

Package ‘CaseCrossover’

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Description An R package for performing case-crossover and case-time-control analyses in an observational database in the OMOP Common Data Model.

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DatabaseConnector (>= 1.3.0),
survival

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CaseControl (>= 1.3.0),
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CaseCrossover	<i>CaseCrossover</i>
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Description

CaseCrossover

createCcrAnalysis	<i>Create a case-crossover analysis specification</i>
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Description

Create a case-crossover analysis specification

Usage

```
createCcrAnalysis(analysisId = 1, description = "", exposureType = NULL,
  outcomeType = NULL, nestingCohortType = NULL, getDbCaseCrossoverDataArgs,
  selectSubjectsToIncludeArgs, getExposureStatusArgs)
```

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.
exposureType	If more than one exposure is provided for each exposureOutcomeNestingCohort, this field should be used to select the specific exposure to use in this analysis.
outcomeType	If more than one outcome is provided for each exposureOutcomeNestingCohort, this field should be used to select the specific outcome to use in this analysis.
nestingCohortType	If more than one nesting cohort is provided for each exposureOutcomeNestingCohort, this field should be used to select the specific nesting cohort to use in this analysis.

getDbCaseCrossoverDataArgs

An object representing the arguments to be used when calling the [createGetDbCaseCrossoverDataA](#) function.

selectSubjectsToIncludeArgs

An object representing the arguments to be used when calling the [selectSubjectsToInclude](#) function.

getExposureStatusArgs

An object representing the arguments to be used when calling the [getExposureStatus](#) function.

Details

Create a set of analysis choices, to be used with the [runCcrAnalyses](#) function.

createExposureOutcomeNestingCohort

Create exposure-outcome-nesting-cohort combinations.

Description

Create exposure-outcome-nesting-cohort combinations.

Usage

```
createExposureOutcomeNestingCohort(exposureId, outcomeId,
  nestingCohortId = NULL)
```

Arguments

- | | |
|-----------------|---|
| exposureId | A concept ID indentifying the target drug in the exposure table. If multiple strategies for picking the exposure 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 exposureType parameter in the createCcrAnalysis function. |
| outcomeId | A concept ID indentifying the outcome in the outcome table. If multiple strategies for picking the outcome 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 outcomeType parameter in the createCcrAnalysis function. |
| nestingCohortId | A concept ID indentifying the nesting cohort in the nesting cohort table. If multiple strategies for picking the nesting cohort 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 nestingCohortType parameter in the createCcrAnalysis function. |

Details

Create a set of hypotheses of interest, to be used with the [runCcrAnalyses](#) function.

```
createGetDbCaseCrossoverDataArgs
```

Create a parameter object for the function getDbCaseCrossoverData

Description

Create a parameter object for the function getDbCaseCrossoverData

Usage

```
createGetDbCaseCrossoverDataArgs(useNestingCohort = FALSE,
  useObservationEndAsNestingEndDate = TRUE, getVisits = FALSE,
  studyStartDate = "", studyEndDate = "", getTimeControlData = FALSE)
```

Arguments

useNestingCohort

Should the study be nested in a cohort (e.g. people with a specific indication)? If not, the study will be nested in the general population.

useObservationEndAsNestingEndDate

When using a nesting cohort, should the observation period end date be used instead of the cohort end date?

getVisits

Get data on visits? This is needed when performing a time- case-control study and matching on visit date is requested later on.

studyStartDate

A calendar date specifying the minimum date where data is used. Date format is 'yyyymmdd'.

studyEndDate

A calendar date specifying the maximum date where data is used. Date format is 'yyyymmdd'.

getTimeControlData

Should data for time controls be fetched? (needed for case-time-control analyses).

Details

Create an object defining the parameter values.

```
createGetExposureStatusArgs
```

Create a parameter object for the function getExposureStatus

Description

Create a parameter object for the function getExposureStatus

Usage

```
createGetExposureStatusArgs(firstExposureOnly = FALSE,
  riskWindowStart = -30, riskWindowEnd = 0, controlWindowOffsets = c(-60))
```

Arguments

firstExposureOnly	Should only the first exposure per subject be included?
riskWindowStart	The start of the risk window (in days) relative to the index date. This number should be non-positive.
riskWindowEnd	The end of the risk window (in days) relative to the index date. This number should be non-positive.
controlWindowOffsets	Offsets in days of the control windows relative to the case window.

Details

Create an object defining the parameter values.

```
createMatchingCriteria
```

Create matching criteria

Description

Create matching criteria

Usage

```
createMatchingCriteria(controlsPerCase = 1, matchOnAge = TRUE,
  ageCaliper = 2, matchOnGender = TRUE, matchOnProvider = FALSE,
  matchOnCareSite = FALSE, matchOnVisitDate = FALSE,
  visitDateCaliper = 30, matchOnTimeInCohort = FALSE,
  daysInCohortCaliper = 30)
```

Arguments

controlsPerCase	Maximum number of controls to select per case.
matchOnAge	Match on age?
ageCaliper	Maximum difference (in years) in age when matching on age.
matchOnGender	Match on gender?
matchOnProvider	Match on provider (as specified in the person table)?
matchOnCareSite	Match on care site (as specified in the person table)?
matchOnVisitDate	Should the index date of the control be changed to the nearest visit date?
visitDateCaliper	Maximum difference (in days) between the index date and the visit date when matching on visit date.

matchOnTimeInCohort

Match on time in nesting cohort? When not using nesting, this is interpreted as time observed prior to index.

daysInCohortCaliper

Maximum difference (in days) in time in cohort.

createSelectSubjectsToIncludeArgs

Create a parameter object for the function selectSubjectsToInclude

Description

Create a parameter object for the function selectSubjectsToInclude

Usage

```
createSelectSubjectsToIncludeArgs(firstOutcomeOnly = TRUE,
  washoutPeriod = 180, matchingCriteria = NULL, minAge = NULL,
  maxAge = NULL)
```

Arguments

firstOutcomeOnly

Use the first outcome per person?

washoutPeriod

Minimum required numbers of days of observation for inclusion as either case or control.

matchingCriteria

If provided, a case-time-control analysis will be performed and controls will be matched based on these criteria.

minAge

Minimum age at which patient time will be included in the analysis. Note that information prior to the min age is still used to determine exposure status after the minimum age (e.g. when a prescription was started just prior to reaching the minimum age). Also, outcomes occurring before the minimum age is reached will be considered as prior outcomes when using first outcomes only. Age should be specified in years, but non-integer values are allowed. If not specified, no age restriction will be applied.

maxAge

Maximum age at which patient time will be included in the analysis. Age should be specified in years, but non-integer values are allowed. If not specified, no age restriction will be applied.

Details

Create an object defining the parameter values.

fitCaseCrossoverModel	<i>Fit case-crossover model</i>
-----------------------	---------------------------------

Description

Fit case-crossover model

Usage

```
fitCaseCrossoverModel(exposureStatus)
```

Arguments

exposureStatus A data frame as generated using the [getExposureStatus](#) function.

Details

Fits a conditional logistic regression on the case-crossover data.

getAttritionTable	<i>Get the attrition table for a set of subjects</i>
-------------------	--

Description

Get the attrition table for a set of subjects

Usage

```
getAttritionTable(subjects)
```

Arguments

subjects A data frame of subjects as generated by the function [selectSubjectsToInclude](#).

Value

A data frame specifying the number of cases and events after various steps of filtering.

getDbCaseCrossoverData

Load case-crossover data from the database

Description

Load all data about the cases from the database.

Usage

```
getDbCaseCrossoverData(connectionDetails, cdmDatabaseSchema,
  oracleTempSchema = cdmDatabaseSchema,
  outcomeDatabaseSchema = cdmDatabaseSchema, outcomeTable = "condition_era",
  outcomeIds = c(), useNestingCohort = FALSE,
  nestingCohortDatabaseSchema = cdmDatabaseSchema,
  nestingCohortTable = "cohort", nestingCohortId = NULL,
  useObservationEndAsNestingEndDate = TRUE, getVisits = FALSE,
  exposureDatabaseSchema = cdmDatabaseSchema, exposureTable = "drug_era",
  exposureIds = c(), studyStartDate = "", studyEndDate = "",
  getTimeControlData = FALSE)
```

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

A schema where temp tables can be created in Oracle.

outcomeDatabaseSchema

The name of the database schema that is the location where the data used to define the outcome cohorts is available. If outcomeTable = CONDITION_ERA, outcomeDatabaseSchema is not used. Requires read permissions to this database.

outcomeTable

The tablename that contains the outcome cohorts. If outcomeTable is not CONDITION_OCCURRENCE or CONDITION_ERA, then expectation is outcomeTable has format of COHORT table: COHORT_DEFINITION_ID, SUBJECT_ID, COHORT_START_DATE, COHORT_END_DATE.

outcomeIds

A list of ids used to define outcomes. If outcomeTable = CONDITION_OCCURRENCE, the list is a set of ancestor CONCEPT_IDS, and all occurrences of all descendant concepts will be selected. If outcomeTable <> CONDITION_OCCURRENCE, the list contains records found in COHORT_DEFINITION_ID field.

useNestingCohort

Should the study be nested in a cohort (e.g. people with a specific indication)? If not, the study will be nested in the general population.

nestingCohortDatabaseSchema

The name of the database schema that is the location where the nesting cohort is defined.

nestingCohortTable	Name of the table holding the nesting cohort. This table should have the same structure as the cohort table.
nestingCohortId	A cohort definition ID identifying the records in the nestingCohortTable to use as nesting cohort.
useObservationEndAsNestingEndDate	When using a nesting cohort, should the observation period end date be used instead of the cohort end date?
getVisits	Get data on visits? This is needed when performing a time- case-control study and matching on visit date is requested later on.
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 but 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.
exposureIds	A list of identifiers to define the exposures of interest. If exposureTable = DRUG_ERA, exposureIds should be CONCEPT_ID. If exposureTable <> DRUG_ERA, exposureIds is used to select the cohort_concept_id in the cohort-like table. If no exposureIds are provided, all drugs or cohorts in the exposureTable are included as exposures.
studyStartDate	A calendar date specifying the minimum date where data is used. Date format is 'yyyymmdd'.
studyEndDate	A calendar date specifying the maximum date where data is used. Date format is 'yyyymmdd'.
getTimeControlData	Should data for time controls be fetched? (needed for case-time-control analyses).

Value

Returns an object of type caseCrossoverData, containing information on the cases, the nesting cohort, exposures, and optionally visits. Information about multiple outcomes can be captured at once for efficiency reasons. The generic summary() function has been implemented for this object.

getExposureStatus	<i>Get the exposure status for cases (and controls).</i>
-------------------	--

Description

Get the exposure status for cases (and controls).

Usage

```
getExposureStatus(subjects, caseCrossoverData, exposureId,
  firstExposureOnly = FALSE, riskWindowStart = -30, riskWindowEnd = 0,
  controlWindowOffsets = c(-60))
```

Arguments

<code>subjects</code>	A data frame as generated using the selectSubjectsToInclude function.
<code>caseCrossoverData</code>	An object of type <code>caseCrossoverData</code> as generated using the getDbCaseCrossoverData function.
<code>exposureId</code>	The identifier of the exposure.
<code>firstExposureOnly</code>	Should only the first exposure per subject be included?
<code>riskWindowStart</code>	The start of the risk window (in days) relative to the index date. This number should be non-positive.
<code>riskWindowEnd</code>	The end of the risk window (in days) relative to the index date. This number should be non-positive.
<code>controlWindowOffsets</code>	Offsets in days of the control windows relative to the case window.

Details

This function determines the exposure status for a give, exposure ID in various windows relative to the index date.

Value

A data frame with these columns:

personId The person ID
indexDate The index date
isCase Is the person a case or a control?
stratumId The ID linking cases and controls in a matched set
isCaseWindow Is this a case window (as opposed to a control window)?
exposed Was the person exposed during the window?

`loadCaseCrossoverData` *Load the case data from a folder*

Description

`loadCaseCrossoverData` loads an object of type `caseCrossoverData` from a folder in the file system.

Usage

```
loadCaseCrossoverData(folder, readOnly = TRUE)
```

Arguments

`folder` 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 caseCrossoverData.

loadCcrAnalysisList	<i>Load a list of ccrAnalysis from file</i>
---------------------	---

Description

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

Usage

```
loadCcrAnalysisList(file)
```

Arguments

file	The name of the file
------	----------------------

Value

A list of objects of type ccrAnalysis.

loadExposureOutcomeNestingCohortList	<i>Load a list of exposureOutcomeNestingCohort from file</i>
--------------------------------------	--

Description

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

Usage

```
loadExposureOutcomeNestingCohortList(file)
```

Arguments

file	The name of the file
------	----------------------

Value

A list of objects of type drugComparatorOutcome.

runCcrAnalyses	<i>Run a list of analyses</i>
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Description

Run a list of analyses

Usage

```
runCcrAnalyses(connectionDetails, cdmDatabaseSchema,
  oracleTempSchema = cdmDatabaseSchema,
  exposureDatabaseSchema = cdmDatabaseSchema, exposureTable = "drug_era",
  outcomeDatabaseSchema = cdmDatabaseSchema, outcomeTable = "condition_era",
  nestingCohortDatabaseSchema = cdmDatabaseSchema,
  nestingCohortTable = "condition_era", outputFolder = "./CcrOutput",
  ccrAnalysisList, exposureOutcomeNestingCohortList,
  getDbCaseCrossoverDataThreads = 1, selectSubjectsToIncludeThreads = 1,
  getExposureStatusThreads = 1, fitCaseCrossoverModelThreads = 1)
```

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

A schema where temp tables can be created in Oracle.

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 but 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 outcomeTable = CONDITION_ERA, outcomeDatabaseSchema is not used. Requires read permissions to this database.

outcomeTable

The tablename that contains the outcome cohorts. If outcomeTable is not CONDITION_OCCURRENCE or CONDITION_ERA, then expectation is outcomeTable has format of COHORT table: COHORT_DEFINITION_ID, SUBJECT_ID, COHORT_START_DATE, COHORT_END_DATE.

nestingCohortDatabaseSchema

The name of the database schema that is the location where the nesting cohort is defined.

nestingCohortTable	Name of the table holding the nesting cohort. This table should have the same structure as the cohort table.
outputFolder	Name of the folder where all the outputs will be written to.
ccrAnalysisList	A list of objects of type ccrAnalysis as created using the createCcrAnalysis function.
exposureOutcomeNestingCohortList	A list of objects of type exposureOutcomeNestingCohort as created using the createExposureOutcomeNestingCohort function.
getDbCaseCrossoverDataThreads	The number of parallel threads to use for building the caseControlData objects.
selectSubjectsToIncludeThreads	The number of parallel threads to use for selecting subjects
getExposureStatusThreads	The number of parallel threads to use for getting exposure status.
fitCaseCrossoverModelThreads	The number of parallel threads to use for fitting the models.

Details

Run a list of analyses for the exposure-outcome-nesting cohorts of interest. This function will run all specified analyses against all hypotheses of interest, meaning that the total number of outcome models is 'length(ccrAnalysisList) * length(exposureOutcomeNestingCohortList)'. 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 control windows are specified then this function will extract the data and select the subjects only once, and re-use this in all the analysis.

saveCaseCrossoverData *Save the case-crossover data to folder*

Description

saveCaseCrossoverData saves an object of type caseCrossoverData to folder.

Usage

```
saveCaseCrossoverData(caseCrossoverData, folder)
```

Arguments

caseCrossoverData	An object of type caseCrossoverData as generated using getDbCaseCrossoverData .
folder	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 specified folder.

saveCcrAnalysisList	<i>Save a list of ccrAnalysis to file</i>
---------------------	---

Description

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

Usage

```
saveCcrAnalysisList(ccrAnalysisList, file)
```

Arguments

ccrAnalysisList	The ccArnalalysis list to be written to file
file	The name of the file where the results will be written

saveExposureOutcomeNestingCohortList	<i>Save a list of drugComparatorOutcome to file</i>
--------------------------------------	---

Description

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

Usage

```
saveExposureOutcomeNestingCohortList(exposureOutcomeNestingCohortList, file)
```

Arguments

exposureOutcomeNestingCohortList	The exposureOutcomeNestingCohort list to be written to file
file	The name of the file where the results will be written

selectSubjectsToInclude

Select subjects to include

Description

Select subjects to include

Usage

```
selectSubjectsToInclude(caseCrossoverData, outcomeId, firstOutcomeOnly = TRUE,
  washoutPeriod = 180, matchingCriteria = NULL, minAge = NULL,
  maxAge = NULL)
```

Arguments

caseCrossoverData	An object of type caseCrossoverData as generated using the getDbCaseCrossoverData function.
outcomeId	The outcome ID of the cases for which we need to pick controls.
firstOutcomeOnly	Use the first outcome per person?
washoutPeriod	Minimum required numbers of days of observation for inclusion as either case or control.
matchingCriteria	If provided, a case-time-control analysis will be performed and controls will be matched based on these criteria.
minAge	Minimum age at which patient time will be included in the analysis. Note that information prior to the min age is still used to determine exposure status after the minimum age (e.g. when a prescription was started just prior to reaching the minimum age). Also, outcomes occurring before the minimum age is reached will be considered as prior outcomes when using first outcomes only. Age should be specified in years, but non-integer values are allowed. If not specified, no age restriction will be applied.
maxAge	Maximum age at which patient time will be included in the analysis. Age should be specified in years, but non-integer values are allowed. If not specified, no age restriction will be applied.

Details

Subject to include in the study are selected for a specific outcome, optionally filtering using a washout period, restricting to first occurrences of the outcome only, and restricting on age. If matching criteria are provided controls will be selected for each case. These controls will be used to adjust for time trends in exposure, turning the analysis into a case-time-control analysis (Suissa, 1995).

Value

A data frame with these columns:

personId The person ID

indexDate The index date

isCase Is the person a case or a control?

stratumId The ID linking cases and controls in a matched set

observationPeriodStartDate The observation period start date

References

Suissa S (1995) The case-time-control design. Epidemiology; 6:248-253.

summarizeCcrAnalyses *Create a summary report of the analyses*

Description

Create a summary report of the analyses

Usage

```
summarizeCcrAnalyses(outcomeReference)
```

Arguments

outcomeReference

A data.frame as created by the [runCcrAnalyses](#) function.

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