

# Package ‘NNTbiomarker’

July 21, 2025

**Type** Package

**Title** Calculate Design Parameters for Biomarker Validation Studies

**Version** 0.29.11

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**Description** Helps a clinical trial team discuss the clinical goals of a well-defined biomarker with a diagnostic, staging, prognostic, or predictive purpose. From this discussion will come a statistical plan for a (non-randomized) validation trial. Both prospective and retrospective trials are supported. In a specific focused discussion, investigators should determine the range of “discomfort” for the NNT, number needed to treat. The meaning of the discomfort range, [NNTlower, NNTupper], is that within this range most physicians would feel discomfort either in treating or withholding treatment. A pair of NNT values bracketing that range, NNTpos and NNTneg, become the targets of the study's design. If the trial can demonstrate that a positive biomarker test yields an NNT less than NNTlower, and that a negative biomarker test yields an NNT less than NNTlower, then the biomarker may be useful for patients. A highlight of the package is visualization of a “contra-Bayes” theorem, which produces criteria for retrospective case-controls studies.

**License** GPL-3

**Imports** shiny, xtable, stringr, magrittr, mvbutils

**Collate** aaa.R ifVerboseCat.R sesp-pv-NNT.R achievable.se.sp.R  
binom.confint.R NNTintervals.R run.R ROCplots.R argmin.R zzz.R

**Suggests** testthat (>= 0.8.1), knitr (>= 1.6), rmarkdown, ggplot2, plyr

**VignetteBuilder** knitr

**NeedsCompilation** no

**Repository** CRAN

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|                      |                                                                                         |
|----------------------|-----------------------------------------------------------------------------------------|
| NNTbiomarker-package | <i>Plan a biomarker validation study by focusing on desired clinical actionability.</i> |
|----------------------|-----------------------------------------------------------------------------------------|

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Description

Clarifying what performance would suffice if the test is to improve medical care makes it possible to design meaningful validation studies.

Details

Package: NNTbiomarker  
Type: Package  
Version: 0.1  
Date: 2015-03-21  
License: What license is it under?

This package bases the design of a biomarker study on the idea of "number needed to treat" (NNT). It postulates a "range of discomfort" for NNT, within which the clinical decision is uncomfortable for a treating physician. provides a shiny window for eliciting the boundaries of the range of number needed to

**Author(s)**

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**References**

See author for unpublished manuscript.

**Examples**

```
NNT.to.pv(NNTpos=5, NNTneg=28)
NNT.from.sesp(se=0.7, sp=0.9, prev=0.1)
pv.to.sesp(pv = cbind(ppv=seq(.5, .9, .1), npv=0.9), prev = 0.2)
```

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|                  |                                                                                          |
|------------------|------------------------------------------------------------------------------------------|
| achievable.se.sp | <i>achievable.se.sp(): target sensitivity and specificity for a retrospective study.</i> |
|------------------|------------------------------------------------------------------------------------------|

---

**Description**

For a retrospective study design, given a prevalence value, produce a plot displaying the achievable contours of either predictive values or NNT values. The calculation uses the "contra-Bayes" theorem, `se.sp.from.pv`.

**Usage**

```
achievable.se.sp(the.prev = 0.5, axes = c("pv", "NNT"),
  sesp.seq = seq(0.5, 1, 0.1), drawNNTaxes = TRUE, drawPVaxes = FALSE,
  drawArrows = TRUE, drawTable = TRUE, latexTable = TRUE,
  placePointLabels = TRUE, cexText = 0.5, cexSubtitle = 0.5,
  cexTitle = 0.7, y0arrow = 0.25, lwdArrow = 1, ltyArrow = 2,
  title = FALSE, mtext = FALSE, contours = TRUE, ...)
```

**Arguments**

|                          |                                                                               |
|--------------------------|-------------------------------------------------------------------------------|
| <code>the.prev</code>    | Prevalence (prior probability)                                                |
| <code>axes</code>        | Should the axes be predictive values ("pv") or NNT values? Default is "pv".   |
| <code>se.sp.seq</code>   | Sequence of values at which the sensitivity and specificity will be explored. |
| <code>drawNNTaxes</code> | (default=TRUE) Option for tweaking the plot.                                  |
| <code>drawPVaxes</code>  | (default=FALSE) Option for tweaking the plot.                                 |
| <code>drawArrows</code>  | (default=TRUE) Arrow option; deprecated.                                      |
| <code>drawTable</code>   | (default=TRUE) Option for tweaking the plot.                                  |
| <code>latexTable</code>  | (default=TRUE) Option for tweaking the plot.                                  |

placePointLabels (default=TRUE) Write A, B, C, ... in circles where sensitivity=specificity.

cexText (default=0.5) Option for tweaking the plot.

cexSubtitle (default=0.5) Option for tweaking the plot.

cexTitle (default=0.7) Option for tweaking the plot.

y0arrow (default=0.25) Arrow option; deprecated.

lwdArrow (default=1) Arrow option; deprecated.

ltyArrow (default=2) Arrow option; deprecated.

title (default=FALSE) Option for tweaking the plot.

mtext (default=FALSE) Option for tweaking the plot.

contours (default=TRUE) Option for tweaking the plot.

... Options to pass to plot.default()

### Value

The predictive values when sensitivity equals specificity: `sest.to.pv(cbind(sesp.seq,sest.seq), prev=the.prev)`

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|        |                                             |
|--------|---------------------------------------------|
| argmin | <i>argmin</i> Argmin function for a vector. |
|--------|---------------------------------------------|

---

### Description

Return the index minimizing distance from v to target.

### Usage

```
argmin(v, target = 0)
```

### Arguments

v The vector to compare to target.

target The value sought in the vector; default=0.

### Value

The index in v of the value which is closest to target.

---

|               |                      |
|---------------|----------------------|
| binom.confint | <i>binom.confint</i> |
|---------------|----------------------|

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**Description**

Exact confidence intervals for a binomial proportion parameter.

**Usage**

```
binom.confint(k, n, alpha = 0.05, side = c("two", "upper", "lower"))
```

**Arguments**

|       |                                                         |
|-------|---------------------------------------------------------|
| k     | #"heads"                                                |
| n     | sample size                                             |
| alpha | Confidence level                                        |
| side  | Sidedness of the hypothesis: c("two", "upper", "lower") |

---

|             |                    |
|-------------|--------------------|
| NNT.from.pv | <i>NNT.from.pv</i> |
|-------------|--------------------|

---

**Description**

Compute NNT values from predictive values.

**Usage**

```
NNT.from.pv(ppv, npv, pv)
```

**Arguments**

|     |                                                              |
|-----|--------------------------------------------------------------|
| ppv | Positive predictive value                                    |
| npv | Negative predictive value                                    |
| pv  | Alternative input of ppv and npv, in matrix or named vector. |

**Value**

```
c(NNTpos=NNTpos, NNTneg=NNTneg)
```

---

NNT.from.sesp

*NNT.from.sesp*


---

### Description

Compute NNT values from sensitivity and specificity.

### Usage

```
NNT.from.sesp(se, sp, sesp, prev)
```

### Arguments

|      |                                                             |
|------|-------------------------------------------------------------|
| se   | Positive predictive value                                   |
| sp   | Negative predictive value                                   |
| sesp | Alternative input for se and sp, as matrix or named vector. |
| prev | Prevalence (prior probability)                              |

### Value

```
c(NNTpos=NNTpos, NNTneg=NNTneg)
```

---

NNT.to.pv

*NNT.to.pv*


---

### Description

Convert between (NNTpos, NNTneg) and (PPV, NPV).

### Usage

```
NNT.to.pv(NNTpos, NNTneg, NNT, prev, calculate.se.sp = F)
```

### Arguments

|                 |                                                                                                         |
|-----------------|---------------------------------------------------------------------------------------------------------|
| NNTpos          | NNT for a patient with positive test result                                                             |
| NNTneg          | NNT for a patient with negative test result                                                             |
| NNT             | A matrix or vector of (NNTpos, NNTneg) values.                                                          |
| prev            | Prevalence of the "BestToTreat" group before testing.                                                   |
| calculate.se.sp | (default=FALSE) If TRUE, also calculate the sensitivity and specificity using the contra-Bayes theorem. |

### Value

For matrix input, cbind(ppv=ppv, npv=npv). For vector input, c(ppv=ppv, npv=npv).

---

NNT.to.sesp

*NNT.to.sesp*


---

**Description**

Compute sensitivity and specificity from NNT values.

**Usage**

```
NNT.to.sesp(NNTpos, NNTneg, NNT, prev)
```

**Arguments**

|        |                                                        |
|--------|--------------------------------------------------------|
| NNTpos | NNT for a positive test result                         |
| NNTneg | NNT for a negative test result                         |
| NNT    | Alternative way in input NNT values (matrix or vector) |
| prev   | Prevalence (prior probability)                         |

**Value**

```
c(se=se, sp=sp)
```

---

NNTintervalsProspective

*NNTintervalsProspective*


---

**Description**

Produce Bayesian and classical intervals for NNT from observations in a prospective study. Useful for "anticipated results" when designing a study, The setting: patients will be tested immediately, and followed to determine the BestToTreat/BestToWait classification. as well as analyzing study results. There were (or will be) Npositives patients with a positive test, Nnegatives with a negative test. The observed NNTs in each group were (or will be) NNTpos and NNTneg.

**Usage**

```
NNTintervalsProspective(Npositives, Nnegatives, NtruePositives, NtrueNegatives,  
  prev = 0.15, alpha = 0.025, prior = c(1/2, 1/2))
```

**Arguments**

|                |                                                                                                                                |
|----------------|--------------------------------------------------------------------------------------------------------------------------------|
| Npositives     | Total number of observed positives.                                                                                            |
| Nnegatives     | Total number of observed negatives.                                                                                            |
| NtruePositives | Observed or anticipated number of "BestToTreat" among the positives.                                                           |
| NtrueNegatives | Observed or anticipated number of "BestToWait" among the negatives.                                                            |
| prev           | = 0.15 Prevalence of "BestToTreat" characteristic.                                                                             |
| alpha          | = 0.025 Significance level (one side).                                                                                         |
| prior          | Beta parameters for prior. Default is the Jeffreys prior = $c(1/2, 1/2)$ . Jaynes prior = $c(0, 0)$ won't work when $\#fp=1$ . |

**Value**

The Bayesian predictive intervals for NNTpos and NNTneg. These are obtained from predictive intervals for PPV and NPV, based on Jeffreys'  $\text{beta}(1/2, 1/2)$  prior.

---

NNTIntervalsRetrospective  
*NNTIntervalsRetrospective*

---

**Description**

Bayes predictive intervals for sensitivity, specificity, NNTpos and NNTneg in a case-control retrospective study.

**Usage**

```
NNTIntervalsRetrospective(Ncases = 10, Ncontrols = 30, NposCases = 6,
  NposControls = 2, prev = 0.15, alpha = 0.025, prior = c(1/2, 1/2))
```

**Arguments**

|              |                                                                                                                                |
|--------------|--------------------------------------------------------------------------------------------------------------------------------|
| Ncases       | Number of cases in the study                                                                                                   |
| Ncontrols    | Number of controls in the study                                                                                                |
| NposCases    | Number of cases with positive test                                                                                             |
| NposControls | Number of controls with positive test                                                                                          |
| prev         | Prevalence of the BestToTreat (versus BestToWait)                                                                              |
| alpha        | Significance level for interval.                                                                                               |
| prior        | Beta parameters for prior. Default is the Jeffreys prior = $c(1/2, 1/2)$ . Jaynes prior = $c(0, 0)$ won't work when $\#fp=1$ . |

**Value**

A list with 3 components containing intervals (predictive or otherwise), with names `intervalsForSN`, `intervalsForSP`, `intervalsForNNT`. The intervals derive from assuming independent Jeffreys priors for SN and SP, sampling from joint independent posteriors for SN and SP incorporating the anticipated results, and applying `NNT.from.sesp` (Bayes theorem) to each sampled pair to obtain a sample of `NNTpos` and `NNTneg`.

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|                           |                     |
|---------------------------|---------------------|
| <code>pv.from.sesp</code> | <i>pv.from.sesp</i> |
|---------------------------|---------------------|

---

**Description**

Computes predictive values from sensitivity and specificity.

**Usage**

```
pv.from.sesp(se = 0.8, sp = 0.8, sesp, prev = 0.001)
```

**Arguments**

|                   |                                                                                        |
|-------------------|----------------------------------------------------------------------------------------|
| <code>se</code>   | Positive predictive value                                                              |
| <code>sp</code>   | Negative predictive value                                                              |
| <code>sesp</code> | Alternative input for <code>se</code> and <code>sp</code> , as matrix or named vector. |
| <code>prev</code> | Prevalence (prior probability). Default = 0.001                                        |

**Value**

```
c(ppv=ppv, npv=npv)
```

---

|                       |                 |
|-----------------------|-----------------|
| <code>ROCplots</code> | <i>ROCplots</i> |
|-----------------------|-----------------|

---

**Description**

A variety of ROC-related plots for a binary target and a single continuous predictor.

**Usage**

```
ROCplots(data, whichPlots = c("density", "raw", "ROC", "pv", "nnt",
  "nntRange"), NNTlower = 3, NNTupper = 10, N = 1000, prev = 0.2,
  diffInSD = 2, ...)
```

**Arguments**

|                         |                                                                                                                                      |
|-------------------------|--------------------------------------------------------------------------------------------------------------------------------------|
| <code>data</code>       | Data frame with columns "class" (binary target variable) and "X" (predictor).                                                        |
| <code>whichPlots</code> | Which plots to do. Options are <code>c("density", "raw", "ROC", "pv", "nnt")</code>                                                  |
| <code>NNTlower</code>   | Subjective input. If $NNT < NNTlower$ , the decision is clearly to Treat.                                                            |
| <code>NNTupper</code>   | Subjective input. If $NNT > NNTupper$ , the decision is clearly to Wait.                                                             |
| <code>N</code>          | For simulated data: sample size                                                                                                      |
| <code>prev</code>       | For simulated data: Prevalence                                                                                                       |
| <code>diffInSD</code>   | For simulated data: Difference: $E(X   \text{group}=1) - E(X   \text{group}=0)$ , measured in units of S.D (common to the 2 groups). |
| <code>...</code>        | Extra arguments for a plot. Do not supply unless <code>length(whichPlots)==1</code> .                                                |

**Details**

The plots display the values achievable by changing the cutoff, in comparison with the desired values as determined by `NNTlower` and `NNTupper`. The "whichPlots" options are as follows:

- "density" Marginal density of X, with rug.
- "raw" X versus class.
- "ROC" Standard ROC curve.
- "pv" Plot of ppv versus npv, with indication of the acceptable range for cutoff.
- "nnt" Plot of NNTpos versus NNTneg, with indication of the acceptable region
- "nntRange" Plot of NNTpos and NNTneg versus cutoff, with indication of the acceptable range.

By default, all the plots are made.

---

run

---

run

---

**Description**

Run a shiny app for this package.

**Usage**

```
run(shinyDir)
```

**Arguments**

|                       |                                                                                                                |
|-----------------------|----------------------------------------------------------------------------------------------------------------|
| <code>shinyDir</code> | Current options are "shinyElicit" and "shinyCombinePlots". If not provided, a menu of the options is provided. |
|-----------------------|----------------------------------------------------------------------------------------------------------------|

**Details**

The selected shiny app is run. See the vignette `Using_the_NNTbiomarker_package` for details, and the vignette `The_Biomarker_Crisis` for an overview.

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|                 |                        |
|-----------------|------------------------|
| runCombinePlots | <i>runCombinePlots</i> |
|-----------------|------------------------|

---

**Description**

Run a shiny app connecting a visual scale for NNT quantities and a "contra-Bayes" plot for mapping from predictive values to sensitivity/specificity (Bayes theorem in reverse).

**Usage**

```
runCombinePlots()
```

**See Also**

run

---

|           |                  |
|-----------|------------------|
| runElicit | <i>runElicit</i> |
|-----------|------------------|

---

**Description**

Run a shiny app outlining the process of specifying a design for a biomarker validation study.

**Usage**

```
runElicit()
```

**See Also**

run

---

|               |                      |
|---------------|----------------------|
| se.sp.from.pv | <i>se.sp.from.pv</i> |
|---------------|----------------------|

---

**Description**

Computes sensitivity and specificity from predictive values.

**Usage**

```
se.sp.from.pv(ppv = 0.1, npv = 0.7, pv, prev = 0.2)
```

**Arguments**

|      |                                                              |
|------|--------------------------------------------------------------|
| ppv  | Positive predictive value                                    |
| npv  | Negative predictive value                                    |
| pv   | Alternative input of ppv and npv, in matrix or named vector. |
| prev | Prevalence (prior probability)                               |

**Value**

c(se=se,sp=sp)

---

sesp.from.pv.feasible    *sesp.from.pv.feasible*

---

**Description**

Computes sensitivity and specificity from predictive values.

**Usage**

```
sesp.from.pv.feasible(ppv, npv, prev, feasible = TRUE)
```

**Arguments**

|          |                                            |
|----------|--------------------------------------------|
| ppv      | Positive predictive value                  |
| npv      | Negative predictive value                  |
| prev     | Prevalence (prior probability)             |
| feasible | Only return results in [0,1]. Default=TRUE |

**Details**

NNT stands for Number Needed to Treat. We have a range, such that if  $NNT < NNT_{pos}$ , all patients will be treated, if  $NNT > NNT_{neg}$  then all patients will not be treated. Suppose  $N = NNT_{pos}$  is the number of patients such that if  $N$  pts are positive, one will be a true positive. The "eq" means that we choose  $NNT_{pos}$  so that treating all or not treating all would be equivalent.  $E(\text{loss} | \text{treat}) = (NNT_{pos} - 1) * L[A, H] = E(\text{loss} | \text{wait}) = 1 * L[W, D]$  Actually we choose  $N$  SMALLER so that TREATing is definitely, comfortably the right thing.  $E(\text{loss} | \text{treat}) = (NNT_{pos} - 1) * L[A, H] \ll E(\text{loss} | \text{wait}) = 1 * L[W, D]$  Suppose  $N = NNT_{neg}$  is the number of patients such that if  $N$  pts are negative, one will be a false negative. The "eq" means that we choose  $NNT_{neg}$  so that treating all or not treating any would be equivalent.  $E(\text{loss} | \text{treat}) = (NNT_{neg} - 1) * L[A, H] = E(\text{loss} | \text{wait}) = 1 * L[W, D]$  Actually we choose  $N$  LARGER so that WAITing is definitely, comfortably the right thing.  $E(\text{loss} | \text{treat}) = (NNT_{pos} - 1) * L[A, H] \gg E(\text{loss} | \text{wait}) = 1 * L[W, D]$

**Value**

c(ppv=ppv, npv=npv, sp=sp, se=se)

---

|                     |                            |
|---------------------|----------------------------|
| setVerboseCatOption | <i>setVerboseCatOption</i> |
|---------------------|----------------------------|

---

**Description**

Allows user to toggle on and off printing messages on a per-function basis. Should be usable in other packages, but not by importing.

**Usage**

setVerboseCatOption(fname, value)

**Arguments**

- |       |                                                         |
|-------|---------------------------------------------------------|
| fname | Name of the function to control.                        |
| value | Boolean value: should this function print out messages? |

**Value**

The new value of the namespace option for fname ifVerboseCat

---

|     |                                 |
|-----|---------------------------------|
| %%% | <i>%%% string concatenation</i> |
|-----|---------------------------------|

---

**Description**

From mvbutils

**Usage**

a %%% b

**Arguments**

- |   |                |
|---|----------------|
| a | a string       |
| b | another string |

**Value**

paste0(a, b)

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