# Package 'CohortMethod'

June 14, 2018

```
Type Package

Title New-user cohort method with large scale propensity and outcome models

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Author Martijn J. Schuemie [aut, cre],
    Marc A. Suchard [aut],
    Patrick B. Ryan [aut]

Maintainer Martijn J. Schuemie <schuemie@ohdsi.org>
```

Description CohortMethod is an R package for performing new-user cohort studies in an observational database in the OMOP Common Data Model. It extracts the necessary data from a database in OMOP Common Data Model format, and uses a large set of covariates for both the propensity and outcome model, including for example all drugs, diagnoses, procedures, as well as age, comorbidity indexes, etc. Large scale regularized regression is used to fit the propensity and outcome models. Functions are included for trimming, stratifying and matching on propensity scores, as well as diagnostic functions, such as propensity score distribution plots and plots showing covariate balance before and after matching and/or trimming. Supported outcome models are (conditional) logistic regression, (conditional) Poisson regression, and (stratified) Cox regression.

```
License Apache License 2.0
VignetteBuilder knitr
Depends R (>= 3.2.2),
      DatabaseConnector (>= 1.11.4),
      Cyclops (>= 1.2.0),
      FeatureExtraction (>= 2.0.0)
Imports methods,
      ggplot2,
      gridExtra,
      grid,
      ff.
      ffbase (>= 0.12.3),
      plyr,
      Rcpp (>= 0.11.2),
      SqlRender (\geq 1.1.1),
      survival,
      OhdsiRTools (>= 1.5.1)
```

2 R topics documented:

Suggests testthat,
pROC,
knitr,
rmarkdown,
EmpiricalCalibration
LinkingTo Rcpp
NeedsCompilation yes
RoxygenNote 6.0.1.9000

# $\mathsf{R}$ topics documented:

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getDbCohortMethodData
getDefaultCmTable1Specifications
getFollowUpDistribution
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# Description

Check is CohortMethod and its dependencies are correctly installed

# Usage

checkCmInstallation(connectionDetails)

# Arguments

connectionDetails

An R object of type

 ${\tt connectionDetails} \ created \ using \ the \ function \ {\tt createConnectionDetails} \ in$ the DatabaseConnector package.

# **Details**

This function checks whether CohortMethod and its dependencies are correctly installed. This will check the database connectivity, large scale regresion engine (Cyclops), and large data object handling (ff).

CohortMethod

CohortMethod

# Description

CohortMethod

 ${\it cohort} {\it MethodDataSimulationProfile} \\ {\it A simulation profile}$ 

# Description

A simulation profile

## Usage

data(cohortMethodDataSimulationProfile)

computeCovariateBalance

Compute covariate balance before and after matching and trimming

# **Description**

For every covariate, prevalence in treatment and comparator groups before and after matching/trimming are computed. When variable ratio matching was used the balance score will be corrected according the method described in Austin et al (2008).

## Usage

```
computeCovariateBalance(population, cohortMethodData,
   subgroupCovariateId = NULL)
```

## **Arguments**

population

A data frame containing the people that are remaining after matching and/or trimming.

 ${\tt cohortMethodData}$ 

 $An \ object \ of \ type \ cohort \texttt{MethodData} \ as \ generated \ using \ \texttt{getDbCohort} \texttt{MethodData}. \\ subgroup \texttt{CovariateId}$ 

Optional: a covariate ID of a binary covariate that indicates a subgroup of interest. Both the before and after populations will be restricted to this subgroup before computing covariate balance.

## **Details**

The population data frame should have at least the following columns:

rowId (integer) A unique identifier for each row (e.g. the person ID)
treatment (integer) Column indicating whether the person is in the target (1) or comparator (0)
group

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#### Value

Returns a date frame describing the covariate balance before and after matching/trimming.

#### References

Austin, P.C. (2008) Assessing balance in measured baseline covariates when using many-to-one matching on the propensity-score. Pharmacoepidemiology and Drug Safety, 17: 1218-1225.

computeMdrr Compute the minimum detectable relative risk

# **Description**

Compute the minimum detectable relative risk

## Usage

```
computeMdrr(population, alpha = 0.05, power = 0.8, twoSided = TRUE,
  modelType = "cox")
```

## **Arguments**

population A data frame describing the study population as created using the createStudyPopulation

function. This should at least have these columns: subjectId, treatment, out-

comeCount, timeAtRisk.

alpha Type I error.

power 1 - beta, where beta is the type II error.

twoSided Consider a two-sided test?

modelType The type of outcome model that will be used. Possible values are "logistic",

"poisson", or "cox". Currently only "cox" is supported.

# **Details**

Compute the minimum detectable relative risk (MDRR) and expected standard error (SE) for a given study population, using the actual observed sample size and number of outcomes. Currently, only computations for Cox models are implemented. For Cox model, the computations by Schoenfeld (1983) is used.

#### Value

A data frame with the MDRR and some counts.

# References

Schoenfeld DA (1983) Sample-size formula for the proportional-hazards regression model, Biometrics, 39(3), 499-503

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computePsAuc

Compute the area under the ROC curve

# **Description**

computePsAuc computes the area under the ROC curve of the propensity score

## Usage

```
computePsAuc(data, confidenceIntervals = FALSE)
```

## **Arguments**

```
data  A \ data \ frame \ with \ at \ least \ the \ two \ columns \ described \ below \ confidence Intervals
```

Compute 95 percent confidence intervals (computationally expensive for large data sets)

## **Details**

The data frame should have a least the following two columns:

```
treatment (integer) Column indicating whether the person is in the target (1) or comparator
```

(0) group

propensityScore (numeric) Propensity score

## Value

A data frame holding the AUC and its 95 percent confidence interval

## **Examples**

```
treatment <- rep(0:1, each = 100)
propensityScore <- c(rnorm(100, mean = 0.4, sd = 0.25), rnorm(100, mean = 0.6, sd = 0.25))
data <- data.frame(treatment = treatment, propensityScore = propensityScore)
data <- data[data$propensityScore > 0 & data$propensityScore < 1, ]
computePsAuc(data)</pre>
```

construct Eras

Build eras

# Description

Constructs eras (continuous periods of exposure or disease).

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#### Usage

```
constructEras(connectionDetails, sourceDatabaseSchema,
  sourceTable = "drug_exposure",
  targetDatabaseSchema = sourceDatabaseSchema, targetTable = "drug_era",
  createTargetTable = FALSE, cdmDatabaseSchema = sourceDatabaseSchema,
  gracePeriod = 30, rollUp = TRUE, rollUpConceptClassId = "Ingredient",
  rollUpVocabularyId = "RxNorm", cdmVersion = "5")
```

## **Arguments**

connectionDetails

An R object of type connectionDetails created using the function createConnectionDetails in the DatabaseConnector package.

sourceDatabaseSchema

The name of the database schema that contains the source table. Requires read permissions to this database. On SQL Server, this should specify both the database and the schema, so for example 'cdm\_instance.dbo'.

sourceTable The name of the source table.

targetDatabaseSchema

The name of the database schema that contains the target table. Requires write permissions to this database. On SQL Server, this should specify both the database and the schema, so for example 'cdm\_instance.dbo'.

targetTable The name of the target table.

createTargetTable

Should the target table be created? If not, the data is inserted in an existing table.

cdmDatabaseSchema

Only needed when rolling up concepts to ancestors: The name of the database schema that contains the vocabulary files. Requires read permissions to this database. On SQL Server, this should specify both the database and the schema, so for example 'cdm\_instance.dbo'.

gracePeriod

The number of days allowed between periods for them to still be considered part of the same era.

rollUp Shoul

Should concepts be rolled up to their ancestors?

rollUpConceptClassId

The identifier of the concept class to which concepts should be rolled up.

rollUpVocabularyId

The identifier of the vocabulary to which concepts should be rolled up.

cdmVersion The verion of the CDM that is being used.

# Details

This function creates eras from source data. For example, one could use this function to create drug eras based on drug exposures. The function allows drugs to be rolled up to ingredients, and prescriptions to the same ingredient that overlap in time are merged into a single ingredient. Note that stockpiling is not assumed to take place (ie. overlap is discarded), but a grace period can be specified allowing for a small gap between prescriptions when merging. The user can specify the source and target table. These tables are assumed to have the same structure as the cohort table in the Common Data Model (CDM), except when the table names are 'drug\_exposure' or 'condition\_occurrence' for the source table, or 'drug\_era' or 'condition\_era' for the target table, in which case the tables are assumed to have the structure defined for those tables in the CDM.

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If both the source and target table specify a field for type\_concept\_id, the era construction will partition by the type\_concept\_id, in other words periods with different type\_concept\_ids will be treated independently.

# **Examples**

```
## Not run:
# Constructing drug eras in CDM v4:
constructEras(connectionDetails,
              sourceDatabaseSchema = cdmDatabaseSchema,
              sourceTable = "drug_exposure",
              targetTable = "drug_era",
              createTargetTable = FALSE,
              gracePeriod = 30,
              rollUpVocabularyId = 8,
              rollUpConceptClassId = "Ingredient",
              cdmVersion = "4")
# Constructing drug eras in CDM v5:
constructEras(connectionDetails,
              sourceDatabaseSchema = cdmDatabaseSchema,
              sourceTable = "drug_exposure",
              targetTable = "drug_era",
              createTargetTable = FALSE,
              gracePeriod = 30,
              rollUpVocabularyId = "RxNorm",
              rollUpConceptClassId = "Ingredient",
              cdmVersion = "5")
## End(Not run)
```

createCmAnalysis

Create a CohortMethod analysis specification

# Description

Create a CohortMethod analysis specification

## Usage

```
createCmAnalysis(analysisId = 1, description = "", targetType = NULL,
  comparatorType = NULL, getDbCohortMethodDataArgs, createStudyPopArgs,
  createPs = FALSE, createPsArgs = NULL, trimByPs = FALSE,
  trimByPsArgs = NULL, trimByPsToEquipoise = FALSE,
  trimByPsToEquipoiseArgs = NULL, matchOnPs = FALSE, matchOnPsArgs = NULL,
  matchOnPsAndCovariates = FALSE, matchOnPsAndCovariatesArgs = NULL,
  stratifyByPs = FALSE, stratifyByPsArgs = NULL,
  stratifyByPsAndCovariates = FALSE, stratifyByPsAndCovariatesArgs = NULL,
  fitOutcomeModel = FALSE, fitOutcomeModelArgs = NULL)
```

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## **Arguments**

analysisId An integer that will be used later to refer to this specific set of analysis choices.

description A short description of the analysis.

targetType If more than one target is provided for each drugComparatorOutcome, this field

should be used to select the specific target to use in this analysis.

comparatorType If more than one comparator is provided for each drugComparatorOutcome, this

field should be used to select the specific comparator to use in this analysis.

getDbCohortMethodDataArgs

An object representing the arguments to be used when calling the getDbCohortMethodData

function.

createStudyPopArgs

An object representing the arguments to be used when calling the createStudyPopulation

function.

createPs Should the createPs function be used in this analysis?

createPsArgs An object representing the arguments to be used when calling the createPs

function.

trimByPs Should the trimByPs function be used in this analysis?

trimByPsArgs An object representing the arguments to be used when calling the trimByPs

function.

trimByPsToEquipoise

Should the trimByPsToEquipoise function be used in this analysis?

trimByPsToEquipoiseArgs

An object representing the arguments to be used when calling the trimByPsToEquipoise

function.

matchOnPs Should the matchOnPs function be used in this analysis?

matchOnPsArgs An object representing the arguments to be used when calling the matchOnPs

function.

matchOnPsAndCovariates

Should the matchOnPsAndCovariates function be used in this analysis?

 ${\tt matchOnPsAndCovariatesArgs}$ 

 $An object \, representing \, the \, arguments \, to \, be \, used \, when \, calling \, the \, {\tt matchOnPsAndCovariates} \,$ 

function.

stratifyByPs Should the stratifyByPs function be used in this analysis?

stratifyByPsArgs

An object representing the arguments to be used when calling the stratifyByPs

function.

stratifyByPsAndCovariates

Should the stratifyByPsAndCovariates function be used in this analysis?

stratifyByPsAndCovariatesArgs

An object representing the arguments to be used when calling the stratifyByPsAndCovariates

function.

fitOutcomeModel

Should the fitOutcomeModel function be used in this analysis?

fitOutcomeModelArgs

An object representing the arguments to be used when calling the fitOutcomeModel

function.

## **Details**

Create a set of analysis choices, to be used with the runCmAnalyses function.

10 createCmTable1

teCmTable1 Create a table 1	

## **Description**

Creates a formatted table of cohort characteristics, to be included in publications or reports.

## Usage

```
createCmTable1(balance, specifications = getDefaultCmTable1Specifications(),
  beforeTargetPopSize, beforeComparatorPopSize, afterTargetPopSize,
  afterComparatorPopSize, beforeLabel = "Before matching",
  afterLabel = "After matching", targetLabel = "Target",
  comparatorLabel = "Comparator", percentDigits = 1, stdDiffDigits = 2)
```

# **Arguments**

balance A data frame created by the computeCovariateBalance funcion.

specifications Specifications of which covariates to display, and how.

beforeTargetPopSize

The number of people in the target cohort before matching/stratification/trimming, to mention in the table header. If not provide, no number will be included in the header.

beforeComparatorPopSize

The number of people in the comparator cohort before matching/stratification/trimming, to mention in the table header. If not provide, no number will be included in the header.

afterTargetPopSize

The number of people in the target cohort after matching/stratification/trimming, to mention in the table header. If not provide, no number will be included in the header.

 $after {\tt Comparator Pop Size}$ 

The number of people in the comparator cohort after matching/stratification/trimming, to mention in the table header. If not provide, no number will be included in the header.

beforeLabel Label for identifying columns before matching / stratification / trimming.

Label for identifying columns after matching / stratification / trimming.

Label for identifying columns of the target cohort.

comparatorLabel

Label for identifying columns of the comparator cohort.

percentDigits Number of digits to be used for percentages.

#### Value

A data frame with the formatted table 1.

 ${\it Create Cohort Method Data Simulation Profile} \\ {\it Create simulation profile}$ 

# Description

createCohortMethodDataSimulationProfile creates a profile based on the provided cohort-MethodData object, which can be used to generate simulated data that has similar characteristics.

## Usage

createCohortMethodDataSimulationProfile(cohortMethodData)

## **Arguments**

cohortMethodData

An object of type cohortMethodData as generated using getDbCohortMethodData.

#### **Details**

The output of this function is an object that can be used by the simulateCohortMethodData function to generate a cohortMethodData object.

## Value

An object of type cohortDataSimulationProfile.

createCreatePsArgs

Create a parameter object for the function createPs

# Description

Create a parameter object for the function createPs

# Usage

```
createCreatePsArgs(excludeCovariateIds = c(), includeCovariateIds = c(),
  maxCohortSizeForFitting = 250000, errorOnHighCorrelation = TRUE,
  stopOnError = TRUE, prior = createPrior("laplace", exclude = c(0),
  useCrossValidation = TRUE), control = createControl(noiseLevel = "silent",
  cvType = "auto", tolerance = 2e-07, cvRepetitions = 10, startingVariance =
  0.01))
```

## **Arguments**

excludeCovariateIds

Exclude these covariates from the propensity model.

includeCovariateIds

Include only these covariates in the propensity model.

maxCohortSizeForFitting

If the target or comparator cohort are larger than this number, theywill be down-sampled before fitting the propensity model. The modelwill be used to compute propensity scores for all subjects. Thepurpose of the sampling is to gain speed. Setting this number to 0means no downsampling will be applied.

errorOnHighCorrelation

If true, the function will test each covariate for correlation withthe treatment assignment. If any covariate has an unusually highcorrelation (either positive or

negative), this will throw anderror.

stopOnError If an error occurrs, should the function stop? Else, the two cohortswill be as-

sumed to be perfectly separable.

prior The prior used to fit the model. SeecreatePrior for details.

control The control object used to control the cross-validation used todetermine the hy-

perparameters of the prior (if applicable). SeecreateControl for details.

## **Details**

Create an object defining the parameter values.

createCreateStudyPopulationArgs

Create a parameter object for the function createStudyPopulation

## **Description**

Create a parameter object for the function createStudyPopulation

# Usage

```
createCreateStudyPopulationArgs(firstExposureOnly = FALSE,
  restrictToCommonPeriod = FALSE, washoutPeriod = 0,
  removeDuplicateSubjects = FALSE, removeSubjectsWithPriorOutcome = TRUE,
  priorOutcomeLookback = 99999, minDaysAtRisk = 1, riskWindowStart = 0,
  addExposureDaysToStart = FALSE, riskWindowEnd = 0,
  addExposureDaysToEnd = TRUE, censorAtNewRiskWindow = FALSE)
```

# **Arguments**

firstExposureOnly

Should only the first exposure per subject be included? Notethat this is typically done in thecreateStudyPopulation function,

restrictToCommonPeriod

Restrict the analysis to the period when both exposures are observed?

washoutPeriod The minimum required continuous observation time prior toindex date for a person to be included in the cohort.

removeDuplicateSubjects

Remove subjects that are in both the target and comparatorcohort? See details for allowed values.

 ${\tt removeSubjectsWithPriorOutcome}$ 

Remove subjects that have the outcome prior to the riskwindow start?

priorOutcomeLookback

How many days should we look back when identifying prioroutcomes?

minDaysAtRisk The minimum required number of days at risk.

riskWindowStart

The start of the risk window (in days) relative to the indexdate (+ days of exposure if theaddExposureDaysToStart parameter is specified).

addExposureDaysToStart

Add the length of exposure the start of the risk window?

riskWindowEnd The end of the risk window (in days) relative to the indexdata (+ days of exposure if the addExposureDaysToEndparameter is specified).

addExposureDaysToEnd

Add the length of exposure the risk window?

censorAtNewRiskWindow

If a subject is in multiple cohorts, should time-at-risk be censoredwhen the new time-at-risk starts to prevent overlap?

## **Details**

Create an object defining the parameter values.

createFitOutcomeModelArgs

Create a parameter object for the function fitOutcomeModel

# Description

Create a parameter object for the function fitOutcomeModel

# Usage

```
createFitOutcomeModelArgs(modelType = "logistic", stratified = FALSE,
  useCovariates = FALSE, inversePtWeighting = FALSE,
  interactionCovariateIds = c(), excludeCovariateIds = c(),
  includeCovariateIds = c(), prior = createPrior("laplace",
  useCrossValidation = TRUE), control = createControl(cvType = "auto",
  startingVariance = 0.01, tolerance = 2e-07, cvRepetitions = 10, noiseLevel =
  "quiet"))
```

## **Arguments**

modelType The type of outcome model that will be used. Possible values are "logistic",

"poisson", or "cox".

stratified Should the regression be conditioned on the strata defined in the population ob-

ject (e.g. by matching or stratifying on propensityscores)?

useCovariates Whether to use the covariate matrix in the cohortMethodDataobject in the out-

come model.

inversePtWeighting

Use inverse probability of treatment weigting?

 $interaction {\tt CovariateIds}$ 

An optional vector of covariate IDs to use to estimate interactions with the main

treatment effect.

excludeCovariateIds

Exclude these covariates from the outcome model.

includeCovariateIds

Include only these covariates in the outcome model.

prior The prior used to fit the model. See createPriorfor details.

control The control object used to control the cross-validation used todetermine the hy-

perparameters of the prior (if applicable). SeecreateControl for details.

## **Details**

Create an object defining the parameter values.

 ${\tt createGetDbCohortMethodDataArgs}$ 

Create a parameter object for the function getDbCohortMethodData

## **Description**

Create a parameter object for the function getDbCohortMethodData

## Usage

```
createGetDbCohortMethodDataArgs(studyStartDate = "", studyEndDate = "",
  excludeDrugsFromCovariates = TRUE, firstExposureOnly = FALSE,
  removeDuplicateSubjects = FALSE, restrictToCommonPeriod = FALSE,
  washoutPeriod = 0, maxCohortSize = 0, covariateSettings)
```

#### **Arguments**

studyStartDate A calendar date specifying the minimum date that a cohort indexdate can appear.

Date format is 'yyyymmdd'.

studyEndDate A calendar date specifying the maximum date that a cohort indexdate can ap-

pear. Date format is 'yyyymmdd'. Important: the studyend data is also used to truncate risk windows, meaning nooutcomes beyond the study end date will be

considered.

## excludeDrugsFromCovariates

Should the target and comparator drugs (and their descendantconcepts) be excluded from the covariates? Note that this willwork if the drugs are actualy drug concept IDs (and not cohortIDs).

#### firstExposureOnly

Should only the first exposure per subject be included? Notethat this is typically done in the createStudyPopulationfunction, but can already be done here for efficiency reasons.

## removeDuplicateSubjects

Remove subjects that are in both the target and comparatorcohort? See details for allowed values.N ote that this is typically done in thecreateStudyPopulation function, but can already be donehere for efficiency reasons.

#### restrictToCommonPeriod

Restrict the analysis to the period when both treatments are observed?

washoutPeriod

The mininum required continuous observation time prior to indexdate for a person to be included in the cohort. Note that thisis typically done in the createStudyPopulation function,but can already be done here for efficiency reasons.

maxCohortSize

If either the target or the comparator cohort is larger thanthis number it will be sampled to this size. maxCohortSize = 0indicates no maximum size.

#### covariateSettings

An object of type covariateSettings as created using thecreateCovariateSettings function in theFeatureExtraction package.

#### **Details**

Create an object defining the parameter values.

createMatchOnPsAndCovariatesArgs

Create a parameter object for the function matchOnPsAndCovariates

## **Description**

Create a parameter object for the function matchOnPsAndCovariates

## Usage

```
createMatchOnPsAndCovariatesArgs(caliper = 0.2,
  caliperScale = "standardized logit", maxRatio = 1, covariateIds)
```

#### **Arguments**

caliper

The caliper for matching. A caliper is the distance which is acceptable for any match. Observations which are outside of the caliper are dropped. A caliper of 0 means no caliper is used.

caliperScale

The scale on which the caliper is defined. Three scales are supported:caliperScale = 'propensity score', caliperScale = 'standardized', or caliperScale = 'standardized logit'. On the standardized scale, the caliper is interpreted in standarddeviations of the propensity score distribution. 'standardized logit' is similar, except that the propensity score is transformed to the logitscale because the PS is more likely to be normally distributed on that scale(Austin, 2011).

maxRatio The maximum number of persons int the comparator arm to be matched to each-

person in the treatment arm. A maxRatio of 0 means no maximum: allcompara-

tors will be assigned to a target person.

covariateIds One or more covariate IDs in the cohortMethodData object on whichsubjects

should be also matched.

## **Details**

Create an object defining the parameter values.

createMatchOnPsArgs

Create a parameter object for the function matchOnPs

## **Description**

Create a parameter object for the function matchOnPs

#### Usage

```
createMatchOnPsArgs(caliper = 0.2, caliperScale = "standardized logit",
   maxRatio = 1, stratificationColumns = c())
```

# **Arguments**

caliper The caliper for matching. A caliper is the distance which isacceptable for any

match. Observations which are outside of thecaliper are dropped. A caliper of 0

means no caliper is used.

caliperScale The scale on which the caliper is defined. Three scales are supported:caliperScale

= 'propensity score', caliperScale = 'standardized', or caliperScale = 'standardized logit'. On the standardized scale, the caliper is interpreted in standarddeviations of the propensity score distribution. 'standardized logit' is similar, except that the propensity score is transformed to the logitscale because the PS is more

likely to be normally distributed on that scale(Austin, 2011).

maxRatio The maximum number of persons int the comparator arm to be matched toeach

person in the treatment arm. A maxRatio of 0 means no maximum:all compara-

tors will be assigned to a target person.

stratificationColumns

Names or numbers of one or more columns in the data data.frameon which subjects should be stratified prior to matching. No personswill be matched with persons outside of the strata identified by thevalues in these columns.

## **Details**

Create an object defining the parameter values.

createPs 17

#### **Description**

createPs creates propensity scores using a regularized logistic regression.

## Usage

```
createPs(cohortMethodData, population, excludeCovariateIds = c(),
  includeCovariateIds = c(), maxCohortSizeForFitting = 250000,
  errorOnHighCorrelation = TRUE, stopOnError = TRUE,
  prior = createPrior("laplace", exclude = c(0), useCrossValidation = TRUE),
  control = createControl(noiseLevel = "silent", cvType = "auto", tolerance =
  2e-07, cvRepetitions = 10, startingVariance = 0.01))
```

## **Arguments**

cohortMethodData

An object of type cohortMethodData as generated using getDbCohortMethodData.

population

A data frame describing the population. This should at least have a 'rowId' column corresponding to the rowId column in the cohortMethodData covariates object and a 'treatment' column. If population is not specified, the full population in the cohortMethodData will be used.

excludeCovariateIds

Exclude these covariates from the propensity model.

includeCovariateIds

Include only these covariates in the propensity model.

maxCohortSizeForFitting

If the target or comparator cohort are larger than this number, they will be down-sampled before fitting the propensity model. The model will be used to compute propensity scores for all subjects. The purpose of the sampling is to gain speed. Setting this number to 0 means no downsampling will be applied.

errorOnHighCorrelation

If true, the function will test each covariate for correlation with the treatment assignment. If any covariate has an unusually high correlation (either positive or negative), this will throw and error.

stopOnError ]

If an error occurrs, should the function stop? Else, the two cohorts will be assumed to be perfectly separable.

prior

The prior used to fit the model. See createPrior for details.

control

The control object used to control the cross-validation used to determine the hyperparameters of the prior (if applicable). See createControl for details.

## **Details**

createPs creates propensity scores using a regularized logistic regression.

#### **Examples**

```
data(cohortMethodDataSimulationProfile)
cohortMethodData <- simulateCohortMethodData(cohortMethodDataSimulationProfile, n = 1000)
ps <- createPs(cohortMethodData)</pre>
```

 ${\tt createStratifyByPsAndCovariatesArgs}$ 

Create a parameter object for the function stratifyByPsAndCovariates

## Description

Create a parameter object for the function stratifyByPsAndCovariates

## Usage

```
createStratifyByPsAndCovariatesArgs(numberOfStrata = 5,
  baseSelection = "all", covariateIds)
```

## **Arguments**

numberOfStrata Into how many strata should the propensity score be divided? Theboundaries of

the strata are automatically defined to contain equalnumbers of target persons.

baseSelection What is the base selection of subjects where the strata bounds areto be deter-

mined? Strata are defined as equally-sized strata insidethis selection. Possible

values are "all", "target", and "comparator".

covariateIds One or more covariate IDs in the cohortMethodData object on whichsubjects

should also be stratified.

## **Details**

Create an object defining the parameter values.

```
createStratifyByPsArgs
```

Create a parameter object for the function stratifyByPs

## **Description**

Create a parameter object for the function stratifyByPs

# Usage

```
createStratifyByPsArgs(numberOfStrata = 5, stratificationColumns = c(),
  baseSelection = "all")
```

createStudyPopulation 19

#### **Arguments**

numberOfStrata How many strata? The boundaries of the strata are automatically defined to contain equal numbers of target persons.

stratificationColumns

Names of one or more columns in the data data.frame on which subjects should also be stratified in addition to stratification on propensity score.

baseSelection

What is the base selection of subjects where the strata bounds areto be determined? Strata are defined as equally-sized strata insidethis selection. Possible values are "all", "target", and "comparator".

#### **Details**

Create an object defining the parameter values.

createStudyPopulation Create a study population

## **Description**

Create a study population

## Usage

```
createStudyPopulation(cohortMethodData, population = NULL, outcomeId,
  firstExposureOnly = FALSE, restrictToCommonPeriod = FALSE,
  washoutPeriod = 0, removeDuplicateSubjects = FALSE,
  removeSubjectsWithPriorOutcome = TRUE, priorOutcomeLookback = 99999,
  minDaysAtRisk = 1, riskWindowStart = 0, addExposureDaysToStart = FALSE,
  riskWindowEnd = 0, addExposureDaysToEnd = TRUE,
  censorAtNewRiskWindow = FALSE)
```

#### **Arguments**

cohortMethodData

An object of type cohortMethodData as generated using getDbCohortMethodData.

population If specified, this population will be used as the starting point instead of the co-

horts in the  ${\tt cohortMethodData}$  object.

will be performed.

firstExposureOnly

Should only the first exposure per subject be included? Note that this is typically done in the createStudyPopulation function,

restrictToCommonPeriod

Restrict the analysis to the period when both exposures are observed?

washoutPeriod The minimum required continuous observation time prior to index date for a person to be included in the cohort.

removeDuplicateSubjects

Remove subjects that are in both the target and comparator cohort? See details for allowed values.

 ${\tt removeSubjectsWithPriorOutcome}$ 

Remove subjects that have the outcome prior to the risk window start?

priorOutcomeLookback

How many days should we look back when identifying prior outcomes?

minDaysAtRisk The minimum required number of days at risk.

riskWindowStart

The start of the risk window (in days) relative to the index date (+ days of exposure if the addExposureDaysToStart parameter is specified).

addExposureDaysToStart

Add the length of exposure the start of the risk window?

riskWindowEnd The end of the risk window (in days) relative to the index data (+ days of exposure if the addExposureDaysToEnd parameter is specified).

addExposureDaysToEnd

Add the length of exposure the risk window?

censorAtNewRiskWindow

If a subject is in multiple cohorts, should time-at-risk be censored when the new time-at-risk starts to prevent overlap?

#### Details

Create a study population by enforcing certain inclusion and exclusion criteria, defining a risk window, and determining which outcomes fall inside the risk window.

The removeduplicateSubjects argument can have one of the following values:

"keep all" Do not remove subjects that appear in both target and comparator cohort

"keep first" When a subjects appear in both target and comparator cohort, only keep whichever cohort is first in time. If both cohorts start simultaneous, the person is removed from the analysis.

"remove all" Remove subjects that appear in both target and comparator cohort completely from the analysis."

# Value

A data frame specifying the study population. This data frame will have the following columns:

rowId A unique identifier for an exposure

subjectId The person ID of the subject

cohortStartdate The index date

outcomeCount The number of outcomes observed during the risk window

timeAtRisk The number of days in the risk window

survivalTime The number of days until either the outcome or the end of the risk window

createTargetComparatorOutcomes

*Create target-comparator-outcomes combinations.* 

## **Description**

Create target-comparator-outcomes combinations.

## Usage

```
createTargetComparatorOutcomes(targetId, comparatorId, outcomeIds,
  excludedCovariateConceptIds = c(), includedCovariateConceptIds = c())
```

## **Arguments**

A concept ID indentifying the target drug in the exposure table. If multiple targetId

strategies for picking the target will be tested in the analysis, a named list of numbers can be provided instead. In the analysis, the name of the number to be used can be specified using the #' targetType parameter in the createCmAnalysis

function.

comparatorId A concept ID indentifying the comparator drug in the exposure table. If multi-

ple strategies for picking the comparator will be tested in the analysis, a named list of numbers can be provided instead. In the analysis, the name of the number to be used can be specified using the #' comparatorType parameter in the

createCmAnalysis function.

outcomeIds A vector of concept IDs indentifying the outcome(s) in the outcome table.

excludedCovariateConceptIds

A list of concept IDs that cannot be used to construct covariates. This argument is to be used only for exclusion concepts that are specific to the drug-comparator

combination.

includedCovariateConceptIds

A list of concept IDs that must be used to construct covariates. This argument is to be used only for inclusion concepts that are specific to the drug-comparator

combination.

## **Details**

Create a set of hypotheses of interest, to be used with the runCmAnalyses function.

createTrimByPsArgs

Create a parameter object for the function trimByPs

## **Description**

Create a parameter object for the function trimByPs

## Usage

```
createTrimByPsArgs(trimFraction = 0.05)
```

22 drawAttritionDiagram

#### **Arguments**

trimFraction

This fraction will be removed from each treatment group. In the treatmentgroup, persons with the highest propensity scores will be removed, in the comparator group person with the lowest scores will be removed.

## **Details**

Create an object defining the parameter values.

createTrimByPsToEquipoiseArgs

Create a parameter object for the function trimByPsToEquipoise

## **Description**

Create a parameter object for the function trimByPsToEquipoise

#### Usage

```
createTrimByPsToEquipoiseArgs(bounds = c(0.25, 0.75))
```

#### **Arguments**

bounds

The upper and lower bound on the preference score for keeping persons

#### **Details**

Create an object defining the parameter values.

drawAttritionDiagram Draw the attrition diagram

## Description

drawAttritionDiagram draws the attition diagram, showing how many people were excluded from the study population, and for what reasons.

## Usage

```
drawAttritionDiagram(object, targetLabel = "Target",
  comparatorLabel = "Comparator", fileName = NULL)
```

## **Arguments**

object

Either an object of type cohortMethodData, a population object generated by functions like createStudyPopulation, or an object of type outcomeModel.

targetLabel

A label to us for the target cohort.

comparatorLabel

A label to us for the comparator cohort.

fileName

Name of the file where the plot should be saved, for example 'plot.png'. See the

function ggsave in the ggplot2 package for supported file formats.

fitOutcomeModel 23

#### Value

A ggplot object. Use the ggsave function to save to file in a different format.

fitOutcomeModel Create an outcome model, and compute the relative risk	fitOutcomeModel	Create an outcome model, and compute the relative risk	
--	-----------------	--	--

## **Description**

fitOutcomeModel creates an outcome model, and computes the relative risk

## Usage

```
fitOutcomeModel(population, cohortMethodData = NULL, modelType = "logistic",
    stratified = FALSE, useCovariates = FALSE, inversePtWeighting = FALSE,
    interactionCovariateIds = c(), excludeCovariateIds = c(),
    includeCovariateIds = c(), prior = createPrior("laplace",
    useCrossValidation = TRUE), control = createControl(cvType = "auto",
    startingVariance = 0.01, tolerance = 2e-07, cvRepetitions = 10, noiseLevel =
    "quiet"))
```

#### **Arguments**

population A population object generated by createStudyPopulation, potentially filtered

by other functions.

cohortMethodData

An object of type cohortMethodData as generated using getDbCohortMethodData.

modelType The type of outcome model that will be used. Possible values are "logistic",

"poisson", or "cox".

stratified Should the regression be conditioned on the strata defined in the population

object (e.g. by matching or stratifying on propensity scores)?

useCovariates Whether to use the covariate matrix in the cohortMethodData object in the

outcome model.

inversePtWeighting

Use inverse probability of treatment weigting?

interaction Covariate Ids

An optional vector of covariate IDs to use to estimate interactions with the main treatment effect.

excludeCovariateIds

Exclude these covariates from the outcome model.

includeCovariateIds

Include only these covariates in the outcome model.

prior The prior used to fit the model. See createPrior for details.

control The control object used to control the cross-validation used to determine the

hyperparameters of the prior (if applicable). See createControl for details.

## Value

An object of class outcomeModel. Generic function summary, coef, and confint are available.

 ${\tt getAttritionTable}$ 

Get the attrition table for a population

## **Description**

Get the attrition table for a population

## Usage

```
getAttritionTable(object)
```

## **Arguments**

object

Either an object of type cohortMethodData, a population object generated by functions like createStudyPopulation, or an object of type outcomeModel.

#### Value

A data frame specifying the number of people and exposures in the population after specific steps of filtering.

getDbCohortMethodData Get the cohort data from the server

# **Description**

This function executes a large set of SQL statements against the database in OMOP CDM format to extract the data needed to perform the analysis.

## Usage

```
getDbCohortMethodData(connectionDetails, cdmDatabaseSchema,
  oracleTempSchema = cdmDatabaseSchema, targetId, comparatorId, outcomeIds,
  studyStartDate = "", studyEndDate = "",
  exposureDatabaseSchema = cdmDatabaseSchema, exposureTable = "drug_era",
  outcomeDatabaseSchema = cdmDatabaseSchema,
  outcomeTable = "condition_occurrence", cdmVersion = "5",
  excludeDrugsFromCovariates = TRUE, firstExposureOnly = FALSE,
  removeDuplicateSubjects = FALSE, restrictToCommonPeriod = FALSE,
  washoutPeriod = 0, maxCohortSize = 0, covariateSettings)
```

## **Arguments**

connectionDetails

An R object of type connectionDetails created using the function createConnectionDetails in the DatabaseConnector package.

#### cdmDatabaseSchema

The name of the database schema that contains the OMOP CDM instance. Requires read permissions to this database. On SQL Server, this should specify both the database and the schema, so for example 'cdm\_instance.dbo'.

### oracleTempSchema

For Oracle only: the name of the database schema where you want all temporary tables to be managed. Requires create/insert permissions to this database.

targetId A unique identifier to define the target cohort. If exposureTable = DRUG\_ERA, targetId is a CONCEPT\_ID and all descendant concepts within that CONCEPT\_ID

will be used to define the cohort. If exposureTable <> DRUG\_ERA, targetId is used to select the cohort\_concept\_id in the cohort-like table.

comparatorId A unique identifier to define the comparator cohort. If exposureTable = DRUG\_ERA,

comparatorId is a CONCEPT\_ID and all descendant concepts within that CON-CEPT\_ID will be used to define the cohort. If exposureTable <> DRUG\_ERA, comparatorId is used to select the cohort\_concept\_id in the cohort-like table.

outcomeIds A list of cohort definition ids used to define outcomes.

studyStartDate A calendar date specifying the minimum date that a cohort index date can ap-

pear. Date format is 'yyyymmdd'.

studyEndDate A calendar date specifying the maximum date that a cohort index date can appear. Date format is 'yyyymmdd'. Important: the study end data is also used to

truncate risk windows, meaning no outcomes beyond the study end date will be

considered.

exposureDatabaseSchema

The name of the database schema that is the location where the exposure data used to define the exposure cohorts is available. If exposureTable = DRUG\_ERA, exposureDatabaseSchema is not used by assumed to be cdmSchema. Requires

read permissions to this database.

exposureTable The tablename that contains the exposure cohorts. If exposureTable <> DRUG\_ERA, then expectation is exposureTable has format of COHORT table: cohort\_concept\_id,

SUBJECT\_ID, COHORT\_START\_DATE, COHORT\_END\_DATE.

outcomeDatabaseSchema

The name of the database schema that is the location where the data used to define the outcome cohorts is available. If exposureTable = CONDITION\_ERA, exposureDatabaseSchema is not used by assumed to be cdmSchema. Requires

read permissions to this database.

outcomeTable The tablename that contains the outcome cohorts. If outcomeTable <> CONDI-

TION\_OCCURRENCE, then expectation is outcomeTable has format of CO-HORT table: COHORT\_DEFINITION\_ID, SUBJECT\_ID, COHORT\_START\_DATE,

COHORT\_END\_DATE.

cdmVersion Define the OMOP CDM version used: currently support "4" and "5".

 ${\tt excludeDrugsFromCovariates}$ 

Should the target and comparator drugs (and their descendant concepts) be excluded from the covariates? Note that this will work if the drugs are actualy drug concept IDs (and not cohort IDs).

firstExposureOnly

Should only the first exposure per subject be included? Note that this is typically done in the createStudyPopulation function, but can already be done here for efficiency reasons.

removeDuplicateSubjects

Remove subjects that are in both the target and comparator cohort? See details for allowed values.N ote that this is typically done in the createStudyPopulation function, but can already be done here for efficiency reasons.

restrictToCommonPeriod

Restrict the analysis to the period when both treatments are observed?

washoutPeriod

The mininum required continuous observation time prior to index date for a person to be included in the cohort. Note that this is typically done in the createStudyPopulation function, but can already be done here for efficiency reasons.

maxCohortSize

If either the target or the comparator cohort is larger than this number it will be sampled to this size. maxCohortSize = 0 indicates no maximum size.

covariateSettings

An object of type covariateSettings as created using the createCovariateSettings function in the FeatureExtraction package.

#### **Details**

Based on the arguments, the treatment and comparator cohorts are retrieved, as well as outcomes occurring in exposed subjects. The treatment and comparator cohorts can be identified using the drug\_era table, or through user-defined cohorts in a cohort table either inside the CDM instance or in a separate schema. Similarly, outcomes are identified using the condition\_era table or through user-defined cohorts in a cohort table either inside the CDM instance or in a separate schema. Covariates are automatically extracted from the appropriate tables within the CDM. Important: The target and comparator drug must not be included in the covariates, including any descendant concepts. If the targetId and comparatorId arguments represent real concept IDs, you can set the excludeDrugsFromCovariates argument to TRUE and automatically the drugs and their descendants will be excluded from the covariates. However, if the targetId and comparatorId arguments do not represent concept IDs, you will need to manually add the drugs and descendants to the excludedCovariateConceptIds of the covariateSettings argument.

The removeduplicateSubjects argument can have one of the following values:

- "keep all" Do not remove subjects that appear in both target and comparator cohort
- "keep first" When a subjects appear in both target and comparator cohort, only keep whichever cohort is first in time.
- "remove all" Remove subjects that appear in both target and comparator cohort completely from the analysis."

## Value

Returns an object of type cohortMethodData, containing information on the cohorts, their outcomes, and baseline covariates. Information about multiple outcomes can be captured at once for efficiency reasons. This object is a list with the following components:

- **outcomes** A data frame listing the outcomes per person, including the time to event, and the outcome id. Outcomes are not yet filtered based on risk window, since this is done at a later stage.
- **cohorts** A data frame listing the persons in each cohort, listing their exposure status as well as the time to the end of the observation period and time to the end of the cohort (usually the end of the exposure era).
- **covariates** An ffdf object listing the baseline covariates per person in the two cohorts. This is done using a sparse representation: covariates with a value of 0 are omitted to save space.

**covariateRef** An ffdf object describing the covariates that have been extracted.

metaData A list of objects with information on how the cohortMethodData object was constructed.

The generic print() and summary() functions have been implemented for this object.

 ${\tt getDefaultCmTable1Specifications}$ 

Get the default table 1 specifications

## **Description**

Loads the default specifications for a table 1, to be used with the createTable1 function. Important: currently only works for binary covariates.

## Usage

```
getDefaultCmTable1Specifications()
```

#### Value

A specifications objects.

getFollowUpDistribution

Get the distribution of follow-up time

## **Description**

Get the distribution of follow-up time

# Usage

```
getFollowUpDistribution(population, quantiles = c(0, 0.25, 0.5, 0.75, 1))
```

# Arguments

population A data frame describing the study population as created using the createStudyPopulation

function. This should at least have these columns: treatment, timeAtRisk.

quantiles The quantiles of the population to compute minimum follow-up time for.

## **Details**

Get the distribution of follow-up time as quantiles. Follow-up time is defined as time-at-risk, so not censored at the outcome.

## Value

A data frame with per treatment group at each quantile the amount of follow-up time available.

28 getPsModel

getOutcomeModel

Get the outcome model

## **Description**

getOutcomeModel shows the full outcome model, so showing the betas of all variables included in the outcome model, not just the treatment variable.

# Usage

```
getOutcomeModel(outcomeModel, cohortMethodData)
```

# **Arguments**

 ${\tt outcomeModel}$ 

An object of type outcomeModel as generated using he createOutcomeMode function.

cohortMethodData

An object of type cohortMethodData as generated using getDbCohortMethodData.

#### **Details**

Shows the coefficients and names of the covariates with non-zero coefficients.

## **Examples**

# todo

getPsModel

Get the propensity model

## **Description**

getPsModel shows the propensity score model

## Usage

```
getPsModel(propensityScore, cohortMethodData)
```

## **Arguments**

```
propensityScore
```

The propensity scores as generated using the createPs function.

cohortMethodData

An object of type cohort Method Data as generated using getDbCohort Method Data.

# Details

Shows the coefficients and names of the covariates with non-zero coefficients.

grepCovariateNames 29

## **Examples**

# todo

grepCovariateNames Extr

Extract covariate names

# Description

Extracts covariate names using a regular-expression.

## Usage

```
grepCovariateNames(pattern, object)
```

## **Arguments**

pattern A regular expression with which to name covariate names object An R object of type cohortMethodData or covariateData.

#### **Details**

This function extracts covariate names that match a regular-expression for a cohortMethodData or covariateData object.

## Value

Returns a data.frame containing information about covariates that match a regular expression. This data.frame has the following columns:

covariateId Numerical identifier for use in model fitting using these covariates
 covariateName Text identifier
 analysisId Analysis identifier
 conceptId OMOP common data model concept identifier, or 0

insertDbPopulation

Insert a population into a database

# **Description**

Insert a population into a database

# Usage

```
insertDbPopulation(population, cohortIds = c(1, 0), connectionDetails, cohortDatabaseSchema, cohortTable = "cohort", createTable = FALSE, dropTableIfExists = TRUE, cdmVersion = "5")
```

30 loadCmAnalysisList

## **Arguments**

population Either an object of type cohortMethodData or a population object generated by

functions like createStudyPopulation.

cohortIds The IDs to be used for the target and comparator cohort, respectively.

connectionDetails

An R object of type

 $connection {\tt Details}\ created\ using\ the\ function\ create{\tt ConnectionDetails}\ in$ 

the DatabaseConnector package.

cohortDatabaseSchema

The name of the database schema where the data will be written. Requires write permissions to this database. On SQL Server, this should specify both the

database and the schema, so for example 'cdm\_instance.dbo'.

cohortTable The name of the table in the database schema where the data will be written.

createTable Should a new table be created? If not, the data will be inserted into an existing

table.

dropTableIfExists

If createTable = TRUE and the table already exists it will be overwritten.

cdmVersion Define the OMOP CDM version used: currently support "4" and "5".

## **Details**

Inserts a population table into a database. The table in the database will have the same structure as the 'cohort' table in the Common Data Model.

loadCmAnalysisList Load a list of cmAnalysis from file

# Description

Load a list of objects of type cmAnalysis from file. The file is in JSON format.

## Usage

loadCmAnalysisList(file)

## **Arguments**

file The name of the file

#### Value

A list of objects of type cmAnalysis.

loadCohortMethodData 31

loadCohortMethodData Load the cohort data from a folder

## **Description**

loadCohortMethodData loads an object of type cohortMethodData from a folder in the file system.

## Usage

```
loadCohortMethodData(file, readOnly = TRUE)
```

## **Arguments**

file The name of the folder containing the data.

readOnly If true, the data is opened read only.

## **Details**

The data will be written to a set of files in the folder specified by the user.

## Value

An object of class cohortMethodData.

## **Examples**

# todo

loadTargetComparatorOutcomesList

Load a list of targetComparatorOutcomes from file

# Description

 $Load\ a\ list\ of\ objects\ of\ type\ {\tt targetComparatorOutcomes}\ from\ file.\ The\ file\ is\ in\ JSON\ format.$ 

# Usage

load Target Comparator Outcomes List (file)

# **Arguments**

file The name of the file

## Value

A list of objects of type targetComparatorOutcomes.

32 matchOnPs

matchOnPs	Match persons by propensity score

#### **Description**

matchOnPs uses the provided propensity scores to match target to comparator persons.

#### Usage

```
matchOnPs(population, caliper = 0.2, caliperScale = "standardized logit",
    maxRatio = 1, stratificationColumns = c())
```

## **Arguments**

population A data frame with the three columns described below.

caliper The caliper for matching. A caliper is the distance which is acceptable for any

match. Observations which are outside of the caliper are dropped. A caliper of

0 means no caliper is used.

caliperScale The scale on which the caliper is defined. Three scales are supported:

caliperScale = 'propensity score', caliperScale = 'standardized',

or

caliperScale = 'standardized logit'. On the standardized scale, the caliper is interpreted in standard deviations of the propensity score distribution. 'standardized logit' is similar, except that the propensity score is transformed to the logit scale because the PS is more likely to be normally distributed on that

scale (Austin, 2011).

maxRatio The maximum number of persons int the comparator arm to be matched to each

person in the treatment arm. A maxRatio of 0 means no maximum: all com-

parators will be assigned to a target person.

stratificationColumns

Names or numbers of one or more columns in the data data.frame on which subjects should be stratified prior to matching. No persons will be matched with

persons outside of the strata identified by the values in these columns.

## **Details**

The data frame should have at least the following three columns:

rowId (numeric) A unique identifier for each row (e.g. the person ID)

treatment (integer) Column indicating whether the person is in the target (1) or comparator

(0) group

propensityScore (numeric) Propensity score

This function implements the greedy variable-ratio matching algorithm described in Rassen et al (2012).

The default caliper (0.2 on the standardized logit scale) is the one recommended by Austin (2011).

matchOnPsAndCovariates 33

#### Value

Returns a date frame with the same columns as the input data plus one extra column: stratumId. Any rows that could not be matched are removed

#### References

Rassen JA, Shelat AA, Myers J, Glynn RJ, Rothman KJ, Schneeweiss S. (2012) One-to-many propensity score matching in cohort studies, Pharmacoepidemiology and Drug Safety, May, 21 Suppl 2:69-80.

Austin, PC. (2011) Optimal caliper widths for propensity-score matching when estimating differences in means and differences in proportions in observational studies, Pharmaceutical statistics, March, 10(2):150-161.

## **Examples**

matchOnPsAndCovariates

Match by propensity score as well as other covariates

# **Description**

 ${\tt matchOnPsAndCovariates}$  uses the provided propensity scores and a set of covariates to match target to comparator persons.

## Usage

```
matchOnPsAndCovariates(population, caliper = 0.2,
  caliperScale = "standardized logit", maxRatio = 1, cohortMethodData,
  covariateIds)
```

## **Arguments**

population A data frame with the three columns described below.

The caliper for matching. A caliper is the distance which is acceptable for any match. Observations which are outside of the caliper are dropped. A caliper of 0 means no caliper is used.

CaliperScale The scale on which the caliper is defined. Three scales are supported: caliperScale = 'propensity score', caliperScale = 'standardized', or caliperScale = 'standardized logit'. On the standardized scale, the

caliper is interpreted in standard deviations of the propensity score distribution. 'standardized logit' is similar, except that the propensity score is transformed to the logit scale because the PS is more likely to be normally distributed on that

scale (Austin, 2011).

maxRatio The maximum number of persons int the comparator arm to be matched to each

person in the treatment arm. A maxRatio of 0 means no maximum: all com-

parators will be assigned to a target person.

cohortMethodData

An object of type cohortMethodData as generated using getDbCohortMethodData.

covariateIds One or more covariate IDs in the cohortMethodData object on which subjects

should be also matched.

#### **Details**

The data frame should have at least the following three columns:

rowId (numeric) A unique identifier for each row (e.g. the person ID)

treatment (integer) Column indicating whether the person is in the target (1) or comparator

(0) group

propensityScore (numeric) Propensity score

This function implements the greedy variable-ratio matching algorithm described in Rassen et al (2012).

The default caliper (0.2 on the standardized logit scale) is the one recommended by Austin (2011).

## Value

Returns a date frame with the same columns as the input data plus one extra column: stratumId. Any rows that could not be matched are removed

#### References

Rassen JA, Shelat AA, Myers J, Glynn RJ, Rothman KJ, Schneeweiss S. (2012) One-to-many propensity score matching in cohort studies, Pharmacoepidemiology and Drug Safety, May, 21 Suppl 2:69-80.

Austin, PC. (2011) Optimal caliper widths for propensity-score matching when estimating differences in means and differences in proportions in observational studies, Pharmaceutical statistics, March, 10(2):150-161.

# **Examples**

# todo

```
plotCovariateBalanceOfTopVariables
```

Plot variables with largest imbalance

## **Description**

Create a plot showing those variables having the largest imbalance before matching, and those variables having the largest imbalance after matching. Requires running computeCovariateBalance first.

#### Usage

```
plotCovariateBalanceOfTopVariables(balance, n = 20, maxNameWidth = 100,
  fileName = NULL, beforeLabel = "before matching",
  afterLabel = "after matching")
```

## **Arguments**

balance	A data frame created by	the computeCovar	iateBalance funcion.

n Count of variates to plot.

maxNameWidth Covariate names longer than this number of characters are truncated to create a

nicer plot.

fileName Name of the file where the plot should be saved, for example 'plot.png'. See the

function ggsave in the ggplot2 package for supported file formats.

beforeLabel Label for identifying data before matching / stratification / trimming.

afterLabel Label for identifying data after matching / stratification / trimming.

## Value

A ggplot object. Use the ggsave function to save to file in a different format.

```
\verb|plotCovariateBalanceScatterPlot|
```

Create a scatterplot of the covariate balance

## **Description**

Create a scatterplot of the covariate balance, showing all variables with balance before and after matching on the x and y axis respectively. Requires running computeCovariateBalance first.

## Usage

```
plotCovariateBalanceScatterPlot(balance, absolute = TRUE, threshold = 0,
  fileName = NULL, beforeLabel = "Before matching",
  afterLabel = "After matching", showCovariateCountLabel = FALSE,
  showMaxLabel = FALSE)
```

## **Arguments**

balance A data frame created by the computeCovariateBalance funcion.

absolute Should the absolute value of the difference be used?

threshold Show a threshold value for after matching standardized difference.

fileName Name of the file where the plot should be saved, for example 'plot.png'. See the

function ggsave in the ggplot2 package for supported file formats.

beforeLabel Label for the x-axis. afterLabel Label for the y-axis.

## Value

A ggplot object. Use the ggsave function to save to file in a different format.

plotFollowUpDistribution

Plot the distribution of follow-up time

## **Description**

Plot the distribution of follow-up time

## Usage

```
plotFollowUpDistribution(population, targetLabel = "Target",
  comparatorLabel = "Comparator", yScale = "percent", logYScale = FALSE,
  dataCutoff = 0.95, title = "Follow-up distribution", fileName = NULL)
```

# **Arguments**

population A data frame describing the study population as created using the createStudyPopulation

function. This should at least have these columns: treatment, timeAtRisk.

targetLabel A label to us for the target cohort.

comparatorLabel

A label to us for the comparator cohort.

yScale Should be either 'percent' or 'count'.
logYScale Should the Y axis be on the log scale?

dataCutoff Fraction of the data (number censored) after which the graph will not be shown.

title The main title of the plot.

fileName Name of the file where the plot should be saved, for example 'plot.png'. See the

function ggsave in the ggplot2 package for supported file formats.

## **Details**

Plot the distribution of follow-up time, stratified by treatment group. Follow-up time is defined as time-at-risk, so not censored at the outcome.

#### Value

A ggplot object. Use the ggsave function to save to file in a different format.

plotKaplanMeier 37

plotKaplanMeier	Plot the Kaplan-Meier curve	

# **Description**

plotKaplanMeier creates the Kaplain-Meier (KM) survival plot. Based (partially) on recommendations in Pocock et al (2002).

When variable-sized strata are detected, an adjusted KM plot is computed to account for stratified data, as described in Galimberti eta al (2002), using the closed form variance estimator described in Xie et al (2005).

# Usage

```
plotKaplanMeier(population, censorMarks = FALSE, confidenceIntervals = TRUE,
  includeZero = FALSE, dataTable = TRUE, dataCutoff = 0.9,
  targetLabel = "Treated", comparatorLabel = "Comparator", title,
  fileName = NULL)
```

## **Arguments**

population A	A population object generated by createStudyPopulation, potentially file	tered
--------------	--	-------

by other functions.

censorMarks Whether or not to include censor marks in the plot.

confidenceIntervals

Plot 95 percent confidence intervals? Default is TRUE, as recommended by

Pocock et al.

includeZero Should the y axis include zero, or only go down to the lowest observed survival?

The default is FALSE, as recommended by Pocock et al.

dataTable Should the numbers at risk be shown in a table? Default is TRUE, as recom-

mended by Pocock et al.

dataCutoff Fraction of the data (number censored) after which the graph will not be shown.

The default is 90 percent as recommended by Pocock et al.

targetLabel A label to us for the target cohort.

comparatorLabel

A label to us for the comparator cohort.

title The main title of the plot.

fileName Name of the file where the plot should be saved, for example 'plot.png'. See the

function ggsave in the ggplot2 package for supported file formats.

## Value

A ggplot object. Use the ggsave function to save to file in a different format.

38 plotPs

#### References

Pocock SJ, Clayton TC, Altman DG. (2002) Survival plots of time-to-event outcomes in clinical trials: good practice and pitfalls, Lancet, 359:1686-89.

Galimberti S, Sasieni P, Valsecchi MG (2002) A weighted Kaplan-Meier estimator for matched data with application to the comparison of chemotherapy and bone-marrow transplant in leukaemia. Statistics in Medicine, 21(24):3847-64.

Xie J, Liu C. (2005) Adjusted Kaplan-Meier estimator and log-rank test with inverse probability of treatment weighting for survival data. Statistics in Medicine, 26(10):2276.

plotPs

Plot the propensity score distribution

## **Description**

plotPs shows the propensity (or preference) score distribution

# Usage

```
plotPs(data, unfilteredData = NULL, scale = "preference",
  type = "density", binWidth = 0.05, targetLabel = "Target",
  comparatorLabel = "Comparator", showCountsLabel = FALSE,
  showAucLabel = FALSE, showEquiposeLabel = FALSE,
  equipoiseBounds = c(0.25, 0.75), fileName = NULL)
```

## **Arguments**

data A data frame with at least the two columns described below

unfilteredData To be used when computing preference scores on data from which subjects have

already been removed, e.g. through trimming and/or matching. This data frame

should have the same structure as data.

scale The scale of the graph. Two scales are supported: scale = 'propensity' or

scale = 'preference'. The preference score scale is defined by Walker et al

(2013).

type Type of plot. Two possible values: type = 'density' or type = 'histogram'

binWidth For histograms, the width of the bins targetLabel A label to us for the target cohort.

comparatorLabel

A label to us for the comparator cohort.

showCountsLabel

Show subject counts?

showAucLabel Show the AUC?

showEquiposeLabel

Show the percentage of the population in equipoise?

equipoiseBounds

The bounds on the preference score to determine whether a subject is in equipoise.

 $\label{eq:normalization} \textbf{Name of the file where the plot should be saved, for example 'plot.png'. See the}$ 

function ggsave in the ggplot2 package for supported file formats.

runCmAnalyses 39

#### **Details**

The data frame should have a least the following two columns:

```
treatment (integer) Column indicating whether the person is in the target (1) or comparator (0) group propensityScore (numeric) Propensity score
```

#### Value

A ggplot object. Use the ggsave function to save to file in a different format.

#### References

Walker AM, Patrick AR, Lauer MS, Hornbrook MC, Marin MG, Platt R, Roger VL, Stang P, and Schneeweiss S. (2013) A tool for assessing the feasibility of comparative effectiveness research, Comparative Effective Research, 3, 11-20

# **Examples**

```
treatment <- rep(0:1, each = 100)
propensityScore <- c(rnorm(100, mean = 0.4, sd = 0.25), rnorm(100, mean = 0.6, sd = 0.25))
data <- data.frame(treatment = treatment, propensityScore = propensityScore)
data <- data[data$propensityScore > 0 & data$propensityScore < 1, ]
plotPs(data)</pre>
```

runCmAnalyses

Run a list of analyses

## **Description**

Run a list of analyses

## Usage

```
runCmAnalyses(connectionDetails, cdmDatabaseSchema,
  oracleTempSchema = cdmDatabaseSchema,
  exposureDatabaseSchema = cdmDatabaseSchema, exposureTable = "drug_era",
  outcomeDatabaseSchema = cdmDatabaseSchema,
  outcomeTable = "condition_occurrence", cdmVersion = 5,
  outputFolder = "./CohortMethodOutput", cmAnalysisList,
  targetComparatorOutcomesList, refitPsForEveryOutcome = FALSE,
  refitPsForEveryStudyPopulation = TRUE, getDbCohortMethodDataThreads = 1,
  createPsThreads = 1, psCvThreads = 1, createStudyPopThreads = 1,
  trimMatchStratifyThreads = 1, fitOutcomeModelThreads = 1,
  outcomeCvThreads = 1, outcomeIdsOfInterest)
```

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#### **Arguments**

connectionDetails

An R object of type connectionDetails created using the function createConnectionDetails in the DatabaseConnector package.

cdmDatabaseSchema

The name of the database schema that contains the OMOP CDM instance. Requires read permissions to this database. On SQL Server, this should specify both the database and the schema, so for example 'cdm\_instance.dbo'.

oracleTempSchema

For Oracle only: the name of the database schema where you want all temporary tables to be managed. Requires create/insert permissions to this database.

exposureDatabaseSchema

The name of the database schema that is the location where the exposure data used to define the exposure cohorts is available. If exposureTable = DRUG\_ERA, exposureDatabaseSchema is not used by assumed to be cdmSchema. Requires read permissions to this database.

exposureTable The tablename that contains the exposure cohorts. If exposureTable <> DRUG\_ERA, then expectation is exposureTable has format of COHORT table: COHORT\_DEFINITION\_ID, SUBJECT\_ID, COHORT\_START\_DATE, COHORT\_END\_DATE.

outcomeDatabaseSchema

The name of the database schema that is the location where the data used to define the outcome cohorts is available. If exposureTable = CONDITION\_ERA, exposureDatabaseSchema is not used by assumed to be cdmSchema. Requires read permissions to this database.

read permissions to this database.

outcomeTable

The tablename that contains the outcome cohorts. If outcomeTable <> CONDITION\_OCCURRENCE, then expectation is outcomeTable has format of CO-

HORT table: COHORT\_DEFINITION\_ID, SUBJECT\_ID, COHORT\_START\_DATE, COHORT\_END\_DATE.

cdmVersion Define the OMOP CDM version used: currently support "4" and "5".

outputFolder Name of the folder where all the outputs will written to.

cmAnalysisList A list of objects of type cmAnalysis as created using the createCmAnalysis function.

target Comparator Outcomes List

A list of objects of type targetComparatorOutcomes as created using the createTargetComparator function.

refitPsForEveryOutcome

Should the propensity model be fitted for every outcome (i.e. after people who already had the outcome are removed)? If false, a single propensity model will be fitted, and people who had the outcome previously will be removed afterwards.

 ${\tt refitPsForEveryStudyPopulation}$ 

Should the propensity model be fitted for every study population definition? If false, a single propensity model will be fitted, and the study population criteria will be applied afterwards.

getDbCohortMethodDataThreads

The number of parallel threads to use for building the cohortMethod data objects.

createPsThreads

The number of parallel threads to use for fitting the propensity models.

runCmAnalyses 41

psCvThreads The number of parallel threads to use for the cross-validation when estimating

the hyperparameter for the propensity model. Note that the total number of CV

threads at one time could be 'createPsThreads' psCvThreads'.

 ${\tt createStudyPopThreads}$ 

The number of parallel threads to use for creating the study population.

trimMatchStratifyThreads

The number of parallel threads to use for trimming, matching and stratifying.

fitOutcomeModelThreads

The number of parallel threads to use for fitting the outcome models.

outcomeCvThreads

The number of parallel threads to use for the cross-validation when estimating the hyperparameter for the outcome model. Note that the total number of CV threads at one time could be 'fitOutcomeModelThreads \* outcomeCvThreads'.

outcomeIdsOfInterest

If provided, creation of non-essential files will be skipped for all other outcome IDs. This could be helpful to speed up analyses with many controls.

## **Details**

Run a list of analyses for the target-comparator-outcomes of interest. This function will run all specified analyses against all hypotheses of interest, meaning that the total number of outcome models is 'length(cmAnalysisList) \* length(targetComparatorOutcomesList)' (if all analyses specify an outcome model should be fitted). When you provide several analyses it will determine whether any of the analyses have anything in common, and will take advantage of this fact. For example, if we specify several analyses that only differ in the way the outcome model is fitted, then this function will extract the data and fit the propensity model only once, and re-use this in all the analysis.

#### Value

A data frame with the following columns:

analysisId The unique identifier for a set of analysis choices.

targetId The ID of the target exposure. comparatorId The ID of the comparator group.

excludedCovariateConceptIds The ID(s) of concepts that cannot be used to construct covariates. IncludedCovariateConceptIds The ID(s) of concepts that should be used to construct covariates.

outcomeId The ID of the outcome cohortMethodDataFolder The ID of the outcome.

sharedPsFile The name of the file containing the propensity scores of the shared

propensity model. This model is used to create the outcome-specific

propensity scores by removing people with prior outcomes.

studyPopFile The name of the file containing the study population (prior

and trimming, matching, or stratification on the PS.

psFile The name of file containing the propensity scores for a specific

outcomes (ie after people with prior outcomes have been removed).

strataFile The name of the file containing the identifiers of the population

after any trimming, matching or stratifying, including their strata.

outcomeModelFile The name of the file containing the outcome model.

42 saveCohortMethodData

 ${\tt save CmAnalysisList}$ 

Save a list of cmAnalysis to file

# Description

Write a list of objects of type cmAnalysis to file. The file is in JSON format.

# Usage

```
saveCmAnalysisList(cmAnalysisList, file)
```

# **Arguments**

cmAnalysisList The cmAnalysis list to be written to file

file The name of the file where the results will be written

saveCohortMethodData Save the cohort data to folder

# Description

saveCohortMethodData saves an object of type cohortMethodData to folder.

# Usage

```
saveCohortMethodData(cohortMethodData, file)
```

# **Arguments**

cohortMethodData

An object of type cohort Method Data as generated using getDbCohort Method Data.

file

The name of the folder where the data will be written. The folder should not yet exist.

# Details

The data will be written to a set of files in the folder specified by the user.

saveTargetComparatorOutcomesList

Save a list of targetComparatorOutcomes to file

# Description

Write a list of objects of type targetComparatorOutcomes to file. The file is in JSON format.

# Usage

save Target Comparator Outcomes List (target Comparator Outcomes List, file)

## **Arguments**

targetComparatorOutcomesList

The targetComparatorOutcomes list to be written to file

The name of the file where the results will be written

simulateCohortMethodData

Generate simulated data

## **Description**

simulateCohortMethodData creates a cohortMethodData object with simulated data.

# Usage

simulateCohortMethodData(profile, n = 10000)

# **Arguments**

profile An object of type cohortMethodDataSimulationProfile as generated using

the

 $create {\tt CohortMethodDataSimulationProfile}\ function.$ 

n The size of the population to be generated.

## **Details**

This function generates simulated data that is in many ways similar to the original data on which the simulation profile is based. The contains same outcome, comparator, and outcome concept IDs, and the covariates and their 1st order statistics should be comparable.

# Value

An object of type cohortMethodData.

44 stratifyByPs

# **Description**

stratifyByPs uses the provided propensity scores to stratify persons. Additional stratification variables for stratifications can also be used.

## Usage

```
stratifyByPs(population, numberOfStrata = 5, stratificationColumns = c(),
baseSelection = "all")
```

# **Arguments**

population A data frame with the three columns described below

numberOfStrata How many strata? The boundaries of the strata are automatically defined to

contain equal numbers of target persons.

stratificationColumns

Names of one or more columns in the data data.frame on which subjects should

also be stratified in addition to stratification on propensity score.

baseSelection What is the base selection of subjects where the strata bounds are to be deter-

mined? Strata are defined as equally-sized strata inside this selection. Possible

values are "all", "target", and "comparator".

## **Details**

The data frame should have the following three columns:

rowId	(numeric)	A unique identifier for each row (e.g. the person ID)
treatment	(integer)	Column indicating whether the person is in the target (1) or comparator
		(0) group

propensityScore (numeric) Propensity score

# Value

Returns a date frame with the same columns as the input data plus one extra column: stratumId.

## **Examples**

```
rowId <- 1:200
treatment <- rep(0:1, each = 100)
propensityScore <- c(runif(100, min = 0, max = 1), runif(100, min = 0, max = 1))
data <- data.frame(rowId = rowId, treatment = treatment, propensityScore = propensityScore)
result <- stratifyByPs(data, 5)</pre>
```

stratifyByPsAndCovariates

Stratify persons by propensity score and other covariates

# **Description**

stratifyByPsAndCovariates uses the provided propensity scores and covariates to stratify persons.

## Usage

```
stratifyByPsAndCovariates(population, numberOfStrata = 5,
  baseSelection = "all", cohortMethodData, covariateIds)
```

# **Arguments**

population A data frame with the three columns described below

numberOfStrata Into how many strata should the propensity score be divided? The boundaries of

the strata are automatically defined to contain equal numbers of target persons.

baseSelection What is the base selection of subjects where the strata bounds are to be deter-

mined? Strata are defined as equally-sized strata inside this selection. Possible

values are "all", "target", and "comparator".

cohortMethodData

An object of type cohortMethodData as generated using getDbCohortMethodData.

covariateIds One or more covariate IDs in the cohortMethodData object on which subjects

should also be stratified.

## **Details**

The data frame should have the following three columns:

rowId (integer) A unique identifier for each row (e.g. the person ID)

treatment (integer) Column indicating whether the person is in the target (1) or comparator

(0) group

propensityScore (numeric) Propensity score

# Value

Returns a date frame with the same columns as the input population plus one extra column: stratumId.

## **Examples**

# todo

46 trimByPs

summarizeAnalyses Create a summary report of the analyses	summarizeAnalyses	Create a summary report of the analyses	
---	-------------------	---	--

# **Description**

Create a summary report of the analyses

## Usage

```
summarizeAnalyses(referenceTable)
```

#### **Arguments**

referenceTable A data.frame as created by the runCmAnalyses function.

#### Value

A data frame with the following columns:

analysisId The unique identifier for a set of analysis choices.

targetId The ID of the target drug.
comparatorId The ID of the comparator group.

indicationConceptIds The ID(s) of indications in which to nest to study.

outcomeId The ID of the outcome.
rr The estimated effect size.

ci95lb The lower bound of the 95 percent confidence interval. ci95ub The upper bound of the 95 percent confidence interval.

target The number of subjects in the target group (after any trimming and matching).

The number of subjects in the comparator group (after any trimming and matching).

eventsTarget The number of outcomes in the target group (after any trimming and matching).

The number of outcomes in the comparator group (after any trimming and matching).

matching).

logRr The log of the estimated relative risk.

seLogRr The standard error of the log of the estimated relative risk.

trimByPs	Trim persons by propensity score

# **Description**

trimByPs uses the provided propensity scores to trim subjects with extreme scores.

# Usage

```
trimByPs(population, trimFraction = 0.05)
```

trimByPsToEquipoise 47

## **Arguments**

population A data frame with the three columns described below

trimFraction This fraction will be removed from each treatment group. In the target group,

persons with the highest propensity scores will be removed, in the comparator

group person with the lowest scores will be removed.

## **Details**

The data frame should have the following three columns:

rowId (numeric) A unique identifier for each row (e.g. the person ID)

treatment (integer) Column indicating whether the person is in the target (1) or comparator

(0) group

propensityScore (numeric) Propensity score

#### Value

Returns a date frame with the same three columns as the input.

# **Examples**

```
rowId <- 1:2000
treatment <- rep(0:1, each = 1000)
propensityScore <- c(runif(1000, min = 0, max = 1), runif(1000, min = 0, max = 1))
data <- data.frame(rowId = rowId, treatment = treatment, propensityScore = propensityScore)
result <- trimByPs(data, 0.05)</pre>
```

trimByPsToEquipoise

Keep only persons in clinical equipoise

#### Description

trimByPsToEquipoise uses the preference score to trim subjects that are not in clinical equipoise

# Usage

```
trimByPsToEquipoise(population, bounds = c(0.25, 0.75))
```

# **Arguments**

population A data frame with at least the three columns described below

bounds The upper and lower bound on the preference score for keeping persons

## **Details**

The data frame should have the following three columns:

rowId (numeric) A unique identifier for each row (e.g. the person ID)

treatment (integer) Column indicating whether the person is in the target (1) or comparator

(0) group

propensityScore (numeric) Propensity score

## Value

Returns a date frame with the same three columns as the input.

## References

Walker AM, Patrick AR, Lauer MS, Hornbrook MC, Marin MG, Platt R, Roger VL, Stang P, and Schneeweiss S. (2013) A tool for assessing the feasibility of comparative effectiveness research, Comparative Effective Research, 3, 11-20

# **Examples**

```
rowId <- 1:2000
treatment <- rep(0:1, each = 1000)
propensityScore <- c(runif(1000, min = 0, max = 1), runif(1000, min = 0, max = 1))
data <- data.frame(rowId = rowId, treatment = treatment, propensityScore = propensityScore)
result <- trimByPsToEquipoise(data)</pre>
```

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