# Package 'AdhereR'

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Title Adherence to Medications

Version 0.8.1

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Description Computation of adherence to medications from Electronic Health care
 Data and visualization of individual medication histories and adherence
 patterns. The package implements a set of S3 classes and
 functions consistent with current adherence guidelines and definitions.

Type Package

functions consistent with current adherence guidelines and definitions. It allows the computation of different measures of adherence (as defined in the literature, but also several original ones), their publication-quality plotting, the estimation of event duration and time to initiation, the interactive exploration of patient medication history and the real-time estimation of adherence given various parameter settings. It scales from very small datasets stored in flat CSV files to very large databases and from single-thread processing on mid-range consumer laptops to parallel processing on large heterogeneous computing clusters. It exposes a standardized interface allowing it to be used from other programming languages and platforms, such as Python.

```
URL https://github.com/ddediu/AdhereR
License GPL (>= 2)
LazyData TRUE
Imports lubridate (>= 1.5), parallel (>= 3.0), data.table (>= 1.9),
    rsvg (>= 1.3), jpeg (>= 0.1), png (>= 0.1), webp (>= 1.0),
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# Description

The function encapsulating all the logics that allows AdhereR to be called from any platform using the generic shell mechanism.

## Usage

callAdhereR(shared.data.directory)

## **Arguments**

shared.data.directory

A *string* containing the path to the directory where all the exchanged (shared) data (both input and output) is. AdhereR needs read and write access to this directory.

## **Details**

In most cases this should not be done directly by the user, but instead used by an appropriate wrapper on the client platform. It allows transparent use of AdhereR from virtually any platform or programming language for which an appropriate wrapper is provided. For more details see the vignette describing the included reference Python 3 wrapper.

## Value

This function displays any messages to the console, tries to also write them to the Adherer-results.txt file in the shared.data.directory directory, and, when finished, forces R to quit with a given shell error code:

- 0 The processing ended without major errors;
- 1 General error (hopefully there are messages in the Adherer-results.txt file;
- 10 The directory shared.data.directory does not exit;
- 11 AdhereR does not have read access to the shared.data.directory directory;
- 12 AdhereR does not have write access to the shared.data.directory directory;
- 13 issues with the parameters file parameters.log;
- 14 issues with the data file dataset.csv;

- 15 plotting issues;
- 16 interactive plotting issues;
- 17 issues exporting the results.

CMA0

CMA0 constructor.

# **Description**

Constructs a basic CMA (continuous multiple-interval measures of medication availability/gaps) object.

# Usage

```
CMA0(
  data = NULL,
  ID.colname = NA,
  event.date.colname = NA,
  event.duration.colname = NA,
  event.daily.dose.colname = NA,
  medication.class.colname = NA,
  medication.groups = NULL,
  flatten.medication.groups = FALSE,
  medication.groups.colname = ".MED_GROUP_ID",
  carryover.within.obs.window = NA,
  carryover.into.obs.window = NA,
  carry.only.for.same.medication = NA,
  consider.dosage.change = NA,
  followup.window.start = 0,
  followup.window.start.unit = c("days", "weeks", "months", "years")[1],
  followup.window.start.per.medication.group = FALSE,
  followup.window.duration = 365 * 2,
  followup.window.duration.unit = c("days", "weeks", "months", "years")[1],
  observation.window.start = 0,
  observation.window.start.unit = c("days", "weeks", "months", "years")[1],
  observation.window.duration = 365 * 2,
  observation.window.duration.unit = c("days", "weeks", "months", "years")[1],
  date.format = "%m/%d/%Y",
  summary = "Base CMA object",
  suppress.warnings = FALSE,
  suppress.special.argument.checks = FALSE,
  arguments.that.should.not.be.defined = NULL,
)
```

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## **Arguments**

data

A data.frame containing the medication events (prescribing or dispensing) used to compute the CMA. Must contain, at a minimum, the patient unique ID, the event date and duration, and might also contain the daily dosage and medication type (the actual column names are defined in the following four parameters).

ID.colname

A *string*, the name of the column in data containing the unique patient ID, or NA if not defined.

event.date.colname

A *string*, the name of the column in data containing the start date of the event (in the format given in the date. format parameter), or NA if not defined.

event.duration.colname

A *string*, the name of the column in data containing the event duration (in days), or NA if not defined.

event.daily.dose.colname

A *string*, the name of the column in data containing the prescribed daily dose, or NA if not defined.

medication.class.colname

A *string*, the name of the column in data containing the classes/types/groups of medication, or NA if not defined.

medication.groups

A *vector* of characters defining medication groups or the name of a column in data that defines such groups. The names of the vector are the medication group unique names, while the content defines them as logical expressions. While the names can be any string of characters except "}", it is recommended to stick to the rules for defining vector names in R. For example,  $c("A"="CATEGORY == 'medA'", "AA"="{A} & PERDAY < 4" defines two medication groups: A which selects all events of type "medA", and B which selects all events already defined by "A" but with a daily dose lower than 4. If NULL, no medication groups are defined. If medication groups are defined, there is one CMA estimate for each group; moreover, there is a special group <math>\_ALL\_OTHERS\_$  automatically defined containing all observations *not* covered by any of the explicitly defined groups.

flatten.medication.groups

Logical, if FALSE (the default) then the CMA and event.info components of the object are lists with one medication group per element; otherwise, they are data.frames with an extra column containing the medication group (its name is given by medication.groups.colname).

medication.groups.colname

a *string* (defaults to ".MED\_GROUP\_ID") giving the name of the column storing the group name when flatten.medication.groups is TRUE.

carryover.within.obs.window

Logical, if TRUE consider the carry-over within the observation window, or NA if not defined.

carryover.into.obs.window

*Logical*, if TRUE consider the carry-over from before the starting date of the observation window, or NA if not defined.

carry.only.for.same.medication

*Logical*, if TRUE the carry-over applies only across medications of the same type, or NA if not defined.

consider.dosage.change

Logical, if TRUE the carry-over is adjusted to reflect changes in dosage, or NA if not defined.

followup.window.start

If a Date object, it represents the actual start date of the follow-up window; if a *string* it is the name of the column in data containing the start date of the follow-up window either as the numbers of followup.window.start.unit units after the first event (the column must be of type numeric) or as actual dates (in which case the column must be of type Date or a string that conforms to the format specified in date.format); if a *number* it is the number of time units defined in the followup.window.start.unit parameter after the begin of the participant's first event; or NA if not defined.

followup.window.start.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.start refers to (when a number), or NA if not defined.

followup.window.start.per.medication.group

a *logical*: if there are medication groups defined and this is TRUE, then the first event considered for the follow-up window start is relative to each medication group separately, otherwise (the default) it is relative to the patient.

followup.window.duration

either a *number* representing the duration of the follow-up window in the time units given in followup.window.duration.unit, or a *string* giving the column containing these numbers. Should represent a period for which relevant medication events are recorded accurately (e.g. not extend after end of relevant treatment, loss-to-follow-up or change to a health care provider not covered by the database).

followup.window.duration.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.duration refers to, or NA if not defined.

observation.window.start, observation.window.start.unit, observation.window.duration, observation.window.the definition of the observation window (see the follow-up window parameters above for details).

date.format A *string* giving the format of the dates used in the data and the other parameters; see the format parameters of the as.Date function for details (NB, this concerns only the dates given as strings and not as Date objects).

summary Metadata as a *string*, briefly describing this CMA.

suppress.warnings

*Logical*, if TRUE don't show any warnings.

suppress.special.argument.checks

*Logical* parameter for internal use; if FALSE (default) check if the important columns in the data have some of the reserved names, if TRUE this check is not performed.

arguments.that.should.not.be.defined

a *list* of argument names and pre-defined values for which a warning should be thrown if passed to the function.

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... other possible parameters

## **Details**

In most cases this should not be done directly by the user, but it is used internally by the other CMAs.

#### Value

An S3 object of class CMA0 with the following fields:

- data The actual event (prescribing or dispensing) data, as given by the data parameter.
- ID. colname the name of the column in data containing the unique patient ID, as given by the ID. colname parameter.
- event.date.colname the name of the column in data containing the start date of the event (in the format given in the date.format parameter), as given by the event.date.colname parameter.
- event.duration.colname the name of the column in data containing the event duration (in days), as given by the event.duration.colname parameter.
- event.daily.dose.colname the name of the column in data containing the prescribed daily dose, as given by the event.daily.dose.colname parameter.
- medication.class.colname the name of the column in data containing the classes/types/groups of medication, as given by the medication.class.colname parameter.
- carryover.within.obs.window whether to consider the carry-over within the observation window, as given by the carryover.within.obs.window parameter.
- carryover.into.obs.window whether to consider the carry-over from before the starting date of the observation window, as given by the carryover.into.obs.window parameter.
- carry.only.for.same.medication whether the carry-over applies only across medication of the same type, as given by the carry.only.for.same.medication parameter.
- consider.dosage.change whether the carry-over is adjusted to reflect changes in dosage, as given by the consider.dosage.change parameter.
- followup.window.start the beginning of the follow-up window, as given by the followup.window.start parameter.
- followup.window.start.unit the time unit of the followup.window.start, as given by the followup.window.start.unit parameter.
- followup.window.duration the duration of the follow-up window, as given by the followup.window.duration parameter.
- followup.window.duration.unit the time unit of the followup.window.duration, as given by the followup.window.duration.unit parameter.
- observation.window.start the beginning of the observation window, as given by the observation.window.start parameter.
- observation.window.start.unit the time unit of the observation.window.start, as given by the observation.window.start.unit parameter.
- observation.window.duration the duration of the observation window, as given by the observation.window.duration parameter.

• observation.window.duration.unit the time unit of the observation.window.duration, as given by the observation.window.duration.unit parameter.

- date. format the format of the dates, as given by the date. format parameter.
- summary the metadata, as given by the summary parameter.

# **Examples**

```
cma0 <- CMA0(data=med.events,</pre>
             ID.colname="PATIENT_ID",
             event.date.colname="DATE",
             event.duration.colname="DURATION",
             event.daily.dose.colname="PERDAY",
             medication.class.colname="CATEGORY",
             followup.window.start=0,
             followup.window.start.unit="days",
             followup.window.duration=2*365,
             followup.window.duration.unit="days",
             observation.window.start=30,
             observation.window.start.unit="days",
             observation.window.duration=365,
             observation. \verb|window|.duration.unit="days"|,\\
             date.format="%m/%d/%Y",
             summary="Base CMA");
```

CMA1

CMA1 and CMA3 constructors.

# **Description**

Constructs a CMA (continuous multiple-interval measures of medication availability/gaps) type 1 or type 3 object.

# Usage

```
CMA1(
    data = NULL,
    ID.colname = NA,
    event.date.colname = NA,
    event.duration.colname = NA,
    medication.groups = NULL,
    flatten.medication.groups = FALSE,
    medication.groups.colname = ".MED_GROUP_ID",
    followup.window.start = 0,
    followup.window.start.unit = c("days", "weeks", "months", "years")[1],
    followup.window.start.per.medication.group = FALSE,
    followup.window.duration = 365 * 2,
    followup.window.duration.unit = c("days", "weeks", "months", "years")[1],
    observation.window.start = 0,
```

```
observation.window.start.unit = c("days", "weeks", "months", "years")[1],
  observation.window.duration = 365 * 2,
  observation.window.duration.unit = c("days", "weeks", "months", "years")[1],
  date.format = "%m/%d/%Y",
  summary = NA,
  event.interval.colname = "event.interval",
  gap.days.colname = "gap.days",
  force.NA.CMA.for.failed.patients = TRUE,
  parallel.backend = c("none", "multicore", "snow", "snow(SOCK)", "snow(MPI)",
    "snow(NWS)")[1],
  parallel.threads = "auto",
  suppress.warnings = FALSE,
  suppress.special.argument.checks = TRUE,
  arguments.that.should.not.be.defined = c(carryover.within.obs.window = FALSE,
    carryover.into.obs.window = FALSE, carry.only.for.same.medication = FALSE,
    consider.dosage.change = FALSE),
)
CMA3(
  data = NULL,
  ID.colname = NA,
  event.date.colname = NA,
  event.duration.colname = NA,
 medication.groups = NULL,
  flatten.medication.groups = FALSE,
 medication.groups.colname = ".MED_GROUP_ID",
  followup.window.start = 0,
  followup.window.start.unit = c("days", "weeks", "months", "years")[1],
  followup.window.start.per.medication.group = FALSE,
  followup.window.duration = 365 \times 2,
  followup.window.duration.unit = c("days", "weeks", "months", "years")[1],
  observation.window.start = 0,
  observation.window.start.unit = c("days", "weeks", "months", "years")[1],
  observation.window.duration = 365 * 2,
  observation.window.duration.unit = c("days", "weeks", "months", "years")[1],
  date.format = "%m/%d/%Y",
  summary = NA,
  event.interval.colname = "event.interval",
  gap.days.colname = "gap.days",
  force.NA.CMA.for.failed.patients = TRUE,
  parallel.backend = c("none", "multicore", "snow", "snow(SOCK)", "snow(MPI)",
    "snow(NWS)")[1],
  parallel.threads = "auto",
  suppress.warnings = FALSE,
  suppress.special.argument.checks = TRUE,
  arguments.that.should.not.be.defined = c(carryover.within.obs.window = FALSE,
    carryover.into.obs.window = FALSE, carry.only.for.same.medication = FALSE,
```

```
consider.dosage.change = FALSE),
...
)
```

## **Arguments**

data

A data.frame containing the events used to compute the CMA. Must contain, at a minimum, the patient unique ID, the event date and duration, and might also contain the daily dosage and medication type (the actual column names are defined in the following four parameters).

ID.colname

A *string*, the name of the column in data containing the unique patient ID; must be present.

event.date.colname

A *string*, the name of the column in data containing the start date of the event (in the format given in the date. format parameter); must be present.

event.duration.colname

A *string*, the name of the column in data containing the event duration (in days); must be present.

medication.groups

A *vector* of characters defining medication groups or the name of a column in data that defines such groups. The names of the vector are the medication group unique names, while the content defines them as logical expressions. While the names can be any string of characters except "}", it is recommended to stick to the rules for defining vector names in R. For example,  $c("A"="CATEGORY == 'medA'", "AA"="{A} & PERDAY < 4" defines two medication groups: A which selects all events of type "medA", and B which selects all events already defined by "A" but with a daily dose lower than 4. If NULL, no medication groups are defined. If medication groups are defined, there is one CMA estimate for each group; moreover, there is a special group <math>\_ALL\_OTHERS\_$  automatically defined containing all observations *not* covered by any of the explicitly defined groups.

flatten.medication.groups

Logical, if FALSE (the default) then the CMA and event.info components of the object are lists with one medication group per element; otherwise, they are data.frames with an extra column containing the medication group (its name is given by medication.groups.colname).

medication.groups.colname

a *string* (defaults to ".MED\_GROUP\_ID") giving the name of the column storing the group name when flatten.medication.groups is TRUE.

followup.window.start

If a Date object, it represents the actual start date of the follow-up window; if a *string* it is the name of the column in data containing the start date of the follow-up window either as the numbers of followup.window.start.unit units after the first event (the column must be of type numeric) or as actual dates (in which case the column must be of type Date or a string that conforms to the format specified in date.format); if a *number* it is the number of time units defined in the followup.window.start.unit parameter after the begin of the participant's first event; or NA if not defined.

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followup.window.start.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.start refers to (when a number), or NA if not defined.

followup.window.start.per.medication.group

a *logical*: if there are medication groups defined and this is TRUE, then the first event considered for the follow-up window start is relative to each medication group separately, otherwise (the default) it is relative to the patient.

followup.window.duration

either a *number* representing the duration of the follow-up window in the time units given in followup.window.duration.unit, or a *string* giving the column containing these numbers. Should represent a period for which relevant medication events are recorded accurately (e.g. not extend after end of relevant treatment, loss-to-follow-up or change to a health care provider not covered by the database).

followup.window.duration.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.duration refers to, or NA if not defined.

observation.window.start, observation.window.start.unit, observation.window.duration, observation.wir the definition of the observation window (see the follow-up window parameters above for details).

date.format

A *string* giving the format of the dates used in the data and the other parameters; see the format parameters of the as. Date function for details (NB, this concerns only the dates given as strings and not as Date objects).

summary

Metadata as a *string*, briefly describing this CMA.

event.interval.colname

A *string*, the name of a newly-created column storing the number of days between the start of the current event and the start of the next one; the default value "event.interval" should be changed only if there is a naming conflict with a pre-existing "event.interval" column in event.info.

gap.days.colname

A *string*, the name of a newly-created column storing the number of days when medication was not available (i.e., the "gap days"); the default value "gap.days" should be changed only if there is a naming conflict with a pre-existing "gap.days" column in event.info.

force.NA.CMA.for.failed.patients

Logical describing how the patients for which the CMA estimation fails are treated: if TRUE they are returned with an NA CMA estimate, while for FALSE they are omitted.

parallel.backend

Can be "none" (the default) for single-threaded execution, "multicore" (using mclapply in package parallel) for multicore processing (NB. not currently implemented on MS Windows and automatically falls back on "snow" on this platform), or "snow", "snow(SOCK)" (equivalent to "snow"), "snow(MPI)" or "snow(NWS)" specifying various types of SNOW clusters (can be on the local machine or more complex setups – please see the documentation of package snow for details; the last two require packages Rmpi and nws, respectively, not automatically installed with AdhereR).

parallel.threads

Can be "auto" (for parallel.backend == "multicore", defaults to the number of cores in the system as given by options("cores"), while for parallel.backend == "snow", defaults to 2), a strictly positive integer specifying the number of parallel threads, or a more complex specification of the SNOW cluster nodes for parallel.backend == "snow" (see the documentation of package snow for details).

suppress.warnings

Logical, if TRUE don't show any warnings.

suppress.special.argument.checks

*Logical* parameter for internal use; if FALSE (default) check if the important columns in the data have some of the reserved names, if TRUE this check is not performed.

arguments.that.should.not.be.defined

a *list* of argument names and pre-defined values for which a warning should be thrown if passed to the function.

... other possible parameters

#### **Details**

CMA1 considers the total number of days with medication supplied in all medication events in the observation window, excluding the last event. CMA3 is identical to CMA1 except that it is capped at 100%.

The formula is

(number of days supply excluding last)/(first to last event)

Thus, the durations of all events are added up, possibly resulting in an CMA estimate (much) bigger than 1.0 (100%).

CMA2 and CMA1 differ in the inclusion or not of the last event.

## Value

An S3 object of class CMA1 (derived from CMA0) with the following fields:

- data The actual event data, as given by the data parameter.
- ID. colname the name of the column in data containing the unique patient ID, as given by the ID. colname parameter.
- event.date.colname the name of the column in data containing the start date of the event (in the format given in the date.format parameter), as given by the event.date.colname parameter.
- event.duration.colname the name of the column in data containing the event duration (in days), as given by the event.duration.colname parameter.
- event.daily.dose.colname the name of the column in data containing the prescribed daily dose, as given by the event.daily.dose.colname parameter.
- medication.class.colname the name of the column in data containing the classes/types/groups of medication, as given by the medication.class.colname parameter.

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• followup.window.start the beginning of the follow-up window, as given by the followup.window.start parameter.

- followup.window.start.unit the time unit of the followup.window.start, as given by the followup.window.start.unit parameter.
- followup.window.duration the duration of the follow-up window, as given by the followup.window.duration parameter.
- followup.window.duration.unit the time unit of the followup.window.duration, as given by the followup.window.duration.unit parameter.
- observation.window.start the beginning of the observation window, as given by the observation.window.start parameter.
- observation.window.start.unit the time unit of the observation.window.start, as given by the observation.window.start.unit parameter.
- observation.window.duration the duration of the observation window, as given by the observation.window.duration parameter.
- observation.window.duration.unit the time unit of the observation.window.duration, as given by the observation.window.duration.unit parameter.
- date. format the format of the dates, as given by the date. format parameter.
- summary the metadata, as given by the summary parameter.
- event.info the data.frame containing the event info (irrelevant for most users; see compute.event.int.gaps for details).
- CMA the data. frame containing the actual CMA estimates for each participant (the ID. colname column).

Please note that if medication.groups are defined and flatten.medication.groups is FALSE, then the CMA and event.info are named lists, each element containing the CMA and event.info corresponding to a single medication group (the element's name), but if flatten.medication.groups is FALSE then they are data.frames with an extra column giving the medication group (the column's name is given by medication.groups.colname).

## See Also

CMAs 1 to 8 are described in:

Vollmer, W. M., Xu, M., Feldstein, A., Smith, D., Waterbury, A., & Rand, C. (2012). Comparison of pharmacy-based measures of medication adherence. *BMC Health Services Research*, **12**, 155. doi: 10.1186/1472696312155.

## **Examples**

CMA2

CMA2 and CMA4 constructors.

# **Description**

Constructs a CMA (continuous multiple-interval measures of medication availability/gaps) type 2 or type 4 object.

# Usage

```
CMA2(
  data = NULL,
  ID.colname = NA,
  event.date.colname = NA,
  event.duration.colname = NA,
  medication.groups = NULL,
  flatten.medication.groups = FALSE,
  medication.groups.colname = ".MED_GROUP_ID",
  followup.window.start = 0,
  followup.window.start.unit = c("days", "weeks", "months", "years")[1],
  followup.window.start.per.medication.group = FALSE,
  followup.window.duration = 365 * 2,
  followup.window.duration.unit = c("days", "weeks", "months", "years")[1],
  observation.window.start = 0,
  observation.window.start.unit = c("days", "weeks", "months", "years")[1],
  observation.window.duration = 365 * 2,
  observation.window.duration.unit = c("days", "weeks", "months", "years")[1],
  date.format = "%m/%d/%Y",
  summary = NA,
  event.interval.colname = "event.interval",
  gap.days.colname = "gap.days",
  force.NA.CMA.for.failed.patients = TRUE,
  parallel.backend = c("none", "multicore", "snow", "snow(SOCK)", "snow(MPI)",
    "snow(NWS)")[1],
  parallel.threads = "auto",
  suppress.warnings = FALSE,
  suppress.special.argument.checks = TRUE,
```

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arguments.that.should.not.be.defined = c(carryover.within.obs.window = FALSE,

```
carryover.into.obs.window = FALSE, carry.only.for.same.medication = FALSE,
    consider.dosage.change = FALSE),
)
CMA4(
  data = NULL,
  ID.colname = NA.
  event.date.colname = NA,
  event.duration.colname = NA,
 medication.groups = NULL,
  flatten.medication.groups = FALSE,
  medication.groups.colname = ".MED_GROUP_ID",
  followup.window.start = 0,
  followup.window.start.unit = c("days", "weeks", "months", "years")[1],
  followup.window.start.per.medication.group = FALSE,
  followup.window.duration = 365 * 2,
  followup.window.duration.unit = c("days", "weeks", "months", "years")[1],
  observation.window.start = 0,
  observation.window.start.unit = c("days", "weeks", "months", "years")[1],
  observation.window.duration = 365 * 2,
  observation.window.duration.unit = c("days", "weeks", "months", "years")[1],
  date.format = "%m/%d/%Y",
  summary = NA,
  event.interval.colname = "event.interval",
  gap.days.colname = "gap.days",
  force.NA.CMA.for.failed.patients = TRUE,
  parallel.backend = c("none", "multicore", "snow", "snow(SOCK)", "snow(MPI)",
    "snow(NWS)")[1],
  parallel.threads = "auto",
  suppress.warnings = FALSE,
  suppress.special.argument.checks = TRUE,
  arguments.that.should.not.be.defined = c(carryover.within.obs.window = FALSE,
    carryover.into.obs.window = FALSE, carry.only.for.same.medication = FALSE,
    consider.dosage.change = FALSE),
)
```

## **Arguments**

data

A data.frame containing the events used to compute the CMA. Must contain, at a minimum, the patient unique ID, the event date and duration, and might also contain the daily dosage and medication type (the actual column names are defined in the following four parameters).

ID.colname

A *string*, the name of the column in data containing the unique patient ID; must be present.

#### event.date.colname

A *string*, the name of the column in data containing the start date of the event (in the format given in the date. format parameter); must be present.

#### event.duration.colname

A *string*, the name of the column in data containing the event duration (in days); must be present.

## medication.groups

A *vector* of characters defining medication groups or the name of a column in data that defines such groups. The names of the vector are the medication group unique names, while the content defines them as logical expressions. While the names can be any string of characters except "}", it is recommended to stick to the rules for defining vector names in R. For example,  $c("A"="CATEGORY == 'medA'", "AA"="{A} & PERDAY < 4" defines two medication groups: A which selects all events of type "medA", and B which selects all events already defined by "A" but with a daily dose lower than 4. If NULL, no medication groups are defined. If medication groups are defined, there is one CMA estimate for each group; moreover, there is a special group <math>\_ALL\_OTHERS\_$  automatically defined containing all observations *not* covered by any of the explicitly defined groups.

## flatten.medication.groups

Logical, if FALSE (the default) then the CMA and event.info components of the object are lists with one medication group per element; otherwise, they are data.frames with an extra column containing the medication group (its name is given by medication.groups.colname).

## medication.groups.colname

a *string* (defaults to ".MED\_GROUP\_ID") giving the name of the column storing the group name when flatten.medication.groups is TRUE.

## followup.window.start

If a Date object, it represents the actual start date of the follow-up window; if a *string* it is the name of the column in data containing the start date of the follow-up window either as the numbers of followup.window.start.unit units after the first event (the column must be of type numeric) or as actual dates (in which case the column must be of type Date or a string that conforms to the format specified in date.format); if a *number* it is the number of time units defined in the followup.window.start.unit parameter after the begin of the participant's first event; or NA if not defined.

## followup.window.start.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.start refers to (when a number), or NA if not defined.

# followup.window.start.per.medication.group

a *logical*: if there are medication groups defined and this is TRUE, then the first event considered for the follow-up window start is relative to each medication group separately, otherwise (the default) it is relative to the patient.

## followup.window.duration

either a *number* representing the duration of the follow-up window in the time units given in followup.window.duration.unit, or a *string* giving the column containing these numbers. Should represent a period for which relevant

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medication events are recorded accurately (e.g. not extend after end of relevant treatment, loss-to-follow-up or change to a health care provider not covered by the database).

followup.window.duration.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.duration refers to, or NA if not defined.

observation.window.start, observation.window.start.unit, observation.window.duration, observation.wir the definition of the observation window (see the follow-up window parameters above for details).

date.format

A *string* giving the format of the dates used in the data and the other parameters; see the format parameters of the as.Date function for details (NB, this concerns only the dates given as strings and not as Date objects).

summary Metadata as a *string*, briefly describing this CMA.

event.interval.colname

A *string*, the name of a newly-created column storing the number of days between the start of the current event and the start of the next one; the default value "event.interval" should be changed only if there is a naming conflict with a pre-existing "event.interval" column in event.info.

gap.days.colname

A *string*, the name of a newly-created column storing the number of days when medication was not available (i.e., the "gap days"); the default value "gap.days" should be changed only if there is a naming conflict with a pre-existing "gap.days" column in event.info.

force.NA.CMA.for.failed.patients

Logical describing how the patients for which the CMA estimation fails are treated: if TRUE they are returned with an NA CMA estimate, while for FALSE they are omitted.

parallel.backend

Can be "none" (the default) for single-threaded execution, "multicore" (using mclapply in package parallel) for multicore processing (NB. not currently implemented on MS Windows and automatically falls back on "snow" on this platform), or "snow", "snow(SOCK)" (equivalent to "snow"), "snow(MPI)" or "snow(NWS)" specifying various types of SNOW clusters (can be on the local machine or more complex setups – please see the documentation of package snow for details; the last two require packages Rmpi and nws, respectively, not automatically installed with AdhereR).

parallel.threads

Can be "auto" (for parallel.backend == "multicore", defaults to the number of cores in the system as given by options ("cores"), while for parallel.backend == "snow", defaults to 2), a strictly positive integer specifying the number of parallel threads, or a more complex specification of the SNOW cluster nodes for parallel.backend == "snow" (see the documentation of package snow for details).

suppress.warnings

*Logical*, if TRUE don't show any warnings.

suppress.special.argument.checks

Logical parameter for internal use; if FALSE (default) check if the important columns in the data have some of the reserved names, if TRUE this check is not performed.

arguments.that.should.not.be.defined

a *list* of argument names and pre-defined values for which a warning should be thrown if passed to the function.

... other possible parameters

## **Details**

CMA2 considers the total number of days with medication supplied in all medication events in the observation window, including the last event. CMA4 is identical to CMA2 except that it is capped at 100%.

The formula is

(number of days supply including last event)/(first to last event)

Thus, the durations of all events are added up, possibly resulting in an CMA estimate (much) bigger than 1.0 (100%)

CMA2 and CMA1 differ in the inclusion or not of the last event.

## Value

An S3 object of class CMA2 (derived from CMA0) with the following fields:

- data The actual event data, as given by the data parameter.
- ID. colname the name of the column in data containing the unique patient ID, as given by the ID. colname parameter.
- event.date.colname the name of the column in data containing the start date of the event (in the format given in the date.format parameter), as given by the event.date.colname parameter.
- event.duration.colname the name of the column in data containing the event duration (in days), as given by the event.duration.colname parameter.
- event.daily.dose.colname the name of the column in data containing the prescribed daily dose, as given by the event.daily.dose.colname parameter.
- medication.class.colname the name of the column in data containing the classes/types/groups of medication, as given by the medication.class.colname parameter.
- followup.window.start the beginning of the follow-up window, as given by the followup.window.start parameter.
- followup.window.start.unit the time unit of the followup.window.start, as given by the followup.window.start.unit parameter.
- followup.window.duration the duration of the follow-up window, as given by the followup.window.duration parameter.
- followup.window.duration.unit the time unit of the followup.window.duration, as given by the followup.window.duration.unit parameter.

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• observation.window.start the beginning of the observation window, as given by the observation.window.start parameter.

- observation.window.start.unit the time unit of the observation.window.start, as given by the observation.window.start.unit parameter.
- observation.window.duration the duration of the observation window, as given by the observation.window.duration parameter.
- observation.window.duration.unit the time unit of the observation.window.duration, as given by the observation.window.duration.unit parameter.
- date. format the format of the dates, as given by the date. format parameter.
- summary the metadata, as given by the summary parameter.
- event.info the data.frame containing the event info (irrelevant for most users; see compute.event.int.gaps for details).
- CMA the data. frame containing the actual CMA estimates for each participant (the ID. colname column).

Please note that if medication groups are defined, then the CMA and event info are named lists, each element containing the CMA and event info corresponding to a single medication group (the element's name).

## See Also

CMAs 1 to 8 are defined in:

Vollmer, W. M., Xu, M., Feldstein, A., Smith, D., Waterbury, A., & Rand, C. (2012). Comparison of pharmacy-based measures of medication adherence. *BMC Health Services Research*, **12**, 155. doi: 10.1186/1472696312155.

## **Examples**

```
## Not run:
cma2 <- CMA2(data=med.events,</pre>
             ID.colname="PATIENT_ID",
             event.date.colname="DATE",
             event.duration.colname="DURATION",
             followup.window.start=30,
             observation.window.start=30,
             observation.window.duration=365,
             date.format="%m/%d/%Y"
            );
cma4 <- CMA4(data=med.events,</pre>
             ID.colname="PATIENT_ID",
             event.date.colname="DATE",
             event.duration.colname="DURATION",
             followup.window.start=30,
             observation.window.start=30,
             observation.window.duration=365,
             date.format="%m/%d/%Y"
            );
## End(Not run)
```

CMA5

CMA5 constructor.

# Description

Constructs a CMA (continuous multiple-interval measures of medication availability/gaps) type 5 object.

# Usage

```
CMA5(
  data = NULL,
  ID.colname = NA,
  event.date.colname = NA,
  event.duration.colname = NA,
  event.daily.dose.colname = NA,
  medication.class.colname = NA,
  medication.groups = NULL,
  flatten.medication.groups = FALSE,
  medication.groups.colname = ".MED_GROUP_ID",
  carry.only.for.same.medication = FALSE,
  consider.dosage.change = FALSE,
  followup.window.start = 0,
  followup.window.start.unit = c("days", "weeks", "months", "years")[1],
  followup.window.start.per.medication.group = FALSE,
  followup.window.duration = 365 * 2,
  followup.window.duration.unit = c("days", "weeks", "months", "years")[1],
  observation.window.start = 0,
  observation.window.start.unit = c("days", "weeks", "months", "years")[1],
  observation.window.duration = 365 * 2,
  observation.window.duration.unit = c("days", "weeks", "months", "years")[1],
  date.format = "%m/%d/%Y",
  summary = NA,
  event.interval.colname = "event.interval",
  gap.days.colname = "gap.days",
  force.NA.CMA.for.failed.patients = TRUE,
  parallel.backend = c("none", "multicore", "snow", "snow(SOCK)", "snow(MPI)",
    "snow(NWS)")[1],
  parallel.threads = "auto",
  suppress.warnings = FALSE,
  suppress.special.argument.checks = TRUE,
  arguments.that.should.not.be.defined = c(carryover.within.obs.window = TRUE,
    carryover.into.obs.window = FALSE),
)
```

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## **Arguments**

data

A data.frame containing the medication events used to compute the CMA. Must contain, at a minimum, the patient unique ID, the event date and duration, and might also contain the daily dosage and medication type (the actual column names are defined in the following four parameters).

ID.colname

A *string*, the name of the column in data containing the unique patient ID; must be present.

event.date.colname

A *string*, the name of the column in data containing the start date of the event (in the format given in the date. format parameter); must be present.

event.duration.colname

A *string*, the name of the column in data containing the event duration (in days); must be present.

event.daily.dose.colname

A *string*, the name of the column in data containing the prescribed daily dose, or NA if not defined.

medication.class.colname

A *string*, the name of the column in data containing the medication type, or NA if not defined.

medication.groups

A *vector* of characters defining medication groups or the name of a column in data that defines such groups. The names of the vector are the medication group unique names, while the content defines them as logical expressions. While the names can be any string of characters except "}", it is recommended to stick to the rules for defining vector names in R. For example,  $c("A"="CATEGORY == 'medA'", "AA"="{A} & PERDAY < 4" defines two medication groups: A which selects all events of type "medA", and B which selects all events already defined by "A" but with a daily dose lower than 4. If NULL, no medication groups are defined. If medication groups are defined, there is one CMA estimate for each group; moreover, there is a special group <math>\_ALL\_OTHERS\_$  automatically defined containing all observations *not* covered by any of the explicitly defined groups.

flatten.medication.groups

Logical, if FALSE (the default) then the CMA and event.info components of the object are lists with one medication group per element; otherwise, they are data.frames with an extra column containing the medication group (its name is given by medication.groups.colname).

medication.groups.colname

a *string* (defaults to ".MED\_GROUP\_ID") giving the name of the column storing the group name when flatten.medication.groups is TRUE.

carry.only.for.same.medication

 $\label{logical} \textit{Logical}, if \ \mathsf{TRUE}, the \ \mathsf{carry-over} \ \mathsf{applies} \ \mathsf{only} \ \mathsf{across} \ \mathsf{medication} \ \mathsf{of} \ \mathsf{the} \ \mathsf{same} \ \mathsf{type}.$   $\mathsf{consider.dosage.change}$ 

Logical, if TRUE, the carry-over is adjusted to also reflect changes in dosage.

followup.window.start

If a Date object, it represents the actual start date of the follow-up window; if a *string* it is the name of the column in data containing the start date of

the follow-up window either as the numbers of followup.window.start.unit units after the first event (the column must be of type numeric) or as actual dates (in which case the column must be of type Date or a string that conforms to the format specified in date.format); if a *number* it is the number of time units defined in the followup.window.start.unit parameter after the begin of the participant's first event; or NA if not defined.

followup.window.start.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.start refers to (when a number), or NA if not defined.

followup.window.start.per.medication.group

a *logical*: if there are medication groups defined and this is TRUE, then the first event considered for the follow-up window start is relative to each medication group separately, otherwise (the default) it is relative to the patient.

followup.window.duration

either a *number* representing the duration of the follow-up window in the time units given in followup.window.duration.unit, or a *string* giving the column containing these numbers. Should represent a period for which relevant medication events are recorded accurately (e.g. not extend after end of relevant treatment, loss-to-follow-up or change to a health care provider not covered by the database).

followup.window.duration.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.duration refers to, or NA if not defined.

observation.window.start, observation.window.start.unit, observation.window.duration, observation.wir the definition of the observation window (see the follow-up window parameters above for details).

date.format

A *string* giving the format of the dates used in the data and the other parameters; see the format parameters of the as.Date function for details (NB, this concerns only the dates given as strings and not as Date objects).

summary

Metadata as a *string*, briefly describing this CMA.

event.interval.colname

A *string*, the name of a newly-created column storing the number of days between the start of the current event and the start of the next one; the default value "event.interval" should be changed only if there is a naming conflict with a pre-existing "event.interval" column in event.info.

gap.days.colname

A *string*, the name of a newly-created column storing the number of days when medication was not available (i.e., the "gap days"); the default value "gap.days" should be changed only if there is a naming conflict with a pre-existing "gap.days" column in event.info.

force.NA.CMA.for.failed.patients

*Logical* describing how the patients for which the CMA estimation fails are treated: if TRUE they are returned with an NA CMA estimate, while for FALSE they are omitted.

parallel.backend

Can be "none" (the default) for single-threaded execution, "multicore" (using mclapply in package parallel) for multicore processing (NB. not currently

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implemented on MS Windows and automatically falls back on "snow" on this platform), or "snow", "snow(SOCK)" (equivalent to "snow"), "snow(MPI)" or "snow(NWS)" specifying various types of SNOW clusters (can be on the local machine or more complex setups – please see the documentation of package snow for details; the last two require packages Rmpi and nws, respectively, not automatically installed with AdhereR).

## parallel.threads

Can be "auto" (for parallel.backend == "multicore", defaults to the number of cores in the system as given by options("cores"), while for parallel.backend == "snow", defaults to 2), a strictly positive integer specifying the number of parallel threads, or a more complex specification of the SNOW cluster nodes for parallel.backend == "snow" (see the documentation of package snow for details).

suppress.warnings

Logical, if TRUE don't show any warnings.

suppress.special.argument.checks

*Logical* parameter for internal use; if FALSE (default) check if the important columns in the data have some of the reserved names, if TRUE this check is not performed.

arguments.that.should.not.be.defined

a *list* of argument names and pre-defined values for which a warning should be thrown if passed to the function.

.. other possible parameters

## **Details**

CMA5 assumes that, within the observation window, the medication is used as prescribed and new medication is "banked" until needed (oversupply from previous events is used first, followed new medication supply). It computes days of theoretical use by extracting the total number of gap days from the total time interval between the first and the last event, accounting for carry over for all medication events within the observation window. Thus, it accounts for timing within the observation window, and excludes the remaining supply at the start of the last event within the observation window.

The formula is

(number of days of the oretical use)/(first to last event)

## Observations:

- the carry.only.for.same.medication parameter controls the transmission of carry-over across medication changes, producing a "standard" CMA5 (default value is FALSE), and an "alternative" CMA5b, respectively;
- the consider.dosage.change parameter controls if dosage changes are taken into account, i.e. if set as TRUE and a new medication event has a different daily dosage recommendation, carry-over is recomputed assuming medication use according to the new prescribed dosage (default value is FALSE).

## Value

An S3 object of class CMA5 (derived from CMA0) with the following fields:

- data The actual event data, as given by the data parameter.
- ID. colname the name of the column in data containing the unique patient ID, as given by the ID. colname parameter.
- event.date.colname the name of the column in data containing the start date of the event (in the format given in the date.format parameter), as given by the event.date.colname parameter.
- event.duration.colname the name of the column in data containing the event duration (in days), as given by the event.duration.colname parameter.
- event.daily.dose.colname the name of the column in data containing the prescribed daily dose, as given by the event.daily.dose.colname parameter.
- medication.class.colname the name of the column in data containing the classes/types/groups of medication, as given by the medication.class.colname parameter.
- carry.only.for.same.medication whether the carry-over applies only across medication of the same type, as given by the carry.only.for.same.medication parameter.
- consider.dosage.change whether the carry-over is adjusted to reflect changes in dosage, as given by the consider.dosage.change parameter.
- followup.window.start the beginning of the follow-up window, as given by the followup.window.start parameter.
- followup.window.start.unit the time unit of the followup.window.start, as given by the followup.window.start.unit parameter.
- followup.window.duration the duration of the follow-up window, as given by the followup.window.duration parameter.

• observation.window.start the beginning of the observation window, as given by the observation.window.start

- followup.window.duration.unit the time unit of the followup.window.duration, as given by the followup.window.duration.unit parameter.
- parameter.
- observation.window.start.unit the time unit of the observation.window.start, as given by the observation.window.start.unit parameter.
- observation.window.duration the duration of the observation window, as given by the observation.window.duration parameter.
- observation.window.duration.unit the time unit of the observation.window.duration, as given by the observation.window.duration.unit parameter.
- date. format the format of the dates, as given by the date. format parameter.
- summary the metadata, as given by the summary parameter.
- event.info the data.frame containing the event info (irrelevant for most users; see compute.event.int.gaps for details).
- CMA the data. frame containing the actual CMA estimates for each participant (the ID. colname column).

Please note that if medication groups are defined, then the CMA and event info are named lists, each element containing the CMA and event info corresponding to a single medication group (the element's name).

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## See Also

CMAs 1 to 8 are defined in:

Vollmer, W. M., Xu, M., Feldstein, A., Smith, D., Waterbury, A., & Rand, C. (2012). Comparison of pharmacy-based measures of medication adherence. *BMC Health Services Research*, **12**, 155. doi: 10.1186/1472696312155.

# **Examples**

CMA6

CMA6 constructor.

# Description

Constructs a CMA (continuous multiple-interval measures of medication availability/gaps) type 6 object.

# Usage

```
CMA6(
  data = NULL,
  ID.colname = NA,
  event.date.colname = NA,
  event.duration.colname = NA,
  event.daily.dose.colname = NA,
  medication.class.colname = NA,
  medication.groups = NULL,
  flatten.medication.groups = FALSE,
  medication.groups.colname = ".MED_GROUP_ID",
  carry.only.for.same.medication = FALSE,
  consider.dosage.change = FALSE,
  followup.window.start = 0,
  followup.window.start.unit = c("days", "weeks", "months", "years")[1],
  followup.window.start.per.medication.group = FALSE,
```

```
followup.window.duration = 365 * 2,
  followup.window.duration.unit = c("days", "weeks", "months", "years")[1],
  observation.window.start = 0,
  observation.window.start.unit = c("days", "weeks", "months", "years")[1],
  observation.window.duration = 365 * 2,
 observation.window.duration.unit = c("days", "weeks", "months", "years")[1],
  date.format = "%m/%d/%Y",
  summary = NA,
  event.interval.colname = "event.interval",
  gap.days.colname = "gap.days",
  force.NA.CMA.for.failed.patients = TRUE,
 parallel.backend = c("none", "multicore", "snow", "snow(SOCK)", "snow(MPI)",
    "snow(NWS)")[1],
  parallel.threads = "auto",
  suppress.warnings = FALSE,
  suppress.special.argument.checks = TRUE,
 arguments.that.should.not.be.defined = c(carryover.within.obs.window = TRUE,
   carryover.into.obs.window = FALSE),
)
```

## **Arguments**

data

A data.frame containing the events used to compute the CMA. Must contain, at a minimum, the patient unique ID, the event date and duration, and might also contain the daily dosage and medication type (the actual column names are defined in the following four parameters).

ID.colname

A *string*, the name of the column in data containing the unique patient ID; must be present.

event.date.colname

A *string*, the name of the column in data containing the start date of the event (in the format given in the date. format parameter); must be present.

event.duration.colname

A *string*, the name of the column in data containing the event duration (in days); must be present.

event.daily.dose.colname

A *string*, the name of the column in data containing the prescribed daily dose, or NA if not defined.

medication.class.colname

A *string*, the name of the column in data containing the medication type, or NA if not defined.

medication.groups

A *vector* of characters defining medication groups or the name of a column in data that defines such groups. The names of the vector are the medication group unique names, while the content defines them as logical expressions. While the names can be any string of characters except "}", it is recommended to stick to the rules for defining vector names in R. For example,  $c("A"="CATEGORY == "medA"", "AA"="{A} & PERDAY < 4" defines two medication groups: A which$ 

selects all events of type "medA", and *B* which selects all events already defined by "A" but with a daily dose lower than 4. If NULL, no medication groups are defined. If medication groups are defined, there is one CMA estimate for each group; moreover, there is a special group \_\_ALL\_OTHERS\_\_ automatically defined containing all observations *not* covered by any of the explicitly defined groups.

flatten.medication.groups

Logical, if FALSE (the default) then the CMA and event.info components of the object are lists with one medication group per element; otherwise, they are data.frames with an extra column containing the medication group (its name is given by medication.groups.colname).

medication.groups.colname

a *string* (defaults to ".MED\_GROUP\_ID") giving the name of the column storing the group name when flatten.medication.groups is TRUE.

carry.only.for.same.medication

*Logical*, if TRUE, the carry-over applies only across medication of the same type.

consider.dosage.change

Logical, if TRUE, the carry-over is adjusted to also reflect changes in dosage.

followup.window.start

If a Date object, it represents the actual start date of the follow-up window; if a *string* it is the name of the column in data containing the start date of the follow-up window either as the numbers of followup.window.start.unit units after the first event (the column must be of type numeric) or as actual dates (in which case the column must be of type Date or a string that conforms to the format specified in date.format); if a *number* it is the number of time units defined in the followup.window.start.unit parameter after the begin of the participant's first event; or NA if not defined.

followup.window.start.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.start refers to (when a number), or NA if not defined.

followup.window.start.per.medication.group

a *logical*: if there are medication groups defined and this is TRUE, then the first event considered for the follow-up window start is relative to each medication group separately, otherwise (the default) it is relative to the patient.

followup.window.duration

either a *number* representing the duration of the follow-up window in the time units given in followup.window.duration.unit, or a *string* giving the column containing these numbers. Should represent a period for which relevant medication events are recorded accurately (e.g. not extend after end of relevant treatment, loss-to-follow-up or change to a health care provider not covered by the database).

followup.window.duration.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.duration refers to, or NA if not defined.

observation.window.start, observation.window.start.unit, observation.window.duration, observation.window.the definition of the observation window (see the follow-up window parameters above for details).

date.format

A *string* giving the format of the dates used in the data and the other parameters; see the format parameters of the as. Date function for details (NB, this concerns only the dates given as strings and not as Date objects).

summary

Metadata as a *string*, briefly describing this CMA.

event.interval.colname

A *string*, the name of a newly-created column storing the number of days between the start of the current event and the start of the next one; the default value "event.interval" should be changed only if there is a naming conflict with a pre-existing "event.interval" column in event.info.

gap.days.colname

A *string*, the name of a newly-created column storing the number of days when medication was not available (i.e., the "gap days"); the default value "gap.days" should be changed only if there is a naming conflict with a pre-existing "gap.days" column in event.info.

force.NA.CMA.for.failed.patients

Logical describing how the patients for which the CMA estimation fails are treated: if TRUE they are returned with an NA CMA estimate, while for FALSE they are omitted.

parallel.backend

Can be "none" (the default) for single-threaded execution, "multicore" (using mclapply in package parallel) for multicore processing (NB. not currently implemented on MS Windows and automatically falls back on "snow" on this platform), or "snow", "snow(SOCK)" (equivalent to "snow"), "snow(MPI)" or "snow(NWS)" specifying various types of SNOW clusters (can be on the local machine or more complex setups – please see the documentation of package snow for details; the last two require packages Rmpi and nws, respectively, not automatically installed with AdhereR).

parallel.threads

Can be "auto" (for parallel.backend == "multicore", defaults to the number of cores in the system as given by options ("cores"), while for parallel.backend == "snow", defaults to 2), a strictly positive integer specifying the number of parallel threads, or a more complex specification of the SNOW cluster nodes for parallel.backend == "snow" (see the documentation of package snow for details).

suppress.warnings

Logical, if TRUE don't show any warnings.

suppress.special.argument.checks

*Logical* parameter for internal use; if FALSE (default) check if the important columns in the data have some of the reserved names, if TRUE this check is not performed.

arguments.that.should.not.be.defined

a *list* of argument names and pre-defined values for which a warning should be thrown if passed to the function.

.. other possible parameters

## **Details**

CMA6 assumes that, within the observation window, the medication is used as prescribed and new medication is "banked" until needed (oversupply from previous events is used first, followed new medication supply). It computes days of theoretical use by extracting the total number of gap days from the total time interval between the first event and the end of the observation window, accounting for carry over for all medication events within the observation window. Thus, it accounts for timing within the observation window, and excludes the remaining supply at the end of the observation window.

The formula is

(number of days of the oretical use)/(first event to end of observation window)

## Observations:

- the carry.only.for.same.medication parameter controls the transmission of carry-over across medication changes, producing a "standard" CMA6 (default value is FALSE), and an "alternative" CMA6b, respectively;
- the consider.dosage.change parameter controls if dosage changes are taken into account, i.e. if set as TRUE and a new medication event has a different daily dosage recommendation, carry-over is recomputed assuming medication use according to the new prescribed dosage (default value is FALSE).

#### Value

An S3 object of class CMA6 (derived from CMA0) with the following fields:

- data The actual event data, as given by the data parameter.
- ID. colname the name of the column in data containing the unique patient ID, as given by the ID. colname parameter.
- event.date.colname the name of the column in data containing the start date of the event (in the format given in the date.format parameter), as given by the event.date.colname parameter.
- event.duration.colname the name of the column in data containing the event duration (in days), as given by the event.duration.colname parameter.
- event.daily.dose.colname the name of the column in data containing the prescribed daily dose, as given by the event.daily.dose.colname parameter.
- medication.class.colname the name of the column in data containing the classes/types/groups of medication, as given by the medication.class.colname parameter.
- carry.only.for.same.medication whether the carry-over applies only across medication of the same type, as given by the carry.only.for.same.medication parameter.
- consider.dosage.change whether the carry-over is adjusted to reflect changes in dosage, as given by the consider.dosage.change parameter.
- followup.window.start the beginning of the follow-up window, as given by the followup.window.start parameter.
- followup.window.start.unit the time unit of the followup.window.start, as given by the followup.window.start.unit parameter.

• followup.window.duration the duration of the follow-up window, as given by the followup.window.duration parameter.

- followup.window.duration.unit the time unit of the followup.window.duration, as given by the followup.window.duration.unit parameter.
- observation.window.start the beginning of the observation window, as given by the observation.window.start parameter.
- observation.window.start.unit the time unit of the observation.window.start, as given by the observation.window.start.unit parameter.
- observation.window.duration the duration of the observation window, as given by the observation.window.duration parameter.
- observation.window.duration.unit the time unit of the observation.window.duration, as given by the observation.window.duration.unit parameter.
- date. format the format of the dates, as given by the date. format parameter.
- summary the metadata, as given by the summary parameter.
- event.info the data.frame containing the event info (irrelevant for most users; see compute.event.int.gaps for details).
- CMA the data. frame containing the actual CMA estimates for each participant (the ID. colname column).

Please note that if medication. groups are defined, then the CMA and event. info are named lists, each element containing the CMA and event. info corresponding to a single medication group (the element's name).

## See Also

CMAs 1 to 8 are defined in:

Vollmer, W. M., Xu, M., Feldstein, A., Smith, D., Waterbury, A., & Rand, C. (2012). Comparison of pharmacy-based measures of medication adherence. *BMC Health Services Research*, **12**, 155. doi: 10.1186/1472696312155.

## **Examples**

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CMA7

CMA7 constructor.

# Description

Constructs a CMA (continuous multiple-interval measures of medication availability/gaps) type 7 object.

# Usage

```
CMA7(
  data = NULL,
  ID.colname = NA,
  event.date.colname = NA,
  event.duration.colname = NA,
  event.daily.dose.colname = NA,
  medication.class.colname = NA,
  medication.groups = NULL,
  flatten.medication.groups = FALSE,
  medication.groups.colname = ".MED_GROUP_ID",
  carry.only.for.same.medication = FALSE,
  consider.dosage.change = FALSE,
  followup.window.start = 0,
  followup.window.start.unit = c("days", "weeks", "months", "years")[1],
  followup.window.start.per.medication.group = FALSE,
  followup.window.duration = 365 * 2,
  followup.window.duration.unit = c("days", "weeks", "months", "years")[1],
  observation.window.start = 0,
  observation.window.start.unit = c("days", "weeks", "months", "years")[1],
  observation.window.duration = 365 * 2,
  observation.window.duration.unit = c("days", "weeks", "months", "years")[1],
  date.format = "%m/%d/%Y",
  summary = NA,
  event.interval.colname = "event.interval",
  gap.days.colname = "gap.days",
  force.NA.CMA.for.failed.patients = TRUE,
  parallel.backend = c("none", "multicore", "snow", "snow(SOCK)", "snow(MPI)",
    "snow(NWS)")[1],
  parallel.threads = "auto",
  suppress.warnings = FALSE,
  suppress.special.argument.checks = TRUE,
  arguments.that.should.not.be.defined = c(carryover.within.obs.window = TRUE,
    carryover.into.obs.window = TRUE),
)
```

## **Arguments**

data

A data.frame containing the events used to compute the CMA. Must contain, at a minimum, the patient unique ID, the event date and duration, and might also contain the daily dosage and medication type (the actual column names are defined in the following four parameters).

ID.colname

A *string*, the name of the column in data containing the unique patient ID; must be present.

event.date.colname

A *string*, the name of the column in data containing the start date of the event (in the format given in the date. format parameter); must be present.

event.duration.colname

A *string*, the name of the column in data containing the event duration (in days); must be present.

event.daily.dose.colname

A *string*, the name of the column in data containing the prescribed daily dose, or NA if not defined.

medication.class.colname

A *string*, the name of the column in data containing the medication type, or NA if not defined.

medication.groups

A *vector* of characters defining medication groups or the name of a column in data that defines such groups. The names of the vector are the medication group unique names, while the content defines them as logical expressions. While the names can be any string of characters except "}", it is recommended to stick to the rules for defining vector names in R. For example,  $c("A"="CATEGORY == 'medA'", "AA"="{A} & PERDAY < 4" defines two medication groups: A which selects all events of type "medA", and B which selects all events already defined by "A" but with a daily dose lower than 4. If NULL, no medication groups are defined. If medication groups are defined, there is one CMA estimate for each group; moreover, there is a special group <math>\_ALL\_OTHERS\_$  automatically defined containing all observations *not* covered by any of the explicitly defined groups.

flatten.medication.groups

Logical, if FALSE (the default) then the CMA and event.info components of the object are lists with one medication group per element; otherwise, they are data.frames with an extra column containing the medication group (its name is given by medication.groups.colname).

medication.groups.colname

a *string* (defaults to ".MED\_GROUP\_ID") giving the name of the column storing the group name when flatten.medication.groups is TRUE.

carry.only.for.same.medication

*Logical*, if TRUE, the carry-over applies only across medication of the same type. consider.dosage.change

Logical, if TRUE, the carry-over is adjusted to also reflect changes in dosage.

followup.window.start

If a Date object, it represents the actual start date of the follow-up window; if a *string* it is the name of the column in data containing the start date of

the follow-up window either as the numbers of followup.window.start.unit units after the first event (the column must be of type numeric) or as actual dates (in which case the column must be of type Date or a string that conforms to the format specified in date.format); if a *number* it is the number of time units defined in the followup.window.start.unit parameter after the begin of the participant's first event; or NA if not defined.

followup.window.start.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.start refers to (when a number), or NA if not defined.

followup.window.start.per.medication.group

a *logical*: if there are medication groups defined and this is TRUE, then the first event considered for the follow-up window start is relative to each medication group separately, otherwise (the default) it is relative to the patient.

followup.window.duration

either a *number* representing the duration of the follow-up window in the time units given in followup.window.duration.unit, or a *string* giving the column containing these numbers. Should represent a period for which relevant medication events are recorded accurately (e.g. not extend after end of relevant treatment, loss-to-follow-up or change to a health care provider not covered by the database).

followup.window.duration.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.duration refers to, or NA if not defined.

observation.window.start, observation.window.start.unit, observation.window.duration, observation.wir the definition of the observation window (see the follow-up window parameters above for details).

date.format

A *string* giving the format of the dates used in the data and the other parameters; see the format parameters of the as.Date function for details (NB, this concerns only the dates given as strings and not as Date objects).

summary

Metadata as a *string*, briefly describing this CMA.

event.interval.colname

A *string*, the name of a newly-created column storing the number of days between the start of the current event and the start of the next one; the default value "event.interval" should be changed only if there is a naming conflict with a pre-existing "event.interval" column in event.info.

gap.days.colname

A *string*, the name of a newly-created column storing the number of days when medication was not available (i.e., the "gap days"); the default value "gap.days" should be changed only if there is a naming conflict with a pre-existing "gap.days" column in event.info.

force.NA.CMA.for.failed.patients

*Logical* describing how the patients for which the CMA estimation fails are treated: if TRUE they are returned with an NA CMA estimate, while for FALSE they are omitted.

parallel.backend

Can be "none" (the default) for single-threaded execution, "multicore" (using mclapply in package parallel) for multicore processing (NB. not currently

implemented on MS Windows and automatically falls back on "snow" on this platform), or "snow", "snow(SOCK)" (equivalent to "snow"), "snow(MPI)" or "snow(NWS)" specifying various types of SNOW clusters (can be on the local machine or more complex setups – please see the documentation of package snow for details; the last two require packages Rmpi and nws, respectively, not automatically installed with AdhereR).

## parallel.threads

Can be "auto" (for parallel.backend == "multicore", defaults to the number of cores in the system as given by options("cores"), while for parallel.backend == "snow", defaults to 2), a strictly positive integer specifying the number of parallel threads, or a more complex specification of the SNOW cluster nodes for parallel.backend == "snow" (see the documentation of package snow for details).

suppress.warnings

Logical, if TRUE don't show any warnings.

suppress.special.argument.checks

*Logical* parameter for internal use; if FALSE (default) check if the important columns in the data have some of the reserved names, if TRUE this check is not performed.

arguments.that.should.not.be.defined

a *list* of argument names and pre-defined values for which a warning should be thrown if passed to the function.

... other possible parameters

## **Details**

CMA7 assumes that, within and before the observation window, the medication is used as prescribed and new medication is "banked" until needed (oversupply from previous events is used first, followed new medication supply). It computes days of theoretical use by extracting the total number of gap days from the total time interval between the start and the end of the observation window, accounting for carry over for all medication events within and before the observation window. All medication events in the follow up window before observation window are considered for carry-over calculation. Thus, it accounts for timing within and before the observation window, and excludes the remaining supply at the end of the observation window.

The formula is

(number of days of the or etical use)/(start to end of observation window)

# Observations:

- the carry.only.for.same.medication parameter controls the transmission of carry-over across medication changes, producing a "standard" CMA7 (default value is FALSE), and an "alternative" CMA7b, respectively;
- the consider.dosage.change parameter controls if dosage changes are taken into account, i.e. if set as TRUE and a new medication event has a different daily dosage recommendation, carry-over is recomputed assuming medication use according to the new prescribed dosage (default value is FALSE).

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## Value

An S3 object of class CMA7 (derived from CMA0) with the following fields:

- data The actual event data, as given by the data parameter.
- ID. colname the name of the column in data containing the unique patient ID, as given by the ID. colname parameter.
- event.date.colname the name of the column in data containing the start date of the event (in the format given in the date.format parameter), as given by the event.date.colname parameter.
- event.duration.colname the name of the column in data containing the event duration (in days), as given by the event.duration.colname parameter.
- event.daily.dose.colname the name of the column in data containing the prescribed daily dose, as given by the event.daily.dose.colname parameter.
- medication.class.colname the name of the column in data containing the classes/types/groups of medication, as given by the medication.class.colname parameter.
- carry.only.for.same.medication whether the carry-over applies only across medication of the same type, as given by the carry.only.for.same.medication parameter.
- consider.dosage.change whether the carry-over is adjusted to reflect changes in dosage, as given by the consider.dosage.change parameter.
- followup.window.start the beginning of the follow-up window, as given by the followup.window.start parameter.
- followup.window.start.unit the time unit of the followup.window.start, as given by the followup.window.start.unit parameter.
- followup.window.duration the duration of the follow-up window, as given by the followup.window.duration parameter.

• observation.window.start the beginning of the observation window, as given by the observation.window.start

- followup.window.duration.unit the time unit of the followup.window.duration, as given by the followup.window.duration.unit parameter.
- parameter.

   observation.window.start.unit the time unit of the observation.window.start, as given
- observation.window.start.unit the time unit of the observation.window.start, as given by the observation.window.start.unit parameter.
- observation.window.duration the duration of the observation window, as given by the observation.window.duration parameter.
- observation.window.duration.unit the time unit of the observation.window.duration, as given by the observation.window.duration.unit parameter.
- date. format the format of the dates, as given by the date. format parameter.
- summary the metadata, as given by the summary parameter.
- event.info the data.frame containing the event info (irrelevant for most users; see compute.event.int.gaps for details).
- CMA the data. frame containing the actual CMA estimates for each participant (the ID. colname column).

Please note that if medication groups are defined, then the CMA and event info are named lists, each element containing the CMA and event info corresponding to a single medication group (the element's name).

## See Also

CMAs 1 to 8 are defined in:

Vollmer, W. M., Xu, M., Feldstein, A., Smith, D., Waterbury, A., & Rand, C. (2012). Comparison of pharmacy-based measures of medication adherence. *BMC Health Services Research*, **12**, 155. doi: 10.1186/1472696312155.

# **Examples**

CMA8

CMA8 constructor.

# Description

Constructs a CMA (continuous multiple-interval measures of medication availability/gaps) type 8 object.

# Usage

```
CMA8(
  data = NULL,
  ID.colname = NA,
  event.date.colname = NA,
  event.duration.colname = NA,
  event.daily.dose.colname = NA,
  medication.class.colname = NA,
  medication.groups = NULL,
  flatten.medication.groups = FALSE,
  medication.groups.colname = ".MED_GROUP_ID",
  carry.only.for.same.medication = FALSE,
  consider.dosage.change = FALSE,
  followup.window.start = 0,
  followup.window.start.unit = c("days", "weeks", "months", "years")[1],
  followup.window.start.per.medication.group = FALSE,
```

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```
followup.window.duration = 365 * 2,
  followup.window.duration.unit = c("days", "weeks", "months", "years")[1],
  observation.window.start = 0,
  observation.window.start.unit = c("days", "weeks", "months", "years")[1],
  observation.window.duration = 365 * 2,
 observation.window.duration.unit = c("days", "weeks", "months", "years")[1],
  date.format = "%m/%d/%Y",
  summary = NA,
  event.interval.colname = "event.interval",
  gap.days.colname = "gap.days",
  force.NA.CMA.for.failed.patients = TRUE,
 parallel.backend = c("none", "multicore", "snow", "snow(SOCK)", "snow(MPI)",
    "snow(NWS)")[1],
  parallel.threads = "auto",
  suppress.warnings = FALSE,
  suppress.special.argument.checks = TRUE,
 arguments.that.should.not.be.defined = c(carryover.within.obs.window = TRUE,
   carryover.into.obs.window = TRUE),
)
```

#### **Arguments**

data

A data.frame containing the events used to compute the CMA. Must contain, at a minimum, the patient unique ID, the event date and duration, and might also contain the daily dosage and medication type (the actual column names are defined in the following four parameters).

ID.colname

A *string*, the name of the column in data containing the unique patient ID; must be present.

event.date.colname

A *string*, the name of the column in data containing the start date of the event (in the format given in the date. format parameter); must be present.

event.duration.colname

A *string*, the name of the column in data containing the event duration (in days); must be present.

event.daily.dose.colname

A *string*, the name of the column in data containing the prescribed daily dose, or NA if not defined.

medication.class.colname

A *string*, the name of the column in data containing the medication type, or NA if not defined.

medication.groups

A *vector* of characters defining medication groups or the name of a column in data that defines such groups. The names of the vector are the medication group unique names, while the content defines them as logical expressions. While the names can be any string of characters except "}", it is recommended to stick to the rules for defining vector names in R. For example,  $c("A"="CATEGORY == "medA"", "AA"="{A} & PERDAY < 4" defines two medication groups: A which$ 

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selects all events of type "medA", and *B* which selects all events already defined by "A" but with a daily dose lower than 4. If NULL, no medication groups are defined. If medication groups are defined, there is one CMA estimate for each group; moreover, there is a special group \_\_ALL\_OTHERS\_\_ automatically defined containing all observations *not* covered by any of the explicitly defined groups.

flatten.medication.groups

Logical, if FALSE (the default) then the CMA and event.info components of the object are lists with one medication group per element; otherwise, they are data.frames with an extra column containing the medication group (its name is given by medication.groups.colname).

medication.groups.colname

a *string* (defaults to ".MED\_GROUP\_ID") giving the name of the column storing the group name when flatten.medication.groups is TRUE.

carry.only.for.same.medication

*Logical*, if TRUE, the carry-over applies only across medication of the same type.

consider.dosage.change

Logical, if TRUE, the carry-over is adjusted to also reflect changes in dosage.

followup.window.start

If a Date object, it represents the actual start date of the follow-up window; if a *string* it is the name of the column in data containing the start date of the follow-up window either as the numbers of followup.window.start.unit units after the first event (the column must be of type numeric) or as actual dates (in which case the column must be of type Date or a string that conforms to the format specified in date.format); if a *number* it is the number of time units defined in the followup.window.start.unit parameter after the begin of the participant's first event; or NA if not defined.

followup.window.start.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.start refers to (when a number), or NA if not defined.

followup.window.start.per.medication.group

a *logical*: if there are medication groups defined and this is TRUE, then the first event considered for the follow-up window start is relative to each medication group separately, otherwise (the default) it is relative to the patient.

followup.window.duration

either a *number* representing the duration of the follow-up window in the time units given in followup.window.duration.unit, or a *string* giving the column containing these numbers. Should represent a period for which relevant medication events are recorded accurately (e.g. not extend after end of relevant treatment, loss-to-follow-up or change to a health care provider not covered by the database).

followup.window.duration.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.duration refers to, or NA if not defined.

observation.window.start, observation.window.start.unit, observation.window.duration, observation.window.the definition of the observation window (see the follow-up window parameters above for details).

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date.format

A *string* giving the format of the dates used in the data and the other parameters; see the format parameters of the as. Date function for details (NB, this concerns only the dates given as strings and not as Date objects).

summary

Metadata as a string, briefly describing this CMA.

### event.interval.colname

A *string*, the name of a newly-created column storing the number of days between the start of the current event and the start of the next one; the default value "event.interval" should be changed only if there is a naming conflict with a pre-existing "event.interval" column in event.info.

### gap.days.colname

A *string*, the name of a newly-created column storing the number of days when medication was not available (i.e., the "gap days"); the default value "gap.days" should be changed only if there is a naming conflict with a pre-existing "gap.days" column in event.info.

# force.NA.CMA.for.failed.patients

Logical describing how the patients for which the CMA estimation fails are treated: if TRUE they are returned with an NA CMA estimate, while for FALSE they are omitted.

### parallel.backend

Can be "none" (the default) for single-threaded execution, "multicore" (using mclapply in package parallel) for multicore processing (NB. not currently implemented on MS Windows and automatically falls back on "snow" on this platform), or "snow", "snow(SOCK)" (equivalent to "snow"), "snow(MPI)" or "snow(NWS)" specifying various types of SNOW clusters (can be on the local machine or more complex setups – please see the documentation of package snow for details; the last two require packages Rmpi and nws, respectively, not automatically installed with AdhereR).

### parallel.threads

Can be "auto" (for parallel.backend == "multicore", defaults to the number of cores in the system as given by options("cores"), while for parallel.backend == "snow", defaults to 2), a strictly positive integer specifying the number of parallel threads, or a more complex specification of the SNOW cluster nodes for parallel.backend == "snow" (see the documentation of package snow for details).

### suppress.warnings

Logical, if TRUE don't show any warnings.

# suppress.special.argument.checks

Logical parameter for internal use; if FALSE (default) check if the important columns in the data have some of the reserved names, if TRUE this check is not performed.

### arguments.that.should.not.be.defined

a *list* of argument names and pre-defined values for which a warning should be thrown if passed to the function.

... other possible parameters

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### **Details**

CMA8 is similar to CMA6 in that it assumes that, within the observation window, the medication is used as prescribed and new medication is "banked" until needed (oversupply from previous events is used first, followed new medication supply). Unlike CMA6 it accounts for carry-over from before the window - but in a different way from CMA7: by adding a time lag at the start of the observation window equal to the duration of carry-over from before. It is designed for situations when an event with a hypothesized causal effect on adherence happens at the start of the observation window (e.g. enrolment in an intervention study); in this case, it may be that the existing supply is not part of the relationship under study (e.g. it delays the actual start of the study for that participant) and needs to be excluded by shortening the time interval examined. The end of the observation window remains the same. Thus, CMA8 computes days of theoretical use by extracting the total number of gap days from the total time interval between the lagged start and the end of the observation window, accounting for carry over for all medication events within the observation window. All medication events in the follow up window before observation window are considered for carryover calculation. Thus, as CMA7, it accounts for timing within the observation window, as well as before (different adjustment than CMA7), and excludes the remaining supply at the end of the observation window.

The formula is

(number of days of theoretical use)/(lagged start to end of observation window)

### Observations:

- the carry.only.for.same.medication parameter controls the transmission of carry-over across medication changes, producing a "standard" CMA8 (default value is FALSE), and an "alternative" CMA8b, respectively;
- the consider.dosage.change parameter controls if dosage changes are taken into account, i.e. if set as TRUE and a new medication event has a different daily dosage recommendation, carry-over is recomputed assuming medication use according to the new prescribed dosage (default value is FALSE).

### Value

An S3 object of class CMA8 (derived from CMA0) with the following fields:

- data The actual event data, as given by the data parameter.
- ID. colname the name of the column in data containing the unique patient ID, as given by the ID. colname parameter.
- event.date.colname the name of the column in data containing the start date of the event (in the format given in the date.format parameter), as given by the event.date.colname parameter.
- event.duration.colname the name of the column in data containing the event duration (in days), as given by the event.duration.colname parameter.
- event.daily.dose.colname the name of the column in data containing the prescribed daily dose, as given by the event.daily.dose.colname parameter.
- medication.class.colname the name of the column in data containing the classes/types/groups of medication, as given by the medication.class.colname parameter.

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• carry.only.for.same.medication whether the carry-over applies only across medication of the same type, as given by the carry.only.for.same.medication parameter.

- consider.dosage.change whether the carry-over is adjusted to reflect changes in dosage, as given by the consider.dosage.change parameter.
- followup.window.start the beginning of the follow-up window, as given by the followup.window.start parameter.
- followup.window.start.unit the time unit of the followup.window.start, as given by the followup.window.start.unit parameter.
- followup.window.duration the duration of the follow-up window, as given by the followup.window.duration parameter.

· observation.window.start the beginning of the observation window, as given by the observation.window.start

- followup.window.duration.unit the time unit of the followup.window.duration, as given by the followup.window.duration.unit parameter.
- parameter.
- observation.window.start.unit the time unit of the observation.window.start, as given by the observation.window.start.unit parameter.
- observation.window.duration the duration of the observation window, as given by the observation.window.duration parameter.
- observation.window.duration.unit the time unit of the observation.window.duration, as given by the observation.window.duration.unit parameter.
- date. format the format of the dates, as given by the date. format parameter.
- summary the metadata, as given by the summary parameter.
- event.info the data.frame containing the event info (irrelevant for most users; see compute.event.int.gaps for details).
- CMA the data. frame containing the actual CMA estimates for each participant (the ID. colname column).

Please note that if medication. groups are defined, then the CMA and event.info are named lists, each element containing the CMA and event.info corresponding to a single medication group (the element's name).

### See Also

CMAs 1 to 8 are defined in:

Vollmer, W. M., Xu, M., Feldstein, A., Smith, D., Waterbury, A., & Rand, C. (2012). Comparison of pharmacy-based measures of medication adherence. *BMC Health Services Research*, **12**, 155. doi: 10.1186/1472696312155.

# **Examples**

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```
medication.class.colname="CATEGORY",
  carry.only.for.same.medication=FALSE,
  consider.dosage.change=FALSE,
  followup.window.start=30,
  observation.window.start=30,
  observation.window.duration=365,
  date.format="%m/%d/%Y"
);
```

CMA9

CMA9 constructor.

## **Description**

Constructs a CMA (continuous multiple-interval measures of medication availability/gaps) type 9 object.

# Usage

```
CMA9(
  data = NULL,
  ID.colname = NA,
  event.date.colname = NA,
  event.duration.colname = NA,
  event.daily.dose.colname = NA,
 medication.class.colname = NA,
 medication.groups = NULL,
  flatten.medication.groups = FALSE,
 medication.groups.colname = ".MED_GROUP_ID",
  carry.only.for.same.medication = FALSE,
  consider.dosage.change = FALSE,
  followup.window.start = 0,
  followup.window.start.unit = c("days", "weeks", "months", "years")[1],
  followup.window.start.per.medication.group = FALSE,
  followup.window.duration = 365 * 2,
  followup.window.duration.unit = c("days", "weeks", "months", "years")[1],
  observation.window.start = 0,
  observation.window.start.unit = c("days", "weeks", "months", "years")[1],
  observation.window.duration = 365 * 2,
  observation.window.duration.unit = c("days", "weeks", "months", "years")[1],
  date.format = "%m/%d/%Y",
  summary = NA,
  event.interval.colname = "event.interval",
  gap.days.colname = "gap.days",
  force.NA.CMA.for.failed.patients = TRUE,
  parallel.backend = c("none", "multicore", "snow", "snow(SOCK)", "snow(MPI)",
    "snow(NWS)")[1],
  parallel.threads = "auto",
```

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## **Arguments**

data

A data.frame containing the events used to compute the CMA. Must contain, at a minimum, the patient unique ID, the event date and duration, and might also contain the daily dosage and medication type (the actual column names are defined in the following four parameters).

ID.colname

A *string*, the name of the column in data containing the unique patient ID; must be present.

event.date.colname

A *string*, the name of the column in data containing the start date of the event (in the format given in the date. format parameter); must be present.

event.duration.colname

A *string*, the name of the column in data containing the event duration (in days); must be present.

event.daily.dose.colname

A *string*, the name of the column in data containing the prescribed daily dose, or NA if not defined.

medication.class.colname

A *string*, the name of the column in data containing the medication type, or NA if not defined.

medication.groups

A *vector* of characters defining medication groups or the name of a column in data that defines such groups. The names of the vector are the medication group unique names, while the content defines them as logical expressions. While the names can be any string of characters except "}", it is recommended to stick to the rules for defining vector names in R. For example,  $c("A"="CATEGORY == 'medA'", "AA"="{A} & PERDAY < 4" defines two medication groups: A which selects all events of type "medA", and B which selects all events already defined by "A" but with a daily dose lower than 4. If NULL, no medication groups are defined. If medication groups are defined, there is one CMA estimate for each group; moreover, there is a special group <math>\_ALL\_OTHERS\_$  automatically defined containing all observations not covered by any of the explicitly defined groups.

flatten.medication.groups

Logical, if FALSE (the default) then the CMA and event.info components of the object are lists with one medication group per element; otherwise, they are data.frames with an extra column containing the medication group (its name is given by medication.groups.colname).

medication.groups.colname

a *string* (defaults to ".MED\_GROUP\_ID") giving the name of the column storing the group name when flatten.medication.groups is TRUE.

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carry.only.for.same.medication

Logical, if TRUE, the carry-over applies only across medication of the same type.

consider.dosage.change

Logical, if TRUE, the carry-over is adjusted to also reflect changes in dosage.

followup.window.start

If a Date object, it represents the actual start date of the follow-up window; if a *string* it is the name of the column in data containing the start date of the follow-up window either as the numbers of followup.window.start.unit units after the first event (the column must be of type numeric) or as actual dates (in which case the column must be of type Date or a string that conforms to the format specified in date.format); if a *number* it is the number of time units defined in the followup.window.start.unit parameter after the begin of the participant's first event; or NA if not defined.

followup.window.start.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.start refers to (when a number), or NA if not defined.

followup.window.start.per.medication.group

a *logical*: if there are medication groups defined and this is TRUE, then the first event considered for the follow-up window start is relative to each medication group separately, otherwise (the default) it is relative to the patient.

followup.window.duration

either a *number* representing the duration of the follow-up window in the time units given in followup.window.duration.unit, or a *string* giving the column containing these numbers. Should represent a period for which relevant medication events are recorded accurately (e.g. not extend after end of relevant treatment, loss-to-follow-up or change to a health care provider not covered by the database).

followup.window.duration.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.duration refers to, or NA if not defined.

observation.window.start, observation.window.start.unit, observation.window.duration, observation.window.the definition of the observation window (see the follow-up window parameters above for details).

date.format

A *string* giving the format of the dates used in the data and the other parameters; see the format parameters of the as. Date function for details (NB, this concerns only the dates given as strings and not as Date objects).

summary Metadata as a *string*, briefly describing this CMA.

event.interval.colname

A *string*, the name of a newly-created column storing the number of days between the start of the current event and the start of the next one; the default value "event.interval" should be changed only if there is a naming conflict with a pre-existing "event.interval" column in event.info.

gap.days.colname

A *string*, the name of a newly-created column storing the number of days when medication was not available (i.e., the "gap days"); the default value "gap.days" should be changed only if there is a naming conflict with a pre-existing "gap.days" column in event.info.

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force.NA.CMA.for.failed.patients

Logical describing how the patients for which the CMA estimation fails are treated: if TRUE they are returned with an NA CMA estimate, while for FALSE they are omitted.

parallel.backend

Can be "none" (the default) for single-threaded execution, "multicore" (using mclapply in package parallel) for multicore processing (NB. not currently implemented on MS Windows and automatically falls back on "snow" on this platform), or "snow", "snow(SOCK)" (equivalent to "snow"), "snow(MPI)" or "snow(NWS)" specifying various types of SNOW clusters (can be on the local machine or more complex setups – please see the documentation of package snow for details; the last two require packages Rmpi and nws, respectively, not automatically installed with AdhereR).

parallel.threads

Can be "auto" (for parallel.backend == "multicore", defaults to the number of cores in the system as given by options ("cores"), while for parallel.backend == "snow", defaults to 2), a strictly positive integer specifying the number of parallel threads, or a more complex specification of the SNOW cluster nodes for parallel.backend == "snow" (see the documentation of package snow for details).

suppress.warnings

*Logical*, if TRUE don't show any warnings.

suppress.special.argument.checks

Logical parameter for internal use; if FALSE (default) check if the important columns in the data have some of the reserved names, if TRUE this check is not performed.

arguments.that.should.not.be.defined

a *list* of argument names and pre-defined values for which a warning should be thrown if passed to the function.

... other possible parameters

# **Details**

CMA9 is similar to CMA7 and CMA8 in that it accounts for carry-over within and before the observation window assuming that new medication is "banked" until needed (oversupply from previous events is used first, followed new medication supply). Yet, unlike these previous CMAs, it does not assume the medication is used as prescribed; in longitudinal studies with multiple CMA measures, this assumption may introduce additional variation in CMA estimates depending on when the observation window starts in relation to the previous medication event. A shorter time distance from the previous event (and longer to the first event in the observation window) results in higher values even if the number of gap days is the same, and it may also be that the patient has had a similar use pattern for that time interval, rather than perfect adherence followed by no medication use. CMA9 applies a different adjustment: it computes a ratio of days supply over each interval between two prescriptions and considers this applies for each day of that interval, up to 100% (moving oversupply to the next event interval). All medication events in the follow up window before observation window are considered for carry-over calculation. The last interval ends at the end of the follow-up window. Thus, it accounts for timing within the observation window, as well as before (but differently from CMA7 and CMA8), and excludes the remaining supply at the end of the observation window, if any.

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#### The formula is

(number of days in the observation window, each weighted by the ratio of days supply applicable to their event interval)/(number of days in the observation window), each weighted by the ratio of days supply applicable to their event interval)/(number of days in the observation window), each weighted by the ratio of days supply applicable to their event interval)/(number of days in the observation window), each weighted by the ratio of days supply applicable to their event interval)/(number of days in the observation window), each weighted by the ratio of days supply applicable to their event interval)/(number of days in the observation window), each weighted by the ratio of days supply applicable to the interval)/(number of days in the observation window), each weighted by the ratio of days supply applicable to the interval)/(number of days in the observation window), each weighted by the ratio of days supply applicable to the observation window window). The results of the observation window w

### Observations:

- the carry.only.for.same.medication parameter controls the transmission of carry-over across medication changes, producing a "standard" CMA7 (default value is FALSE), and an "alternative" CMA7b, respectively;
- the consider.dosage.change parameter controls if dosage changes are taken into account, i.e. if set as TRUE and a new medication event has a different daily dosage recommendation, carry-over is recomputed assuming medication use according to the new prescribed dosage (default value is FALSE).

### Value

An S3 object of class CMA9 (derived from CMA0) with the following fields:

- data The actual event data, as given by the data parameter.
- ID. colname the name of the column in data containing the unique patient ID, as given by the ID. colname parameter.
- event.date.colname the name of the column in data containing the start date of the event (in the format given in the date.format parameter), as given by the event.date.colname parameter.
- event.duration.colname the name of the column in data containing the event duration (in days), as given by the event.duration.colname parameter.
- event.daily.dose.colname the name of the column in data containing the prescribed daily dose, as given by the event.daily.dose.colname parameter.
- medication.class.colname the name of the column in data containing the classes/types/groups of medication, as given by the medication.class.colname parameter.
- carry.only.for.same.medication whether the carry-over applies only across medication of the same type, as given by the carry.only.for.same.medication parameter.
- consider.dosage.change whether the carry-over is adjusted to reflect changes in dosage, as given by the consider.dosage.change parameter.
- followup.window.start the beginning of the follow-up window, as given by the followup.window.start parameter.
- followup.window.start.unit the time unit of the followup.window.start, as given by the followup.window.start.unit parameter.
- followup.window.duration the duration of the follow-up window, as given by the followup.window.duration parameter.
- followup.window.duration.unit the time unit of the followup.window.duration, as given by the followup.window.duration.unit parameter.
- observation.window.start the beginning of the observation window, as given by the observation.window.start parameter.
- observation.window.start.unit the time unit of the observation.window.start, as given by the observation.window.start.unit parameter.

• observation.window.duration the duration of the observation window, as given by the observation.window.duration parameter.

- observation.window.duration.unit the time unit of the observation.window.duration, as given by the observation.window.duration.unit parameter.
- date. format the format of the dates, as given by the date. format parameter.
- summary the metadata, as given by the summary parameter.
- event.info the data.frame containing the event info (irrelevant for most users; see compute.event.int.gaps for details).
- CMA the data. frame containing the actual CMA estimates for each participant (the ID. colname column).

Please note that if medication.groups are defined, then the CMA and event.info are named lists, each element containing the CMA and event.info corresponding to a single medication group (the element's name).

## **Examples**

CMA\_per\_episode

CMA\_per\_episode constructor.

### **Description**

Applies a given CMA to each treatment episode and constructs a CMA\_per\_episode object.

# Usage

```
CMA_per_episode(
   CMA.to.apply,
   data,
   treat.epi = NULL,
   ID.colname = NA,
   event.date.colname = NA,
   event.duration.colname = NA,
```

```
event.daily.dose.colname = NA,
 medication.class.colname = NA,
 medication.groups = NULL,
  flatten.medication.groups = FALSE,
 medication.groups.colname = ".MED_GROUP_ID",
  carry.only.for.same.medication = NA,
  consider.dosage.change = NA,
 medication.change.means.new.treatment.episode = TRUE,
 dosage.change.means.new.treatment.episode = FALSE,
 maximum.permissible.gap = 180,
 maximum.permissible.gap.unit = c("days", "weeks", "months", "years", "percent")[1],
 maximum.permissible.gap.append.to.episode = FALSE,
  followup.window.start = 0,
  followup.window.start.unit = c("days", "weeks", "months", "years")[1],
  followup.window.start.per.medication.group = FALSE,
  followup.window.duration = 365 * 2,
  followup.window.duration.unit = c("days", "weeks", "months", "years")[1],
  observation.window.start = 0,
  observation.window.start.unit = c("days", "weeks", "months", "years")[1],
  observation.window.duration = 365 \times 2,
  observation.window.duration.unit = c("days", "weeks", "months", "years")[1],
  return.inner.event.info = FALSE,
  date.format = "%m/%d/%Y",
  summary = "CMA per treatment episode",
  event.interval.colname = "event.interval",
  gap.days.colname = "gap.days",
  force.NA.CMA.for.failed.patients = TRUE,
  return.mapping.events.episodes = FALSE,
  parallel.backend = c("none", "multicore", "snow", "snow(SOCK)", "snow(MPI)",
    "snow(NWS)")[1],
 parallel.threads = "auto",
  suppress.warnings = FALSE,
  suppress.special.argument.checks = TRUE,
)
```

### Arguments

data

CMA. to. apply A *string* giving the name of the CMA function (1 to 9) that will be computed for each treatment episode.

A data. frame containing the events (prescribing or dispensing) used to compute the CMA. Must contain, at a minimum, the patient unique ID, the event date and duration, and might also contain the daily dosage and medication type (the actual column names are defined in the following four parameters).

A data.frame containing the treatment episodes. Must contain the patient ID (as given in ID.colname), the episode unique ID (increasing sequentially, episode.ID), the episode start date (episode.start), the episode duration in days (episode.duration), and the episode end date (episode.end).

ID.colname

A *string*, the name of the column in data containing the unique patient ID; must be present.

event.date.colname

A *string*, the name of the column in data containing the start date of the event (in the format given in the date. format parameter); must be present.

event.duration.colname

A *string*, the name of the column in data containing the event duration (in days); must be present.

event.daily.dose.colname

A *string*, the name of the column in data containing the prescribed daily dose, or NA if not defined.

medication.class.colname

A *string*, the name of the column in data containing the medication type, or NA if not defined.

medication.groups

A *vector* of characters defining medication groups or the name of a column in data that defines such groups. The names of the vector are the medication group unique names, while the content defines them as logical expressions. While the names can be any string of characters except "}", it is recommended to stick to the rules for defining vector names in R. For example,  $c("A"="CATEGORY == 'medA'", "AA"="{A} & PERDAY < 4" defines two medication groups: A which selects all events of type "medA", and B which selects all events already defined by "A" but with a daily dose lower than 4. If NULL, no medication groups are defined. If medication groups are defined, there is one CMA estimate for each group; moreover, there is a special group <math>\_ALL\_OTHERS\_$  automatically defined containing all observations *not* covered by any of the explicitly defined groups.

flatten.medication.groups

Logical, if FALSE (the default) then the CMA and event.info components of the object are lists with one medication group per element; otherwise, they are data.frames with an extra column containing the medication group (its name is given by medication.groups.colname).

medication.groups.colname

a *string* (defaults to ".MED\_GROUP\_ID") giving the name of the column storing the group name when flatten.medication.groups is TRUE.

carry.only.for.same.medication

Logical, if TRUE, the carry-over applies only across medication of the same type; valid only for CMAs 5 to 9, in which case it is coupled (i.e., the same value is used for computing the treatment episodes and the CMA on each treatment episode).

consider.dosage.change

Logical, if TRUE, the carry-over is adjusted to also reflect changes in dosage; valid only for CMAs 5 to 9, in which case it is coupled (i.e., the same value is used for computing the treatment episodes and the CMA on each treatment episode).

medication.change.means.new.treatment.episode

*Logical*, should a change in medication automatically start a new treatment episode?

dosage.change.means.new.treatment.episode

Logical, should a change in dosage automatically start a new treatment episode? maximum.permissible.gap

The *number* of units given by maximum.permissible.gap.unit representing the maximum duration of permissible gaps between treatment episodes (can also be a percent, see maximum.permissible.gap.unit for details).

maximum.permissible.gap.unit

can be either "days", "weeks", "months", "years" or "percent", and represents the time units that maximum.permissible.gap refers to; if percent, then maximum.permissible.gap is interpreted as a percent (can be greater than 100%) of the duration of the current prescription.

maximum.permissible.gap.append.to.episode

a *logical* value specifying of the maximum.permissible.gap should be append at the end of an episode with a gap larger than the maximum.permissible.gap; FALSE (the default) mean no addition, while TRUE mean that the full maximum.permissible.gap is added.

followup.window.start

If a Date object, it represents the actual start date of the follow-up window; if a *string* it is the name of the column in data containing the start date of the follow-up window either as the numbers of followup.window.start.unit units after the first event (the column must be of type numeric) or as actual dates (in which case the column must be of type Date or a string that conforms to the format specified in date.format); if a *number* it is the number of time units defined in the followup.window.start.unit parameter after the begin of the participant's first event; or NA if not defined.

followup.window.start.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.start refers to (when a number), or NA if not defined.

followup.window.start.per.medication.group

a *logical*: if there are medication groups defined and this is TRUE, then the first event considered for the follow-up window start is relative to each medication group separately, otherwise (the default) it is relative to the patient.

followup.window.duration

either a *number* representing the duration of the follow-up window in the time units given in followup.window.duration.unit, or a *string* giving the column containing these numbers. Should represent a period for which relevant medication events are recorded accurately (e.g. not extend after end of relevant treatment, loss-to-follow-up or change to a health care provider not covered by the database).

followup.window.duration.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.duration refers to, or NA if not defined.

observation.window.start, observation.window.start.unit, observation.window.duration, observation.wir the definition of the observation window (see the follow-up window parameters above for details).

return.inner.event.info

Logical specifying if the function should also return the event.info for all the individual events in each sliding window; by default it is FALSE as this informa-

tion is useful only in very specific cases (e.g., plotting the event intervals) and adds a small but non-negligible computational overhead.

date.format

A *string* giving the format of the dates used in the data and the other parameters; see the format parameters of the as. Date function for details (NB, this concerns only the dates given as strings and not as Date objects).

summary

Metadata as a string, briefly describing this CMA.

#### event.interval.colname

A *string*, the name of a newly-created column storing the number of days between the start of the current event and the start of the next one; the default value "event.interval" should be changed only if there is a naming conflict with a pre-existing "event.interval" column in event.info.

### gap.days.colname

A *string*, the name of a newly-created column storing the number of days when medication was not available (i.e., the "gap days"); the default value "gap.days" should be changed only if there is a naming conflict with a pre-existing "gap.days" column in event.info.

## force.NA.CMA.for.failed.patients

Logical describing how the patients for which the CMA estimation fails are treated: if TRUE they are returned with an NA CMA estimate, while for FALSE they are omitted.

### return.mapping.events.episodes

A *Logical*, if TRUE then the mapping between events and episodes is returned as an extra component mapping.episodes.to.events, which is a data.table giving, for each episode, the events that belong to it (an event is given by its row number in the data). Please note that the episodes returned are specific to the particular simple CMA used, and should preferentially used over those returned by compute.treatment.episodes(). This component can also be accessed using the getEventsToEpisodesMapping() function.

## parallel.backend

Can be "none" (the default) for single-threaded execution, "multicore" (using mclapply in package parallel) for multicore processing (NB. not currently implemented on MS Windows and automatically falls back on "snow" on this platform), or "snow", "snow(SOCK)" (equivalent to "snow"), "snow(MPI)" or "snow(NWS)" specifying various types of SNOW clusters (can be on the local machine or more complex setups – please see the documentation of package snow for details; the last two require packages Rmpi and nws, respectively, not automatically installed with AdhereR).

### parallel.threads

Can be "auto" (for parallel.backend == "multicore", defaults to the number of cores in the system as given by options("cores"), while for parallel.backend == "snow", defaults to 2), a strictly positive integer specifying the number of parallel threads, or a more complex specification of the SNOW cluster nodes for parallel.backend == "snow" (see the documentation of package snow for details).

### suppress.warnings

Logical, if TRUE don't show any warnings.

suppress.special.argument.checks

*Logical* parameter for internal use; if FALSE (default) check if the important columns in the data have some of the reserved names, if TRUE this check is not performed.

... other possible parameters

#### **Details**

CMA\_per\_episode first identifies the treatment episodes for the whole follo-up window (using the compute.treatment.episodes function), and then computes the given "simple" CMA for each treatment episode that intersects with the observation window. NB: the CMA is computed for the period of the episode that is part of the observations window; thus, if an episode starts earlier or ends later than the observation window, CMA will be computed for a section of that episode. Thus, as opposed to the "simple" CMAs 1 to 9, it returns a set of CMAs, with possibly more than one element.

It is highly similar to CMA\_sliding\_window which computes a CMA for a set of sliding windows.

### Value

An S3 object of class CMA\_per\_episode with the following fields:

- data The actual event data, as given by the data parameter.
- ID. colname the name of the column in data containing the unique patient ID, as given by the ID. colname parameter.
- event.date.colname the name of the column in data containing the start date of the event (in the format given in the date.format parameter), as given by the event.date.colname parameter.
- event.duration.colname the name of the column in data containing the event duration (in days), as given by the event.duration.colname parameter.
- event.daily.dose.colname the name of the column in data containing the prescribed daily dose, as given by the event.daily.dose.colname parameter.
- medication.class.colname the name of the column in data containing the classes/types/groups of medication, as given by the medication.class.colname parameter.
- carry.only.for.same.medication whether the carry-over applies only across medication of the same type, as given by the carry.only.for.same.medication parameter.
- consider.dosage.change whether the carry-over is adjusted to reflect changes in dosage, as given by the consider.dosage.change parameter.
- followup.window.start the beginning of the follow-up window, as given by the followup.window.start parameter.
- followup.window.start.unit the time unit of the followup.window.start, as given by the followup.window.start.unit parameter.
- followup.window.duration the duration of the follow-up window, as given by the followup.window.duration parameter.
- followup.window.duration.unit the time unit of the followup.window.duration, as given by the followup.window.duration.unit parameter.

• observation.window.start the beginning of the observation window, as given by the observation.window.start parameter.

- observation.window.start.unit the time unit of the observation.window.start, as given by the observation.window.start.unit parameter.
- observation.window.duration the duration of the observation window, as given by the observation.window.duration parameter.
- observation.window.duration.unit the time unit of the observation.window.duration, as given by the observation.window.duration.unit parameter.
- date. format the format of the dates, as given by the date. format parameter.
- summary the metadata, as given by the summary parameter.
- event.info the data.frame containing the event info (irrelevant for most users; see compute.event.int.gaps for details).
- computed.CMA the class name of the computed CMA.
- CMA the data. frame containing the actual CMA estimates for each participant (the ID. colname column) and treatment episode, with columns:
  - ID. colname the patient ID as given by the ID. colname parameter.
  - episode. ID the unique treatment episode ID (within patients).
  - episode.start the treatment episode's start date (as a Date object).
  - end.episode.gap.days the corresponding gap days of the last event in this episode.
  - episode.duration the treatment episode's duration in days.
  - episode.end the treatment episode's end date (as a Date object).
  - CMA the treatment episode's estimated CMA.

Please note that if medication. groups are defined, then the CMA and event. info are named lists, each element containing the CMA and event. info corresponding to a single medication group (the element's name).

#### See Also

CMA\_sliding\_window is very similar, computing a "simple" CMA for each of a set of same-size sliding windows. The "simple" CMAs that can be computed comprise CMA1, CMA2, CMA3, CMA4, CMA5, CMA6, CMA7, CMA8, CMA9, as well as user-defined classes derived from CMA0 that have a CMA component giving the estimated CMA per patient as a data.frame. If return.mapping.events.episodes is TRUE, then this also has a component mapping.episodes.to.events that gives the mapping between episodes and events as a data.table with the following columns:

- patid the patient ID.
- episode. ID the episode unique ID (increasing sequentially).
- event.index.in.data the event given by its row number in the data.

# Examples

CMA\_polypharmacy

CMA constructor for polypharmacy.

### **Description**

Constructs a CMA (continuous multiple-interval measures of medication availability/gaps) object for polypharmacy.

## Usage

```
CMA_polypharmacy(
  data = data,
  medication.groups = medication.class.colname,
 CMA.to.apply = NA,
  aggregate.first = TRUE,
  aggregation.method = NA,
  aggregation.method.arguments = NA,
  thresholds = NA,
  ID.colname = NA.
  event.date.colname = NA,
  event.duration.colname = NA,
  event.daily.dose.colname = NA,
 medication.class.colname = NA,
  carry.only.for.same.medication = NA,
  consider.dosage.change = NA,
  followup.window.start = 0,
  followup.window.start.unit = c("days", "weeks", "months", "years")[1],
  followup.window.duration = 365 * 2,
  followup.window.duration.unit = c("days", "weeks", "months", "years")[1],
  observation.window.start = 0,
  observation.window.start.unit = c("days", "weeks", "months", "years")[1],
  observation.window.duration = 365 * 2,
  observation.window.duration.unit = c("days", "weeks", "months", "years")[1],
  date.format = "%m/%d/%Y",
  summary = "CMA for polypharmacy",
```

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```
force.NA.CMA.for.failed.patients = TRUE,
parallel.backend = c("none", "multicore", "snow", "snow(SOCK)", "snow(MPI)",
    "snow(NWS)")[1],
parallel.threads = "auto",
suppress.warnings = FALSE,
suppress.special.argument.checks = TRUE,
...
)
```

## **Arguments**

data

A data.frame containing the events (prescribing or dispensing) used to compute the CMA. Must contain, at a minimum, the patient unique ID, the event date and duration, medication type, and might also contain the daily dosage (the actual column names are defined in the following four parameters).

### medication.groups

A *string* with the name of the column containing the medication groups. If multiple medication classes should belong to the same treatment group, they can be differentiated here (important to investigate treatment switches)

CMA.to.apply

A *string* giving the name of the CMA function (1 to 9) that will be computed for each treatment group.

#### aggregate.first

*Logical*, if TRUE, aggregate across treatment groups before summarizing over time during OW.

### aggregation.method

A *string* giving the name of the function to aggregate CMA values of medication group, or NA to return only raw CMA estimates per medication group. Accepts summary functions such as "mean", "sd", "var", "min", "max", and "median". Custom functions are possible as long as they take a numeric vector as input and return a single numeric value.

## aggregation.method.arguments

optional, A *named list* of additional arguments to the function given in aggregation method, e.g. na.rm = TRUE.

thresholds

optional, a *number* to apply as threshold between aggregation and summarizing.

ID.colname

A *string*, the name of the column in data containing the medication type. Defaults to medication.class.colname.

#### event.date.colname

A *string*, the name of the column in data containing the start date of the event (in the format given in the date. format parameter); must be present.

### event.duration.colname

A *string*, the name of the column in data containing the event duration (in days); must be present.

### event.daily.dose.colname

A *string*, the name of the column in data containing the prescribed daily dose, or NA if not defined.

medication.class.colname

A *string*, the name of the column in data containing the medication type, or NA if not defined.

carry.only.for.same.medication

Logical, if TRUE, the carry-over applies only across medication of the same type; valid only for CMAs 5 to 9, in which case it is coupled (i.e., the same value is used for computing the treatment episodes and the CMA on each treatment episode).

consider.dosage.change

Logical, if TRUE, the carry-over is adjusted to also reflect changes in dosage; valid only for CMAs 5 to 9, in which case it is coupled (i.e., the same value is used for computing the treatment episodes and the CMA on each treatment episode).

followup.window.start

If a Date object, it represents the actual start date of the follow-up window; if a *string* it is the name of the column in data containing the start date of the follow-up window either as the numbers of followup.window.start.unit units after the first event (the column must be of type numeric) or as actual dates (in which case the column must be of type Date); if a *number* it is the number of time units defined in the followup.window.start.unit parameter after the begin of the participant's first event; or NA if not defined.

followup.window.start.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.start refers to (when a number), or NA if not defined.

followup.window.duration

either a *number* representing the duration of the follow-up window in the time units given in followup.window.duration.unit, or a *string* giving the column containing these numbers. Should represent a period for which relevant medication events are recorded accurately (e.g. not extend after end of relevant treatment, loss-to-follow-up or change to a health care provider not covered by the database).

followup.window.duration.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.duration refers to, or NA if not defined.

observation.window.start, observation.window.start.unit, observation.window.duration, observation.wir the definition of the observation window (see the follow-up window parameters above for details). Can be defined separately for each patient and treatment group.

date.format A *string* giving the format of the dates used in the data and the other parameters; see the format parameters of the as.Date function for details (NB, this concerns only the dates given as strings and not as Date objects).

summary Metadata as a *string*, briefly describing this CMA.

force.NA.CMA.for.failed.patients

Logical describing how the patients for which the CMA estimation fails are treated: if TRUE they are returned with an NA CMA estimate, while for FALSE they are omitted.

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#### parallel.backend

Can be "none" (the default) for single-threaded execution, "multicore" (using mclapply in package parallel) for multicore processing (NB. not currently implemented on MS Windows and automatically falls back on "snow" on this platform), or "snow", "snow(SOCK)" (equivalent to "snow"), "snow(MPI)" or "snow(NWS)" specifying various types of SNOW clusters (can be on the local machine or more complex setups – please see the documentation of package snow for details; the last two require packages Rmpi and nws, respectively, not automatically installed with AdhereR).

#### parallel.threads

Can be "auto" (for parallel.backend == "multicore", defaults to the number of cores in the system as given by options("cores"), while for parallel.backend == "snow", defaults to 2), a strictly positive integer specifying the number of parallel threads, or a more complex specification of the SNOW cluster nodes for parallel.backend == "snow" (see the documentation of package snow for details).

suppress.warnings

Logical, if TRUE don't show any warnings.

suppress.special.argument.checks

Logical parameter for internal use; if FALSE (default) check if the important columns in the data have some of the reserved names, if TRUE this check is not performed.

.. other possible parameters

#### Value

An S3 object of class CMA\_polypharmacy with the following fields:

- data The actual event data, as given by the data parameter.
- ID. colname the name of the column in data containing the unique patient ID, as given by the ID. colname parameter.
- event.date.colname the name of the column in data containing the start date of the event (in the format given in the date.format parameter), as given by the event.date.colname parameter.
- event.duration.colname the name of the column in data containing the event duration (in days), as given by the event.duration.colname parameter.
- event.daily.dose.colname the name of the column in data containing the prescribed daily dose, as given by the event.daily.dose.colname parameter.
- medication.class.colname the name of the column in data containing the classes/types/groups of medication, as given by the medication.class.colname parameter.
- carry.only.for.same.medication whether the carry-over applies only across medication of the same type, as given by the carry.only.for.same.medication parameter.
- consider.dosage.change whether the carry-over is adjusted to reflect changes in dosage, as given by the consider.dosage.change parameter.
- followup.window.start the beginning of the follow-up window, as given by the followup.window.start parameter.

- followup.window.start.unit the time unit of the followup.window.start, as given by the followup.window.start.unit parameter.
- followup.window.duration the duration of the follow-up window, as given by the followup.window.duration parameter.
- followup.window.duration.unit the time unit of the followup.window.duration, as given by the followup.window.duration.unit parameter.
- observation.window.start the beginning of the observation window, as given by the observation.window.start parameter.
- observation.window.start.unit the time unit of the observation.window.start, as given by the observation.window.start.unit parameter.
- observation.window.duration the duration of the observation window, as given by the observation.window.duration parameter.
- observation.window.duration.unit the time unit of the observation.window.duration, as given by the observation.window.duration.unit parameter.
- date. format the format of the dates, as given by the date. format parameter.
- summary the metadata, as given by the summary parameter.
- event.info the data.frame containing the event info (irrelevant for most users; see compute.event.int.gaps for details).
- aggregation.method the aggregation method to combine CMA values from different groups.
- computed. CMA the class name of the computed CMA.
- medication.groups a data.frame with medication groups and classes
- CMA the data. frame containing the actual CMA estimates for each participant (the ID. colname column) and sometimes treatment group, with columns:
  - ID. colname the patient ID as given by the ID. colname parameter.
  - medication.groups only when no aggregation method is used (aggregation.method
     NA); the treatment group as given by the medication.groups parameter.
  - CMA the treatment episode's estimated CMA.

# **Examples**

```
## Not run:
CMA_PP <- CMA_polypharmacy(data = med.events.pp,
medication.groups = med.groups,
CMA.to.apply = "CMA7",
aggregate.first = TRUE, # aggregate before summarizing
aggregation.method = "mean", # compute mean of CMAs
aggregation.method.arguments = list(na.rm = TRUE), # remove NA's during calculation
thresholds = NA, # don't apply threshold
ID.colname="PATIENT_ID",
event.date.colname="DATE",
event.duration.colname="DURATION",
event.daily.dose.colname="PERDAY",
medication.class.colname="CATEGORY",
followup.window.start=0,
observation.window.start=180,</pre>
```

CMA\_sliding\_window

```
observation.window.duration=365,
carry.only.for.same.medication = TRUE);
## End(Not run)
```

CMA\_sliding\_window

CMA\_sliding\_window constructor.

### **Description**

Applies a given CMA to each sliding window and constructs a CMA\_sliding\_window object.

### Usage

```
CMA_sliding_window(
  CMA.to.apply,
  data,
  ID.colname = NA,
  event.date.colname = NA,
  event.duration.colname = NA,
  event.daily.dose.colname = NA,
  medication.class.colname = NA,
 medication.groups = NULL,
  flatten.medication.groups = FALSE,
 medication.groups.colname = ".MED_GROUP_ID",
  carry.only.for.same.medication = NA,
  consider.dosage.change = NA,
  followup.window.start = 0,
  followup.window.start.unit = c("days", "weeks", "months", "years")[1],
  followup.window.start.per.medication.group = FALSE,
  followup.window.duration = 365 * 2,
  followup.window.duration.unit = c("days", "weeks", "months", "years")[1],
  observation.window.start = 0,
  observation.window.start.unit = c("days", "weeks", "months", "years")[1],
  observation.window.duration = 365 * 2,
  observation.window.duration.unit = c("days", "weeks", "months", "years")[1],
  sliding.window.start = 0,
  sliding.window.start.unit = c("days", "weeks", "months", "years")[1],
  sliding.window.duration = 90,
  sliding.window.duration.unit = c("days", "weeks", "months", "years")[1],
  sliding.window.step.duration = 30,
  sliding.window.step.unit = c("days", "weeks", "months", "years")[1],
  sliding.window.no.steps = NA,
  return.inner.event.info = FALSE,
  date.format = "%m/%d/%Y",
  summary = "CMA per sliding window",
  event.interval.colname = "event.interval",
  gap.days.colname = "gap.days",
```

```
force.NA.CMA.for.failed.patients = TRUE,
  return.mapping.events.sliding.window = FALSE,
  parallel.backend = c("none", "multicore", "snow", "snow(SOCK)", "snow(MPI)",
        "snow(NWS)")[1],
  parallel.threads = "auto",
  suppress.warnings = FALSE,
  suppress.special.argument.checks = FALSE,
  ...
)
```

### **Arguments**

CMA. to. apply A *string* giving the name of the CMA function (1 to 9) that will be computed for

each treatment episode.

A data. frame containing the events used to compute the CMA. Must contain, at a minimum, the patient unique ID, the event date and duration, and might also contain the daily dosage and medication type (the actual column names are

defined in the following four parameters).

 $\hbox{ID. colname} \qquad \quad A \textit{ string}, \text{ the name of the column in data containing the unique patient ID; must}$ 

be present.

event.date.colname

A *string*, the name of the column in data containing the start date of the event (in the format given in the date. format parameter); must be present.

event.duration.colname

A *string*, the name of the column in data containing the event duration (in days); must be present.

event.daily.dose.colname

A *string*, the name of the column in data containing the prescribed daily dose, or NA if not defined.

medication.class.colname

A *string*, the name of the column in data containing the medication type, or NA if not defined.

medication.groups

A *vector* of characters defining medication groups or the name of a column in data that defines such groups. The names of the vector are the medication group unique names, while the content defines them as logical expressions. While the names can be any string of characters except "}", it is recommended to stick to the rules for defining vector names in R. For example,  $c("A"="CATEGORY == 'medA'", "AA"="{A} & PERDAY < 4" defines two medication groups: A which selects all events of type "medA", and B which selects all events already defined by "A" but with a daily dose lower than 4. If NULL, no medication groups are defined. If medication groups are defined, there is one CMA estimate for each group; moreover, there is a special group <math>\_ALL\_OTHERS\_$  automatically defined containing all observations *not* covered by any of the explicitly defined groups.

flatten.medication.groups

*Logical*, if FALSE (the default) then the CMA and event.info components of the object are lists with one medication group per element; otherwise, they are

data.frames with an extra column containing the medication group (its name is given by medication.groups.colname).

medication.groups.colname

a *string* (defaults to ".MED\_GROUP\_ID") giving the name of the column storing the group name when flatten.medication.groups is TRUE.

carry.only.for.same.medication

 $\label{logical} \textit{Logical}, \text{ if TRUE}, \text{ the carry-over applies only across medication of the same type.} \\ \text{consider.dosage.change}$ 

Logical, if TRUE, the carry-over is adjusted to also reflect changes in dosage.

followup.window.start

If a Date object, it represents the actual start date of the follow-up window; if a *string* it is the name of the column in data containing the start date of the follow-up window either as the numbers of followup.window.start.unit units after the first event (the column must be of type numeric) or as actual dates (in which case the column must be of type Date or a string that conforms to the format specified in date.format); if a *number* it is the number of time units defined in the followup.window.start.unit parameter after the begin of the participant's first event; or NA if not defined.

followup.window.start.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.start refers to (when a number), or NA if not defined.

followup.window.start.per.medication.group

a *logical*: if there are medication groups defined and this is TRUE, then the first event considered for the follow-up window start is relative to each medication group separately, otherwise (the default) it is relative to the patient.

followup.window.duration

either a *number* representing the duration of the follow-up window in the time units given in followup.window.duration.unit, or a *string* giving the column containing these numbers. Should represent a period for which relevant medication events are recorded accurately (e.g. not extend after end of relevant treatment, loss-to-follow-up or change to a health care provider not covered by the database).

followup.window.duration.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.duration refers to, or NA if not defined.

observation.window.start, observation.window.start.unit, observation.window.duration, observation.window.the definition of the observation window (see the follow-up window parameters above for details).

sliding.window.start, sliding.window.start.unit, sliding.window.duration, sliding.window.duration.unithe definition of the first sliding window (see the follow-up window parameters above for details).

sliding.window.step.duration, sliding.window.step.unit

if not missing (NA), these give the step (or "jump") to the right of the sliding window in time units.

sliding.window.no.steps

a *integer* specifying the desired number of sliding windows to cover the observation window (if possible); trumps sliding.window.step.duration and sliding.window.step.unit.

return.inner.event.info

Logical specifying if the function should also return the event.info for all the individual events in each sliding window; by default it is FALSE as this information is useful only in very specific cases (e.g., plotting the event intervals) and adds a small but non-negligible computational overhead.

date.format

A *string* giving the format of the dates used in the data and the other parameters; see the format parameters of the as. Date function for details (NB, this concerns only the dates given as strings and not as Date objects).

summary

Metadata as a *string*, briefly describing this CMA.

event.interval.colname

A *string*, the name of a newly-created column storing the number of days between the start of the current event and the start of the next one; the default value "event.interval" should be changed only if there is a naming conflict with a pre-existing "event.interval" column in event.info.

gap.days.colname

A *string*, the name of a newly-created column storing the number of days when medication was not available (i.e., the "gap days"); the default value "gap.days" should be changed only if there is a naming conflict with a pre-existing "gap.days" column in event.info.

force.NA.CMA.for.failed.patients

Logical describing how the patients for which the CMA estimation fails are treated: if TRUE they are returned with an NA CMA estimate, while for FALSE they are omitted.

return.mapping.events.sliding.window

A *Logical*, if TRUE then the mapping between events and sliding windows is returned as the component mapping.windows.to.events, which is a data.table giving, for each sliding window, the events that belong to it (an event is given by its row number in the data).

parallel.backend

Can be "none" (the default) for single-threaded execution, "multicore" (using mclapply in package parallel) for multicore processing (NB. not currently implemented on MS Windows and automatically falls back on "snow" on this platform), or "snow", "snow(SOCK)" (equivalent to "snow"), "snow(MPI)" or "snow(NWS)" specifying various types of SNOW clusters (can be on the local machine or more complex setups – please see the documentation of package snow for details; the last two require packages Rmpi and nws, respectively, not automatically installed with AdhereR).

parallel.threads

Can be "auto" (for parallel.backend == "multicore", defaults to the number of cores in the system as given by options("cores"), while for parallel.backend == "snow", defaults to 2), a strictly positive integer specifying the number of parallel threads, or a more complex specification of the SNOW cluster nodes for parallel.backend == "snow" (see the documentation of package snow for details).

suppress.warnings

Logical, if TRUE don't show any warnings.

suppress.special.argument.checks

*Logical* parameter for internal use; if FALSE (default) check if the important columns in the data have some of the reserved names, if TRUE this check is not performed.

... other possible parameters

### **Details**

CMA\_sliding\_window first computes a set of fixed-size (possibly partly overlapping) sliding windows, each sliding to the right by a fixed timelag, and then, for each of them, it computes the given "simple" CMA. Thus, as opposed to the "simple" CMAs 1 to 9, it returns a set of CMAs, with possibly more than one element.

It is highly similar to CMA\_per\_episode which computes a CMA for a set of treatment episodes.

#### Value

An S3 object of class CMA\_sliding\_window with the following fields:

- data The actual event data, as given by the data parameter.
- ID. colname the name of the column in data containing the unique patient ID, as given by the ID. colname parameter.
- event.date.colname the name of the column in data containing the start date of the event (in the format given in the date.format parameter), as given by the event.date.colname parameter.
- event.duration.colname the name of the column in data containing the event duration (in days), as given by the event.duration.colname parameter.
- event.daily.dose.colname the name of the column in data containing the prescribed daily dose, as given by the event.daily.dose.colname parameter.
- medication.class.colname the name of the column in data containing the classes/types/groups of medication, as given by the medication.class.colname parameter.
- carry.only.for.same.medication whether the carry-over applies only across medication of the same type, as given by the carry.only.for.same.medication parameter.
- consider.dosage.change whether the carry-over is adjusted to reflect changes in dosage, as given by the consider.dosage.change parameter.
- followup.window.start the beginning of the follow-up window, as given by the followup.window.start parameter.
- followup.window.start.unit the time unit of the followup.window.start, as given by the followup.window.start.unit parameter.
- followup.window.duration the duration of the follow-up window, as given by the followup.window.duration parameter.
- followup.window.duration.unit the time unit of the followup.window.duration, as given by the followup.window.duration.unit parameter.
- observation.window.start the beginning of the observation window, as given by the observation.window.start parameter.

- observation.window.start.unit the time unit of the observation.window.start, as given by the observation.window.start.unit parameter.
- observation.window.duration the duration of the observation window, as given by the observation.window.duration parameter.
- observation.window.duration.unit the time unit of the observation.window.duration, as given by the observation.window.duration.unit parameter.
- date. format the format of the dates, as given by the date. format parameter.
- summary the metadata, as given by the summary parameter.
- event.info the data.frame containing the event info (irrelevant for most users; see compute.event.int.gaps for details).
- computed. CMA the class name of the computed CMA.
- CMA the data. frame containing the actual CMA estimates for each participant (the ID. colname column) and sliding window, with columns:
  - ID. colname the patient ID as given by the ID. colname parameter.
  - window. ID the unique window ID (within patients).
  - window. start the window's start date (as a Date object).
  - window. end the window's end date (as a Date object).
  - CMA the window's estimated CMA.

Please note that if medication. groups are defined, then the CMA and event. info are named lists, each element containing the CMA and event. info corresponding to a single medication group (the element's name).

#### See Also

CMA\_per\_episode is very similar, computing a "simple" CMA for each of the treatment episodes. The "simple" CMAs that can be computed comprise CMA1, CMA2, CMA3, CMA4, CMA5, CMA6, CMA7, CMA8, CMA9, as well as user-defined classes derived from CMA0 that have a CMA component giving the estimated CMA per patient as a data.frame. If return.mapping.events.sliding.window is TRUE, then this also has an attribute mapping.windows.to.events that gives the mapping between episodes and events as a data.table with the following columns:

- patid the patient ID.
- window. ID the episode unique ID (increasing sequentially).
- event.index.in.data the event given by its row number in the data.

# **Examples**

compute.event.int.gaps 65

```
consider.dosage.change=FALSE,
followup.window.start=0,
observation.window.start=0,
observation.window.duration=365,
sliding.window.start=0,
sliding.window.start.unit="days",
sliding.window.duration=90,
sliding.window.duration.unit="days",
sliding.window.step.duration=7,
sliding.window.step.unit="days",
sliding.window.no.steps=NA,
date.format="%m/%d/%Y"
);
```

## End(Not run)

compute.event.int.gaps

Gap Days and Event (prescribing or dispensing) Intervals.

### **Description**

For a given event (prescribing or dispensing) database, compute the gap days and event intervals in various scenarious.

# Usage

```
compute.event.int.gaps(
  data,
  ID.colname = NA,
  event.date.colname = NA,
  event.duration.colname = NA,
  event.daily.dose.colname = NA,
 medication.class.colname = NA,
  event.interval.colname = "event.interval",
  gap.days.colname = "gap.days",
  carryover.within.obs.window = FALSE,
  carryover.into.obs.window = FALSE,
  carry.only.for.same.medication = FALSE,
  consider.dosage.change = FALSE,
  followup.window.start = 0,
  followup.window.start.unit = c("days", "weeks", "months", "years")[1],
  followup.window.duration = 365 * 2,
  followup.window.duration.unit = c("days", "weeks", "months", "years")[1],
  observation.window.start = 0,
  observation.window.start.unit = c("days", "weeks", "months", "years")[1],
  observation.window.duration = 365 * 2,
  observation.window.duration.unit = c("days", "weeks", "months", "years")[1],
  date.format = "%m/%d/%Y",
```

# **Arguments**

data

A data.frame containing the events used to compute the CMA. Must contain, at a minimum, the patient unique ID, the event date and duration, and might also contain the daily dosage and medication type (the actual column names are defined in the following four parameters); the CMA constructors call this parameter data.

ID.colname

A *string*, the name of the column in data containing the unique patient ID; must be present.

event.date.colname

A *string*, the name of the column in data containing the start date of the event (in the format given in the date. format parameter); must be present.

event.duration.colname

A *string*, the name of the column in data containing the event duration (in days); must be present.

event.daily.dose.colname

A *string*, the name of the column in data containing the prescribed daily dose, or NA if not defined.

medication.class.colname

A *string*, the name of the column in data containing the classes/types/groups of medication, or NA if not defined.

event.interval.colname

A *string*, the name of a newly-created column storing the number of days between the start of the current event and the start of the next one; the default value "event.interval" should be changed only if there is a naming conflict with a pre-existing "event.interval" column in event.info.

gap.days.colname

A *string*, the name of a newly-created column storing the number of days when medication was not available (i.e., the "gap days"); the default value "gap.days" should be changed only if there is a naming conflict with a pre-existing "gap.days" column in event.info.

carryover.within.obs.window

*Logical*, if TRUE consider the carry-over within the observation window, or NA if not defined.

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carryover.into.obs.window

*Logical*, if TRUE consider the carry-over from before the starting date of the observation window, or NA if not defined.

carry.only.for.same.medication

Logical, if TRUE the carry-over applies only across medication of the same type, or NA if not defined.

consider.dosage.change

Logical, if TRUE the carry-over is adjusted to reflect changes in dosage, or NA if not defined.

followup.window.start

If a Date object, it represents the actual start date of the follow-up window; if a *string* it is the name of the column in data containing the start date of the follow-up window either as the numbers of followup.window.start.unit units after the first event (the column must be of type numeric) or as actual dates (in which case the column must be of type Date); if a *number* it is the number of time units defined in the followup.window.start.unit parameter after the begin of the participant's first event.

followup.window.start.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.start refers to (when a number), or NA if not defined.

followup.window.duration

either a *number* representing the duration of the follow-up window in the time units given in followup.window.duration.unit, or a *string* giving the column containing these numbers. Should represent a period for which relevant medication events are recorded accurately (e.g. not extend after end of relevant treatment, loss-to-follow-up or change to a health care provider not covered by the database).

followup.window.duration.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.duration refers to, or NA if not defined.

observation.window.start, observation.window.start.unit, observation.window.duration, observation.wir the definition of the observation window (see the follow-up window parameters above for details).

date.format A *string* giving the format of the dates used in the data and the other parameters; see the format parameters of the as.Date function for details (NB, this concerns only the dates given as strings and not as Date objects).

keep.window.start.end.dates

Logical, should the computed start and end dates of the windows be kept?

remove.events.outside.followup.window

Logical, should the events that fall outside the follo-wup window be removed from the results?

keep.event.interval.for.all.events

Logical, should the computed event intervals be kept for all events, or NA'ed for those outside the OW?

parallel.backend

Can be "none" (the default) for single-threaded execution, "multicore" (using mclapply in package parallel) for multicore processing (NB. not currently

implemented on MS Windows and automatically falls back on "snow" on this platform), or "snow", "snow(SOCK)" (equivalent to "snow"), "snow(MPI)" or "snow(NWS)" specifying various types of SNOW clusters (can be on the local machine or more complex setups – please see the documentation of package snow for details; the last two require packages Rmpi and nws, respectively, not automatically installed with AdhereR).

### parallel.threads

Can be "auto" (for parallel.backend == "multicore", defaults to the number of cores in the system as given by options("cores"), while for parallel.backend == "snow", defaults to 2), a strictly positive integer specifying the number of parallel threads, or a more complex specification of the SNOW cluster nodes for parallel.backend == "snow" (see the documentation of package snow for details).

suppress.warnings

Logical, if TRUE don't show any warnings.

suppress.special.argument.checks

*Logical* parameter for internal use; if FALSE (default) check if the important columns in the data have some of the reserved names, if TRUE this check is not performed.

return.data.table

Logical, if TRUE return a data. table object, otherwise a data. frame.

.. extra arguments.

#### **Details**

This should in general not be called directly by the user, but is provided as a basis for the extension to new CMAs.

# Value

A data.frame or data.table extending the event.info parameter with:

- event.interval Or any other name given in event.interval.colname, containing the number of days between the start of the current event and the start of the next one.
- gap.days Or any other name given in gap.days.colname, containing the number of days when medication was not available for the current event (i.e., the "gap days").
- .FU.START.DATE, .FU.END.DATE if kept, the actual start and end dates of the follow-up window (after adjustments due to the various parameters).
- .OBS.START.DATE, .OBS.END.DATE if kept, the actual start and end dates of the observation window (after adjustments due to the various parameters).
- .EVENT.STARTS.BEFORE.OBS.WINDOW if kept, TRUE if the current event starts before the start of the observation window.
- .TDIFF1, .TDIFF2 if kept, various auxiliary time differences (in days).
- .EVENT.STARTS.AFTER.OBS.WINDOW if kept, TRUE if the current event starts after the end of the observation window.
- .CARRY.OVER.FROM.BEFORE if kept, the carry-over (if any) from the previous events.
- .EVENT.WITHIN.FU.WINDOW if kept, TRUE if the current event is within the follow-up window.

```
compute.treatment.episodes
```

Compute Treatment Episodes.

### **Description**

For a given event (prescribing or dispensing) database, compute the treatment episodes for each patient in various scenarious.

# Usage

```
compute.treatment.episodes(
  data,
  ID.colname = NA,
  event.date.colname = NA,
  event.duration.colname = NA,
  event.daily.dose.colname = NA,
 medication.class.colname = NA,
  carryover.within.obs.window = TRUE,
  carry.only.for.same.medication = TRUE,
  consider.dosage.change = TRUE,
 medication.change.means.new.treatment.episode = TRUE,
  dosage.change.means.new.treatment.episode = FALSE,
  maximum.permissible.gap = 90,
 maximum.permissible.gap.unit = c("days", "weeks", "months", "years", "percent")[1],
 maximum.permissible.gap.append.to.episode = FALSE,
  followup.window.start = 0,
  followup.window.start.unit = c("days", "weeks", "months", "years")[1],
  followup.window.duration = 365 * 2,
  followup.window.duration.unit = c("days", "weeks", "months", "years")[1],
  event.interval.colname = "event.interval",
  gap.days.colname = "gap.days",
  return.mapping.events.episodes = FALSE,
  date.format = "%m/%d/%Y",
  parallel.backend = c("none", "multicore", "snow", "snow(SOCK)", "snow(MPI)",
    "snow(NWS)")[1],
  parallel.threads = "auto",
  suppress.warnings = FALSE,
  suppress.special.argument.checks = FALSE,
  return.data.table = FALSE,
)
```

#### **Arguments**

data

A data. frame containing the events used to compute the CMA. Must contain, at a minimum, the patient unique ID, the event date and duration, and might also

contain the daily dosage and medication type (the actual column names are defined in the following four parameters); the CMA constructors call this parameter data

ID.colname

A *string*, the name of the column in data containing the unique patient ID, or NA if not defined.

event.date.colname

A *string*, the name of the column in data containing the start date of the event (in the format given in the date. format parameter), or NA if not defined.

event.duration.colname

A *string*, the name of the column in data containing the event duration (in days), or NA if not defined.

event.daily.dose.colname

A *string*, the name of the column in data containing the prescribed daily dose, or NA if not defined.

medication.class.colname

A *string*, the name of the column in data containing the classes/types/groups of medication, or NA if not defined.

carryover.within.obs.window

*Logical*, if TRUE consider the carry-over within the observation window, or NA if not defined.

carry.only.for.same.medication

*Logical*, if TRUE the carry-over applies only across medication of the same type, or NA if not defined.

consider.dosage.change

*Logical*, if TRUE the carry-over is adjusted to reflect changes in dosage, or NA if not defined.

medication.change.means.new.treatment.episode

Logical, should a change in medication automatically start a new treatment episode?

 ${\tt dosage.change.means.new.treatment.episode}$ 

Logical, should a change in dosage automatically start a new treatment episode?

maximum.permissible.gap

The *number* of units given by maximum.permissible.gap.unit representing the maximum duration of permissible gaps between treatment episodes (can also be a percent, see maximum.permissible.gap.unit for details).

maximum.permissible.gap.unit

can be either "days", "weeks", "months", "years" or "percent", and represents the time units that maximum.permissible.gap refers to; if percent, then maximum.permissible.gap is interpreted as a percent (can be greater than 100%) of the duration of the current prescription.

maximum.permissible.gap.append.to.episode

a *logical* value specifying of the maximum.permissible.gap should be append at the end of an episode with a gap larger than the maximum.permissible.gap; FALSE (the default) mean no addition, while TRUE mean that the full maximum.permissible.gap is added.

followup.window.start

If a Date object it is the actual start date of the follow-up window; if a *string* it is the name of the column in data containing the start date of the follow-up window; if a *number* it is the number of time units defined in the followup.window.start.unit parameter after the begin of the participant's first event; or NA if not defined.

followup.window.start.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.start refers to (when a number), or NA if not defined.

followup.window.duration

a *number* representing the duration of the follow-up window in the time units given in followup.window.duration.unit, or NA if not defined.

followup.window.duration.unit

can be either "days", "weeks", "months" or "years", and represents the time units that followup.window.duration refers to, or NA if not defined.

event.interval.colname

A *string*, the name of a newly-created column storing the number of days between the start of the current event and the start of the next one; the default value "event.interval" should be changed only if there is a naming conflict with a pre-existing "event.interval" column in event.info.

gap.days.colname

A *string*, the name of a newly-created column storing the number of days when medication was not available (i.e., the "gap days"); the default value "gap.days" should be changed only if there is a naming conflict with a pre-existing "gap.days" column in event.info.

return.mapping.events.episodes

A *Logical*, if TRUE then the mapping between events and episodes is returned as the attribute mapping.episodes.to.events, which is a data.table giving, for each episode, the events that belong to it (an event is given by its row number in the data). Please note that the episodes returned are quite "generic" (e.g., they include all the events in the FUW), because which events will be actually used in the computation of a CMA\_per\_episode depend on which simple CMA is used (see also CMA\_per\_episode), and should be used with care (we recommend using the mappings given by CMA\_per\_episode instead).

date.format

A *string* giving the format of the dates used in the data and the other parameters; see the format parameters of the as.Date function for details (NB, this concerns only the dates given as strings and not as Date objects).

parallel.backend

Can be "none" (the default) for single-threaded execution, "multicore" (using mclapply in package parallel) for multicore processing (NB. not currently implemented on MS Windows and automatically falls back on "snow" on this platform), or "snow", "snow(SOCK)" (equivalent to "snow"), "snow(MPI)" or "snow(NWS)" specifying various types of SNOW clusters (can be on the local machine or more complex setups – please see the documentation of package snow for details; the last two require packages Rmpi and nws, respectively, not automatically installed with AdhereR).

parallel.threads

Can be "auto" (for parallel.backend == "multicore", defaults to the number of cores in the system as given by options ("cores"), while for parallel.backend

== "snow", defaults to 2), a strictly positive integer specifying the number of parallel threads, or a more complex specification of the SNOW cluster nodes for parallel.backend == "snow" (see the documentation of package snow for details).

suppress.warnings

Logical, if TRUE don't show any warnings.

suppress.special.argument.checks

*Logical* parameter for internal use; if FALSE (default) check if the important columns in the data have some of the reserved names, if TRUE this check is not performed.

return.data.table

*Logical*, if TRUE return a data. table object, otherwise a data. frame.

... extra arguments.

#### **Details**

This should in general not be called directly by the user, but is provided as a basis for the extension to new CMAs.

For the last treatment episode, the gap is considered only when longer than the maximum permissible gap. Please note the following:

- episode starts at first medication event for a particular medication,
- episode ends on the day when the last supply of that medication finished or if a period longer than the permissible gap preceded the next medication event, or at the end of the FUW,
- end episode gap days represents either the number of days after the end of the treatment episode (if medication changed, or if a period longer than the permissible gap preceded the next medication event) or at the end of (and within) the episode, i.e. the number of days after the last supply finished (if no other medication event followed until the end of the FUW),
- the duration of the episode is the interval between the episode start and episode end (and may include the gap days at the end, in the latter condition described above),
- the number of gap days after the end of the episode can be computed as all values larger than the permissible gap and 0 otherwise,
- if medication change starts new episode, then previous episode ends when the last supply is finished (irrespective of the length of gap compared to a maximum permissible gap); any days before the date of the new medication supply are considered a gap; this maintains consistency with gaps between episodes (whether they are constructed based on the maximum permissible gap rule or the medication change rule).

# Value

A data. frame or data. table with the following columns (or NULL if no treatment episodes could be computed):

- patid the patient ID.
- episode. ID the episode unique ID (increasing sequentially).
- episode.start the episode start date.

- end.episode.gap.days the corresponding gap days of the last event in this episode.
- episode.duration the episode duration in days.
- episode.end the episode end date.

If mapping.episodes.to.events is TRUE, then this also has an *attribute* mapping.episodes.to.events that gives the mapping between episodes and events as a data.table with the following columns:

- patid the patient ID.
- episode. ID the episode unique ID (increasing sequentially).
- event.index.in.data the event given by its row number in the data.

compute\_event\_durations

Computation of event durations.

# **Description**

Computes event durations based on dispensing, prescription, and other data (e.g. hospitalization data) and returns a data. frame which can be used with the CMA constructors in AdhereR.

# Usage

```
compute_event_durations(
 disp.data = NULL,
  presc.data = NULL,
  special.periods.data = NULL,
  ID.colname,
 medication.class.colnames,
  disp.date.colname,
  total.dose.colname,
  presc.date.colname,
 presc.daily.dose.colname,
 presc.duration.colname,
  visit.colname,
  split.on.dosage.change = TRUE,
  force.init.presc = FALSE,
  force.presc.renew = FALSE,
  trt.interruption = c("continue", "discard", "carryover")[1],
  special.periods.method = trt.interruption,
  carryover = FALSE,
  date.format = "%d.%m.%Y",
  suppress.warnings = FALSE,
  return.data.table = FALSE,
 progress.bar = TRUE,
)
```

#### **Arguments**

disp.data

A data frame or data table containing the dispensing events. Must contain, at a minimum, the patient unique ID, one medication identifier, the dispensing date, and total dispensed dose, and might also contain additional columns to identify and group medications (the actual column names are defined in the medication class colnames parameter).

presc.data

A data.frame containing the prescribing events. Must contain, at a minimum, the same unique patient ID and medication identifier(s) as the dispensing data, the prescription date, the daily prescribed dose, and the prescription duration. Optionally, it might also contain a visit number.

special.periods.data

Optional, NULL or a data.frame containing the information about special periods (e.g., hospitalizations or other situations where medication use may differ, e.g. during incarcerations or holidays). Must contain the same unique patient ID as dispensing and prescription data, the start and end dates of the special periods with the exact column names DATE.IN and DATE.OUT. Optional columns are TYPE (indicating the type of special situation), customized instructions how to handle a specific period (see special.periods.method), and any of those specified in medication.class.colnames.

ID.colname

A *string*, the name of the column in disp.data, presc.data, and special.periods.data containing the unique patient ID.

medication.class.colnames

A Vector of *strings*, the name(s) of the column(s) in disp. data and presc. data containing the classes/types/groups of medication.

disp.date.colname

A *string*, the name of the column in disp.data containing the dispensing date (in the format given in the date.format parameter).

total.dose.colname

A *string*, the name of the column in disp.data containing the total dispensed dose as numeric (e.g. 500 for 10 tablets of 50 mg).

presc.date.colname

A *string*, the name of the column in presc.data containing the prescription date (in the format given in the date.format parameter).

presc.daily.dose.colname

A *string*, the name of the column in presc.data containing the daily prescribed dose as numeric (e.g. 50 for 50 mg once per day, or 25 for 50 mg once ever 2 days).

presc.duration.colname

A *string*, the name of the column in presc.data containing the duration of the prescription as numeric or NA if duration is unknown.

visit.colname A *string*, the name of the column in presc.data containing the number of the visit or a new column name if the prescribing data does not contain such a column.

split.on.dosage.change

*Logical* or *string*. If TRUE split the dispensing event on days with dosage change and create a new event with the new dosage for the remaining supply. If *string*,

the name of the column containing the Logical in *disp.data* for each medication class separatly. Important if carryover should be considered later on.

force.init.presc

Logical. If TRUE advance the date of the first prescription event to the date of the first dispensing event, if the first prescription event is after the first dispensing event for a specific medication. Only if the first prescription event is not limited in duration (as indicated in the presc.duration.colname).

force.presc.renew

Logical or string. If TRUE require a new prescription for all medications for every prescription event (visit), otherwise prescriptions end on the first visit without renewal. If string, the name of the column in disp.data containing the Logical for each medication class separatly.

trt.interruption

can be either of "continue", "discard", "carryover", or a string. It indicates how to handle durations during treatment interruptions (see special.periods.method). If string, the name of the (character) column in disp.data containing the information ("continue", "discard", or "carryover") for each medication class separatly.

special.periods.method

can be either of *continue*, *discard*, *carryover*, or *custom*. It indicates how to handle durations during special periods. With *continue*, special periods have no effect on durations and event start dates. With *discard*, durations are truncated at the beginning of special periods and the remaining quantity is discarded. With *carryover*, durations are truncated at the beginning of a special period and a new event with the remaining duration is created after the end of the end of the special period. With *custom*, the mapping has to be included in special.periods.data.

carryover

Logical, if TRUE apply carry-over to medications of the same type (according to medication.class.colnames). Can only be used together with CMA7 and above in combination with carry.only.for.same.medication = TRUE.

date.format

A *string* giving the format of the dates used in the data and the other parameters; see the format parameters of the as.Date function for details (NB, this concerns only the dates given as strings and not as Date objects).

suppress.warnings

Logical, if TRUE don't show any warnings.

return.data.table

Logical, if TRUE return a data. table object, otherwise a data. frame.

progress.bar Log

Logical, if TRUE show a progress bar.

... other possible parameters.

#### **Details**

Computation of CMAs requires a supply duration for medications dispensed to patients. If medications are not supplied for fixed durations but as a quantity that may last for various durations based on the prescribed dose, the supply duration has to be calculated based on dispensed and prescribed doses. Treatments may be interrupted and resumed at later times, for which existing supplies may or

may not be taken into account. Patients may be hospitalized or incarcerated, and may not use their own supplies during these periods. This function calculates supply durations, taking into account the aforementioned situations and providing various parameters for flexible adjustments.

#### Value

#### A list with the following elements:

- event\_durations: A data.table or data.frame with the following columns:
  - ID. colname the unique patient ID, as given by the ID. colname parameter.
  - medication.class.colnames the column(s) with classes/types/groups of medication, as given by the medication.class.colnames parameter.
  - disp.date.colname the date of the dispensing event, as given by the disp.date.colnema parameter.
  - total.dose.colname the total dispensed dose, as given by the total.dose.colname parameter.
  - presc.daily.dose.colname the prescribed daily dose, as given by the presc.daily.dose.colname parameter.
  - DISP. START the start date of the dispensing event, either the same as in disp. date.colname
    or a later date in case of dosage changes or treatment interruptions/hospitalizations.
  - DURATION the calculated duration of the supply, based on the total dispensed dose and the prescribed daily dose, starting from the DISP. START date.
  - episode.start: the start date of the current prescription episode.
  - episode.end: the end date of the current prescription episode. Can be before the start date of the dispensing event if dispensed during a treatment interruption.
  - SPECIAL.DURATION the number of days during the current duration affected by special durations or treatment interruptions of type "continue".
  - CARRYOVER. DURATION the number of days *after* the current duration affected by special durations or treatment interruptions of type "carryover".
  - EVENT. ID: in case of multiple events with the same dispensing date (e.g. for dosage changes or interruptions); a unique ID starting at 1 for the first event
  - tot.presc.interruptions the total number of prescription interruptions per patient for a specific medication.
  - tot.dosage.changes the total number of dosage changes per patient for a specific medication.
- prescription\_episodes: A data.table or data.frame with the following columns:
  - ID. colname: the unique patient ID, as given by the ID. colname parameter.
  - medication.class.colnames: the column(s) with classes/types/groups of medication, as given by the medication.class.colnames parameter.
  - presc.daily.dose.colname: the prescribed daily dose, as given by the presc.daily.dose.colname parameter.
  - episode.start: the start date of the prescription episode.
  - episode.duration: the duration of the prescription episode in days.
  - episode.end: the end date of the prescription episode.
- special\_periods: A data.table or data.frame, the special.periods.data with an additional column SPECIAL.DURATION: the number of days between DATE.IN and DATE.OUT

- ID.colname the name of the columns containing the unique patient ID, as given by the ID.colname parameter.
- medication.class.colnames the name(s) of the column(s) in disp.data and presc.data containing the classes/types/groups of medication, as given by the medication.class.colnames parameter.
- disp.date.colname the name of the column in disp.data containing the dispensing date, as given in the disp.date.colname parameter.
- total.dose.colname the name of the column in disp.data containing the total dispensed dose, as given by the total.dose.colname parameter.
- presc.date.colname the name of the column in presc.data containing the prescription date, as given in the presc.date.colname parameter.
- presc.daily.dose.colname the name of the column in presc.data containing the daily prescribed dose, as given by the presc.daily.dose.colname parameter.
- presc.duration.colname the name of the column in presc.data containing the duration of the prescription, as given by the presc.duration.colname parameter.
- visit.colname the name of the column containing the number of the visit, as given by the visit.colname parameter
- split.on.dosage.change whether to split the dispensing event on days with dosage changes
  and create a new event with the new dosage for the remaining supply, as given by the split.on.dosage.change
  parameter.
- force.init.presc whether the date of the first prescription event was set back to the date of the first dispensing event, when the first prescription event was after the first dispensing event for a specific medication, as given by the force.init.presc parameter.
- force.presc.renew whether a new prescription was required for all medications for every prescription event (visit), as given by the force.presc.renew parameter.
- trt.interruption how durations during treatment interruptions were handled, as given by the trt.interruption parameter.
- special.periods.method as given by the special.periods.method parameter.
- date. format the format of the dates, as given by the date. format parameter.

## **Examples**

```
force.init.presc = TRUE,
force.presc.renew = TRUE,
trt.interruption = "continue",
special.periods.method = "continue",
date.format = "%Y-%m-%d",
suppress.warnings = FALSE,
return.data.table = TRUE);
```

## End(Not run)

cover\_special\_periods Cover special periods.

#### **Description**

Identifies special periods that are in proximity to already covered durations and adds additional events for these durations.

# Usage

```
cover_special_periods(
  events.data,
  special.periods.data,
  ID.colname,
  medication.class.colnames,
  disp.date.colname,
  disp.start.colname,
  episode.start.colname,
  episode.end.colname,
  duration.colname,
  days.before,
  days.after,
  date.format,
  suppress.warnings = FALSE,
  return.data.table = FALSE,
)
```

## **Arguments**

```
events.data A data.frame or data.table with the event durations. special.periods.data
```

a data.frame or or data.table containing the information about special periods (e.g., hospitalizations or other situations where medication use may differ, e.g. during incarcerations or holidays). Must contain the same unique patient ID as dispensing and prescription data, the start and end dates of the special periods with the exact column names DATE.IN and DATE.OUT.

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ID.colname

A *string*, the name of the column in events.data and special.periods.data containing the unique patient ID.

medication.class.colnames

A Vector of *strings*, the name(s) of the column(s) in the events.data identify medication classes.

disp.date.colname

A *string*, the name of the column in events.data containing the dispensation start date (in the format given in the date.format parameter).

disp.start.colname, episode.start.colname, episode.end.colname column names in events.data.

duration.colname

A *string*, the name of the column in events. data containing the duration of the

medication event.

days.before an integer, the number of days before the start of a special period within which

an event duration must end to consider the special period as covered.

days.after an integer, the number of days after a special period within which an event

duration must start to consider the special period as covered.

date.format A string giving the format of the dates used in the data and the other param-

eters; see the format parameters of the as.Date function for details (NB, this

concerns only the dates given as strings and not as Date objects).

suppress.warnings

Logical, if TRUE don't show any warnings.

return.data.table

Logical, if TRUE return a data. table object, otherwise a data. frame.

... other possible parameters.

#### **Details**

Special periods may appear as gaps, possibly leading to underestimation of implementation or even assumption of discontinuation and non-persistence. To consider such periods as covered, this function adds additional durations, for example when it is assumed that hospitalized patients are adherent during the hospitalization period. This function should be used after pruning with prune\_event\_durations.

#### Value

A data.frame or data.table, the events.data with the additional durations for special periods covered.

## **Examples**

80 durcomp.dispensing

```
special.periods.data = durcomp.hospitalisation,
                                                 special.periods.method = "carryover",
                                                 ID.colname = "ID",
                                                 presc.date.colname = "DATE.PRESC",
                                                 disp.date.colname = "DATE.DISP",
                                                 date.format = "%Y-%m-%d",
                                                medication.class.colnames = c("ATC.CODE",
                                                                                "FORM"),
                                                 total.dose.colname = "TOTAL.DOSE",
                                                 presc.daily.dose.colname = "DAILY.DOSE",
                                               presc.duration.colname = "PRESC.DURATION",
                                                 visit.colname = "VISIT",
                                                 force.init.presc = TRUE,
                                                 force.presc.renew = TRUE,
                                                 split.on.dosage.change = TRUE,
                                                 trt.interruption = "carryover",
                                                 suppress.warnings = FALSE,
                                                 return.data.table = TRUE,
                                                 progress.bar = FALSE)
event_durations <- prune_event_durations(event_durations_list,</pre>
                                          include = c("special periods"),
                                          medication.class.colnames = "ATC.CODE",
                                          days.within.out.date.1 = 7,
                                          days.within.out.date.2 = 30,
                                          keep.all = TRUE)
# cover special periods
special_periods <- event_durations_list$special_periods</pre>
event_durations_covered <- cover_special_periods(events.data = event_durations,
                                                  special.periods.data = special_periods,
                                                  ID.colname = "ID",
                                                  medication.class.colnames = "ATC.CODE",
                                                  disp.start.colname = "DISP.START",
                                                  duration.colname = "DURATION",
                                                  days.before = 7,
                                                  days.after = 7,
                                                  date.format = "%Y-%m-%d")
## End(Not run)
```

durcomp.dispensing

Example dispensing events for 16 patients.

## **Description**

A sample dataset containing dispensing events (one per row) for 16 patients over a period of roughly 24 months (1794 events in total). This is the appropriate format to compute event durations with the compute\_event\_durations function. Each row represents an individual dispensing record for

a specific dose of a specific medication for a patient at a given date. More than one column to group medications can be supplied (such as ATC code, Form and Unit).

# Usage

durcomp.dispensing

#### **Format**

A data frame with 1794 rows and 6 variables:

**ID** integer here; patient unique identifier. Can also be string.

**DATE.DISP** *Date* here; the dispensing event date, by default in the yyyy-mm-dd format. Can also be *string*.

ATC.CODE character; the medication type, according to the WHO ATC classification system. This can be a researcher-defined classification depending on study aims (e.g., based on therapeutic use, mechanism of action, chemical molecule, or pharmaceutical formulation). The compute\_event\_durations function will match prescribed medication to dispensed medications based on this variable.

**UNIT** *integer*; the unit of the dispensed dose. This is optional and can be used as a separate variable to match between prescription and dispensing events.

**FORM** *character*; the galenic form of the dispensed preparation. This is optional and can be used as a separate variable to match between prescription and dispensing events.

**TOTAL.DOSE** *numeric*; the total dispensed dose supplied at this medication event (e.g., 5000 for 10 tables of 500 mg).

durcomp.hospitalisation

Example special periods for 10 patients.

# Description

A sample dataset containing special periods (one per row) for 10 patients over a period of roughly 18 months (28 events in total). This is the appropriate format to compute event durations with the compute\_event\_durations function. Each row represents an individual special period of type "hospitalization" of a patient for whom event durations should be calculated. Besides hospitalizations, this could cover other situations where medication use may differ, e.g. during incarcerations or holidays. All column names must match the format provided in this example.

#### Usage

durcomp.hospitalisation

82 durcomp.prescribing

#### **Format**

A data frame with 28 rows and 3 variables:

**ID** *Integer* here; patient unique identifier. Can also be *string*.

**DATE.IN** *Date* here; the start of the hospitalization period, by default in the yyyy-mm-dd format. Can also be *string*.

**DATE.OUT** *Date*; the end of the hospitalization period, by default in the yyyy-mm-dd format. Can also be *string*.

durcomp.prescribing

Example prescription events for 16 patients.

## **Description**

A sample dataset containing prescription events (one per row) for 16 patients over a period of roughly 15 months (1502 events in total). This is the appropriate format to compute event durations with the compute\_event\_durations function. Each row represents an individual prescription record for a specific dose of a specific medication for a patient at a given date. Visit number and Duration are optional, and more than one column to group medications can be supplied (such as ATC Code, Form or Unit).

#### Usage

durcomp.prescribing

#### **Format**

A data table with 1502 rows and 8 variables:

**ID** *integer* here; patient unique identifier. Can also be *string*.

**DATE.PRESC** *Date* here; the prescription event date, by default in the yyyy-mm-dd format. Can also be *string*.

**VISIT** *integer*; the consecutive number of the prescription instances. This column is optional and will be generated internally when not supplied. It is used to identify treatment interruptions.

ATC.CODE character; the medication type, according to the WHO ATC classification system. This can be a researcher-defined classification depending on study aims (e.g., based on therapeutic use, mechanism of action, chemical molecule, or pharmaceutical formulation). The compute\_event\_durations function will match prescribed medication to dispensed medications based on this variable.

**FORM** *character*; the galenic form of the prescribed preparation. This is optional and can be used as a separate variable to match between prescription and dispensing events.

**UNIT** *integer*; the unit of the prescribed dose. This is optional and can be used as a separate variable to match between prescription and dispensing events.

**PRESC.DURATION** *numeric*; the duration (in days) for which the prescription is intended. Can be NA if the prescription is continuous without a fixed end date.

**DAILY.DOSE** *numeric*; the daily dose prescribed during this event (e.g., 50 for 1 tablet of 50 mg per day or 25 for 1 tablet of 50 mg every two days).

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```
get.event.plotting.area
```

Get the actual plotting area.

# **Description**

Returns the actual plotting area rectangle in plotting coordinates.

## Usage

```
get.event.plotting.area(
  plot.type = c("baseR", "SVG")[1],
  suppress.warnings = FALSE
)
```

# **Arguments**

```
plot.type Can be either "baseR" or "SVG" and specifies to which type of plotting the mapping applies.

suppress.warnings

Logical, if TRUE don't show any warnings.
```

# **Details**

This is intended for advanced users only.

#### Value

A numeric vector with components x.min, x.max, y.min and y.max, or NULL in case of error.

```
get.legend.plotting.area

Get the legend plotting area.
```

# Description

Returns the legend plotting area rectangle in plotting coordinates (if any).

# Usage

```
get.legend.plotting.area(
  plot.type = c("baseR", "SVG")[1],
  suppress.warnings = FALSE
)
```

84 get.plotted.events

# **Arguments**

plot.type Can be either "baseR" or "SVG" and specifies to which type of plotting the mapping applies.

suppress.warnings

Logical, if TRUE don't show any warnings.

#### **Details**

This is intended for advanced users only.

#### Value

A numeric vector with components *x.min*, *x.max*, *y.min* and *y.max*, or NULL in case of error or no legend being shown.

get.plotted.events

Get info about the plotted events.

#### **Description**

Returns a data. frame where each row contains info about one plotted event; the order of the rows reflects the y-axis (first row on bottom).

## Usage

```
get.plotted.events(plot.type = c("baseR", "SVG")[1], suppress.warnings = FALSE)
```

## **Arguments**

plot.type Can be either "baseR" or "SVG" and specifies to which type of plotting the mapping applies.

suppress.warnings

Logical, if TRUE don't show any warnings.

#### **Details**

This is intended for advanced users only.

#### Value

A data. frame that, besides the info about each event, also contains info about:

- the corresponding follow-up and observation windows (and, for CMA8, the "real" observation window), given as the corners of the area .X...START, .X...END, .Y...START and .Y...END (where the mid dot stands for FUW, OW and ROW, respectively).
- the area occupied by the graphic representation of the event given by its four corners .X.START, .X.END, .Y.START and .Y.END, as well as the line width .EV.LWD.

get.plotted.partial.cmas 85

- the dose text's (if any) position (.X.DOSE, .Y.DOSE) and font size .FONT.SIZE.DOSE.
- if event corvered and not covered are plotted, also give their areas as .X.EVC.START, .X.EVC.END, .Y.EVC.START, .Y.EVC.END, .X.EVNC.START, .X.EVNC.END, .Y.EVNC.START and .Y.EVNC.END.
- the continuation lines area as .X.CNT.START, .X.CNT.END, .Y.CNT.START and .Y.CNT.END.
- and the corresponding summary CMA (if any) given as the area .X.SCMA.START, .X.SCMA.END, .Y.SCMA.START and .Y.SCMA.END.

Please note that even if with follow-up and ("real") observation window, and the summary CMA info is repeated for each event, they really make sense at the level of the patient.

# **Examples**

```
cma7 <- CMA7(data=med.events[med.events$PATIENT_ID %in% c(1,2),],</pre>
             ID.colname="PATIENT_ID",
             event.date.colname="DATE",
             event.duration.colname="DURATION",
             event.daily.dose.colname="PERDAY",
             medication.class.colname="CATEGORY",
             followup.window.start=0,
             followup.window.start.unit="days",
             followup.window.duration=2*365,
             followup.window.duration.unit="days",
             observation.window.start=30,
             observation.window.start.unit="days",
             observation.window.duration=365,
             observation.window.duration.unit="days",
             date.format="%m/%d/%Y",
             summary="Base CMA");
plot(cma7);
tmp <- get.plotted.events();</pre>
head(tmp);
# "Mask" the first event:
rect(tmp$.X.START[1], tmp$.Y.START[1]-0.5, tmp$.X.END[1], tmp$.Y.END[1]+0.5,
     col=adjustcolor("white",alpha.f=0.75), border="black");
# "Mask" the first patient's summary CMA:
rect(tmp$.X.SCMA.START[1], tmp$.Y.SCMA.START[1],
     tmp$.X.SCMA.END[1], tmp$.Y.SCMA.END[1],
     col=adjustcolor("white",alpha.f=0.75), border="black");
```

```
get.plotted.partial.cmas
```

Get info about the plotted partial CMAs.

# **Description**

Returns a data. frame where each row contains info about one plotted partial CMA (partial CMAs make sense only for "complex" CMAs, i.e., per episode and sliding windows).

## Usage

```
get.plotted.partial.cmas(
  plot.type = c("baseR", "SVG")[1],
  suppress.warnings = FALSE
)
```

# **Arguments**

```
plot.type Can be either "baseR" or "SVG" and specifies to which type of plotting the mapping applies.

suppress.warnings

Logical, if TRUE don't show any warnings.
```

## **Details**

This is intended for advanced users only.

#### Value

A data. frame that contains info about:

- the patient ID (pid) to which the partial CMA belongs.
- the *type* of partial CMA (see the help for plotting "complex" CMAs).
- the corners of the whole area covered by the partial CMA plot given as *x.region.start*, *y.region.start*, *x.region.end* and *y.region.end*.
- for each element of the partial CMA plot, its area as *x.partial.start*, *y.partial.start*, *x.partial.end* and *y.partial.end*.

Please note that this contains one row per partial CMA element (e.g., if plotting stacked, one row for each rectangle).

```
{\it getCallerWrapperLocation}. {\it getCallerWrapperLocation}.
```

# **Description**

This function returns the full path to where the various wrappers that can call AdhereR are installed.

## Usage

```
getCallerWrapperLocation(callig.platform = c("python3")[1], full.path = FALSE)
```

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# **Arguments**

callig.platform

A string specifying the desired wrapper. Currently it can be "python3".

full.path

A *logical* specifying if the returned path should also include the wrapper's main file name.

## **Details**

In most cases, these wrappers are one or more files in the calling language that may be directly used as such. For more details see the vignette describing the included reference Python 3 wrapper.

#### Value

The full path to the requested wrapper or NULL if none exists.

getCMA

Access the actual CMA estimate from a CMA object.

# **Description**

Retrieve the actual CMA estimate(s) encapsulated in a simple, per episode, or sliding window CMA object.

#### Usage

```
getCMA(
    x,
    flatten.medication.groups = FALSE,
    medication.groups.colname = ".MED_GROUP_ID"
)
```

#### **Arguments**

a CMA object.

flatten.medication.groups

*Logical*, if TRUE and there are medication groups defined, then the return value is flattened to a single data. frame with an extra column containing the medication group (its name is given by medication.groups.colname).

medication.groups.colname

a *string* (defaults to ".MED\_GROUP\_ID") giving the name of the column storing the group name when flatten.medication.groups is TRUE.

#### Value

a data.frame containing the CMA estimate(s).

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## **Examples**

```
cma1 <- CMA1(data=med.events,</pre>
             ID.colname="PATIENT_ID",
             event.date.colname="DATE",
             event.duration.colname="DURATION",
             followup.window.start=30,
             observation.window.start=30,
             observation.window.duration=365,
             date.format="%m/%d/%Y"
            );
getCMA(cma1);
## Not run:
cmaE <- CMA_per_episode(CMA="CMA1",</pre>
                         data=med.events,
                         ID.colname="PATIENT_ID",
                         event.date.colname="DATE",
                         event.duration.colname="DURATION",
                         event.daily.dose.colname="PERDAY",
                        medication.class.colname="CATEGORY",
                         carry.only.for.same.medication=FALSE,
                         consider.dosage.change=FALSE,
                         followup.window.start=0,
                         observation.window.start=0,
                         observation.window.duration=365,
                         date.format="%m/%d/%Y"
                        );
getCMA(cmaE);
## End(Not run)
```

getEventInfo

Access the event info from a CMA object.

# **Description**

Retrieve the event info encapsulated in a simple, per episode, or sliding window CMA object.

# Usage

```
getEventInfo(
    x,
    flatten.medication.groups = FALSE,
    medication.groups.colname = ".MED_GROUP_ID"
)
```

# **Arguments**

x a CMA object.

flatten.medication.groups

*Logical*, if TRUE and there are medication groups defined, then the return value is flattened to a single data. frame with an extra column containing the medication group (its name is given by medication.groups.colname).

medication.groups.colname

a *string* (defaults to ".MED\_GROUP\_ID") giving the name of the column storing the group name when flatten.medication.groups is TRUE.

## Value

a data.frame containing the CMA estimate(s).

## **Examples**

getEventsToEpisodesMapping

getEventsToEpisodesMapping

## Description

This function returns the event-to-episode mapping, if this information exists.

#### Usage

```
getEventsToEpisodesMapping(x)
```

#### **Arguments**

x Either a data.frame as returned by compute.treatment.episodes() or an CMA\_per\_episode object.

## **Details**

There are cases where it is interesting to know which events belong to which episodes and which events have been actually used in computing the simple CMA for each episode. This information can be returned by compute.treatment.episodes() and CMA\_per\_episode() if the parameter return.mapping.events.episodes is set to TRUE.

90 getInnerEventInfo

#### Value

The mapping between events and episodes, if it exists either as the attribute mapping.episodes.to.events of the data.frame or as the mapping.episodes.to.events component of the CMA\_per\_episode object object, or NULL otherwise.

## **Description**

This function returns the event-to-sliding-window mapping, if this information exists.

## Usage

```
getEventsToSlidingWindowsMapping(x)
```

## **Arguments**

x is an CMA\_sliding\_window object.

#### **Details**

There are cases where it is interesting to know which events belong to which sliding windows and which events have been actually used in computing the simple CMA for each sliding window This information can be returned by CMA\_sliding\_window() if the parameter return.mapping.events.episodes is set to TRUE.

#### Value

The mapping between events and episodes, if it exists as the mapping.windows.to.events component of the CMA\_sliding\_window object object, or NULL otherwise.

getInnerEventInfo

Access the inner event info from a complex CMA object.

## **Description**

Retrieve the event info encapsulated in a complex (i.e., per episode or sliding window) CMA object.

# Usage

```
getInnerEventInfo(
    x,
    flatten.medication.groups = FALSE,
    medication.groups.colname = ".MED_GROUP_ID"
)
```

getMGs 91

# **Arguments**

a CMA object.

flatten.medication.groups

*Logical*, if TRUE and there are medication groups defined, then the return value is flattened to a single data. frame with an extra column containing the medication group (its name is given by medication.groups.colname).

medication.groups.colname

a *string* (defaults to ".MED\_GROUP\_ID") giving the name of the column storing the group name when flatten.medication.groups is TRUE.

#### Value

a data.frame containing the CMA estimate(s).

getMGs

Access the medication groups of a CMA object.

# Description

Retrieve the medication groups and the observations they refer to (if any).

# Usage

getMGs(x)

## **Arguments**

Χ

a CMA object.

#### Value

a *list* with two members:

- defs A data.frame containing the names and definitions of the medication classes; please note that there is an extra class \_\_ALL\_OTHERS\_\_ containing all the observations not selected by any of the explicitly given medication classes.
- obs A logical matrix where the columns are the medication classes (the last being  $\_ALL\_OTHERS\_\_$ ), and the rows the observations in the x's data; element (i,j) is TRUE iff observation j was selected by medication class i.

92 last.plot.get.info

last.plot.get.info Access last adherence plot info.

# **Description**

Returns the full info the last adherence plot, to be used to modify and/or to add new elements to this plot.

### Usage

```
last.plot.get.info()
```

#### **Details**

This is intended for advanced users only. It may return NULL if no plotting was generated yet, but if one was, a list containing one named element for each type of plot produced (currently only *baseR* and *SVG* are used). For all types of plots there are a set of *mapping* functions useful for transforming events in plotting coordinates: .map.event.x(x) takes a number of days x, .map.event.date(d, adjust.for.earliest.date=TRUE) takes a Date d (and implictely adjusts for the earilerst date plotted), and .map.event.y(y) takes a row ("event" number) y. Besides the shared elements (see the returned value), there are specific ones as well. For *baseR*, the members *old.par* and *used.par* contain the original (pre-plot) par() environment and the one used within plot(), respectively, in case these need restoring.

## Value

A list (possibly empty) containing one named element for each type of plot produced (currently only *baseR* and *SVG*). Each may contain shared and specific fields concerning:

- the values of the parameters with which plot() was invoked.
- actual plot size and other characteristics.
- actual title, axis names and labels and their position and size.
- legend size, position and size and position of its components.
- expanded cma\$data containing, for each event, info about its plotting, including the corresponding fullow-uo and observation windows, event start and end, dose text (if any) and other graphical elements.
- position, size of the partial CMAs (if any) and of their components.
- position, size of the plotted CMAs (if any) and of their components.
- rescaling function(s) useful for mapping events to plotting coordinates.

## **Examples**

```
cma7 <- CMA7(data=med.events[med.events$PATIENT_ID %in% c(1,2),],</pre>
             ID.colname="PATIENT_ID",
             event.date.colname="DATE",
             event.duration.colname="DURATION".
             event.daily.dose.colname="PERDAY",
             medication.class.colname="CATEGORY",
             followup.window.start=0,
             followup.window.start.unit="days",
             followup.window.duration=2*365,
             followup.window.duration.unit="days",
             observation.window.start=30,
             observation.window.start.unit="days",
             observation.window.duration=365,
             observation.window.duration.unit="days",
             date.format="%m/%d/%Y",
             summary="Base CMA");
plot(cma7);
tmp <- last.plot.get.info();</pre>
names(tmp);
tmp$baseR$legend$box; # legend position and size
head(tmp$baseR$cma$data); # events + plotting info
# Add a transparent blue rect between days 270 and 900:
rect(tmp$baseR$.map.event.x(270), tmp$baseR$.map.event.y(1-0.5),
     tmp$baseR$.map.event.x(900), tmp$baseR$.map.event.y(nrow(tmp$baseR$cma$data)+0.5),
     col=adjustcolor("blue",alpha.f=0.5), border="blue");
# Add a transparent rect rect between dates 03/15/2036 and 03/15/2037:
rect(tmp$baseR$.map.event.date(as.Date("03/15/2036", format="%m/%d/%Y")),
     tmp$baseR$.map.event.y(1-0.5),
     tmp$baseR$.map.event.date(as.Date("03/15/2037", format="%m/%d/%Y")),
     tmp$baseR$.map.event.y(nrow(tmp$baseR$cma$data)+0.5),
     col=adjustcolor("red",alpha.f=0.5), border="blue");
```

```
map.event.coords.to.plot
```

Map from event to plot coordinates.

## **Description**

Maps the (x,y) coordinates in the event space to the plotting space.

# Usage

```
map.event.coords.to.plot(
    x = NA,
    y = NA,
    x.is.Date = FALSE,
    x.date.format = "%m/%d/%Y",
    adjust.for.earliest.date = TRUE,
```

```
plot.type = c("baseR", "SVG")[1],
suppress.warnings = FALSE
)
```

## **Arguments**

X	The <i>x</i> coordinate in the event space, either a number giving the number of days since the earliest plotted date, or a Date or a string in the format given by the <i>x.date.format</i> parameter giving the actual calendar date.
У	The y coordinate in the event space, thus a number giving the plot row.
x.is.Date	A logical, being TRUE if <i>x</i> is a string giving the date in the <i>x.date.format</i> format.
x.date.format	A string giving the format of the <i>x</i> date, if <i>x.is.Date</i> id TRUE.
adjust.for.earliest.date	
	A logical which is TRUE if $x$ is a calendar date that must be adjusted for the earliest plotted date (by default TRUE).
plot.type	Can be either "baseR" or "SVG" and specifies to which type of plotting the mapping applies.
suppress.warnings	
	Logical, if TRUE don't show any warnings.

#### **Details**

This is intended for advanced users only. In the event space, the *x* coordinate can be either given as the number of days since the first plotted event, or as an actual calendar date (either as a Date object or a string with a given format; a date may or may not be corrected relative to the first displayed date). On the *y* coordinate, the plotting is divided in equally spaced rows, each row corresponding to a single event or an element of a partial CMA plot (one can specify in between rows using fractions). Any or both of *x* and *y* can be missing.

## Value

A numeric vector with x and y components giving the plotting coordinates, or NULL in case of error.

## **Examples**

med.events 95

med.events

Example medication events records for 100 patients.

## **Description**

An artificial dataset containing medication events (one per row) for 100 patients (1080 events in total). This is the dataset format appropriate for medication adherence analyses performed with the R package AdhereR. Medication events represent individual records of prescribing or dispensing a specific medication for a patient at a given date. Dosage and medication type is optional (only needed if calculation of adherence or persistence takes into account changes in dosage and type of medication).

## Usage

med.events

## Format

A data frame with 1080 rows and 5 variables:

**PATIENT\_ID** integer here; patient unique identifier. Can also be string.

**DATE** *character*; the medication event date, by default in the mm/dd/yyyy format. It may represent a prescribing or dispensing date.

**PERDAY** *integer*; the daily dosage prescribed for the medication supplied at this medication event (i.e. how many doses should be taken daily according to the prescription). This column is optional, as it is not considered in all functions but may be relevant for specific research or clinical contexts. All values should be > 0.

**CATEGORY** *character*; the medication type, here two placeholder labels, 'medA' and 'medB'. This is a researcher-defined classification depending on study aims (e.g., based on therapeutic use, mechanism of action, chemical molecule, or pharmaceutical formulation). This column is optional, as it is not considered in all functions but may be relevant for specific research or clinical contexts.

**DURATION** *integer*; the medication event duration in days (i.e. how many days the mediation supplied would last if used as prescribed); may be available in the extraction or computed based on quantity supplied (the number of doses prescribed or dispensed on that occasion) and daily dosage. All values should be > 0.

96 med.groups

med.events.ATC

Example of medication events with ATC codes.

# Description

An artificial dataset containing medication events (one per row) for 16 patients (1564 events in total), containing ATC codes. This dataset is derived from the durcomp datasets using the compute\_event\_durations function. See @med.events for more details.

## Usage

med.events.ATC

#### **Format**

A data frame with 1564 rows and 7 variables:

PATIENT\_ID the patient unique identifier.

**DATE** the medication event date.

**DURATION** the duration in days.

**PERDAY** the daily dosage.

**CATEGORY** the ATC code.

**CATEGORY\_L1** explicitation of the first field of the ATC code (e.g., "A"="ALIMENTARY TRACT AND METABOLISM").

**CATEGORY\_L2** explicitation of the first and second fields of the ATC code (e.g., "A02"="DRUGS FOR ACID RELATED DISORDERS").

med.groups

Example of medication groups.

# Description

An example defining 6 medication groups for med.events.ATC. It is a *named character vector*, where the names are the medication group unique *names* (e.g., "Vitamines") and the elements are the medication group *definitions* (e.g., "(CATEGORY\_L2 == 'VITAMINS')"). The definitions are R logical expressions using *column names* and *values* that appear in the dataset, as well as references to other medication groups using the construction "NAME".

# Usage

med.groups

# **Format**

An object of class character of length 6.

## **Details**

In the above example, "CATEGORY\_L2" is a column name in the med.events.ATC dataset, and 'VITAMINS' one of its possible values, and which selects all events that have prescribed ATC codes "A11" (aka "VITAMINS"). Another example is "NotVita" defined as "(!Vitamines)", which selects all events that do not have Vitamines prescribed.

For more details, please see the acompanying vignette.

plot.CMA0

Plot CMA0 objects.

#### **Description**

Plots the events (prescribing or dispensing) data encapsulated in a basic CMA0 object.

# Usage

```
## S3 method for class 'CMA0'
plot(
 Х,
  patients.to.plot = NULL,
  duration = NA,
  align.all.patients = FALSE,
  align.first.event.at.zero = FALSE,
  show.period = c("dates", "days")[2],
  period.in.days = 90,
  show.legend = TRUE,
  legend.x = "right",
  legend.y = "bottom",
  legend.bkg.opacity = 0.5,
  legend.cex = 0.75,
  legend.cex.title = 1,
  cex = 1,
  cex.axis = 0.75,
  cex.lab = 1,
  xlab = c(dates = "Date", days = "Days"),
  ylab = c(withoutCMA = "patient", withCMA = "patient (& CMA)"),
  title = c(aligned = "Event patterns (all patients aligned)", notaligned =
    "Event patterns"),
  col.cats = rainbow,
  unspecified.category.label = "drug",
  medication.groups.to.plot = NULL,
 medication.groups.separator.show = TRUE,
 medication.groups.separator.lty = "solid",
  medication.groups.separator.lwd = 2,
  medication.groups.separator.color = "blue",
```

```
medication.groups.allother.label = "*",
  lty.event = "solid",
  lwd.event = 2,
  pch.start.event = 15,
  pch.end.event = 16,
  plot.events.vertically.displaced = TRUE,
 print.dose = FALSE,
  cex.dose = 0.75,
  print.dose.outline.col = "white",
  print.dose.centered = FALSE,
 plot.dose = FALSE,
  lwd.event.max.dose = 8,
 plot.dose.lwd.across.medication.classes = FALSE,
  col.continuation = "black",
 lty.continuation = "dotted",
  lwd.continuation = 1,
  col.na = "lightgray",
  highlight.followup.window = TRUE,
  followup.window.col = "green",
  highlight.observation.window = TRUE,
  observation.window.col = "yellow",
  observation.window.density = 35,
  observation.window.angle = -30,
  observation.window.opacity = 0.3,
  alternating.bands.cols = c("white", "gray95"),
  rotate.text = -60,
  force.draw.text = FALSE,
  bw.plot = FALSE,
 min.plot.size.in.characters.horiz = 0,
 min.plot.size.in.characters.vert = 0,
  suppress.warnings = FALSE,
 max.patients.to.plot = 100,
  export.formats = NULL,
 export.formats.fileprefix = "AdhereR-plot",
  export.formats.height = NA,
  export.formats.width = NA,
  export.formats.save.svg.placeholder = TRUE,
  export.formats.svg.placeholder.type = c("jpg", "png", "webp")[2],
  export.formats.svg.placeholder.embed = FALSE,
  export.formats.html.template = NULL,
  export.formats.html.javascript = NULL,
 export.formats.html.css = NULL,
 export.formats.directory = NA,
  generate.R.plot = TRUE,
 do.not.draw.plot = FALSE
)
```

#### **Arguments**

x A CMA0 or derived object, representing the CMA to plot

... other possible parameters

patients.to.plot

A vector of *strings* containing the list of patient IDs to plot (a subset of those in the cma object), or NULL for all

duration A *number*, the total duration (in days) of the whole period to plot; in NA it is automatically determined from the event data such that the whole dataset fits.

align.all.patients

*Logical*, should all patients be aligned (i.e., the actual dates are discarded and all plots are relative to the earliest date)?

align.first.event.at.zero

*Logical*, should the first event be placed at the origin of the time axis (at 0)?

show.period A *string*, if "dates" show the actual dates at the regular grid intervals, while for "days" (the default) shows the days since the beginning; if align.all.patients == TRUE, show.period is taken as "days".

period.in.days The *number* of days at which the regular grid is drawn (or 0 for no grid).

show. legend *Logical*, should the legend be drawn?

legend.x The position of the legend on the x axis; can be "left", "right" (default), or a numeric value.

legend.y The position of the legend on the y axis; can be "bottom" (default), "top", or a *numeric* value.

legend.bkg.opacity

A *number* between 0.0 and 1.0 specifying the opacity of the legend background.

cex, cex.axis, cex.lab, legend.cex, legend.cex.title

numeric values specifying the cex of the various types of text.

Named vector of x-axis labels to show for the two types of periods ("days" and "dates"), or a single value for both, or NULL for nothing.

ylab Named vector of y-axis labels to show without and with CMA estimates, or a single value for both, or NULL for nonthing.

title Named vector of titles to show for and without alignment, or a single value for both, or NULL for nonthing.

A *color* or a *function* that specifies the single colour or the colour palette used to

plot the different medication; by default rainbow, but we recommend, whenever possible, a colorblind-friendly palette such as viridis or colorblind\_pal.

unspecified.category.label

col.cats

A string giving the name of the unspecified (generic) medication category.

medication.groups.to.plot

the names of the medication groups to plot or NULL (the default) for all.

medication.groups.separator.show

a *boolean*, if TRUE (the default) visually mark the medication groups the belong to the same patient, using horizontal lines and alternating vertical lines.

medication.groups.separator.lty, medication.groups.separator.lwd, medication.groups.separator.color graphical parameters (line type, line width and colour describing the visual marking og medication groups as beloning to the same patient.

medication.groups.allother.label

a *string* giving the label to use for the implicit \_\_ALL\_OTHERS\_\_ medication group (defaults to "\*").

lty.event, lwd.event, pch.start.event, pch.end.event

The style of the event (line style, width, and start and end symbols).

plot.events.vertically.displaced

Should consecutive events be plotted on separate rows (i.e., separated vertically, the default) or on the same row?

print.dose Logical, should the daily dose be printed as text?

cex.dose *Numeric*, if daily dose is printed, what text size to use?

print.dose.outline.col

If NA, don't print dose text with outline, otherwise a color name/code for the outline.

print.dose.centered

Logical, print the daily dose centered on the segment or slightly below it?

plot.dose *Logical*, should the daily dose be indicated through segment width?

lwd.event.max.dose

*Numeric*, the segment width corresponding to the maximum daily dose (must be >= lwd.event but not too big either).

plot.dose.lwd.across.medication.classes

*Logical*, if TRUE, the line width of the even is scaled relative to all medication classes (i.e., relative to the global minimum and maximum doses), otherwise it is scale relative only to its medication class.

col.continuation, lty.continuation, lwd.continuation

The style of the "continuation" lines connecting consecutive events (colour, line style and width).

col.na The colour used for missing event data.

highlight.followup.window

Logical, should the follow-up window be plotted?

followup.window.col

The follow-up window's colour.

highlight.observation.window

Logical, should the observation window be plotted?

observation.window.col, observation.window.density, observation.window.angle, observation.window.opac Attributes of the observation window (colour, shading density, angle and opacity).

alternating.bands.cols

The colors of the alternating vertical bands distinguishing the patients; can be NULL = don't draw the bandes; or a vector of colors.

rotate.text *Numeric*, the angle by which certain text elements (e.g., axis labels) should be rotated.

force.draw.text

Logical, if TRUE, always draw text even if too big or too small

bw.plot Logical, should the plot use grayscale only (i.e., the gray colors function)?

min.plot.size.in.characters.horiz, min.plot.size.in.characters.vert

*Numeric*, the minimum size of the plotting surface in characters; horizontally (min.plot.size.in.characters.horiz) refers to the the whole duration of the events to plot; vertically (min.plot.size.in.characters.vert) refers to a single event. If the plotting is too small, possible solutions might be: if within RStudio, try to enlarge the "Plots" panel, or (also valid outside RStudio but not if using RStudio server start a new plotting device (e.g., using X11(), quartz() or windows(), depending on OS) or (works always) save to an image (e.g., jpeg(...); ...; dev.off()) and display it in a viewer.

suppress.warnings

Logical: show or hide the warnings?

max.patients.to.plot

Numeric, the maximum patients to attempt to plot.

export.formats a *string* giving the formats to export the figure to (by default NULL, meaning no exporting); can be any combination of "svg" (just an SVG file), "html" (SVG + HTML + CSS + JavaScript, all embedded within one HTML document), "jpg", "png", "webp", "ps" or "pdf".

export.formats.fileprefix

a *string* giving the file name prefix for the exported formats (defaults to "AdhereR-plot").

export.formats.height, export.formats.width

*numbers* giving the desired dimensions (in pixels) for the exported figure (defaults to sane values if NA).

export.formats.save.svg.placeholder

a *logical*, if TRUE, save an image placeholder of type given by export. formats.svg.placeholder.typ for the SVG image.

export.formats.svg.placeholder.type

a *string*, giving the type of placeholder for the SVG image to save; can be "jpg", "png" (the default) or "webp".

 ${\tt export.formats.svg.placeholder.embed}$ 

a *logical*, if TRUE, embed the placeholder image in the HTML document (if any) using base64 encoding, otherwise (the default) leave it as an external image file (works only when an HTML document is exported and only for JPEG or PNG images.

export.formats.html.template, export.formats.html.javascript, export.formats.html.css character strings or NULL (the default) giving the path to the HTML, JavaScript and CSS templates, respectively, to be used when generating the HTML+CSS semi-interactive plots; when NULL, the default ones included with the package will be used. If you decide to define new templates please use the default ones for inspiration and note that future version are not guaranteed to be backwards compatible!

export.formats.directory

a *string*; if exporting, which directory to export to; if NA (the default), creates the files in a temporary directory.

```
generate.R.plot

a logical, if TRUE (the default), generate the standard (base R) plot for plotting within R.

do.not.draw.plot

a logical, if TRUE (not the default), does not draw the plot itself, but only the legend (if show.legend is TRUE) at coordinates (0,0) irrespective of the given legend coordinates. This is intended to allow (together with the get.legend.plotting.area() function) the separate plotting of the legend.
```

#### **Details**

The x-axis represents time (either in days since the earliest date or as actual dates), with consecutive events represented as ascending on the y-axis.

Each event is represented as a segment with style lty.event and line width lwd.event starting with a pch.start.event and ending with a pch.end.event character, coloured with a unique color as given by col.cats, extending from its start date until its end date. Consecutive events are thus represented on consecutive levels of the y-axis and are connected by a "continuation" line with col.continuation colour, lty.continuation style and lwd.continuation width; these continuation lines are purely visual guides helping to perceive the sequence of events, and carry no information about the availability of medication in this interval.

When several patients are displayed on the same plot, they are organized vertically, and alternating bands (white and gray) help distinguish consecutive patients. Implicitly, all patients contained in the cma object will be plotted, but the patients.to.plot parameter allows the selection of a subset of patients.

## **Examples**

```
cma0 <- CMA0(data=med.events,</pre>
             ID.colname="PATIENT_ID",
             event.date.colname="DATE",
             event.duration.colname="DURATION",
             event.daily.dose.colname="PERDAY",
             medication.class.colname="CATEGORY",
             followup.window.start=0,
             followup.window.start.unit="days",
             followup.window.duration=2*365,
             followup.window.duration.unit="days",
             observation.window.start=30,
             observation.window.start.unit="days",
             observation.window.duration=365,
             observation.window.duration.unit="days",
             date.format="%m/%d/%Y",
             summary="Base CMA");
plot(cma0, patients.to.plot=c("1","2"));
```

plot.CMA1

Plot CMA0-derived objects.

## Description

Plots the event data and estimated CMA encapsulated in objects derived from CMA0.

# Usage

```
## S3 method for class 'CMA1'
plot(
 х,
 patients.to.plot = NULL,
  duration = NA,
  align.all.patients = FALSE,
  align.first.event.at.zero = FALSE,
  show.period = c("dates", "days")[2],
  period.in.days = 90,
  show.legend = TRUE,
  legend.x = "right",
  legend.y = "bottom",
  legend.bkg.opacity = 0.5,
  legend.cex = 0.75,
  legend.cex.title = 1,
  cex = 1,
  cex.axis = 0.75,
  cex.lab = 1,
  show.cma = TRUE,
  col.cats = rainbow,
  unspecified.category.label = "drug",
 medication.groups.to.plot = NULL,
 medication.groups.separator.show = TRUE,
 medication.groups.separator.lty = "solid",
 medication.groups.separator.lwd = 2,
 medication.groups.separator.color = "blue",
 medication.groups.allother.label = "*",
  lty.event = "solid",
  lwd.event = 2,
  pch.start.event = 15,
  pch.end.event = 16,
  show.event.intervals = TRUE,
  col.na = "lightgray",
  print.CMA = TRUE,
  CMA.cex = 0.5,
  plot.CMA = TRUE,
  CMA.plot.ratio = 0.1,
```

```
CMA.plot.col = "lightgreen",
  CMA.plot.border = "darkgreen",
  CMA.plot.bkg = "aquamarine",
  CMA.plot.text = CMA.plot.border,
  highlight.followup.window = TRUE,
  followup.window.col = "green",
  highlight.observation.window = TRUE,
  observation.window.col = "yellow",
  observation.window.density = 35,
  observation.window.angle = -30,
  observation.window.opacity = 0.3,
  show.real.obs.window.start = TRUE,
  real.obs.window.density = 35,
  real.obs.window.angle = 30,
  print.dose = FALSE,
  cex.dose = 0.75,
  print.dose.outline.col = "white",
  print.dose.centered = FALSE,
  plot.dose = FALSE,
  lwd.event.max.dose = 8,
  plot.dose.lwd.across.medication.classes = FALSE,
  alternating.bands.cols = c("white", "gray95"),
  bw.plot = FALSE,
  rotate.text = -60,
  force.draw.text = FALSE,
 min.plot.size.in.characters.horiz = 0,
 min.plot.size.in.characters.vert = 0,
 max.patients.to.plot = 100,
  export.formats = NULL,
  export.formats.fileprefix = "AdhereR-plot",
  export.formats.height = NA,
  export.formats.width = NA,
  export.formats.save.svg.placeholder = TRUE,
  export.formats.svg.placeholder.type = c("jpg", "png", "webp")[2],
  export.formats.svg.placeholder.embed = FALSE,
  export.formats.directory = NA,
  export.formats.html.template = NULL,
  export.formats.html.javascript = NULL,
  export.formats.html.css = NULL,
  generate.R.plot = TRUE,
  do.not.draw.plot = FALSE
)
## S3 method for class 'CMA2'
plot(...)
## S3 method for class 'CMA3'
plot(...)
```

```
## S3 method for class 'CMA4'
    plot(...)
    ## S3 method for class 'CMA5'
    plot(...)
    ## S3 method for class 'CMA6'
    plot(...)
    ## S3 method for class 'CMA7'
    plot(...)
    ## S3 method for class 'CMA8'
    plot(...)
    ## S3 method for class 'CMA9'
    plot(...)
Arguments
                      A CMA0 or derived object, representing the CMA to plot
    Х
                      other possible parameters
    patients.to.plot
                      A vector of strings containing the list of patient IDs to plot (a subset of those in
                      the cma object), or NULL for all
    duration
                      A number, the total duration (in days) of the whole period to plot; in NA it is
                      automatically determined from the event data such that the whole dataset fits.
    align.all.patients
                      Logical, should all patients be aligned (i.e., the actual dates are discarded and
                      all plots are relative to the earliest date)?
    align.first.event.at.zero
                      Logical, should the first event be placed at the origin of the time axis (at 0)?
    show.period
                      A string, if "dates" show the actual dates at the regular grid intervals, while for
                      "days" (the default) shows the days since the beginning; if align.all.patients
                      == TRUE, show.period is taken as "days".
    period.in.days The number of days at which the regular grid is drawn (or 0 for no grid).
    show.legend
                      Logical, should the legend be drawn?
    legend.x
                      The position of the legend on the x axis; can be "left", "right" (default), or a
                      numeric value.
    legend.y
                      The position of the legend on the y axis; can be "bottom" (default), "top", or a
                      numeric value.
    legend.bkg.opacity
                      A number between 0.0 and 1.0 specifying the opacity of the legend background.
    cex, cex.axis, cex.lab, legend.cex, legend.cex.title, CMA.cex
                      numeric values specifying the cex of the various types of text.
```

show.cma *Logical*, should the CMA type be shown in the title?

A *color* or a *function* that specifies the single colour or the colour palette used to plot the different medication; by default rainbow, but we recommend, whenever possible, a colorblind-friendly palette such as viridis or colorblind\_pal.

unspecified.category.label

A *string* giving the name of the unspecified (generic) medication category.

medication.groups.to.plot

the names of the medication groups to plot or NULL (the default) for all.

medication.groups.separator.show

a *boolean*, if TRUE (the default) visually mark the medication groups the belong to the same patient, using horizontal lines and alternating vertical lines.

medication.groups.separator.lty, medication.groups.separator.lwd, medication.groups.separator.color graphical parameters (line type, line width and colour describing the visual marking og medication groups as beloning to the same patient.

medication.groups.allother.label

a *string* giving the label to use for the implicit \_\_ALL\_OTHERS\_\_ medication group (defaults to "\*").

lty.event, lwd.event, pch.start.event, pch.end.event

The style of the event (line style, width, and start and end symbols).

show.event.intervals

Logical, should the actual event intervals be shown?

col.na The colour used for missing event data.

print.CMA Logical, should the CMA values be printed?

plot.CMA Logical, should the CMA values be represented graphically?

CMA.plot.ratio A *number*, the proportion of the total horizontal plot space to be allocated to the CMA plot.

CMA.plot.col, CMA.plot.border, CMA.plot.bkg, CMA.plot.text

Strings giving the colours of the various components of the CMA plot.

highlight.followup.window

*Logical*, should the follow-up window be plotted?

followup.window.col

The follow-up window's colour.

highlight.observation.window

*Logical*, should the observation window be plotted?

observation.window.col, observation.window.density, observation.window.angle, observation.window.opac Attributes of the observation window (colour, shading density, angle and opacity).

show.real.obs.window.start, real.obs.window.density, real.obs.window.angle

For some CMAs, the observation window might be adjusted, in which case should it be plotted and with that attributes?

print.dose Logical, should the daily dose be printed as text?

cex.dose *Numeric*, if daily dose is printed, what text size to use?

print.dose.outline.col

If NA, don't print dose text with outline, otherwise a color name/code for the outline.

print.dose.centered

Logical, print the daily dose centered on the segment or slightly below it?

plot.dose Logical, should the daily dose be indicated through segment width?

lwd.event.max.dose

*Numeric*, the segment width corresponding to the maximum daily dose (must be >= lwd.event but not too big either).

plot.dose.lwd.across.medication.classes

Logical, if TRUE, the line width of the even is scaled relative to all medication classes (i.e., relative to the global minimum and maximum doses), otherwise it is scale relative only to its medication class.

alternating.bands.cols

The colors of the alternating vertical bands distinguishing the patients; can be NULL = don't draw the bandes; or a vector of colors.

bw.plot Logical, should the plot use grayscale only (i.e., the gray.colors function)?

rotate.text *Numeric*, the angle by which certain text elements (e.g., axis labels) should be rotated.

force.draw.text

Logical, if TRUE, always draw text even if too big or too small

min.plot.size.in.characters.horiz, min.plot.size.in.characters.vert

*Numeric*, the minimum size of the plotting surface in characters; horizontally (min.plot.size.in.characters.horiz) refers to the the whole duration of the events to plot; vertically (min.plot.size.in.characters.vert) refers to a single event. If the plotting is too small, possible solutions might be: if within RStudio, try to enlarge the "Plots" panel, or (also valid outside RStudio but not if using RStudio server start a new plotting device (e.g., using X11(), quartz() or windows(), depending on OS) or (works always) save to an image (e.g., jpeg(...); ...; dev.off()) and display it in a viewer.

max.patients.to.plot

*Numeric*, the maximum patients to attempt to plot.

export.formats a *string* giving the formats to export the figure to (by default NULL, meaning no exporting); can be any combination of "svg" (just an SVG file), "html" (SVG + HTML + CSS + JavaScript, all embedded within one HTML document), "jpg", "png", "webp", "ps" or "pdf".

export.formats.fileprefix

a *string* giving the file name prefix for the exported formats (defaults to "AdhereR-plot").

export.formats.height, export.formats.width

*numbers* giving the desired dimensions (in pixels) for the exported figure (defaults to sane values if NA).

export.formats.save.svg.placeholder

a *logical*, if TRUE, save an image placeholder of type given by export. formats.svg.placeholder.typ for the SVG image.

export.formats.svg.placeholder.type

a *string*, giving the type of placeholder for the SVG image to save; can be "jpg", "png" (the default) or "webp".

export.formats.svg.placeholder.embed

a *logical*, if TRUE, embed the placeholder image in the HTML document (if any) using base64 encoding, otherwise (the default) leave it as an external image file (works only when an HTML document is exported and only for JPEG or PNG images.

export.formats.directory

a *string*; if exporting, which directory to export to; if NA (the default), creates the files in a temporary directory.

export.formats.html.template, export.formats.html.javascript, export.formats.html.css character strings or NULL (the default) giving the path to the HTML, JavaScript and CSS templates, respectively, to be used when generating the HTML+CSS semi-interactive plots; when NULL, the default ones included with the package will be used. If you decide to define new templates please use the default ones for inspiration and note that future version are not guaranteed to be backwards compatible!

generate.R.plot

a *logical*, if TRUE (the default), generate the standard (base R) plot for plotting within R.

do.not.draw.plot

a *logical*, if TRUE (*not* the default), does not draw the plot itself, but only the legend (if show.legend is TRUE) at coordinates (0,0) irrespective of the given legend coordinates. This is intended to allow (together with the get.legend.plotting.area() function) the separate plotting of the legend.

#### **Details**

Please note that this function plots objects inheriting from CMA0 but not objects of type CMA0 itself (these are plotted by plot.CMA0).

The x-axis represents time (either in days since the earliest date or as actual dates), with consecutive events represented as ascending on the y-axis.

Each event is represented as a segment with style lty.event and line width lwd.event starting with a pch.start.event and ending with a pch.end.event character, coloured with a unique color as given by col.cats, extending from its start date until its end date. Superimposed on these are shown the event intervals and gap days as estimated by the particular CMA method, more precisely plotting the start and end of the available events as solid filled-in rectangles, and the event gaps as shaded rectangles.

The follow-up and the observation windows are plotted as an empty rectangle and as shaded rectangle, respectively (for some CMAs the observation window might be adjusted in which case the adjustment may also be plotted using a different shading).

The CMA estimates can be visually represented as well in the left side of the figure using bars (sometimes the estimates can go above 100%, in which case the maximum possible bar filling is adjusted to reflect this).

When several patients are displayed on the same plot, they are organized vertically, and alternating bands (white and gray) help distinguish consecutive patients. Implicitly, all patients contained in

plot.CMA\_per\_episode

the cma object will be plotted, but the patients.to.plot parameter allows the selection of a subset of patients.

Finally, the y-axis shows the patient ID and possibly the CMA estimate as well.

# Examples

# Description

Plots the event data and the estimated CMA per treatment episode and sliding window, respectively.

```
## S3 method for class 'CMA_per_episode'
plot(
 Х,
 patients.to.plot = NULL,
 duration = NA,
  align.all.patients = FALSE,
  align.first.event.at.zero = FALSE,
  show.period = c("dates", "days")[2],
  period.in.days = 90,
  show.legend = TRUE,
  legend.x = "right",
  legend.y = "bottom",
  legend.bkg.opacity = 0.5,
  legend.cex = 0.75,
  legend.cex.title = 1,
  cex = 1,
  cex.axis = 0.75,
  cex.lab = 1,
  show.cma = TRUE,
  xlab = c(dates = "Date", days = "Days"),
  ylab = c(withoutCMA = "patient", withCMA = "patient (& CMA)"),
  title = c(aligned = "Event patterns (all patients aligned)", notaligned =
```

```
"Event patterns"),
col.cats = rainbow,
unspecified.category.label = "drug",
medication.groups.to.plot = NULL,
medication.groups.separator.show = TRUE,
medication.groups.separator.lty = "solid",
medication.groups.separator.lwd = 2,
medication.groups.separator.color = "blue",
medication.groups.allother.label = "*",
lty.event = "solid",
lwd.event = 2,
pch.start.event = 15,
pch.end.event = 16,
show.event.intervals = FALSE,
show.overlapping.event.intervals = c("first", "last", "min gap", "max gap",
  "average")[1],
plot.events.vertically.displaced = TRUE,
print.dose = FALSE,
cex.dose = 0.75,
print.dose.outline.col = "white",
print.dose.centered = FALSE,
plot.dose = FALSE,
lwd.event.max.dose = 8,
plot.dose.lwd.across.medication.classes = FALSE,
col.na = "lightgray",
col.continuation = "black",
lty.continuation = "dotted",
lwd.continuation = 1,
print.CMA = TRUE,
CMA.cex = 0.5,
plot.CMA = TRUE,
plot.CMA.as.histogram = TRUE,
plot.partial.CMAs.as = c("stacked", "overlapping", "timeseries")[1],
plot.partial.CMAs.as.stacked.col.bars = "gray90",
plot.partial.CMAs.as.stacked.col.border = "gray30";
plot.partial.CMAs.as.stacked.col.text = "black",
plot.partial.CMAs.as.timeseries.vspace = 7,
plot.partial.CMAs.as.timeseries.start.from.zero = TRUE,
plot.partial.CMAs.as.timeseries.col.dot = "darkblue",
plot.partial.CMAs.as.timeseries.col.interval = "gray70",
plot.partial.CMAs.as.timeseries.col.text = "firebrick",
plot.partial.CMAs.as.timeseries.interval.type = c("none", "segments", "arrows",
  "lines", "rectangles")[2],
plot.partial.CMAs.as.timeseries.lwd.interval = 1,
plot.partial.CMAs.as.timeseries.alpha.interval = 0.25,
plot.partial.CMAs.as.timeseries.show.0perc = TRUE,
plot.partial.CMAs.as.timeseries.show.100perc = FALSE,
plot.partial.CMAs.as.overlapping.alternate = TRUE,
```

```
plot.partial.CMAs.as.overlapping.col.interval = "gray70",
  plot.partial.CMAs.as.overlapping.col.text = "firebrick",
  CMA.plot.ratio = 0.1,
  CMA.plot.col = "lightgreen",
  CMA.plot.border = "darkgreen",
  CMA.plot.bkg = "aquamarine",
  CMA.plot.text = CMA.plot.border,
  highlight.followup.window = TRUE,
  followup.window.col = "green",
  highlight.observation.window = TRUE,
  observation.window.col = "yellow",
  observation.window.opacity = 0.3,
  print.episode.or.sliding.window = FALSE,
  alternating.bands.cols = c("white", "gray95"),
  bw.plot = FALSE,
  rotate.text = -60,
  force.draw.text = FALSE,
  min.plot.size.in.characters.horiz = 0,
 min.plot.size.in.characters.vert = 0,
 max.patients.to.plot = 100,
  export.formats = NULL,
  export.formats.fileprefix = "AdhereR-plot",
  export.formats.height = NA,
  export.formats.width = NA,
  export.formats.save.svg.placeholder = TRUE,
  export.formats.svg.placeholder.type = c("jpg", "png", "webp")[2],
  export.formats.svg.placeholder.embed = FALSE,
  export.formats.html.template = NULL,
  export.formats.html.javascript = NULL,
  export.formats.html.css = NULL,
  export.formats.directory = NA,
  generate.R.plot = TRUE,
  do.not.draw.plot = FALSE,
  suppress.warnings = FALSE,
)
## S3 method for class 'CMA_sliding_window'
plot(
  х,
 patients.to.plot = NULL,
  duration = NA,
  align.all.patients = FALSE,
  align.first.event.at.zero = FALSE,
  show.period = c("dates", "days")[2],
  period.in.days = 90,
  show.legend = TRUE,
  legend.x = "right",
```

```
legend.y = "bottom",
legend.bkg.opacity = 0.5,
legend.cex = 0.75,
legend.cex.title = 1,
cex = 1,
cex.axis = 0.75,
cex.lab = 1,
show.cma = TRUE,
xlab = c(dates = "Date", days = "Days"),
ylab = c(withoutCMA = "patient", withCMA = "patient (& CMA)"),
title = c(aligned = "Event patterns (all patients aligned)", notaligned =
  "Event patterns"),
col.cats = rainbow,
unspecified.category.label = "drug",
medication.groups.to.plot = NULL,
medication.groups.separator.show = TRUE,
medication.groups.separator.lty = "solid",
medication.groups.separator.lwd = 2,
medication.groups.separator.color = "blue",
medication.groups.allother.label = "*",
lty.event = "solid",
lwd.event = 2,
pch.start.event = 15,
pch.end.event = 16,
show.event.intervals = FALSE,
show.overlapping.event.intervals = c("first", "last", "min gap", "max gap",
  "average")[1],
plot.events.vertically.displaced = TRUE,
print.dose = FALSE,
cex.dose = 0.75,
print.dose.outline.col = "white",
print.dose.centered = FALSE,
plot.dose = FALSE,
lwd.event.max.dose = 8,
plot.dose.lwd.across.medication.classes = FALSE,
col.na = "lightgray",
col.continuation = "black",
lty.continuation = "dotted",
lwd.continuation = 1,
print.CMA = TRUE,
CMA.cex = 0.5,
plot.CMA = TRUE,
plot.CMA.as.histogram = TRUE,
plot.partial.CMAs.as = c("stacked", "overlapping", "timeseries")[1],
plot.partial.CMAs.as.stacked.col.bars = "gray90",
plot.partial.CMAs.as.stacked.col.border = "gray30",
plot.partial.CMAs.as.stacked.col.text = "black",
plot.partial.CMAs.as.timeseries.vspace = 7,
```

```
plot.partial.CMAs.as.timeseries.start.from.zero = TRUE,
  plot.partial.CMAs.as.timeseries.col.dot = "darkblue",
  plot.partial.CMAs.as.timeseries.col.interval = "gray70",
  plot.partial.CMAs.as.timeseries.col.text = "firebrick"
 plot.partial.CMAs.as.timeseries.interval.type = c("none", "segments", "arrows",
    "lines", "rectangles")[2],
  plot.partial.CMAs.as.timeseries.lwd.interval = 1,
  plot.partial.CMAs.as.timeseries.alpha.interval = 0.25,
  plot.partial.CMAs.as.timeseries.show.0perc = TRUE,
  plot.partial.CMAs.as.timeseries.show.100perc = FALSE,
  plot.partial.CMAs.as.overlapping.alternate = TRUE,
  plot.partial.CMAs.as.overlapping.col.interval = "gray70",
  plot.partial.CMAs.as.overlapping.col.text = "firebrick",
  CMA.plot.ratio = 0.1,
  CMA.plot.col = "lightgreen",
  CMA.plot.border = "darkgreen",
  CMA.plot.bkg = "aquamarine",
  CMA.plot.text = CMA.plot.border,
  highlight.followup.window = TRUE,
  followup.window.col = "green",
  highlight.observation.window = TRUE,
  observation.window.col = "yellow",
  observation.window.opacity = 0.3,
  print.episode.or.sliding.window = FALSE,
  alternating.bands.cols = c("white", "gray95"),
  bw.plot = FALSE,
  rotate.text = -60,
  force.draw.text = FALSE,
  min.plot.size.in.characters.horiz = 0,
 min.plot.size.in.characters.vert = 0,
  max.patients.to.plot = 100,
  export.formats = NULL,
  export.formats.fileprefix = "AdhereR-plot",
  export.formats.height = NA,
  export.formats.width = NA,
  export.formats.save.svg.placeholder = TRUE,
  export.formats.svg.placeholder.type = c("jpg", "png", "webp")[2],
  export.formats.svg.placeholder.embed = FALSE,
  export.formats.html.template = NULL,
  export.formats.html.javascript = NULL,
  export.formats.html.css = NULL,
  export.formats.directory = NA,
  generate.R.plot = TRUE,
  do.not.draw.plot = FALSE,
  suppress.warnings = FALSE,
)
```

#### **Arguments**

A CMA0 or derived object, representing the CMA to plot

patients.to.plot

A vector of *strings* containing the list of patient IDs to plot (a subset of those in the cma object), or NULL for all

duration A number, the total duration (in days) of the whole period to plot; in NA it is automatically determined from the event data such that the whole dataset fits.

align.all.patients

Logical, should all patients be aligned (i.e., the actual dates are discarded and all plots are relative to the earliest date)?

align.first.event.at.zero

Logical, should the first event be placed at the origin of the time axis (at 0)?

show.period A string, if "dates" show the actual dates at the regular grid intervals, while for "days" (the default) shows the days since the beginning; if align.all.patients == TRUE, show.period is taken as "days".

period.in.days The *number* of days at which the regular grid is drawn (or 0 for no grid).

show.legend Logical, should the legend be drawn?

legend.x The position of the legend on the x axis; can be "left", "right" (default), or a numeric value.

legend.y The position of the legend on the y axis; can be "bottom" (default), "top", or a numeric value.

legend.bkg.opacity

A *number* between 0.0 and 1.0 specifying the opacity of the legend background.

legend.cex, legend.cex.title

The legend and legend title font sizes.

cex, cex.axis, cex.lab

numeric values specifying the cex of the various types of text.

show.cma Logical, should the CMA type be shown in the title?

xlab Named vector of x-axis labels to show for the two types of periods ("days" and

"dates"), or a single value for both, or NULL for nothing.

ylab Named vector of y-axis labels to show without and with CMA estimates, or a

single value for both, or NULL for nonthing.

title Named vector of titles to show for and without alignment, or a single value for

both, or NULL for nonthing.

col.cats A color or a function that specifies the single colour or the colour palette used to

> plot the different medication; by default rainbow, but we recommend, whenever possible, a colorblind-friendly palette such as viridis or colorblind\_pal.

unspecified.category.label

A *string* giving the name of the unspecified (generic) medication category.

medication.groups.to.plot

the names of the medication groups to plot or NULL (the default) for all.

medication.groups.separator.show

a boolean, if TRUE (the default) visually mark the medication groups the belong to the same patient, using horizontal lines and alternating vertical lines.

medication.groups.separator.lty, medication.groups.separator.lwd, medication.groups.separator.color graphical parameters (line type, line width and colour describing the visual marking og medication groups as beloning to the same patient.

medication.groups.allother.label

a *string* giving the label to use for the implicit \_\_ALL\_OTHERS\_\_ medication group (defaults to "\*").

lty.event, lwd.event, pch.start.event, pch.end.event

The style of the event (line style, width, and start and end symbols).

show.event.intervals

*Logical*, should the actual event intervals be shown? As per-episode and sliding windows might have overlapping intervals, it is better not to show them by default (FALSE).

show.overlapping.event.intervals

specifies how to plot the event intervals that appear in multiple sliding windows or episodes. We can plot how thye look in the *first* sliding window or episode (the default), how they appear in the *last*, pick the one that minimizes the gap (*min gap*) or maximizes it (*max gap*), or compute their *average* across all sliding windows or episodes containing them.

plot.events.vertically.displaced

Should consecutive events be plotted on separate rows (i.e., separated vertically, the default) or on the same row?

print.dose, cex.dose, print.dose.outline.col, print.dose.centered

Print daily dose as a number and, if so, how (color, size, position...).

plot.dose, lwd.event.max.dose, plot.dose.lwd.across.medication.classes

Show dose through the width of the event lines and, if so, what the maximum width should be, and should this maximum be by medication class or overall.

col.na The colour used for missing event data.

col.continuation, lty.continuation, lwd.continuation

The color, style and width of the contuniation lines connecting consecutive events.

print.CMA Logical, should the CMA values be printed?

CMA. cex ... and, if printed, what cex (numeric) to use?

plot.CMA Logical, should the distribution of the CMA values across episodes/sliding windows be plotted? If TRUE (the default), the distribution is shown on the left-hand side of the plot, otherwise it is not.

plot.CMA.as.histogram

Logical, should the CMA plot be a histogram or a (truncated) density plot? Please note that it is TRUE by deafult for CMA\_per\_episode and FALSE for CMA\_sliding\_window, because usually there are more sliding windows than episodes. Also, the density estimate cannot be estimated for less than three different values.

plot.partial.CMAs.as

Should the partial CMAs be plotted? Possible values are "stacked", "overlapping" or "timeseries", or NULL for no partial CMA plots. Please note that plot.CMA and plot.partial.CMAs.as are independent of each other.

plot.partial.CMAs.as.stacked.col.bars, plot.partial.CMAs.as.stacked.col.border, plot.partial.CMAs.as If plotting the partial CMAs as stacked bars, define their graphical attributes.

plot.partial.CMAs.as.timeseries.vspace, plot.partial.CMAs.as.timeseries.start.from.zero, plot.partia If plotting the partial CMAs as imeseries, these are their graphical attributes.

plot.partial.CMAs.as.overlapping.alternate, plot.partial.CMAs.as.overlapping.col.interval, plot.part

If plotting the partial CMAs as overlapping segments, these are their graphical

attributes.

CMA.plot.ratio A *number*, the proportion of the total horizontal plot space to be allocated to the CMA plot.

CMA.plot.col, CMA.plot.border, CMA.plot.bkg, CMA.plot.text

Strings giving the colours of the various components of the CMA plot.

highlight.followup.window

*Logical*, should the follow-up window be plotted?

followup.window.col

The follow-up window colour.

highlight.observation.window

Logical, should the observation window be plotted?

observation.window.col, observation.window.opacity

Attributes of the observation window (colour, transparency).

print.episode.or.sliding.window

Logical, should we show which events belong to which episode or sliding window? To work, the CMA must have been constructed with return.mapping.events.episodes or return.mapping.events.sliding.window set to TRUE, respectively.

alternating.bands.cols

The colors of the alternating vertical bands distinguishing the patients; can be NULL = don't draw the bandes; or a vector of colors.

bw.plot

*Logical*, should the plot use grayscale only (i.e., the gray.colors function)?

rotate.text

*Numeric*, the angle by which certain text elements (e.g., axis labels) should be rotated.

force.draw.text

Logical, if TRUE, always draw text even if too big or too small

min.plot.size.in.characters.horiz, min.plot.size.in.characters.vert

*Numeric*, the minimum size of the plotting surface in characters; horizontally (min.plot.size.in.characters.horiz) refers to the the whole duration of the events to plot; vertically (min.plot.size.in.characters.vert) refers to a single event. If the plotting is too small, possible solutions might be: if within RStudio, try to enlarge the "Plots" panel, or (also valid outside RStudio but not if using RStudio server start a new plotting device (e.g., using X11(), quartz() or windows(), depending on OS) or (works always) save to an image (e.g., jpeg(...); ...; dev.off()) and display it in a viewer.

max.patients.to.plot

Numeric, the maximum patients to attempt to plot.

export.formats a *string* giving the formats to export the figure to (by default NULL, meaning no exporting); can be any combination of "svg" (just an SVG file), "html" (SVG + HTML + CSS + JavaScript, all embedded within one HTML document), "jpg", "png", "webp", "ps" or "pdf".

export.formats.fileprefix

a *string* giving the file name prefix for the exported formats (defaults to "AdhereR-plot").

export.formats.height, export.formats.width

*numbers* giving the desired dimensions (in pixels) for the exported figure (defaults to sane values if NA).

export.formats.save.svg.placeholder

a *logical*, if TRUE, save an image placeholder of type given by export.formats.svg.placeholder.typ for the SVG image.

export.formats.svg.placeholder.type

a *string*, giving the type of placeholder for the SVG image to save; can be "jpg", "png" (the default) or "webp".

export.formats.svg.placeholder.embed

a *logical*, if TRUE, embed the placeholder image in the HTML document (if any) using base64 encoding, otherwise (the default) leave it as an external image file (works only when an HTML document is exported and only for JPEG or PNG images.

export.formats.html.template, export.formats.html.javascript, export.formats.html.css character strings or NULL (the default) giving the path to the HTML, JavaScript and CSS templates, respectively, to be used when generating the HTML+CSS semi-interactive plots; when NULL, the default ones included with the package will be used. If you decide to define new templates please use the default ones for inspiration and note that future version are not guaranteed to be backwards compatible!

export.formats.directory

a *string*; if exporting, which directory to export to; if NA (the default), creates the files in a temporary directory.

generate.R.plot

a *logical*, if TRUE (the default), generate the standard (base R) plot for plotting within R.

do.not.draw.plot

a *logical*, if TRUE (*not* the default), does not draw the plot itself, but only the legend (if show.legend is TRUE) at coordinates (0,0) irrespective of the given legend coordinates. This is intended to allow (together with the get.legend.plotting.area() function) the separate plotting of the legend.

suppress.warnings

Logical, if TRUE don't show any warnings.

.. other parameters (to be passed to the estimation and plotting of the simple CMA)

#### **Details**

The x-axis represents time (either in days since the earliest date or as actual dates), with consecutive events represented as ascending on the y-axis.

Each event is represented as a segment with style lty.event and line width lwd.event starting with a pch.start.event and ending with a pch.end.event character, coloured with a unique color as given by col.cats, extending from its start date until its end date. Consecutive events are thus represented on consecutive levels of the y-axis and are connected by a "continuation" line

with col.continuation colour, lty.continuation style and lwd.continuation width; these continuation lines are purely visual guides helping to perceive the sequence of events, and carry no information about the avilability of medicine in this interval.

Above these, the treatment episodes or the sliding windows are represented in a stacked manner from the earlieast (left, bottom of the stack) to the latest (right, top of the stack), each showing the CMA as percent fill (capped at 100% even if CMA values may be higher) and also as text.

The follow-up and the observation windows are plotted as empty an rectangle and as shaded rectangle, respectively (for some CMAs the observation window might be adjusted in which case the adjustment may also be plotted using a different shading).

The kernel density ("smoothed histogram") of the CMA estimates across treatment episodes/sliding windows (if more than 2) can be visually represented as well in the left side of the figure (NB, their horizontal scales may be different across patients).

When several patients are displayed on the same plot, they are organized vertically, and alternating bands (white and gray) help distinguish consecutive patients. Implicitely, all patients contained in the cma object will be plotted, but the patients.to.plot parameter allows the selection of a subset of patients.

Finally, the y-axis shows the patient ID and possibly the CMA estimate as well.

Any not explicitly defined arguments are passed to the simple CMA estimation and plotting function; therefore, for more info about possible estimation parameters plese see the help for the appropriate simple CMA, and for possible aesthetic tweaks, please see the help for their plotting.

#### See Also

See the simple CMA estimation CMA1 to CMA9 and plotting plot. CMA1 functions for extra parameters

## **Examples**

```
## Not run:
cmaW <- CMA_sliding_window(CMA=CMA1,</pre>
                        data=med.events,
                        ID.colname="PATIENT_ID"
                        event.date.colname="DATE",
                        event.duration.colname="DURATION".
                        event.daily.dose.colname="PERDAY",
                        medication.class.colname="CATEGORY"
                        carry.only.for.same.medication=FALSE,
                        consider.dosage.change=FALSE,
                        followup.window.start=0,
                        observation.window.start=0,
                        observation.window.duration=365,
                        sliding.window.start=0,
                        sliding.window.start.unit="days",
                        sliding.window.duration=90,
                        sliding.window.duration.unit="days",
                        sliding.window.step.duration=7,
                        sliding.window.step.unit="days",
                        sliding.window.no.steps=NA,
                        date.format="%m/%d/%Y"
```

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```
);
plot(cmaW, patients.to.plot=c("1","2"));
cmaE <- CMA_per_episode(CMA=CMA1,</pre>
                        data=med.events,
                        ID.colname="PATIENT_ID",
                         event.date.colname="DATE",
                         event.duration.colname="DURATION",
                         event.daily.dose.colname="PERDAY",
                        medication.class.colname="CATEGORY",
                         carry.only.for.same.medication=FALSE,
                         consider.dosage.change=FALSE,
                         followup.window.start=0,
                         observation.window.start=0,
                         observation.window.duration=365,
                         date.format="%m/%d/%Y"
                        );
plot(cmaE, patients.to.plot=c("1","2"));
## End(Not run)
```

## **Description**

Interactively plot a given patient's data, allowing the real-time exploration of the various CMAs and their parameters. It can use Rstudio's manipulate library or Shiny.

## Usage

```
plot_interactive_cma(...)
```

#### **Arguments**

... Parameters to be passed to plot\_interactive\_cma() in package AdhereRViz.

## **Details**

This is merely a stub for the actual implementation in package AdhereRViz: it just checks if this package is installed and functional, in which case it calls the actual implementation, otherwise warns the user that AdhereRViz must be installed.

#### Value

Nothing

## See Also

Function plot\_interactive\_cma in package AdhereRViz.

print.CMA0

## **Examples**

print.CMA0

Print CMA0 (and derived) objects.

## Description

Prints and summarizes a basic CMA0, or derived, object.

```
## S3 method for class 'CMA0'
print(
 х,
  . . . ,
  inline = FALSE,
  format = c("text", "latex", "markdown"),
  print.params = TRUE,
  print.data = TRUE,
  exclude.params = c("event.info", "real.obs.windows"),
  skip.header = FALSE,
  cma.type = class(cma)[1]
)
## S3 method for class 'CMA1'
print(...)
## S3 method for class 'CMA2'
print(...)
## S3 method for class 'CMA3'
print(...)
## S3 method for class 'CMA4'
print(...)
## S3 method for class 'CMA5'
print(...)
```

print.CMA0

```
## S3 method for class 'CMA6'
print(...)
## S3 method for class 'CMA7'
print(...)
## S3 method for class 'CMA8'
print(...)
## S3 method for class 'CMA9'
print(...)
## S3 method for class 'CMA_per_episode'
print(
 Х,
  ...,
  inline = FALSE,
  format = c("text", "latex", "markdown"),
 print.params = TRUE,
 print.data = TRUE,
 exclude.params = c("event.info", "inner.event.info", "mapping.episodes.to.events"),
 skip.header = FALSE,
  cma.type = class(x)[1]
)
## S3 method for class 'CMA_sliding_window'
print(...)
```

## **Arguments**

x	A CMA0 or derived object, representing the CMA to print.
	other possible parameters
inline	Logical, should print inside a line of text or as a separate, extended object?
format	A <i>string</i> , the type of output: plain text ("text"; default), LaTeX ("latex") or R Markdown ("markdown").
print.params	Logical, should print the parameters?
print.data	Logical, should print a summary of the data?
exclude.params	A vector of <i>strings</i> , the names of the object fields to exclude from printing (usually, internal information irrelevant to the end-user).
skip.header	Logical, should the header be printed?
cma.type	A string, used to override the reported object's class.

## **Details**

Can produce output for the console (text), R Markdown or LaTeX, showing various types of information.

prune\_event\_durations

## **Examples**

```
cma0 <- CMA0(data=med.events,</pre>
             ID.colname="PATIENT_ID",
             event.date.colname="DATE",
             event.duration.colname="DURATION".
             event.daily.dose.colname="PERDAY",
             medication.class.colname="CATEGORY",
             followup.window.start=0,
             followup.window.start.unit="days",
             followup.window.duration=2*365,
             followup.window.duration.unit="days",
             observation.window.start=30,
             observation.window.start.unit="days",
             observation.window.duration=365,
             observation.window.duration.unit="days",
             date.format="%m/%d/%Y",
             summary="Base CMA");
cma0;
print(cma0, format="markdown");
cma1 <- CMA1(data=med.events,</pre>
             ID.colname="PATIENT_ID",
             event.date.colname="DATE",
             event.duration.colname="DURATION",
             followup.window.start=30,
             observation.window.start=30,
             observation.window.duration=365,
             date.format="%m/%d/%Y"
            );
cma1;
```

prune\_event\_durations Prune event durations.

## Description

Flags or removes leftover supply durations after dosage changes, the end of a special period, or treatment interruption. The function accepts the raw list output of compute\_event\_durations and additional arguments to specify event durations that need to be removed.

```
prune_event_durations(
   data,
   include = c("special periods", "treatment interruptions", "dosage changes"),
   medication.class.colnames = data$medication.class.colnames,
   days.within.out.date.1,
   days.within.out.date.2,
   keep.all = TRUE,
   suppress.warnings = FALSE,
```

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```
return.data.table = FALSE,
...
)
```

## **Arguments**

data

A list, the output of compute\_event\_durations.

include

A Vector of *strings* indicating whether to include dosage changes, special periods, and/or treatment interruptions.

medication.class.colnames

A Vector of *strings*, the name(s) of the column(s) in the event\_durations element of data to identify medication classes. Defaults to the columns used in compute\_event\_durations.

days.within.out.date.1

event durations from before the dosage change, special period, or treatment interruptions are removed if there is a new dispensing event within the number of days specified as *integer* after the dosage change or end of the special period/treatment interruption.

days.within.out.date.2

event durations from before dosage change, special period, or treatment interruption are removed if there is *NO* new dispensing event within the number of days specified as *integer* after the dosage change or end of the special period/treatment interruption.

keep.all

*Logical*, should events be kept and marked for removal? If TRUE, a new column .prune.event will be added to event\_durations, if FALSE the events will be removed from the output.

suppress.warnings

Logical, if TRUE don't show any warnings.

return.data.table

Logical, if TRUE return a data. table object, otherwise a data. frame.

.. other possible parameters.

#### **Details**

Dosage changes, special periods, and treatment interruptions may lead to overestimation of implementation, e.g. if patients get a refill after discharge from hospital and don't continue to use their previous supply. Likewise, it may also lead to overestimation of persistence, e.g. when patients discontinue treatments after the end of a special period or treatment interruption.

#### Value

A data.frame or data.table, the pruned event\_durations.

## **Examples**

```
## Not run:
```

# select medication class of interest and compute event durations

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```
disp_data <- durcomp.dispensing[ID == 3 & grepl("J01EE01", ATC.CODE)]</pre>
presc_data <- durcomp.prescribing[ID == 3 & grepl("J01EE01", ATC.CODE)]</pre>
# compute event durations
event_durations_list <- compute_event_durations(disp.data = disp_data,</pre>
                                                 presc.data = presc_data,
                                          special.periods.data = durcomp.hospitalisation,
                                                 ID.colname = "ID",
                                                 presc.date.colname = "DATE.PRESC",
                                                 disp.date.colname = "DATE.DISP",
                                                 date.format = "%Y-%m-%d",
                                                medication.class.colnames = c("ATC.CODE",
                                                                                 "UNIT",
                                                                                 "FORM"),
                                                 total.dose.colname = "TOTAL.DOSE",
                                                 presc.daily.dose.colname = "DAILY.DOSE",
                                               presc.duration.colname = "PRESC.DURATION",
                                                 visit.colname = "VISIT",
                                                 force.init.presc = TRUE,
                                                 force.presc.renew = TRUE,
                                                 split.on.dosage.change = TRUE,
                                                 trt.interruption = "carryover",
                                                 special.periods.method = "carryover",
                                                 suppress.warnings = FALSE,
                                                 return.data.table = TRUE,
                                                 progress.bar = FALSE)
# prune event durations
event_durations <- prune_event_durations(event_durations_list,</pre>
                                          include = c("special periods"),
                                          medication.class.colnames = "ATC.CODE",
                                          days.within.out.date.1 = 7,
                                          days.within.out.date.2 = 30,
                                          keep.all = FALSE)
## End(Not run)
```

subsetCMA

Restrict a CMA object to a subset of patients.

## **Description**

Restrict a CMA object to a subset of patients.

```
subsetCMA(cma, patients, suppress.warnings)
```

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## Arguments

```
cma a CMA object.

patients a list of patient IDs to keep.

suppress.warnings

Logical, if TRUE don't show any warnings.
```

## Value

a CMA object containing only the information for the given patients.

## **Examples**

time\_to\_initiation

Computation of initiation times.

## Description

Computes the time between the start of a prescription episode and the first dispensing event for each medication class.

```
time_to_initiation(
  presc.data = NULL,
  disp.data = NULL,
  ID.colname = NA,
  medication.class.colnames = NA,
  presc.start.colname = NA,
  disp.date.colname = NA,
  date.format = "%d.%m.%Y",
  suppress.warnings = FALSE,
  return.data.table = FALSE,
  ...
)
```

time\_to\_initiation

#### **Arguments**

presc.data A data.frame or data.table containing the prescription episodes. Must con-

tain, at a minimum, the patient unique ID, one medication identifier, and the start date of the prescription episode, and might also contain additional columns to identify and group medications (the actual column names are defined in the

medication.class.colnames parameter).

disp.data A data.frame or data.table containing the dispensing events. Must contain,

at a minimum, the patient unique ID, one medication identifier, the dispensing date, and might also contain additional columns to identify and group medications (the actual column names are defined in the medication.class.colnames

parameter).

ID. colname A *string*, the name of the column in presc.data and disp.data containing the

unique patient ID, or NA if not defined.

medication.class.colnames

A Vector of *strings*, the name(s) of the column(s) in data containing the classes/types/groups of medication, or NA if not defined.

presc.start.colname

A *string*, the name of the column in presc.data containing the prescription date (in the format given in the date.format parameter), or NA if not defined.

disp.date.colname

A *string*, the name of the column in disp.data containing the dispensing date (in the format given in the date.format parameter), or NA if not defined.

date. format A string giving the format of the dates used in the data and the other param-

eters; see the format parameters of the as.Date function for details (NB, this concerns only the dates given as strings and not as Date objects).

suppress.warnings

Logical, if TRUE don't show any warnings.

return.data.table

Logical, if TRUE return a data.table object, otherwise a data.frame.

.. other possible parameters

## Details

The period between the start of a prescription episode and the first dose administration may impact health outcomes differently than omitting doses once on treatment or interrupting medication for longer periods of time. Primary non-adherence (not acquiring the first prescription) or delayed initiation may have a negative impact on health outcomes. The function time\_to\_initiation calculates the time between the start of a prescription episode and the first dispensing event, taking into account multiple variables to differentiate between treatments.

#### Value

A data. frame or data. table with the following columns:

- ID. colname the unique patient ID, as given by the ID. colname parameter.
- medication.class.colnames the column(s) with classes/types/groups of medication, as given by the medication.class.colnames parameter.

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- episode.start the date of the first prescription event.
- first.disp the date of the first dispensing event.
- time.to.initiation the difference in days between the first dispensing date and the first prescription date.

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