Computing Drug Order Compliance with Guidelines Using an OWL2 Reasoner and Standard Drug Resources

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Guideline compliance

- Fact: medical practice variability
- Effort to promote “best practice” - quality, safety, and costs
  - Clinical practices guidelines (CPGs) and recommendations
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2/15
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Focus on medical treatments
The drug order

- A set of drugs (+ posology)
- Using commercial names
- For several patient health problems
  
  eg. \textit{P2: tareg® 160 ; lipanthyl® 160 1 cp/j}
The drug order

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- Using commercial names
- For several patient health problems
  eg. P2: tareg® 160 ; lipanthyl® 160 1 cp/j
- Computerized physician order entry (CPOE)
The prescription recommendation(s)

- The recommended treatment according to guidelines for THE patient
- A set a drug
- Using drug classes (eg. ARBs, Th, BB, ACEi, CCBs...)
- For one given health problem (eg. AHT)
  
  *eg. bi*ther*apy* of “ARBs and Th”*
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  *eg.* bitherapy of “ARBs and Th”

- Guideline-based clinical decision support systems (CDSSs)
Problem statement

*Does a patient’s drug order comply with the patient’s recommended treatment for a given pathology?*
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Eg. Does “tareg® 160 ; lipanthyl® 160 1 cp/j” comply with the AHT guidelines? ie. is an antihypertensive bitherapy of “ARBs and Th”?

- Orders may address multiple pathologies whereas CPGs don’t
- Orders and recommendations refer to drugs at different levels of abstraction
- Some drugs are combinations of drug classes (bitherapies)
Objectives

The semantic web community has produced

- Standard syntaxes and associated tools *(OWL2)*
- Representing knowledge and reasoning with ontologies
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  - Internationally widespread
  - Available for every commercialized drug
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Propose a generic model to calculate the conformity relationship between a drug prescription $P$ and a prescription recommendation $R^a$ as a subsumption relationship between their representations using:

1. the OWL2 syntax and ontological reasoners
2. the ATC as a standard drug resource and as a “quasi”-ontology

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In the domain of hypertensive patient management.
Tools and resources

- OWL2 – Web Ontology Language
  - Standardized language for representing hierarchical structures and defining logical concept
  - SHOINQ interpretation to handle quantified cardinality restriction (QCR) (*to identify levels of drug associations*)
  - Appropriate reasoners (eg. HermiT)
Tools and resources

- OWL2 – Web Ontology Language
  - Standardized language for representing hierarchical structures and defining logical concept
  - SHOINQ interpretation to handle quantified cardinality restriction (QCR) (to identify levels of drug associations)
  - Appropriate reasoners (e.g., HermiT)
- The WHO ATC classification as a “quasi”-ontology
  - Hierarchical drug classes, ARBs and valsartan
  - Plain drug subclasses can be considered as ontologies
  - Each commercial drug has an ATC code per indication
Monographie de TAREG 160 mg Comprimé pelliculé sécable Boîte de 30

Composition

(exprimée par Comprimé)

<table>
<thead>
<tr>
<th>Principes Actifs</th>
<th>160 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valsartan</td>
<td></td>
</tr>
</tbody>
</table>

Excipients

Comprimé nu :
- Cellulose microcristalline (E460)
- Crospovidone (E1202) type A
- Silice (E551) colloidale anhydre
- Magnésium stéarate (E572)

Pelliculage :
- Hypromellose (E464)
- Titane dioxyde (E171)
- Macrogol 8000
- Fer oxyde (E172) rouge
- Fer oxyde (E172) jaune
- Fer oxyde (E172) noir

Contenance totale : 4800 mg ou 30 comprimés

Classification ATC

SYSTEME CARDIOVASCULAIRE
- MEDICAMENTS AGISSANT SUR LE SYSTEME RENINE-ANGIOTENSINE
  - ANTAGONISTES DE L'ANGIOTENSINE II
    - Antagonistes de l'angiotensine II non associés
    - Valsartan (C09CA03)
**Tools and ressources**

**Cardiovascular System**

**C09 Agents Acting on the Renin-Angiotensin System**

The DDDs are based on the treatment of mild-moderate hypertension.

See comments to C02L concerning the principles for assignment of DDDs for combined preparations.

**C09C Angiotensin II Antagonists, Plain**

**C09CA Angiotensin II antagonists, plain**

<table>
<thead>
<tr>
<th>ATC code</th>
<th>Name</th>
<th>DDD</th>
<th>U</th>
<th>Adm.R</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>C09CA01</td>
<td>losartan</td>
<td>50</td>
<td>mg</td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>C09CA02</td>
<td>eprosartan</td>
<td>0.6</td>
<td>g</td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>C09CA03</td>
<td>valsartan</td>
<td>80</td>
<td>mg</td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>C09CA04</td>
<td>irbesartan</td>
<td>0.15</td>
<td>g</td>
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<td>O</td>
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<tr>
<td>C09CA05</td>
<td>tasosartan</td>
<td></td>
<td></td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>C09CA06</td>
<td>candesartan</td>
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<td>mg</td>
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<td></td>
<td>O</td>
</tr>
<tr>
<td>C09CA08</td>
<td>olmesartan medoxomil</td>
<td>20</td>
<td>mg</td>
<td></td>
<td>O</td>
</tr>
</tbody>
</table>
OWL2 prescription model

- Simply based on composition relationship
- \text{genericPrescription} = \text{Thing} \land \text{(hasComp some Drug)}.
- Drug is the root class of the ATC hierarchy
- Representation of P2

\begin{align*}
P2: & \text{tareg}^{\text{®}} 160 \text{ ; lipanthyl}^{\text{®}} 160 \text { cp/j} \\
& \text{valsartan} \quad \text{fenofibrate} \\
& \text{C09CA03} \quad \text{C10AB05}
\end{align*}

\begin{align*}
P2 & = \text{Prescription} \\
& \land \text{(hasComp only (C09CA03 or C10AB05))} \\
& \land \text{(hasComp exactly 1 C09CA03)} \\
& \land \text{(hasComp exactly 1 C10AB05)}.\end{align*}
OWL2 recommendation model

- Intermediate concepts
  - Antihypertensive drugs used in the CPGs
    \[\text{antiAHT} = (\text{C09A OR C09C OR C03A OR C08C OR C07A}).\]
  - \(n\)-therapies
    \[
    \begin{align*}
    \text{monoAntiAHT} &= \text{genericPrescription} \\
    & \quad \text{and (hasComp exactly 1 antiAHT)}. \\
    \text{biAntiAHT} &= \text{genericPrescription} \\
    & \quad \text{and (hasComp exactly 2 antiAHT)}. 
    \end{align*}
    \]

- Representation of 2 recommendations:
  - “ARBs alone” or “ARBs + Thiazides”
    \[
    \begin{align*}
    \text{R-ARBs} &= \text{monoAntiAHT} \\
    & \quad \text{and (hasComp some C09CA)}. \\
    \text{R-ARBs-Th} &= \text{biAntiAHT} \\
    & \quad \text{and (hasComp some C09CA)} \\
    & \quad \text{and (hasComp some C03A)}. 
    \end{align*}
    \]
## 5 prescriptions wrt R-ARBs and R-ARBs+Th

<table>
<thead>
<tr>
<th>Prescription</th>
<th>Medication Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>P1:</strong></td>
<td>pravastatine 40 1/jour; coaprovel® 300/12,5 1/jour (pravastatin [ARBs+Th])</td>
</tr>
<tr>
<td><strong>P2:</strong></td>
<td>tareg® 160; lipanthyl® 160 1 cp/j (ARBs fenofibrate)</td>
</tr>
<tr>
<td><strong>P3:</strong></td>
<td>aprovel® 300; esidrex®; lipanthyl® 160 (ARBs Th fenofibrate)</td>
</tr>
<tr>
<td><strong>P4:</strong></td>
<td>hydrochlorothiazide 25mg 1 cp; lipanthyl® 160mg 1/j (Th fenofibrate)</td>
</tr>
<tr>
<td><strong>P5:</strong></td>
<td>amlor®; lasilix® 20; lipanthyl® 60; metformine (CCBs loopD fenofibrate metformine)</td>
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</table>
Ontological reasoning: an example

- 5 prescriptions wrt R-ARBs and R-ARBs+Th
Ontological reasoning: an example

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Ontological reasoning: an example

- 5 prescriptions wrt R-ARBs and R-ARBs+Th
Web-based on-line study of ASTI-GM DSS

Chronic disease clinical cases to solve – AHT case #2

**Case:** Mrs C., 52-year-old non-smoking patient, has hypertension since the age of 42 years. She is obese with a BMI of 43. Her mother has type 2 diabetes and hyperlipidemia. Mrs C. has no personal history of diabetes and her renal function is normal. Her BP is measured today at 125 - 85 mm Hg. She was initially taken care by beta-blockers (BBs). Her treatment has been modified one month ago for an angiotensin-converting enzyme inhibitor (ACE inhibitor) because her BP had increased. She consults today complaining about a persistent cough lasting for 3 weeks.

**Current treatment:** Captopril 50 mg, 2 pills/day, Lipanthyl 160 mg, 1/day.

**Biology:** Total cholesterol: 1.65 g/l; LDL-C: 0.94 g/l; HDL-C: 0.36 g/l; Triglycerides: 1.75 g/l; Creatinine clearance: 78 ml/min; Glycemia: 1.12 g/l.
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The question: What would you prescribe?
Experimental context

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- Chronic disease clinical cases to solve – AHT case #2

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**The question:** What would you prescribe?

- Guideline-based recommendations for the case:
  - ARBs monotherapy
  - ARBs+Th bitherapy
Issued order dataset

- 2 month experiment (2009) – 266 volunteering GPs
- 442 drug prescription orders collected for case #2
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Gold standard for the compliance module assessment
### Results

- Compliance module applied to collected orders \((n = 442)\)

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<tr>
<td></td>
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<tr>
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<td>TP</td>
<td>FP</td>
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<td>FN</td>
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Concordance rate = 99.5%

Sensibility = 0.99; Specificity = 1.0

No false positive
2 false negatives

Use of a combination of “ARBs+Th” (ATC code: C09DA04)

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pravastatin [ARBs+Th]

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  - Not an exact test due to drug resources
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Perspectives
- Model extensions (drug posology, cancer care plan...)
- Standardized, validated, and legal drug resources
Thank you