

Creating Cohort Subset Definitions

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1 Introduction

This guide describes the process for creating cohort subsets using `CohortGenerator`. OHDSI defines a cohort as *a set of persons who satisfy one or more criteria for a duration of time* and the aim with cohort subsets is to apply additional criteria to cohorts to define more specific subgroups for use in various analyses. This is done by defining a **subset definition** that includes one or more **subset operators** to apply to cohorts that are a part of your cohort definition set.

1.1 Subset Operators

Cohort generator contains three types of subset operators that are described below.

Demographic subset operator

The demographic subset operator allows you to subset a cohort by age, gender, race or ethnicity.

Limit subset operator

The limit subset operator is designed to subset a cohort to limit based on some time or ordinal criteria. For example, we might want to consider the first event for a person in a cohort. We can use the limit subset operator to limit a cohort based on prior observation time, cohort duration or even a calendar start/end date.

Cohort subset operator

This type of operation allows you to subset a cohort to subjects included in one or more other cohorts. As an example, we might be interested in new users of metformin who have the indication of Type 2 diabetes.

We can define this population using 2 cohorts: 1) new users of metformin and 2) Type 2 diabetes patients. We can then use these 2 cohorts to define our target population where we describe “new users of metformin who’s start date overlaps within a Type 2 diabetes episode.” In this way, cohorts become reusable building blocks to create new populations using existing cohort definitions.

1.2 Subset Definition

Subset definitions are named sets of one or more operators (from above) that can be applied to a set of one or more cohorts. Operators can be sequentially chained within subset definitions and all outputs are full cohorts that can be passed into to other analytical tasks.

2 Creating cohort subset definitions

This section will provide an overview and some examples of how to define a subset definition using the various operators.

2.1 Cohort Definition Set

We will start by loading a cohort definition set with two cohorts for this example:

```
jsonFilePath <- system.file("testdata", "CohortsToSubset.JSON", package = "CohortGenerator")
cohortDefinitionSet <- jsonlite::fromJSON(jsonFilePath)
cohortDefinitionSet <- cohortDefinitionSet |>
  dplyr::filter(cohortId %in% c(1, 2))

cohortDefinitionSet |>
  dplyr::select("cohortId", "cohortName") |>
  knitr::kable()
```

cohortId	cohortName
1	Celcoxib
2	Ibuprofen

We will use these two cohorts in the subsequent examples.

2.2 Subset operators

In this section we will show you can create and use the various subset operators to create different subset definitions using the two cohorts in our example cohort definition set.

Demographic Subset Operator

Here is an example of a demographic subset operator called `ageCriteria` that identifies cohort subjects between the ages 20 - 50 years old.

```
ageCriteria <- CohortGenerator::createDemographicSubsetOperator(
  ageMin = 20,
  ageMax = 50
)
```

Limit Subset Operator

This is an example of how we can create a limit subset operator called `limitToLastEver` to identify the last cohort event that happens between 1 January 2000 and 31 December 2008.

```

limitToLastEver <- CohortGenerator::createLimitSubsetOperator(
  name = "Last event during 1 January 2000 and 31 December 2008",
  priorTime = 0,
  followUpTime = 0,
  limitTo = "lastEver",
  calendarStartDate = as.Date("2000-01-01"),
  calendarEndDate = as.Date("2008-12-31")
)

```

Cohort Subset Operator

The following example shows how we can identify patients that have an ibuprofen event that starts during the target cohort start and end date:

```

ibuprofenSubset <- CohortGenerator::createCohortSubsetOperator(
  name = "ibuprofen exposure",
  cohortIds = 2, # Ibuprofen cohort
  cohortCombinationOperator = "any", # Look for any Ibuprofen exposure
  negate = FALSE, # We want to include (not exclude) participants exposed to Ibuprofen,
  windows = list(
    CohortGenerator::createSubsetCohortWindow(
      startDay = 0,
      endDay = 9999,
      targetAnchor = "cohortStart",
      subsetAnchor = "cohortStart"
    ),
    CohortGenerator::createSubsetCohortWindow(
      startDay = -9999,
      endDay = 0,
      targetAnchor = "cohortEnd",
      subsetAnchor = "cohortStart"
    )
  )
)

```

In this subset, we use **cohortId = 2** to identify all the subjects exposed to ibuprofen. The **combination-Operation = all**, states that persons must exist in all of the **cohortIds**. We define the **windows** to evaluate the start/end date of the subset cohort (ibuprofen) relative to the start/end date of the target cohort. The **windows** is defined as:

The subset cohort start date is on or after the target cohort start date

AND

the subset cohort start date must end on or before the target cohort end date

2.3 Create the subset definition

Now we can use one or more of the subset operators in a subset definition. Here is how to create a subset definition for patients aged between 20 to 50:

```

ageRequirementSubset <- CohortGenerator::createCohortSubsetDefinition(
  name = "Patients 20 to 50 years old ",
  definitionId = 10,
  subsetOperators = list(
    ageCriteria
  ),
)

```

```

subsetCohortNameTemplate = "@baseCohortName - @subsetDefinitionName"
)

```

We can combine multiple subset operators in a single subset definition. Here is how to create subset for patients aged 20-50 that are exposed to ibuprofen at the start of the cohort and to extract the last event from 1 January 2000 and 31 December 2008:

```

ibuprofenWCelcoxib <- CohortGenerator::createCohortSubsetDefinition(
  name = "Aged 20-50 yrs, last ibuprofen exposure from 2000-2008",
  definitionId = 11, # Unique ID for this subset
  subsetOperators = list(
    ageCriteria,
    ibuprofenSubset,
    limitToLastEver
  ),
  subsetCohortNameTemplate = "@baseCohortName - @subsetDefinitionName"
)

```

2.4 Adding subsets to Cohort Definition Set

Cohort subset definitions must be added to a cohort definition set to generate these subsets using CohortGenerator. To do this, we use the `addCohortSubsetDefinition` function to add the subset definition to the cohort definition set. This function allows us to specify the `targetCohortIds` that should receive the subset definition and operators. Here we will apply the subset definitions to the target cohort celecoxib (`cohortId == 1`).

```

cohortDefinitionSet <- cohortDefinitionSet |>
  CohortGenerator::addCohortSubsetDefinition(ageRequirementSubset, targetCohortIds = c(1)) |>
  CohortGenerator::addCohortSubsetDefinition(ibuprofenWCelcoxib, targetCohortIds = c(1))
cohortDefinitionSet |>
  dplyr::select("cohortId", "cohortName") |>
  knitr::kable()

```

cohortId	cohortName
1	Celecoxib
2	Ibuprofen
1010	Celecoxib - Patients 20 to 50 years old
1011	Celecoxib - Aged 20-50 yrs, last ibuprofen exposure from 2000-2008

3 Generating subsets

Next, we'll use some test data included in the CohortGenerator package to demonstrate how to generate subsets. We will begin by creating an empty OMOP data model and populating it with person and drug exposure entries. For reference, the script used to generate the test data in `extras/PackageMaintenance.R`.

```

databaseFile <- tempfile(fileext = ".duckdb")
duckdbConnectionDetails <- DatabaseConnector::createConnectionDetails(
  dbms = "duckdb",
  server = databaseFile
)
resultsSchema <- "main"
connection <- DatabaseConnector::connect(duckdbConnectionDetails)

DatabaseConnector::insertTable(

```

```

connection = connection,
databaseSchema = resultsSchema,
tableName = "person",
data = omopCdmPerson
)
# Insert updated data into the 'drug_exposure' table
DatabaseConnector::insertTable(
  connection = connection,
  databaseSchema = resultsSchema,
  tableName = "drug_exposure",
  data = omopCdmDrugExposure
)

```

We can now use this sample data to generate the subsets:

```

cohortTableNames <- CohortGenerator::getCohortTableNames()
CohortGenerator::createCohortTables(
  connection = connection,
  cohortDatabaseSchema = "main",
  cohortTableNames = cohortTableNames
)

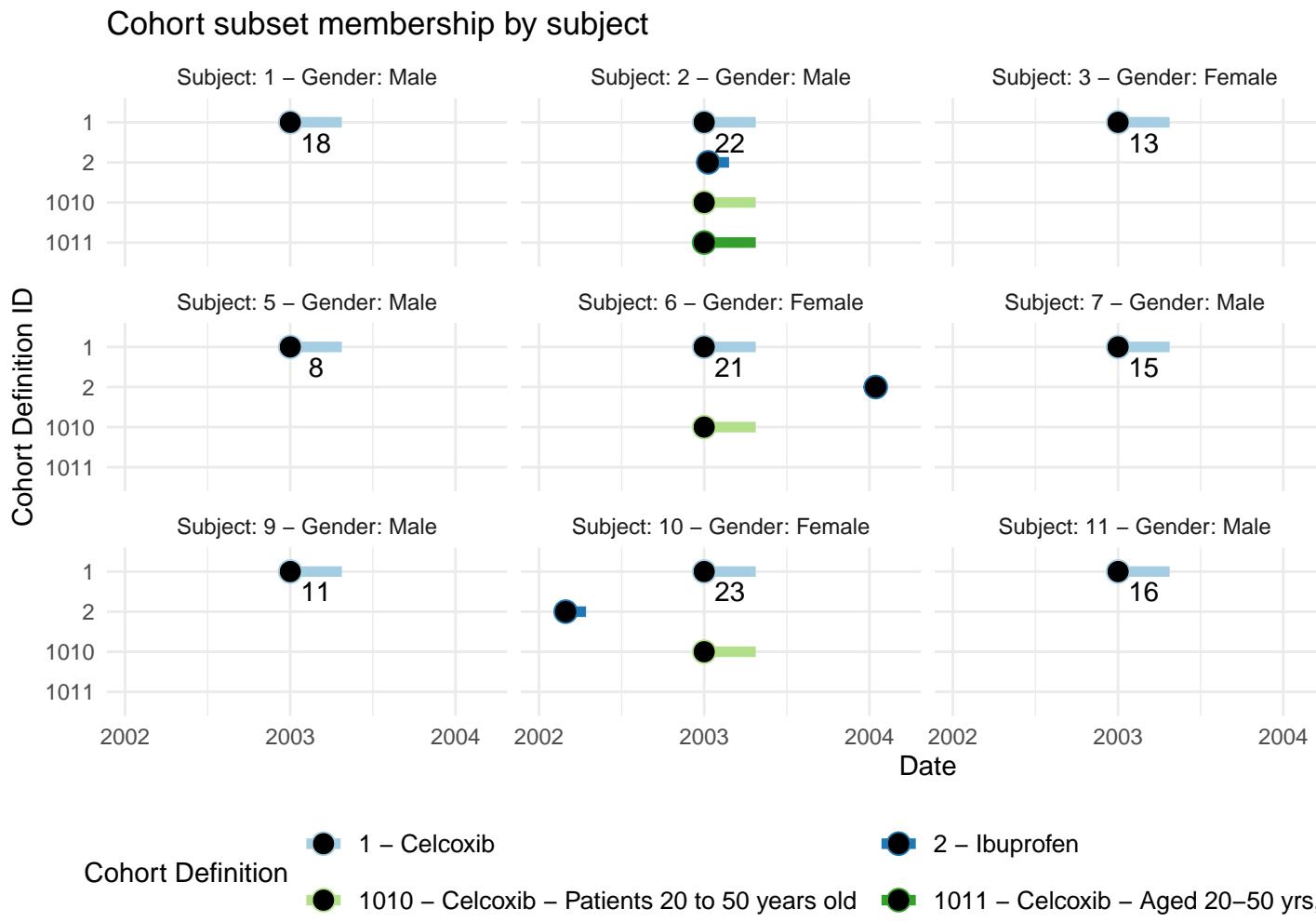
### As subsets are a big side effect we need to be clear what was generated and have good naming convention
CohortGenerator::generateCohortSet(
  connection = connection,
  cdmDatabaseSchema = "main",
  cohortDatabaseSchema = "main",
  cohortTableNames = CohortGenerator::getCohortTableNames(),
  cohortDefinitionSet = cohortDefinitionSet
)

```

Cohort subset definitions can be run incrementally. In fact, if the base cohort definition changes for any reason, any subsets will automatically be re-executed when calling `generateCohortSet`.

3.1 Visualizing subset membership

In the graph below we show the 12 subjects who are in our sample data set. Each subject's graph is labeled with their subject ID, gender and their age at index for the celecoxib exposure. The y-axis describes the eras of time where a subject is a member of that cohort. The x-axis represents the observation period for each subject.



A subject may have 0 or more ibuprofen (cohort ID = 2) exposures. When a subject is a member of one of the two subsets in our example, they will have an era for the cohort ID on that row. For example, subject 6 qualifies for cohort ID 1010 which identifies patients aged 20-50 years at the start of the celecoxib exposure. Similarly, subject ID 2 qualifies for all subsets since they are aged 22 and also have an ibuprofen exposure during their exposure to celecoxib.

4 Saving and loading subset definitions

4.1 Saving to packages/directories

Saving applied subsets can automatically be added to a project using `saveCohortDefinitionSet`

```
saveCohortDefinitionSet(cohortDefinitionSet,
  subsetJsonFolder = "<path_to_my_subset_definition>"
)
```

loading is also achieved with `getCohortDefinitionSet`

```
cohortDefinitionSet <- getCOhortDefinitionSet(  
  subsetJsonFolder = "<path_to_my_subset_definition>"  
)
```

Any subset definitions should automatically be loaded and applied to the cohort definition set.

4.2 Writing json objects

Subset definitions can be converted to JSON objects as follows:

```
jsonDefinition <- subsetDef$toJSON()
```

For the purpose of writing to disk we recommend the use of `ParallelLogger` for consistency.

```
# Save to a file  
ParallelLogger::saveSettingsToJson(subsetDef$list(), "subsetDefinition1.json")
```