Automatic Medical Knowledge Acquisition Using Question-Answering

Emilie Pasche, Douglas Teodoro, Julien Gobeill, Patrick Ruch, Christian Lovis
Introduction
Introduction

Antibiotic usage

Large choice of antibiotics
- ~ 100 available antibiotics
- Several families (beta-lactams, macrolides, …)
- Microbial spectrum (broad, narrow)

Analysis
- Culture
- Antibiogram

Recommendations
- Local guidelines (i.e. to a specific department of an hospital)
- National guidelines (i.e. National Guideline ClearingHouse)
Introduction

The consequences of inappropriate antibiotic usage

• Health care costs
• Hospitalization stays
• Adverse effects
• Increase of bacterial resistance
Introduction

DebugIT

*Detecting and Eliminating Bacteria Using Information Technology*

European project FP7 (grant #712139)

- **Collect** clinical data
- **Learn** with multimodal data mining
- **Store** the extracted knowledge
- **Apply** decision support and monitoring

Our objective:

- Automatic generation of prescription rules, using Question-Answering
Methods
Methods

Manual generation of rules
• Based on guidelines

Benchmark

Automatic generation of rules
• Using a question-answering engine

Evaluation
• Of the automatic generated rules using the manual rules
## Methods: Manual generation of rules

<table>
<thead>
<tr>
<th>Pathologies</th>
<th>Pathogenic agents</th>
<th>Antibiotics</th>
<th>Alternatives</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diverticulitis</td>
<td>Enterobacteriaceae</td>
<td>amoxicillin/clavulanate 1.2 g/8h iv (1000mg/200mg)</td>
<td>ciprofloxacin 500 mg/12h po + metronidazole 500 mg/8h po</td>
<td>7 to 10 days</td>
</tr>
<tr>
<td></td>
<td>Bacteroides</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Enterococcus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diverticulitis severe or Peritonitis community-acquired</td>
<td>Enterobacteriaceae</td>
<td>ceftriaxone 1 à 2 g/24h iv + metronidazole 500 mg/8h po</td>
<td>Piperacillin/tazobac. 4,5 g/8h iv</td>
<td>10 to 14 days</td>
</tr>
<tr>
<td></td>
<td>Bacteroides</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Enterococcus</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Translation / Normalization**

<table>
<thead>
<tr>
<th>Pathologies</th>
<th>Pathogenic agents</th>
<th>Antibiotics</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diverticulitis (D004238)</td>
<td>Enterobacteriaceae (543)</td>
<td>Amoxicillin-Clavulanate (J01CR02) Ciprofloxacin (J01MA02) Metronidazole (J01XD01)</td>
<td></td>
</tr>
<tr>
<td>Diverticulitis (D004238)</td>
<td>Bacteroides (816)</td>
<td>Amoxicillin-Clavulanate (J01CR02) Ciprofloxacin (J01MA02) Metronidazole (J01XD01)</td>
<td></td>
</tr>
<tr>
<td>Diverticulitis (D004238)</td>
<td>Enterobacteriaceae (543)</td>
<td>Ceftriaxone (J01DD04) Metronidazole (J01XD01) Piperacillin+Tazobactam (J01CR05)</td>
<td>severe</td>
</tr>
</tbody>
</table>

64 tuples generated from the geriatrics guidelines
Methods: Automatic generation of rules

What **antibiotic A** should be prescribed to treat a **disease D** which is caused by a **pathogen P** under **conditions D**?

**Answers obtained by EAGLi**
(Engine for Question-Answering in Genomic Literature)

http://eagl.unige.ch/EAGLi
Methods: Automatic generation of rules

EAGLi

- Search engine
  - easyIR
  - PubMed

- Target terminologies
  Antibiotic
  - MeSH
  - WHO-ATC
  - Combination

- Corpus
  - MEDLINE
Evaluation

• Tool
  – TrecEval
    Developed to evaluate TREC results
    (Text REtrieval Conferences)

• Benchmark
  – 64 manually-generated rules

• Measures
  – Top-precision
  – Recall at 5 documents
Results
## Results

### Search engine

<table>
<thead>
<tr>
<th></th>
<th>easyIR</th>
<th>PubMed</th>
<th>Combination</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Search model</strong></td>
<td>Vector-space</td>
<td>Boolean</td>
<td>Combined</td>
</tr>
<tr>
<td><strong>Coverage</strong></td>
<td>64/64</td>
<td>41/64</td>
<td>64/64</td>
</tr>
<tr>
<td><strong>Top-precision</strong></td>
<td>54.5%</td>
<td>53.8%</td>
<td>55.4%</td>
</tr>
<tr>
<td><strong>Recall at 5 docs</strong></td>
<td>0.37</td>
<td>0.42</td>
<td>0.38</td>
</tr>
</tbody>
</table>

- easyIR has a better coverage
- Top-precision is very similar
- PubMed has a better recall

⇒ Combination of the two engines to combine strength
Results

Target terminologies

MeSH (UMLS T195)
- **Synonymous terms** (37 terms for Trimethoprim and Sulfamethoxazole)
- **191 possible answers** (Contains generic terms: Antibacterial Agents)

WHO-ATC
- **No synonymous term** (1 term for Trimethoprim and Sulfamethoxazole)
- **70 possible answers** (Only antibiotics)

Combination
- **Synonymous terms**
- **70 possible answers**

<table>
<thead>
<tr>
<th></th>
<th>MeSH</th>
<th>WHO-ATC</th>
<th>Combin.</th>
</tr>
</thead>
<tbody>
<tr>
<td>easyIR</td>
<td>P0 = 12%</td>
<td>P0 = 51%</td>
<td>P0 = 54%</td>
</tr>
<tr>
<td>PubMed</td>
<td>P0 = 16%</td>
<td>P0 = 52%</td>
<td>P0 = 54%</td>
</tr>
</tbody>
</table>
Results

Corpus MEDLINE

Limitation by publication type:

- **Review**
  - Slight decrease of P0
- **Practice Guideline**
  - Strong increase of P0,
  - but coverage much weaker
- **Case Reports**
  - Strong decrease of P0

Library content drift:

- Resistance profiles evolve
- Limiting search to one year results in high variations

<table>
<thead>
<tr>
<th></th>
<th>P0</th>
<th>Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review</td>
<td>51%</td>
<td>33/64</td>
</tr>
<tr>
<td>Practice guidelines</td>
<td>75%</td>
<td>4/64</td>
</tr>
<tr>
<td>Case Reports</td>
<td>28%</td>
<td>21/64</td>
</tr>
</tbody>
</table>
Results

In more than half of the cases, the system answers correctly to the questions.

How can we improve our results?

• Why are the answers not correct?
  – Some antibiotics could be appropriate but not recommended in priority
  ⇒ Acceptable vs. Wrong
Results

Relaxing constraints

Methods:
• Analyze outputs regarding more generic hierarchical level

Example:
• Gastroenteritis caused by Campylobacter
  – Recommended: Clarithromycin
  – Top-returned answer: Erythromycin
  ⇒ Both are macrolides

<table>
<thead>
<tr>
<th>ANTINFECTIVES FOR SYSTEMIC USE</th>
<th>ANTIINFECTIVES FOR SYSTEMIC USE</th>
</tr>
</thead>
<tbody>
<tr>
<td>301 ANTIBACTERIALS FOR SYSTEMIC USE</td>
<td>301 ANTIBACTERIALS FOR SYSTEMIC USE</td>
</tr>
<tr>
<td>301F MACROLIDES, LINCOSAMIDES AND STREPTOGRAMINS</td>
<td>301F MACROLIDES, LINCOSAMIDES AND STREPTOGRAMINS</td>
</tr>
<tr>
<td>301FA Macrolides</td>
<td>301FA Macrolides</td>
</tr>
<tr>
<td>DDD</td>
<td>DDD</td>
</tr>
<tr>
<td>Unit</td>
<td>Unit</td>
</tr>
<tr>
<td>Admin. route</td>
<td>Admin. route</td>
</tr>
<tr>
<td>Notes</td>
<td>Notes</td>
</tr>
<tr>
<td>301FA09 clarithromycin</td>
<td>301FA01 erythromycin</td>
</tr>
<tr>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>g</td>
<td>g</td>
</tr>
<tr>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>301FA09 clarithromycin</td>
<td>301FA01 erythromycin</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>g</td>
<td>g</td>
</tr>
<tr>
<td>P</td>
<td>P</td>
</tr>
<tr>
<td>301FA01 erythromycin</td>
<td>301FA01 erythromycin</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>g</td>
<td>g</td>
</tr>
<tr>
<td>O</td>
<td>P</td>
</tr>
<tr>
<td>Erythromycin ophthalmic</td>
<td>Erythromycin ophthalmic</td>
</tr>
<tr>
<td>301FA01 erythromycin</td>
<td>301FA01 erythromycin</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>g</td>
<td>g</td>
</tr>
<tr>
<td>P</td>
<td>P</td>
</tr>
</tbody>
</table>

⇒ Both are macrolides
Results

Relaxing constraints

Results

• **Level 1**
  – P0 = 64% with easyIR
  – P0 = 59% with PubMed

• **Level 2**
  – P0 = 81% with easyIR
  – P0 = 77% with PubMed

In four cases out of five, the top-returned antibiotic corresponds to an antibiotic of the same class than the recommended antibiotic.
Conclusion
Conclusion

Further investigations

• Corpus
  – Search answers in other corpora
  – National Guidelines ClearingHouse, Google, …

• Questions
  – Search for other types of information
  – What disease is caused by pathogen P and treated by antibiotic A?

• Benchmark
  – Evaluation with benchmarks providing from other clinical centres
  – Variation of bacterial resistance among geographic localization
Conclusion

How to use this approach?

• Integration into an interactive tool for creating and validating prescription rules
  – Kind of generation assistant: propose a list of antibiotics given some conditions
  – Expert users validate/invalidate propositions

• Prescription rules are then used by a decision support system
  – Improvement of antibiotic usage
Acknowledgments

DebugIT
http://www.debugit.eu

EAGLi
http://eagl.unige.ch/EAGLi
Thanks for your attention

Questions?