n0 + n1`.

CP Conditional consistency probability, without rounding.

Design assumptions

Regional inputs may be scalars or vectors of length `length(f)`. The calculation uses a normal random-effects approximation and the sample-size equation in `ssCPnorm()`. Invalid inputs and designs with no finite solution raise errors. CP uses the continuous design; returned group counts are rounded recommendations.

References

Ren, Xinru, and Jin Xu. 2026. "Consistency Assessment and Regional Sample Size Calculation for MRCT under Random Effects Model." *Pharmaceutical Statistics* 25 (3): e70090. doi:10.1002/pst.70090.

See Also

`ssCPnorm()`, `CPlbd()`.

Examples

```
ssCPbinary(alpha = 0.025, beta = 0.2, p0r = 0.3,
           p1r = c(0.6, 0.55, 0.5), target = 1, f = rep(1/3, 3))
```

---

ssCPnorm *Random-effects design for a normal endpoint: Method I*

Description

Calculate overall sample size and conditional Method I consistency probability for an empirical shrinkage regional estimator.

Usage

```
ssCPnorm(
  alpha,
  beta,
  delta,
  tau,
  sigma1r,
  sigma0r,
  pi = 0.5,
  randRatio = 1,
  target,
  f
)
```

Arguments

`alpha`	One-sided significance level, between 0 and 0.5.
`beta`	Type II error probability; `alpha < 1 - beta < 1`.
`delta`	Positive mean of the regional treatment-effect distribution.
`tau`	Nonnegative standard deviation of regional treatment effects.
`sigma1r`, `sigma0r`	Positive treatment and control outcome standard deviations, as scalars or vectors with one value per region.
`pi`	Fraction of the overall effect to preserve; `0 <= pi < 1`.
`randRatio`	Treatment-to-control allocation ratio, strictly positive.
`target`	Index of the region of interest in `f`.
`f`	Positive regional fractions summing to one. At least two regions are required.

Details

Let ℓ be `randRatio`, $z = z_{1-\alpha} + z_{1-\beta}$ and $\Omega_r = \sigma_{1r}^2/\ell + \sigma_{0r}^2$. The continuous control count solves

$$\sum_r \left(\tau^2 + \frac{\Omega_r}{n_0 f_r}\right)^{-1} = \frac{z^2}{\delta^2}.$$

A finite solution requires $\tau z/\delta < \sqrt{R}$, where R is the number of regions.

The target-region criterion is

$$\Pr(\widetilde{D}_r \geq \pi \widetilde{D} \mid T > z_{1-\alpha}).$$

It uses the shrinkage estimator, not the raw regional mean difference. At `tau = 0`, regional and overall shrinkage estimates coincide, so CP is one.

Value

A list with:

n0, n1 Recommended overall control and treatment counts.

n Total count, `n0 + n1`.

CP Conditional consistency probability, without rounding.

Design assumptions

Regional inputs may be scalars or vectors of length `length(f)`. The calculation uses a normal random-effects approximation and the sample-size equation above. Invalid inputs and designs with no finite solution raise errors. CP uses the continuous design; returned group counts are rounded recommendations.

References

Ren, Xinru, and Jin Xu. 2026. "Consistency Assessment and Regional Sample Size Calculation for MRCT under Random Effects Model." *Pharmaceutical Statistics* 25 (3): e70090. doi:10.1002/pst.70090.

See Also

ssCPbinary(), ssCPsurvPH(), ssCPsurvNPH(), CPlbd().

Examples

```
ssCPnorm(alpha = 0.025, beta = 0.2, delta = 0.25, tau = 0.1,
         sigma1r = 1, sigma0r = 1, target = 1, f = rep(1/3, 3))
```

---

ssCPsurvNPH *Random-effects design using RMST: Method I*

Description

Calculate sample size and shrinkage-based Method I consistency probability for a treatment-minus-control restricted mean survival time (RMST) difference, allowing non-proportional hazards.

Usage

```
ssCPsurvNPH(
  alpha,
  beta,
  lambda0a,
  lambda0b,
  lambda1a,
  lambda1b,
  breakpoint,
  shape0,
  scale0,
  shape1,
  scale1,
  PW = TRUE,
  unimin,
  unimax,
  pi = 0.5,
  randRatio = 1,
  target,
  f,
  eta
)
```

Arguments

alpha	One-sided significance level, between 0 and 0.5.
beta	Type II error probability; alpha < 1 - beta < 1.
lambda0a, lambda0b	Positive control hazard rates before and after breakpoint. Used only when PW = TRUE.

`lambda1a`, `lambda1b`
: Positive treatment hazard rates before and after `breakpoint`. Used only when `PW = TRUE`.

`breakpoint`
: Nonnegative, common hazard change time. Used only when `PW = TRUE`.

`shape0`, `shape1`
: Positive Weibull shape parameters for control and treatment. Used only when `PW = FALSE`.

`scale0`, `scale1`
: Positive Weibull scale parameters for control and treatment. Used only when `PW = FALSE`.

`PW`
: Use piecewise exponential survival (`TRUE`) or Weibull survival (`FALSE`).

`unimin`, `unimax`
: Uniform censoring limits, with `0 <= unimin < unimax`.

`pi`
: Fraction of the overall effect to preserve; `0 <= pi < 1`.

`randRatio`
: Treatment-to-control allocation ratio, strictly positive.

`target`
: Index of the region of interest in `f`.

`f`
: Positive regional fractions summing to one. At least two regions are required.

`eta`
: Positive common RMST horizon; must be below every `unimax`.

Details

Supply only the survival parameters needed by `PW`. All regional model parameters can be scalars or vectors of length `length(f)`. Use the same time units for `eta`, `breakpoint`, censoring limits and scales.

With `PW = TRUE`, hazards change once at `breakpoint`. With `PW = FALSE`, Weibull survival is $S(t) = \exp\{-(t/\text{scale})^{\text{shape}}\}$. Scale equals the reciprocal exponential rate only when shape is one. Event and censoring times are independent. Before `unimin`, censoring survival equals one.

Regional effects are RMST differences; their mean and sample standard deviation define `delta` and `tau`. The mean must be positive. RMST variance is integrated numerically, with $\Omega_r = \sigma_{1r}^2/\ell + \sigma_{0r}^2$.

Value

A list containing `n0`, `n1`, `n` and `CP` as in `ssCPnorm()`, plus:

Dr Treatment-minus-control RMST difference in each region.

sigma2.1r, sigma2.0r Treatment and control RMST variance coefficients. Divide each by its regional arm count to obtain the estimator variance.

Design assumptions

Regional inputs may be scalars or vectors of length `length(f)`. The calculation uses a normal random-effects approximation and the sample-size equation in `ssCPnorm()`. Invalid inputs and designs with no finite solution raise errors. CP uses the continuous design; returned group counts are rounded recommendations.

References

Ren, Xinru, and Jin Xu. 2026. "Consistency Assessment and Regional Sample Size Calculation for MRCT under Random Effects Model." *Pharmaceutical Statistics* 25 (3): e70090. doi:10.1002/pst.70090.

See Also

ssCPsurvPH(), ssCPnorm().

Examples

```
# Piecewise exponential survival
ssCPsurvNPH(alpha = 0.025, beta = 0.2,
            lambda0a = 0.07, lambda0b = 0.04,
            lambda1a = c(0.02, 0.03, 0.04), lambda1b = 0.04,
            breakpoint = 10, unimin = 0, unimax = 240,
            target = 1, f = rep(1/3, 3), eta = 80)

# Weibull survival: shape = 1 gives exponential survival
ssCPsurvNPH(alpha = 0.025, beta = 0.2, PW = FALSE,
            shape0 = 1, scale0 = 10, shape1 = 1, scale1 = 15,
            unimin = 20, unimax = 30, eta = 10,
            target = 1, f = rep(1/3, 3))
```

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ssCPsurvPH *Random-effects design for a PH endpoint: Method I*

Description

Calculate sample size and shrinkage-based Method I consistency probability for exponential survival with a common fixed follow-up time.

Usage

```
ssCPsurvPH(alpha, beta, lambda0r, hr, pi = 0.5, randRatio = 1, target, f, L)
```

Arguments

alpha	One-sided significance level, between 0 and 0.5.
beta	Type II error probability; alpha < 1 - beta < 1.
lambda0r	Positive control hazard rates, as a scalar or regional vector.
hr	Positive treatment-to-control hazard ratios, as a scalar or regional vector. The mean of -log(hr) must be positive.
pi	Fraction of the overall effect to preserve; 0 <= pi < 1.
randRatio	Treatment-to-control allocation ratio, strictly positive.
target	Index of the region of interest in f.
f	Positive regional fractions summing to one. At least two regions are required.
L	Positive follow-up duration, in the same time units as the hazard rates.

Details

All participants are followed for `L` time units. Administrative censoring at `L` is the only censoring mechanism. Regional effects are `-log(hr)`; their mean and sample standard deviation define `delta` and `tau`. With event probabilities $P_{kr} = 1 - \exp(-\lambda_{kr} L)$,

$$\Omega_r = \frac{(\ell + 1)^2}{\ell(P_{0r} + \ell P_{1r})}.$$

For delayed effects or crossing survival curves, use `ssCPsurvNPH()`.

Value

A list with:

n0, n1 Recommended overall control and treatment counts.

n Total count, `n0 + n1`.

CP Conditional consistency probability, without rounding.

Design assumptions

Regional inputs may be scalars or vectors of length `length(f)`. The calculation uses a normal random-effects approximation and the sample-size equation in `ssCPnorm()`. Invalid inputs and designs with no finite solution raise errors. CP uses the continuous design; returned group counts are rounded recommendations.

References

Ren, Xinru, and Jin Xu. 2026. "Consistency Assessment and Regional Sample Size Calculation for MRCT under Random Effects Model." *Pharmaceutical Statistics* 25 (3): e70090. doi:10.1002/pst.70090.

See Also

`ssCPnorm()`, `ssCPsurvNPH()`.

Examples

```
ssCPsurvPH(alpha = 0.025, beta = 0.2, lambda0r = 0.05,
           hr = c(0.7, 0.6, 0.4), target = 1, f = rep(1/3, 3), L = 36)
```

Index

conProb, *2*, 3
conProb(), *6, 7*, *15*
conProb2, *2*, 4
conProb2(), *4*, *10*, *15*
conProbII, *2*, 6
conProbII(), *10*, *16*
conProbII2, *2*, 8
conProbII2(), *7*
CPlbd, *2*, 10
CPlbd(), *17*, *19*

regATE_dr, *2*, 12
regFrac, *2*, 14
regFrac(), *4*
regFrac2, *2*, 15
regFrac2(), *6*, *15*

ssCPbinary, *2*, 16
ssCPbinary(), *19*
ssCPnorm, *2*, 17
ssCPnorm(), *11*, *17*, *20–22*
ssCPsurvNPH, *2*, 19
ssCPsurvNPH(), *19*, *22*
ssCPsurvPH, *2*, 21
ssCPsurvPH(), *19*, *21*
ssMRCT *(*ssMRCT-package*)*, 2
ssMRCT-package, 2