Daily Dose Assessment of Medicines Administered in Intensive Care Unit and Inpatient Settings in Hospital del Mar Barcelona

European OHDSI Symposium, Rotterdam, 1-3 June 2024

Background
The European Medicines Agency (EMA) is focusing on crisis preparedness by assessing medicine shortages during public health emergencies through the DARWIN EU initiative. This initiative oversees an observational study analyzing the use of essential medicines in Intensive Care Units (ICU) to identify usage patterns and potential shortfalls. The study measures administration rates, dosages, and treatment durations to aid EMA's monitoring efforts.

The main objective of this study is to show how drug_exposure data from inpatient and emergency room visits is organized in Hospital del Mar EHR database (IMASIS) and how it can be used for the reliable assessment of daily dose.

Methods
IMASIS medications from inpatient visits in the drug_exposure table are:

- labelled with drug_type_concept_id = 32819 (EHR administration record). Prescribed and Dispensed drugs in outpatient visits (not considered in the study) have different values
- recorded as single drug_exposure events at a specific time (start_datetime = end_datetime)
- ‘drug_exposure.quantity’ values are generally expressed in terms of “single dose items” (e.g. 1 oral tablet, 1 actuat) and not in terms of boxes of drug.
- mapped to ‘quantified’ concepts when available (otherwise to unquantified concepts like “Clinical Drug”)

In general, ‘Daily dose’ calculations need to consider several drug_exposure records in the same day or time window.

We suggest how to assess dose calculations for a specific drug_exposure record regardless of whether the drug_concept_id belongs to a quantified or an unquantified concept_class. Dose in a drug_exposure record (di) can be calculated as follows:

1. When the amount of ingredient is available in the ds.amount_value:
   \[d_i = ds.de.quantity \times ds.amount_value\] expressed in terms of ds.amount_unit_concept_id where de and ds stand for drug_exposure and drug_strength, respectively.

2. When the amount of ingredient is expressed in ds.numerator_value and ds.denominator_value:
   \[d_i = ds.de.quantity \times (ds.numerator_value/ds.denominator_value)\] if ds.denominator_value is NULL it has to be set to 1;
   expressed in terms of ds.numerator_unit_concept_id/ds.denominator_unit_concept_id

The Daily Dose of an ingredient can be derived from the collapse of different single drug_exposure events/records (including different drug_concept_ids including this ingredient) within a time window. Every record takes place at a specific datetime, and the corresponding dose di can be calculated according to formula 1 or 2.

Dose within a day DDate can be calculated as the sum of doses this day
3. \[D_{DDate} = \sum d_i\] in this date

Thereby, total dose DTotal in this time window can be calculated as
4. \[D_{Total} = D_{DDate}\] within the time window.

Daily dosage during this time window can be calculated as
5. \[D_{Daily} = D_{Total}/number\ of\ days\]

Results

Table 1. Calculation of dose (d) in records with ‘quantity’ values expressed as “single dose items” and the amount of ingredient is expressed according to (1)

<table>
<thead>
<tr>
<th>concept_id</th>
<th>concept_name</th>
<th>concept_class_id</th>
<th>ingredient_id</th>
<th>box_size</th>
<th>amount_value</th>
<th>amount_unit_concept_id</th>
<th>d (de.quantity = 1 oral 1d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>38274912</td>
<td>Acetaminophen 1000 MG Oral Tablet Box of 120</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40077527</td>
<td>Acetaminophen 500 MG Oral Tablet Box of 10 by Hemopharm</td>
<td>1125315</td>
<td>10</td>
<td>500</td>
<td>1</td>
<td>8576 (milligram)</td>
<td></td>
</tr>
<tr>
<td>19020053</td>
<td>Acetaminophen 500 MG Oral Tablet Box of 120</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Calculation of dose (d) in records with ‘quantity’ values expressed as “single dose items” and the amount of ingredient is expressed according to (2)

<table>
<thead>
<tr>
<th>concept_id</th>
<th>concept_name</th>
<th>concept_class_id</th>
<th>ingredient_id</th>
<th>box_size</th>
<th>numerator_value</th>
<th>denominator_value</th>
<th>d (de.quantity = 1 Actuat)</th>
</tr>
</thead>
<tbody>
<tr>
<td>784967</td>
<td>120 ACTUAT furosemide 0.25 MG/ACTUAT / salmeterol 0.025 MG/ACTUAT Inhalation Solution [Artusol] Box of 1 by Sandoz</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>784969</td>
<td>120 ACTUAT furosemide 0.25 MG/ACTUAT / salmeterol 0.025 MG/ACTUAT Inhalation Solution Box of 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>23167699</td>
<td>120 ACTUAT furosemide 0.25 MG/ACTUAT / salmeterol 0.025 MG/ACTUAT Inhalation Solution</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>784241</td>
<td>furosemide 0.25 MG/ACTUAT / salmeterol 0.025 MG/ACTUAT Inhalation Solution</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21079794</td>
<td>furosemide 0.25 MG/ACTUAT / salmeterol 0.025 MG/ACTUAT Inhalation Solution</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21109284</td>
<td>furosemide 0.25 MG/ACTUAT / salmeterol 0.025 MG/ACTUAT Inhalation Solution</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

All rows have numerator_unit_concept_id values set to 8576 (milligram) and denominator_unit_concept_id set to 45744809 (Actuat).

If “de.quantity” values are expressed as “single dose items” (e.g. Oral Tablet), the “box_size” value in the drug_strength table available in quantified concept_classes (“Marketed Product” and “Clinical Drug”) is not involved in the calculation of doses. Otherwise (de.quantity expressed as number of boxes of Acetaminophen tablets), the box_size value would be needed and “Clinical Drug” concept would not be useful for dose calculations.

Figure 1. Daily dose calculation from a set of drug exposure records within a time window embedded in an inpatient visit

acacetominophen 1000 MG Oral Tablet of 120 | concept_id = 38274912

23:00h drug_exp.quantity = 2; d1 = x 1000 = 2000 (mg)
15:00h drug_exp.quantity = 1; d2 = x 1000 = 1000 (mg)
07:00h drug_exp.quantity = 1; d3 = x 1000 = 1000 (mg)

D_{Daily} = 500 mg/day

Figure 1 shows a set of drug exposure records involving a patient within a time window embedded in an inpatient visit. Doses for every record (d1 to d3) have been calculated according to (1). Doses within a day (D_{Daily}) have been calculated according to (3). Total Dose (D_{Total}) and Daily Dose within this period have been calculated according formula (4) and (5), respectively.

Conclusions
We explain how drug_exposure data from inpatient visits is organized in IMASIS to assess daily dose values, which could be considered for the implementation of the analytical tools used in observational studies on medications administered in hospitals using the OMOP CDM.