



# **Conceptual bases for the standardization of calculation approaches for assigning** exposure duration to single drug utilization records in multi-database studies

G. Roberto<sup>1</sup>, N. Thurin<sup>2</sup>, J. Riera<sup>3</sup>, O. Paoletti<sup>1</sup>, P.C. Souverein<sup>4</sup>, R. Pajouheshnia<sup>4</sup>, Rosa Gini<sup>1</sup>

<sup>1</sup>Agenzia Regionale di Sanità Toscana, Florence, Italy <sup>2</sup>Bordeaux PharmacoEpi, INSERM CIC-P1401, Univ. Bordeaux, 33000 Bordeaux, France <sup>3</sup>Department of Datascience and Biostatistics, Julius Centrum, University Medical Center of Utrecht (UMCU), The Netherlands

<sup>4</sup>Division of Pharmacoepidemiology and Clinical Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Utrecht University

#### Background

In observational multi-database studies, prescribing, dispensing or administrations records, are usually leveraged for exposure assessment. The number of days of treatment (DOT) associated with each drug utilization record of interest can be calculated in several ways. Therefore, standardization of calculation approaches is paramount to document study methods and facilitate comparison of results between data sources.

#### **Objectives**

To define a set of calculation choices (recipes), for standardizing DOT calculation of single DURs from any observational healthcare datasource.

#### Methods

A list of recipes to calculate DOT from electronic DUR was created based on literature search and researchers' experience. Concepts needed to implement the recipes were defined using the standard terms of the European Directorate for the Quality of Medicine.

#### Results

Five concepts corresponding to paramenters possibly recorded in the data source of interest and useful to calculate DOT were identified. A total of five recipies were created and classified in two main families according to calculation approach chosen by the investigator: Daily Dose(DD)-based (n=3) recipies and Fixed duration-based (n=2) recipies.

### CONCEPTS (N=5)

1)UNIT OF PRESENTATIONS i.e. unit in which the strength(s) of the manufactured item or pharmaceutical product is presented and described, e.g. tablet, bottle;

2)ACTIVE SUBSTANCE AMOUNT e.g. mass or volume;

3)PHARMACEUTICAL PRODUCT AMOUNT e.g. mass of cream, volume of oral solution;

4)**MEDICINAL PRODUCT** as identified by the marketing authorization number;

5)**DRUG UTILIZATION RECORD** i.e. prescription/dispensing/administration record corresponding to ≥1 medicinal product unit.

#### FAMILIES OF RECIPIES (N=2)

#### DAILY DOSE(DD)-BASED RECIPIES (n=3)

a prescribed or assumed DD is necessary for the application

## Number of unit of presentations

DOT=number of medicinal products\*number of units of presentation per medicinal product÷DD

e.g. applying this recipe to a dru utilization record containing 2 units of "Atorvastatin 40mg 30 tablets", assuming a DD of 1 tablet/day

## Amont of active substance

DOT=number of medicinal products\*pharmaceutical product amount per medicinal product÷DD

e.g. applying this recipe to a drug utilization record containing 2 units of "DEPAKIN\*OS FL 40ML 200MG/ML" (valproate),

## Amont of pharmaceutical product DOT=number of medicinal products\*active substance

amount per medicinal product÷DD

e.g. applying this recipe to a drug utilization record containing 1 units of "CLOBESOL\*CREMA 30G

#### FIXED DURATION-BASED RECIPIES (n=2)

A fixed duration is associated to each drug utilization record or medicinal product of interest

> **Fixed medicinal product**duration

DOT=fixed-duration

e.g. applying this recipe to a drug utilization record containing 2 units of "Aimovig 1PEN 70mg 1ml" or tp a record containing 2 units of "Aimovig 1PEN 140mg

#### **Fixed-record duration**

DOT= number of medicinal products\*fixed-duration

e.g. applying this recipe to a drug utilization record containing 3 units of "Acitretin 30mg 30 tablets" or a record containing 2 units of "Acitretin 25mg 20



## Conclusions

We provided comprehensive conceptual bases to standardize calculation approaches to assign exposure duration to drug utilization records. Within this framework, investigators can choose a daily dose-based recipe whenever the true daily dose is considered reasonably predictable, according to the available data. Otherwise, when the true daily dose is difficult to predict, a fixed duration recipe might be preferred if it is considered a more reliable assumption based on the expected utilization pattern.