Package ‘EBASS’

October 2, 2016

Type Package

Title Sample Size Calculation Method for Cost-Effectiveness Studies
Based on Expected Value of Perfect Information

Version 0.1

Date 2016-10-02

Maintainer Sebastien Cossin <cossin.sebastien@gmail.com>

URL https://github.com/scossin/EBASS

BugReports https://github.com/scossin/EBASS/issues

Description We propose a new sample size calculation method for trial-based
cost-effectiveness analyses. Our strategy is based on the value of perfect
information that would remain after the completion of the study.

License GPL-3

LazyData TRUE

RoxygenNote 5.0.1

Collate 'POP.R' 'INMB_DIRECT.R' 'VAR_INMB_DIRECT.R' 'EVPLR'
  'internal.R' 'INMB.R' 'Lambda.R' 'VAR_INMB.R' 'VAR_INMB_DIFF.R'
  'fonctions_sujets.R'

Imports methods

Suggests knitr, rmarkdown

VignetteBuilder knitr

NeedsCompilation no

Author Sebastien Cossin [aut, cre],
  Clement Bader [ctb],
  Morgane Donadel [ctb],
  Aline Maillard [ctb],
  Antoine Benard [ctb]

Repository CRAN

Date/Publication 2016-10-02 13:18:36
create_object_evpi_decrease

Create an object evpi_decrease

Description

An object that combines three others objects: object_inmb, object_pop, object_var_inmb. It contains methods to compute the value of perfect information (EVPI) that would remain after a study of n participants (EVPIn). For each additional individual included, the EVPI decreases. So EVPIn is a decreasing vector. It is used to determine the optimal sample size.

Usage

create_object_evpi_decrease(object_inmb, object_pop, object_var_inmb,
                             step_exp = 1, step_ref = 1)

Arguments

object_inmb : an object that represents the INMB (Incremental Net Monetary Benefit) Create an object with one of these functions: create_object_inmb_direct, create_object_inmb

object_pop : an object that represents the size of the targeted population. Create an object with create_object_pop
create_object_inmb

object_var_inmb : an object that represents the variance of INMB. The variance of INMB can be directly hypothesized, or calculated through sdc, sde, rho and lambda, or calculated through sdc_ref, sde_ref, sdc_exp, sde_exp, rho and lambda. Create an object with one of these functions: create_object_var_inmb_direct, create_object_var_inmb, create_object_var_inmb_diff

step_exp (default=1) : the minimal number of individuals to be included in the experimental group to respect the allocation ratio. If the allocation ratio is 2:1 in favor of the experimental group, step_exp=2 and step_ref=1.

step_ref (default=1) : the minimal number of individuals to be included in the reference group to respect the allocation ratio. If the allocation ratio is 2:1 in favor of the reference group, step_ref=2 and step_exp=1.

Value

create_object_evpi_decrease returns an object of class EVPI DECREASE

Examples

```r
## First, create 3 objects : inmb, pop and var_inmb, then create the evpi_decrease object
object_lambda <- create_object_lambda (20000)
object_inmb <- create_object_inmb(de = 0.04, dc=168, object_lambda = object_lambda)
object_var_inmb <- create_object_var_inmb(sde=0.12, sdc=2100, rho=0.1, object_lambda=object_lambda)
object_pop <- create_object_pop(horizon = 20, discount=0.04, N_year = 52000)
object_evpi_decrease <- create_object_evpi_decrease(object_inmb, object_pop, object_var_inmb)
```

create_object_inmb Create an object INMB

Description

The net monetary benefit (NMB) of an intervention is given by \( E \times \text{Lambda} - C \), where \( E \) and \( C \) are the effectiveness and cost of this intervention, and \( \text{Lambda} \) is the threshold value for a unit of effectiveness, the ceiling incremental cost-effectiveness ratio. When the NMB is positive, the value of the intervention’s effectiveness overpasses its cost. When evaluating the cost-effectiveness of a new intervention in comparison with the reference, one can estimate the difference between the net monetary benefit of the new or experimental intervention (NMBn) and the net monetary benefit of the reference (NMBr). This difference is known as the incremental net monetary benefit (INMB), which is given by: \( \text{INMB} = \text{NMBn} - \text{NMBr} = de \times \text{lambda} - dc \). The new intervention is cost-effective if INMB is positive.

Usage

```r
create_object_inmb(de, dc, object_lambda)
```
Arguments

- **de**: Expected point estimate of the difference in mean effectiveness (effectiveness in the experimental group minus effectiveness in the reference group)
- **dc**: Expected point estimate of the difference in mean cost (cost in the experimental group minus cost in the reference group)
- **object_lambda**: object containing the ceiling cost-effectiveness ratio or maximum acceptable cost of a unit of effectiveness. See `create_object_lambda`

Value

`create_object_inmb` returns an object of class `INMB` which inherits from the class `INMB_DIRECT`

See Also

- `create_object_inmb_direct` for INMB directly defined

Examples

```r
## First, create a lambda object
object_lambda <- create_object_lambda (20000)
## Then, create an inmb object
object_inmb <- create_object_inmb(de = 0.04, dc=-168, object_lambda = object_lambda)
## inmb is calculated by methods inside the object. Retrieve the inmb :
object_inmb$get_inmb()
```
create_object_lambda

See Also
create_object_inmb

Examples

## Create an object inmb_direct
object_inmb_direct <- create_object_inmb_direct(968)

---

create_object_lambda Create an object lambda

Description

Lambda is known as the willingness to pay. That is the ceiling cost-effectiveness ratio or the maximum acceptable cost of a unit of effectiveness. It must be coherent with the criteria of effectiveness used in the analysis (year of life, QALY, life saved, or a criteria related to morbidity).

Usage

create_object_lambda(lambda)

Arguments

lambda : Lambda is a monetary value. For example, the value of lambda is usually between 20 000 and 40 000 pounds/QALY in UK.

Value

create_object_lambda returns an object of class Lambda

Examples

## Create an object lambda
object_lambda <- create_object_lambda(20000)
## retrieve the lambda value from the object
object_lambda$get_lambda()
create_object_pop

Create an object POP

Description

The expected value of perfect information (EVPI) is estimated for the entire population targeted by the evaluated intervention. This object represents this target population. The size of the target population (POP) can be estimated through prevalence and incidence data from registries, large cohort studies, medico-administrative databases, or surveillance systems. POP has to be calculated over the entire time horizon used for the estimation of the EVPI. It is usually easier to gather data on the annual number of individual susceptible to benefit for the new intervention. If this number is expected to be constant over the time horizon, POP is the product of this time horizon (in years) and the annual number of individual. If the time horizon is longer than one year, POP has to be discounted.

Usage

create_object_pop(horizon, discount, N_year)

Arguments

- **horizon**: Time horizon in years considered in the estimation of the EVPI. Finite time horizons are recommended in order to control for the complex and uncertain process of future changes. Furthermore, because of discounting, the impact of a time horizon over 15 or 20 years on the estimation of EVPI is insignificant.
- **discount**: Annual discount rate considered in the estimation of the EVPI. The annual discount rate is defined in each country, usually within 3 to 6%.
- **N_year**: Number of individuals likely to be targeted by the evaluated intervention each year

Value

create_object_pop returns an object of class POP

Examples

object_pop <- create_object_pop(horizon = 20, discount=0.04, N_year = 52000)
**create_object_var_inmb**

Create an object var_inmb

**Description**

Hypothetical variance of the Incremental Net Monetary Benefit. If data are available this variance can be calculated based of the common standard deviation of costs in each group (sdc), the common standard deviation of effectiveness in each group (sde), lambda (create_object_lambda), and the coefficient of correlation (rho) between the difference in costs (dc) and the difference in effectiveness (de)

**Usage**

```r
create_object_var_inmb(sdc, sde, rho, object_lambda)
```

**Arguments**

- **sdc**: common standard deviation of costs in each group
- **sde**: common standard deviation of effectiveness in each group
- **rho**: coefficient of correlation between the difference in costs (dc) and the difference in effectiveness (de)
- **object_lambda**: an object lambda. Create one with create_object_lambda. It contains lambda
  - **lambda**: the ceiling cost-effectiveness ratio or maximum acceptable cost of a unit of effectiveness

**Value**

create_object_var_inmb returns an object of class VAR_INMB which inherits from the class VAR_INMB_DIRECT

**See Also**

create_object_var_inmb_direct to directly provide a value for the variance of the Incremental Net Monetary Benefit

create_object_var_inmb_diff to calculate the theoretical standard deviation of the expected INB with different standard deviation in the reference and the experimental group

**Examples**

```r
## First, create a lambda object
object_lambda <- create_object_lambda (20000)
## Then, create a var_inmb object
var_inmb <- create_object_var_inmb(sde=0.12, sdc=2100, rho=0.1, object_lambda=object_lambda)
var_inmb$get_var_inmb()
```
create_object_var_inmb_diff

Create an object var_inmb_diff

Description

The variance of the Incremental Net Monetary Benefit may also be calculated in a hypothetical situation when the standard deviation of costs and effectiveness in each group differ.

Usage

create_object_var_inmb_diff(sdc_refL, sdc_expL, sde_refL, sde_expL, rhoL, object_lambdaI)

Arguments

sdc_ref : standard deviation of costs in the reference group
sdc_exp : standard deviation of costs in the experimental group
sde_ref : standard deviation of effectiveness in the reference group
sde_exp : standard deviation of effectiveness in the experimental group
rho : coefficient of correlation between the difference in costs (dc) and the difference in effectiveness (de)
object_lambda : object containing the ceiling cost-effectiveness ratio or maximum acceptable cost of a unit of effectiveness. See create_object_lambda

Value

create_object_var_inmb_diff returns an object of class VAR_INMB_DIFF which inherits from the class VAR_INMB_DIRECT

See Also

create_object_var_inmb_direct to directly provide a value for the variance of the Incremental Net Monetary Benefit
create_object_var_inmb to calculate the theoretical standard deviation of the expected INB with the same standard deviation in the reference and the experimental group

Examples

## First, create a lambda object
object_lambda <- create_object_lambda (20000)
## Then, create a var_inmb_diff object
var_inmb_diff <- create_object_var_inmb_diff(sdc_ref=2100, sdc_exp=2100, sde_ref = 0.12, sde_exp = 0.12, rho = 0.1,object_lambda = object_lambda)
Description

When absolutely no data regarding the variability of costs and effectiveness are available, it is possible to directly provide a value for the variance of the Incremental Net Monetary Benefit in this object.

Usage

create_object_var_inmb_direct(var_inmb)

Arguments

var_inmb : variance of the Incremental Net Monetary Benefit

Value

create_object_var_inmb_direct returns an object of class VAR_INMB_DIRECT

See Also

create_object_var_inmb_diff to calculate the theoretical standard deviation of the expected INB with different standard deviation in the reference and the experimental group

create_object_var_inmb to calculate the theoretical standard deviation of the expected INB with the same standard deviation in the reference and the experimental group

Examples

## Create a var_inmb object:
object_var_inmb <- create_object_var_inmb_direct(var_inmb = 18324000)
## retrieve the inmb value from the object
object_var_inmb$get_var_inmb()

---

**EVPI_DECREASE**  
_A Reference Class to represent the EVPI_

Description

An object that combines three others objects: object_inmb, object_pop, object_var_inmb.
gamma_risk

Fields

object_inmb : an instance that inherits the INMB_DIRECT
object_var_inmb : an instance that inherits the VAR_INMB_DIRECT
object_pop : an instance that inherits the POP
step_ref (default=1) : to define the ratio (step_ref/step_exp) for group allocation during the study
step_exp (default=1) : to define the ratio (step_ref/step_exp) for group allocation during the study

Methods

get_N(): return the estimated optimal sample size for the study
get_N_exp(): return the estimated number of individuals in the experimental group
get_N_ref(): return the estimated number of participants to include in the reference group
get_k(N_exp): return the ratio (step_ref/step_exp) for group allocation
set_N_ref(N_ref): sets the number of individuals in the reference group (N_exp will be automatically calculated according to the ratio)
set_N_exp(N_exp): sets the number of individuals in the experimental group (N_ref will be automatically calculated according to the ratio)
set_object_inmb(object_inmb): sets object_inmb for this EVPI_DECREASE object
set_object_var_inmb(object_var_inmb): sets object_var_inmb for this EVPI_DECREASE object
set_object_pop(object_pop): sets object_pop for this EVPI_DECREASE object

gamma_risk

Function to estimate the gamma risk

Description

The gamma risk is the probability that a decision based on the expected mean of the Incremental Net Monetary Benefit (INMB) is wrong. In other terms, it is one minus the cost-effectiveness probability of an intervention. Use sample_size function first to estimate the sample size.

Usage

gamma_risk(object_evpi_decrease)

Arguments

object_evpi_decrease

: evpi_decrease object. See create_object_evpi_decrease
Explain the estimated sample size calculated

Description

Produces a plot to explain the estimated sample size calculated based on the EVPI gain after the inclusion of new participants and inclusion costs. Use `sample_size` function first to estimate the sample size.

Usage

`graph_gain_n(object_evpi_decrease, cost_indiv)`

Arguments

- `object_evpi_decrease`: evpi_decrease object. See `create_object_evpi_decrease`.
- `cost_indiv`: mean costs induced by the inclusion and follow-up of one participant in the study.

INMB

A Reference Class to represent the INMB (Incremental Net Monetary Benefit)

Description

The net monetary benefit (NMB) of an intervention is given by E x Lambda - C, where E and C are the effectiveness and cost of this intervention, and Lambda is the threshold value for a unit of effectiveness, the ceiling incremental cost-effectiveness ratio. When the NMB is positive, the value of the intervention’s effectiveness overpasses its cost. When evaluating the cost-effectiveness of a new intervention in comparison with the reference, one can estimate the difference between the net monetary benefit of the new or experimental intervention (NMBn) and the net monetary benefit of the reference (NMBr). This difference is known as the incremental net monetary benefit (INMB), which is given by: INMB = NMBn - NMBr = de x lambda - dc. The new intervention is cost-effective if INMB is positive.

Fields

- `de`: Expected point estimate of the difference in mean effectiveness (effectiveness in the experimental group minus effectiveness in the reference group).
- `dc`: Expected point estimate of the difference in mean cost (cost in the experimental group minus cost in the reference group).
- `object_lambda`: object containing the ceiling cost-effectiveness ratio or maximum acceptable cost of a unit of effectiveness. See `create_object_lambda`.
Methods

get_inmb(): Returns the calculated Incremental Net Monetary Benefit (inmb)
set_de(dc): sets the dc of this INMB object
set_de(de): sets the de of this INMB object
set_object_lambda(object_lambda): sets the object_lambda of this INMB object

See Also

INMB_DIRECT the parent class
create_object_inmb the constructor

Examples

```r
## First, create a lambda object
goal <- create_object_lambda(20000)
## Then, create an inmb object
inmb <- create_object_inmb(de = 0.04, dc = 158, object_lambda = object_lambda)
## inmb is calculated by methods inside the object. Retrieve the inmb:
inmb$get_inmb()
```

INMB_DIRECT A Reference Class to represent the INMB (Incremental Net Monetary Benefit)

Description

If the INMB can be drawn from de, dc and lambda with create_object_inmb, one can also make directly an hypothesis on the value of the INMB.

Fields

inmb: INMB expected Incremental Net monetary Benefit.

Methods

get_inmb(): Returns the Incremental Net Monetary Benefit (inmb)
set_inmb(inmb): sets the inmb of this INMB_DIRECT object

See Also

create_object_inmb_direct the constructor
create_object_inmb to calculate the INMB
Lambda

A Reference Class to represent the lambda value

Description

Lambda is known as the willingness to pay. That is the ceiling cost-effectiveness ratio or the maximum acceptable cost of a unit of effectiveness.

Fields

lambda : Lambda is a monetary value. For example, the value of lambda is usually between 20,000 and 40,000 pounds/QALY in UK.

Methods

set_lambda(lambda): sets the lambda value of this Lambda object

See Also

create_object_lambda the constructor

POP

A Reference Class to represent the target population

Description

The expected value of perfect information (EVPI) is estimated for the entire population targeted by the evaluated intervention.

Fields

horizon : Time horizon in years considered in the estimation of the EVPI. Finite time horizons are recommended in order to control for the complex and uncertain process of future changes. Furthermore, because of discounting, the impact of a time horizon over 15 or 20 years on the estimation of EVPI is insignificant.

discount : Annual discount rate considered in the estimation of the EVPI. The annual discount rate is defined in each country, usually within 3 to 6%.

N_year : Number of individuals likely to be targeted by the evaluated intervention each year

Methods

set_discount(discount): sets the discount for this POP object

set_N_year(N_year): sets the N_year of this POP object

set_horizon(horizon): sets the horizon of this POP object
See Also

create_object_pop the constructor

Examples

object_pop <- create_object_pop(horizon = 20, discount=0.04, N_year = 52000)

VAR_INMB
A Reference Class to represent the Hypothetical variance of the Incremental Net Monetary Benefit

Description

Hypothetical variance of the Incremental Net Monetary Benefit.
VAR_INMB_DIFF

Fields

- **sdc**: common standard deviation of costs in each group
- **sde**: common standard deviation of effectiveness in each group
- **rho**: coefficient of correlation between the difference in costs (dc) and the difference in effectiveness (de)
- **object_lambda**: an object lambda. Create one with `create_object_lambda`. It contains lambda: the ceiling cost-effectiveness ratio or maximum acceptable cost of a unit of effectiveness

Methods

- **set_sdc(sdc)**: Sets the common standard deviation of costs in each group for this VAR_INMB object
- **set_sde(sde)**: Sets the common standard deviation of effectiveness in each group for this VAR_INMB object
- **set_rho(rho)**: Sets the coefficient of correlation between the difference in costs (dc) and the difference in effectiveness (de)
- **set_object_lambda(object_lambda)**: Sets the object_lambda of this VAR_INMB object
- **get_var_inmb()**: Return the calculated hypothetical variance of the Incremental Net Monetary Benefit (INMB)

See Also

- `create_object_var_inmb_direct` to directly provide a value for the variance of the Incremental Net Monetary Benefit
- `create_object_var_inmb_diff` to calculate the theoretical standard deviation of the expected INB with different standard deviation in the reference and the experimental group
- `create_object_var_inmb` the constructor

Examples

```r
# First, create a lambda object
object_lambda <- create_object_lambda(20000)
# Then, create a var_inmb object
var_inmb <- create_object_var_inmb(sde=0.12, sdc=2100, rho=0.1, object_lambda=object_lambda)
var_inmb$get_var_inmb()
```

**Description**

The variance of the Incremental Net Monetary Benefit may also be calculated in a hypothetical situation when the standard deviation of costs and effectiveness in each group differ.
VAR_INMB_DIFF

Fields

- `sdc_ref`: standard deviation of costs in the reference group
- `sdc_exp`: standard deviation of costs in the experimental group
- `sde_exp`: standard deviation of effectiveness in the experimental group
- `sde_ref`: standard deviation of effectiveness in the reference group
- `rho`: coefficient of correlation between the difference in costs (dc) and the difference in effectiveness (de)
- `object_lambda`: object containing the ceiling cost-effectiveness ratio or maximum acceptable cost of a unit of effectiveness. See `create_object_lambda`

See Also

- `create_object_var_inmb_direct` to directly provide a value for the variance of the Incremental Net Monetary Benefit
- `create_object_var_inmb` to calculate the theoretical standard deviation of the expected INB with the same standard deviation in the reference and the experimental group
- `create_object_var_inmb_diff` the constructor

- `set_sdc_ref(sdc_ref)`: sets the standard deviation of costs in the reference group of this VAR_INMB_DIFF object
- `set_sdc_exp(sdc_exp)`: sets the standard deviation of costs in the experimental group of this VAR_INMB_DIFF object
- `set_sde_exp(sde_exp)`: sets the standard deviation of effectiveness in the experimental group of this VAR_INMB_DIFF object
- `set_sde_ref(sde_ref)`: sets the standard deviation of effectiveness in the reference group of this VAR_INMB_DIFF object
- `set_rho(rho)`: Sets the coefficient of correlation between the difference in costs (dc) and the difference in effectiveness (de) of this VAR_INMB_DIFF object
- `set_lambda(lambda)`: sets the lambda value of this VAR_INMB_DIFF object
- `get_var_inmb()`: Return the calculated variance of the Incremental Net Monetary Benefit when the standard deviation of costs and effectiveness in each group differ.

Examples

```r
## First, create a lambda object
object_lambda <- create_object_lambda (20000)
## Then, create a var_inmb_diff object
var_inmb_diff <- create_object_var_inmb_diff(sdc_ref=2100, sdc_exp=2100, sde_ref = 0.12, sde_exp = 0.12, rho = 0.1, object_lambda = object_lambda)
```
**VAR_INMB_DIRECT**

A Reference Class to represent the theoretical standard deviation of the expected INB

**Description**

When absolutely no data regarding the variability of costs and effectiveness are available, it is possible to directly provide a value for the variance of the Incremental Net Monetary Benefit in this object.

**Fields**

- `var_inmb`: variance of the Incremental Net Monetary Benefit

**Methods**

- `set_var_inmb(inmb)`: sets the `var_inmb` for this VAR_INMB_DIRECT object

**See Also**

- `create_object_var_inmb_diff` to calculate the theoretical standard deviation of the expected INB with different standard deviation in the reference and the experimental group
- `create_object_var_inmb` to calculate the theoretical standard deviation of the expected INB with the same standard deviation in the reference and the experimental group
- `create_object_var_inmb_direct` the constructor

**Examples**

```r
## Create a var_inmb object:
object_var_inmb <- create_object_var_inmb_direct(var_inmb = 18324000)
## retrieve the inmb value from the object
object_var_inmb$get_var_inmb()
```
Index

create_object_evpi_decrease, 2, 10, 11, 14
create_object_inmb, 2, 3, 4, 5, 12
create_object_inmb_direct, 2, 4, 4, 12
create_object_lambda, 4, 5, 7, 8, 11, 13, 15, 16
create_object_pop, 2, 6, 14
create_object_var_inmb, 3, 7, 8, 9, 15–17
create_object_var_inmb_diff, 3, 7, 8, 9, 15–17
create_object_var_inmb_direct, 3, 7, 8, 9, 15–17

EVPI_DECREASE, 3, 9

gamma_risk, 10
graph_gain_n, 11

INMB, 4, 11
INMB_DIRECT, 4, 10, 12, 12

Lambda, 5, 13

POP, 6, 10, 13

sample_size, 10, 11, 14

VAR_INMB, 7, 14
VAR_INMB_DIFF, 8, 15
VAR_INMB_DIRECT, 7–10, 17