# ${\bf Package\ 'Self Controlled Case Series'}$

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Author Martijn Schuemie, Patrick Ryan, Trevor Shaddox, Marc A. Suchard
Maintainer Martijn Schuemie <schuemie@ohdsi.org></schuemie@ohdsi.org>
<b>Description</b> SelfControlledCaseSeries is an R package for performing self-controlled case series (SCCS) analyses in an observational database in the OMOP Common Data Model.
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 $Compute \ the \ minimum \ detectable \ relative \ risk$ 

### Description

computeMdrr

Compute the minimum detectable relative risk

### Usage

```
computeMdrr(sccsEraData, exposureCovariateId, alpha = 0.05,
   power = 0.8, twoSided = TRUE, method = "binomial")
```

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#### **Arguments**

sccsEraData An object containing study population observation time, outcomesa and covari-

ates as created using the  ${\tt createSccsEraData}$  function. This should include the

following dataframes: outcomes, covariates, and covariateRef.

exposureCovariateId

Covariate Id for the health exposure of interest.

alpha Type I error.

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

twoSided Consider a two-sided test?

method The type of sample size formula that will be used. Allowable values are "pro-

portion", "binomial", "SRL1", "SRL2", or "ageEffects". Currently "ageEffects"

is not supported.

#### **Details**

Compute the minimum detectable relative risk (MDRR) for a given study population, using the observerd time at risk and total time in days and number of events. Five sample size formulas are implemented: sampling proportion, binomial proportion, 2 signed root likelihood ratio methods, and likelihood extension for age effects. The expressions by Musonda (2006) are used.

#### Value

A data frame with the MDRR, number of events, time at risk, and total time.

#### References

Musonda P, Farrington CP, Whitaker HJ (2006) Samples sizes for self-controlled case series studies, Statistics in Medicine, 15;25(15):2618-31

createAgeSettings

Create age settings

#### **Description**

Create age settings

#### Usage

```
createAgeSettings(includeAge = FALSE, ageKnots = 5,
   allowRegularization = FALSE, computeConfidenceIntervals = FALSE,
   minAge = NULL, maxAge = NULL)
```

#### **Arguments**

includeAge Should age be included in the model?

ageKnots If a single number is provided this is assumed to indicate the number of knots

to use for the spline, and the knots are automatically spaced according to equal percentiles of the data. If more than one number is provided these are assumed

to be the exact location of the knots in age-days

allowRegularization

When fitting the model, should the covariates defined here be allowed to be regularized?

computeConfidenceIntervals

Should confidence intervals be computed for the covariates defined here? Setting this to FALSE might save computing time when fitting the model. Will be turned to FALSE automatically when allowRegularization = TRUE.

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 specifing whether and how age should be included in the model. Age can be included by splitting patient time into calendar months. During a month, the relative risk attributed to age is assumed to be constant, and the risk from month to month is modeled using a cubic spline.

### Value

An object of type ageSettings.

createCovariateSettings

Create covariate settings

### **Description**

Create covariate settings

### Usage

```
createCovariateSettings(includeCovariateIds = NULL,
  excludeCovariateIds = NULL, label = "Covariates",
  stratifyById = TRUE, start = 0, addExposedDaysToStart = FALSE,
  end = 0, addExposedDaysToEnd = FALSE, firstOccurrenceOnly = FALSE,
  splitPoints = c(), allowRegularization = FALSE)
```

#### **Arguments**

includeCovariateIds

One or more IDs of variables in the sccsData object that should be used to construct this covariate. If no IDs are specified, all variables will be used.

excludeCovariateIds

One or more IDs of variables in the sccsData object that should not be used to construct this covariate.

label A label used to identify the covariates created using these settings.

stratifyById Should a single covariate be created for every ID in the sccsData object, or

should a single covariate be constructed? For example, if the IDs identify exposures to different drugs, should a covariate be constructed for every drug, or a single covariate for exposure to any of these drugs. Note that overlap will be

considered a single exposure.

start The start of the risk window in days, relative to the exposure start date.

 $add {\tt Exposed Days To Start}$ 

Should the length of exposure be added to the start date?

end The start of the risk window in days, relative to the exposure start date.

 $add {\sf ExposedDaysToEnd}$ 

Should the length of exposure be added to the end date?

firstOccurrenceOnly

Should only the first occurrence of the exposure be used?

splitPoints To split the risk window into several smaller windows, specify the end of each

sub- window relative to the start of the main risk window. If addExposed-DaysToStart is TRUE, the split points will be considered to be relative to the

end of the main risk window instead.

allowRegularization

When fitting the model, should the covariates defined here be allowed to be

regularized?

#### **Details**

Create an object specifying how to create a (set of) covariates.

### Value

An object of type covariateSettings.

createCreateSccsEraDataArgs

Create a parameter object for the function createSccsEraData

#### **Description**

Create a parameter object for the function createSccsEraData

#### Usage

```
createCreateSccsEraDataArgs(naivePeriod = 0, firstOutcomeOnly = FALSE,
  covariateSettings, ageSettings = createAgeSettings(includeAge = FALSE),
  seasonalitySettings = createSeasonalitySettings(includeSeasonality =
  FALSE), minCasesForAgeSeason = 10000,
  eventDependentObservation = FALSE)
```

#### **Arguments**

naivePeriod

The number of days at the start of a patient's observation periodthat should not be included in the risk calculations. Note thatthe naive period can be used to determine current covariatestatus right after the naive period, and whether an outcome is the first one.

firstOutcomeOnly

Whether only the first occurrence of an outcome should beconsidered.

covariateSettings

Either an object of type covariateSettings as createdusing the createCovariateSettings function, or alist of such objects.

 $\label{thm:constraints} age Settings \ as \ created \ using \ the create Age Settings \ function.$  seasonality Settings

An object of type seasonalitySettings as created using thecreateSeasonalitySettings function.

minCasesForAgeSeason

Minimum number of cases to use to fit age and season splines. IFneeded (and available), cases that are not exposed will be included.#'

eventDependentObservation

Should the extension proposed by Farrington et al. be used toadjust for event-dependent observation time?

#### Details

Create an object defining the parameter values.

createExposureOutcome Create a exposure-outcome combination.

### **Description**

Create a exposure-outcome combination.

#### Usage

```
createExposureOutcome(exposureId, outcomeId, ...)
```

#### **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

createSccsAnalysis function.

outcomeId A concept ID indentifying the outcome in the outcome table.

... Custom variables, to be used in the analyses.

#### **Details**

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

createFitSccsModelArgs

Create a parameter object for the function fitSccsModel

#### **Description**

Create a parameter object for the function fitSccsModel

### Usage

#### Arguments

prior The prior used to fit the model. See createPrior fordetails.

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

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

#### **Details**

Create an object defining the parameter values.

createGetDbSccsDataArgs

Create a parameter object for the function getDbSccsData

### Description

Create a parameter object for the function getDbSccsData

#### Usage

```
createGetDbSccsDataArgs(useCustomCovariates = FALSE,
  useNestingCohort = FALSE, nestingCohortId = NULL,
  deleteCovariatesSmallCount = 100, studyStartDate = "",
  studyEndDate = "", maxCasesPerOutcome = 0,
  exposureIds = "exposureId", customCovariateIds = "")
```

#### **Arguments**

useCustomCovariates

Create covariates from a custom table?

 ${\tt useNestingCohort}$ 

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.

nestingCohortId

A cohort definition ID identifying the records in thenestingCohortTable to use as nesting cohort.

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deleteCovariatesSmallCount

The minimum count for a covariate to appear in the data to bekept.

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 isused. Date format is

'yyyymmdd'.

maxCasesPerOutcome

If there are more than this number of cases for a singleoutcome cases will be sampled to this size. maxCasesPerOutcome = 0indicates no maximum size.

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 selectthe cohort\_concept\_id in the cohort-like table. If noexposureIds are provided, all drugs or cohorts in theexposureTable are included as

exposures.

customCovariateIds

A list of cohort definition IDS identifying the records in the customCovariateTable to use for building customcovariates.

#### **Details**

Create an object defining the parameter values.

createSccsAnalysis

Create a SelfControlledCaseSeries analysis specification

#### **Description**

Create a SelfControlledCaseSeries analysis specification

### Usage

```
createSccsAnalysis(analysisId = 1, description = "",
  exposureType = NULL, outcomeType = NULL, getDbSccsDataArgs,
  createSccsEraDataArgs, fitSccsModelArgs)
```

#### **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.

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

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

getDbSccsDataArgs

An object representing the arguments to be used when calling the getDbSccsData function.

createSccsEraDataArgs

An object representing the arguments to be used when calling the createSccsEraData function.

fitSccsModelArgs

An object representing the arguments to be used when calling the fitSccsModel function.

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#### **Details**

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

createSccsEraData

Create SCCS era data

#### **Description**

Create SCCS era data

### Usage

```
createSccsEraData(sccsData, outcomeId = NULL, naivePeriod = 0,
  firstOutcomeOnly = FALSE, covariateSettings,
  ageSettings = createAgeSettings(includeAge = FALSE),
  seasonalitySettings = createSeasonalitySettings(includeSeasonality =
  FALSE), minCasesForAgeSeason = 10000,
  eventDependentObservation = FALSE)
```

### **Arguments**

sccsData An object of type sccsData as created using the getDbSccsData function.

outcomeId The outcome to create the era data for. If not specified it is assumed to be the

one outcome for which the data was loaded from the database.

naivePeriod The number of days at the start of a patient's observation period that should not

be included in the risk calculations. Note that the naive period can be used to determine current covariate status right after the naive period, and whether an

outcome is the first one.

firstOutcomeOnly

Whether only the first occurrence of an outcome should be considered.

covariateSettings

Either an object of type covariateSettings as created using the createCovariateSettings

function, or a list of such objects.

ageSettings An object of type ageSettings as created using the createAgeSettings func-

tion.

seasonalitySettings

An object of type seasonalitySettings as created using the createSeasonalitySettings

function.

 ${\tt minCasesForAgeSeason}$ 

Minimum number of cases to use to fit age and season splines. IF needed (and

available), cases that are not exposed will be included.#'

eventDependentObservation

Should the extension proposed by Farrington et al. be used to adjust for event-

dependent observation time?

### Details

This function creates covariates based on the data in the sccsData object, according to the provided settings. It chops patient time into periods during which all covariates remain constant. The output details these periods, their durations, and a sparse representation of the covariate values.

#### Value

An object of type sccsEraData.

#### References

Farrington, C. P., Anaya-Izquierdo, A., Whitaker, H. J., Hocine, M.N., Douglas, I., and Smeeth, L. (2011). Self-Controlled case series analysis with event-dependent observation periods. Journal of the American Statistical Association 106 (494), 417-426

createSccsSimulationSettings

Create SCCS simulation settings

#### **Description**

Create SCCS simulation settings

### Usage

```
createSccsSimulationSettings(meanPatientTime = 4 * 365,
    sdPatientTime = 2 * 365, minAge = 18 * 365, maxAge = 65 * 365,
    minBaselineRate = 0.001, maxBaselineRate = 0.01,
    covariateIds = c(1, 2), patientUsages = c(0.2, 0.1),
    usageRate = c(0.01, 0.01), meanPrescriptionDurations = c(14, 30),
    sdPrescriptionDurations = c(7, 14),
    simulationRiskWindows = list(createSimulationRiskWindow(relativeRisks = 1), createSimulationRiskWindow(relativeRisks = 1),
    includeAgeEffect = TRUE, ageKnots = 5, includeSeasonality = TRUE,
    seasonKnots = 5, outcomeId = 10)
```

#### **Arguments**

meanPatientTime

Mean number of observation days per patient.

sdPatientTime Standard deviation of the observation days per patient.

minAge The minimum age in days.

maxAge The maximum age in days.

minBaselineRate

The minimum baseline rate (per day).

maxBaselineRate

The maximum baseline rate (per day).

covariateIds The IDs for the covariates to be generated.

patientUsages The fraction of patients that use the drugs.

usageRate The rate of prescriptions per person that uses the drug.

 ${\it mean Prescription Durations}$ 

The mean duration of a prescription, per drug.

sdPrescriptionDurations

The standard deviation of the duration of a prescription, per drug.

simulationRiskWindows

One or a list of objects of type simulationRiskWindow as created using the createSimulationRiskWindow function.

includeAgeEffect

Include an age effect for the outcome?

ageKnots Number of knots in the age spline.

includeSeasonality

Include seasonality for the outcome?

seasonKnots Number of knots in the seasonality spline.

outcomeId The ID to be used for the outcome.

#### **Details**

Create an object of settings for an SCCS simulation.

#### Value

An object of type sccsSimulationSettings.

createSeasonalitySettings

Create seasonality settings

### Description

Create seasonality settings

#### Usage

```
createSeasonalitySettings(includeSeasonality = FALSE, seasonKnots = 5,
   allowRegularization = FALSE, computeConfidenceIntervals = FALSE)
```

### **Arguments**

includeSeasonality

Should seasonlaity be included in the model?

seasonKnots

If a single number is provided this is assumed to indicate the number of knots to use for the spline, and the knots are automatically equaly spaced across the year. If more than one number is provided these are assumed to be the exact location of the knots in days relative to the start of the year.

 ${\it allow} Regularization$ 

When fitting the model, should the covariates defined here be allowed to be regularized?

computeConfidenceIntervals

Should confidence intervals be computed for the covariates defined here? Setting this to FALSE might save computing time when fitting the model. Will be turned to FALSE automatically when allowRegularization = TRUE.

#### **Details**

Create an object specifing whether and how seasonality should be included in the model. Seasonality can be included by splitting patient time into calendar months. During a month, the relative risk attributed to season is assumed to be constant, and the risk from month to month is modeled using a cyclic cubic spline.

#### Value

An object of type seasonalitySettings.

createSimulationRiskWindow

Create a risk window definition for simulation

### **Description**

Create a risk window definition for simulation

#### Usage

```
createSimulationRiskWindow(start = 0, end = 0,
  addExposedDaysToEnd = TRUE, splitPoints = c(),
  relativeRisks = c(0))
```

### **Arguments**

start Start of the risk window relative to exposure start.

end End of risk window relative to exposure start, or if addExposedDaysToEnd is

TRUE, relative to the end date.

 $add {\sf ExposedDaysToEnd}$ 

Should the length of exposure be added to the end date? In other words, should the exposure end date be used as reference point for the risk window end?

splitPoints Subdivision of the risk window in to smaller sub-windows.

relativeRisks Either a single number representing the relative risk in the risk window, or when

splitPoints have been defined a vector of relative risks, one for each sub-window.

#### Value

An object of type simulationRiskWindow.

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cyclicSplineDesign Create a design matrix for a cyclic spline	
---------------------------------------------------------------	--

### **Description**

Create a design matrix for a cyclic spline

#### Usage

```
cyclicSplineDesign(x, knots, ord = 4)
```

#### **Arguments**

x Vector of coordinates of the points to be interpolated.

knots Location of the knots.

ord Order of the spline function.

#### **Details**

This function is used by other functions in this package.

fitSccsModel	Fit the SCCS model	

### **Description**

Fit the SCCS model

### Usage

```
fitSccsModel(sccsEraData, prior = createPrior("laplace",
  useCrossValidation = TRUE), control = createControl(cvType = "auto",
  selectorType = "byPid", startingVariance = 0.1, noiseLevel = "quiet"))
```

### Arguments

sccsEraData An object of type sccsEraData as created using the createSccsEraData func-

tion.

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**

Fits the SCCS model as a conditional Poisson regression. When allowed, coefficients for some or all covariates can be regularized.

#### Value

An object of type sccsModel. Generic functions summary, coef, and confint are available.

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#### References

Suchard, M.A., Simpson, S.E., Zorych, I., Ryan, P., and Madigan, D. (2013). Massive parallelization of serial inference algorithms for complex generalized linear models. ACM Transactions on Modeling and Computer Simulation 23, 10

forceSccsEraDataIntoRam

Force a loaded SCCS era data in RAM

#### **Description**

 $force Sccs EraData Into Ram\ converts\ the\ ffdf\ components\ of\ an\ sccs EraData\ object\ into\ data. table\ components$ 

#### Usage

```
forceSccsEraDataIntoRam(sccsEraData)
```

#### **Arguments**

sccsEraData Exisiting sccsEraData object.

#### **Details**

Uses ff::as.ram() to move virtual data into data.table objects

#### Value

An object of class sccsEraData

getDbSccsData

Load data for SCCS from the database

### **Description**

Load all data needed to perform an SCCS analysis from the database.

### Usage

```
getDbSccsData(connectionDetails, cdmDatabaseSchema,
  oracleTempSchema = cdmDatabaseSchema,
  outcomeDatabaseSchema = cdmDatabaseSchema,
  outcomeTable = "condition_era", outcomeIds,
  exposureDatabaseSchema = cdmDatabaseSchema,
  exposureTable = "drug_era", exposureIds = c(),
  useCustomCovariates = FALSE,
  customCovariateDatabaseSchema = cdmDatabaseSchema,
  customCovariateTable = "cohort", customCovariateIds = c(),
  useNestingCohort = FALSE,
  nestingCohortDatabaseSchema = cdmDatabaseSchema,
```

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```
nestingCohortTable = "cohort", nestingCohortId = NULL,
deleteCovariatesSmallCount = 100, studyStartDate = "",
studyEndDate = "", cdmVersion = "5", maxCasesPerOutcome = 0)
```

#### **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 CON-DITION\_OCCURRENCE or CONDITION\_ERA, then expectation is outcomeTable has format of COHORT table: COHORT\_DEFINITION\_ID, SUBJECT\_ID, COHORT\_START\_DATE, COHORT\_END\_DATE.

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.

exposureDatabaseSchema

outcomeIds

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.

useCustomCovariates

Create covariates from a custom table?

customCovariateDatabaseSchema

The name of the database schema that is the location where the custom covariate data is available.

customCovariateTable

Name of the table holding the custom covariates. This table should have the same structure as the cohort table.

customCovariateIds

A list of cohort definition IDS identifying the records in the customCovariateTable to use for building custom covariates.

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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.

 ${\tt nestingCohortDatabaseSchema}$ 

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.

deleteCovariatesSmallCount

The minimum count for a covariate to appear in the data to be kept.

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'.

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

maxCasesPerOutcome

If there are more than this number of cases for a single outcome cases will be sampled to this size. maxCasesPerOutcome = 0 indicates no maximum size.

#### Details

This function downloads several types of information:

- Information on the occurrences of the outcome(s) of interest. Note that information for multiple outcomes can be fetched in one go, and later the specific outcome can be specified for which we want to build a model.
- Information on the observation time and age for the people with the outcomes.
- Information on exposures of interest which we want to include in the model.

Five different database schemas can be specified, for five different types of information: The cdmDatabaseSchema is used to extract patient age and observation period. The outcomeDatabaseSchema is used to extract information about the outcomes, the exposureDatabaseSchema is used to retrieve information on exposures, and the customCovariateDatabaseSchema is optionally used to find additional, user-defined covariates. All four locations could point to the same database schema. nestingCohortDatabaseSchema is optionally used to define a cohort in which the analysis is nested, for example a cohort of diabetics patients.

All five locations could point to the same database schema.

#### Value

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

cases An ffdf object listing the persons that have the outcome(s), their age, and observation time.

eras An ffdf object listing the exposures, outcomes and other covariates.

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

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

The generic summary() function has been implemented for this object.

getModel

Output the full model

### **Description**

Output the full model

### Usage

```
getModel(sccsModel)
```

### **Arguments**

sccsModel

An object of type sccsModel as created using the fitSccsModel function.

#### Value

A data frame with the coefficients and confidence intervals (when not-regularized) for all covariates in the model.

loadExposureOutcomeList

Load a list of exposureOutcome from file

### Description

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

### Usage

loadExposureOutcomeList(file)

### **Arguments**

file

The name of the file

### Value

A list of objects of type exposureOutcome.

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loadSccsAnalysisList Load a list of sccsAnalysis from file

### Description

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

### Usage

```
loadSccsAnalysisList(file)
```

### **Arguments**

file

The name of the file

### Value

A list of objects of type sccsAnalysis.

loadSccsData

Load the SCCS data from a folder

### Description

loadSccsData loads an object of type sccsData from a folder in the file system.

### Usage

```
loadSccsData(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 cohortData.

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### **Description**

loadSccsEraData loads an object of type sccsEraData from a folder in the file system.

#### Usage

```
loadSccsEraData(folder, readOnly = FALSE)
```

### **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 sccsEraData

plotAgeEffect	Plot the age effect

### Description

Plot the age effect

### Usage

```
plotAgeEffect(sccsModel, rrLim = c(0.1, 10), fileName = NULL)
```

### **Arguments**

sccsModel An object of type sccsModel as created using the fitSccsModel function.

rrLim The limits on the incidence rate ratio scale in 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 spline curve of the age effect.

#### Value

20 plotAgeSpans

plotAgeSpans	Plot the age ranges spanned by each observation period.	

### **Description**

Plot the age ranges spanned by each observation period.

### Usage

```
plotAgeSpans(sccsData, outcomeId = NULL, firstOutcomeOnly = FALSE,
    naivePeriod = 0, minAge = NULL, maxAge = NULL, fileName = NULL)
```

#### **Arguments**

sccsData	An object of type sccsData as created using the getDbSccsData function.
outcomeId	The outcome to create the era data for. If not specified it is assumed to be the
	one outcome for which the data was loaded from the database.

firstOutcomeOnly

Whether only the first occurrence of an outcome should be considered.

naivePeriod The number of days at the start of a patient's observation period that should not

be included in the risk calculations. Note that the naive period can be used to determine current covariate status right after the naive period, and whether an

outcome is the first one.

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.

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**

If parameters such as naivePeriod, minAge, and maxAge are provided, these will first be applied to curtail the observation period prior to plotting. Similarly, firstOutcomeOnly can be provided so subjects where the first outcome falls before the true observation start are removed before plotting.

#### Value

plotEventObservationDependence

Plot time from event to observation end for censored and uncensored time.

#### **Description**

Plot time from event to observation end for censored and uncensored time.

#### Usage

```
plotEventObservationDependence(sccsData, outcomeId = NULL,
    naivePeriod = 0, minAge = NULL, maxAge = NULL, fileName = NULL)
```

### **Arguments**

~	,	
	sccsData	An object of type sccsData as created using the getDbSccsData function.
	outcomeId	The outcome to create the era data for. If not specified it is assumed to be the one outcome for which the data was loaded from the database.
	naivePeriod	The number of days at the start of a patient's observation period that should not be included in the risk calculations. Note that the naive period can be used to determine current covariate status right after the naive period, and whether an outcome is the first one.
	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.
	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**

This plot shows whether there is a difference in time between (first) event and the observation period end for periods that are 'censored' and those that are 'uncensored'. By 'censored' we mean periods that end before we would normally expect. Here, we define periods to be uncensored if they end at either the study end date (if specified), database end date (i.e. the date after which no data is captured in the database), or maximum age (if specified). All other periods are assumed to be censored.

As proposed by Farrington et al., by comparing the two plots, we can gain some insight into whether the censoring is dependend on the occurrence of the event.

If parameters such as naivePeriod, minAge, and maxAge are provided, these will first be applied to curtail the observation period prior to plotting. Similarly, firstOutcomeOnly can be provided so subjects where the first outcome falls before the true observation start are removed before plotting.

#### Value

A Ggplot object. Use the ggsave function to save to file.

### References

Farrington P, Whitaker H, Ghebremichael Weldeselassie Y (2018), Self-controlled case series studies: A modelling guide with R, Taylor & Francis

```
plotEventToCalendarTime
```

Plot the count of events over calendar time.

### Description

Plot the count of events over calendar time.

### Usage

```
plotEventToCalendarTime(sccsData, outcomeId = NULL, naivePeriod = 0,
    minAge = NULL, maxAge = NULL, fileName = NULL)
```

### **Arguments**

sccsData	An object of type sccsData as created using the getDbSccsData function.
outcomeId	The outcome to create the era data for. If not specified it is assumed to be the one outcome for which the data was loaded from the database.
naivePeriod	The number of days at the start of a patient's observation period that should not be included in the risk calculations. Note that the naive period can be used to determine current covariate status right after the naive period, and whether an outcome is the first one.
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.
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

plotExposureCentered Plot information centered around the start of exposure

#### **Description**

Plot information centered around the start of exposure

### Usage

```
plotExposureCentered(sccsData, outcomeId = NULL, exposureId = NULL,
  naivePeriod = 0, firstOutcomeOnly = FALSE, minAge = NULL,
  maxAge = NULL, fileName = NULL)
```

#### **Arguments**

minAge

sccsData	An object of type sccsData as created using the getDbSccsData function.
outcomeId	The outcome to create the era data for. If not specified it is assumed to be the one outcome for which the data was loaded from the database.
exposureId	The exposure to create the era data for. If not specified it is assumed to be the one exposure for which the data was loaded from the database.
naivePeriod	The number of days at the start of a patient's observation period that should not be included in the risk calculations. Note that the naive period can be used to determine current covariate status right after the naive period, and whether an outcome is the first one.
firstOutcomeOn	ly

Whether only the first occurrence of an outcome should be considered.

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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.

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**

This plot shows the number of events and the number of subjects under observation in week-sized intervals relative to the start of the first exposure.

If parameters such as naivePeriod, minAge, and maxAge are provided, these will first be applied to curtail the observation period prior to plotting. Similarly, firstOutcomeOnly can be provided so subjects where the first outcome falls before the true observation start are removed before plotting.

#### Value

24 plotPerPersonData

plotPerPersonData	Plot exposures and outcomes per person

### **Description**

Plot exposures and outcomes per person

#### Usage

```
plotPerPersonData(sccsData, outcomeId = NULL, exposureId = NULL,
  naivePeriod = 0, firstOutcomeOnly = FALSE, minAge = NULL,
  maxAge = NULL, fileName = NULL)
```

#### **Arguments**

sccsData	An object of type sccsData as created using the getDbSccsData function.
outcomeId	The outcome to create the era data for. If not specified it is assumed to be the one outcome for which the data was loaded from the database.
exposureId	The exposure to create the era data for. If not specified it is assumed to be the one exposure for which the data was loaded from the database.
naivePeriod	The number of days at the start of a patient's observation period that should not be included in the risk calculations. Note that the naive period can be used to determine current covariate status right after the naive period, and whether an outcome is the first one.

#### firstOutcomeOnly

minAge

Whether only the first occurrence of an outcome should be considered.

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.

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**

This plot shows the observation time (black), exposures (red), and outcomes (yellow) per person.

If parameters such as naivePeriod, minAge, and maxAge are provided, these will first be applied to curtail the observation period prior to plotting. Similarly, firstOutcomeOnly can be provided so subjects where the first outcome falls before the true observation start are removed before plotting.

### Value

plotSeasonality 25

plotSeasonality	Pi
protocasonarity	1 (

Plot the seasonality effect

#### **Description**

Plot the seasonality effect

#### Usage

```
plotSeasonality(sccsModel, rrLim = c(0.1, 10), fileName = NULL)
```

#### **Arguments**

sccsModel An object of type sccsModel as created using the fitSccsModel function.

rrLim The limits on the incidence rate ratio scale in 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 spline curve of the seasonality effect.

#### Value

A Ggplot object. Use the ggsave function to save to file.

runSccsAnalyses

Run a list of analyses

### Description

Run a list of analyses

### Usage

```
runSccsAnalyses(connectionDetails, cdmDatabaseSchema,
  oracleTempSchema = cdmDatabaseSchema,
  exposureDatabaseSchema = cdmDatabaseSchema,
  exposureTable = "drug_era",
  outcomeDatabaseSchema = cdmDatabaseSchema,
  outcomeTable = "condition_era",
  customCovariateDatabaseSchema = cdmDatabaseSchema,
  customCovariateTable = "cohort",
  nestingCohortDatabaseSchema = cdmDatabaseSchema,
  nestingCohortTable = "cohort", cdmVersion = 5,
  outputFolder = "./SccsOutput", sccsAnalysisList, exposureOutcomeList,
  combineDataFetchAcrossOutcomes = TRUE,
  compressSccsEraDataFiles = FALSE, getDbSccsDataThreads = 1,
  createSccsEraDataThreads = 1, fitSccsModelThreads = 1,
  cvThreads = 1)
```

26 runSccsAnalyses

#### **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 specifiy 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 exposure Table = 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 exposure Table <> DRUG\_ERA, then expectation is exposure Table 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 outcome Table = CONDITION\_ERA, outcomeDatabaseSchema is not used. Requires read permissions to this database.

outcomeTable

The tablename that contains the outcome cohorts. If outcome Table is not CON-DITION\_OCCURRENCE or CONDITION\_ERA, then expectation is outcomeTable has format of COHORT table: COHORT\_DEFINITION\_ID, SUBJECT\_ID, COHORT\_START\_DATE, COHORT\_END\_DATE.

### $\verb|customCovariateDatabaseSchema| \\$

The name of the database schema that is the location where the custom covariate data is available.

#### customCovariateTable

Name of the table holding the custom covariates. This table should have the same structure as the cohort table.

#### 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.

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

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

### sccsAnalysisList

A list of objects of type sccsAnalysis as created using the createSccsAnalysis function.

#### exposureOutcomeList

A list of objects of type exposureOutcome as created using the createExposureOutcome function.

### combineDataFetchAcrossOutcomes

Should fetching data from the database be done one outcome at a time, or for all outcomes in one fetch? Combining fetches will be more efficient if there is large overlap in the subjects that have the different outcomes.

compressSccsEraDataFiles

Should compression be used when saving? IF TRUE, the zip program needs to be available on the command prompt.

 ${\tt getDbSccsDataThreads}$ 

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

createSccsEraDataThreads

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

fitSccsModelThreads

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

cvThreads 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 'fitSccsModelThreads \* cvThreads'.

#### **Details**

Run a list of analyses for the drug-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(drugComparatorOutcomesList)' (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.

exposureId The ID of the target drug. outcomeId The ID of the outcome.

sccsDataFolder The folder where the sccsData object is stored.
sccsEraDataFolder The folder where the sccsEraData object is stored.
sccsModelFile The file where the fitted SCCS model is stored.

save Exposure Outcome List

Save a list of exposureOutcome to file

### Description

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

### Usage

saveExposureOutcomeList(exposureOutcomeList, file)

28 saveSccsData

#### **Arguments**

exposureOutcomeList

The exposureOutcome list to be written to file

The name of the file where the results will be written

saveSccsAnalysisList Save a list of sccsAnalysis to file

### **Description**

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

### Usage

```
saveSccsAnalysisList(sccsAnalysisList, file)
```

### **Arguments**

sccsAnalysisList

The sccsAnalysis list to be written to file

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

saveSccsData Save the SCCS data to folder

#### **Description**

sccsData saves an object of type sccsData to folder.

### Usage

```
saveSccsData(sccsData, folder)
```

### Arguments

sccsData An object of type sccsData as generated using getDbSccsData.

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.

#### **Examples**

# todo

saveSccsEraData 29

saveSccsEraData Save the SCCS era data to folder

### **Description**

saveSccsEraData saves an object of type sccsEraData to folder.

### Usage

```
saveSccsEraData(sccsEraData, folder, compress = FALSE)
```

### **Arguments**

sccsEraData An object of type sccsEraData as generated using createSccsEraData.

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

exist.

compress Should compression be used when saving?

### **Details**

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

SelfControlledCaseSeries

Self Controlled Case Series

### Description

SelfControlledCaseSeries

simulateSccsData Simulate SCCS data

### **Description**

Simulate SCCS data

### Usage

simulateSccsData(nCases, settings)

### **Arguments**

nCases The number of cases to simulate.

 $Settings \hspace{1cm} \textbf{An object of type sccsSimulationSettings as created using the } \hspace{0.1cm} \textbf{createSccsSimulationSettings} \\$ 

#### Value

An object of type sccsData.

summarizeSccsAnalyses Create a summary report of the analyses

### **Description**

Create a summary report of the analyses

#### Usage

summarizeSccsAnalyses(outcomeReference, outputFolder)

#### **Arguments**

outcomeReference

A data.frame as created by the runSccsAnalyses function.

outputFolder Name of the folder where all the outputs have been written to.

#### 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.

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

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

The number of outcomes in the treated 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.

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