Modeling Antipsychotic Treatment Patterns Evolution in Schizophrenia

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REES France (Health Economics Evaluation Network)
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Model Objectives

• French guidelines recommend the use of atypical antipsychotics as a first line treatment for new onset schizophrenia*.

• Typical antipsychotics cost less (generic forms available) but have more side effects (extrapyramidal symptoms).

• What is the economical burden of antipsychotic prescription for schizophrenia and how is it supposed to evolve?

METHODS
Data Sources: “EpiSurvey”

- Cross-sectional epidemiological survey;
- Representative sample of ambulatory schizophrenic patients;
- 177 psychiatrists surveyed:
  - 116 in private practice;
  - 61 in hospital consultations (out-patients).
- Two-level survey:
  - Patient registry: 2732 patients ➔ Treatment patterns
  - Detailed survey: 1855 patients ➔ Treatment switches
General Markov Model

- 6 classes of antipsychotics can be prescribed as the principal treatment;
- Patients can switch between these six treatments (or remain under their treatment);
- $6 \times 6 = 36$ transition probabilities;
- 3 one-year cycles simulated.
General Markov Model

Available drugs in France in 2003

- CLOZAPINE
- RISPERIDONE
- OLANZAPINE
- DEPOT, TYPICAL
- AMISULPRIDE
- STANDARD, TYPICAL
Differing Prescription Patterns
Ambulatory Schizophrenic patients

Legend
- Standard, typical
- Depot, typical
- A amisulpride
- O olanzapine
- R risperidone
- C clozapine

Private practice
Diagnosis < 1 year
Age < 42 in 2003
Age ≥ 42 in 2003

Hospital out-patients
4 Markov Models

- Patients stratified according to age in 2003 and prescription settings (hospital/private practice).
- Differing transition probabilities.
- Every year, patients:
  - Enter the “Age < 42” models;
  - Leave the “Age ≥ 42” models;
  - Total entry proportion = total exit proportion (stable prevalence in France).
# Transition Probabilities Example

Private practice patients, Age < 42 in 2003

<table>
<thead>
<tr>
<th>From</th>
<th>To</th>
<th>St typical</th>
<th>Dp typical</th>
<th>Amis.</th>
<th>Cloz.</th>
<th>Risp.</th>
<th>Olan.</th>
</tr>
</thead>
<tbody>
<tr>
<td>St typical</td>
<td>St typical</td>
<td>69.27%</td>
<td>5.36%</td>
<td>5.90%</td>
<td>0.00%</td>
<td>9.89%</td>
<td>9.58%</td>
</tr>
<tr>
<td>Dp typical</td>
<td>St typical</td>
<td>0.95%</td>
<td>90.81%</td>
<td>0.47%</td>
<td>0.78%</td>
<td>2.96%</td>
<td>4.03%</td>
</tr>
<tr>
<td>Amis.</td>
<td>St typical</td>
<td>0.36%</td>
<td>5.13%</td>
<td>75.84%</td>
<td>1.05%</td>
<td>7.54%</td>
<td>10.08%</td>
</tr>
<tr>
<td>Cloz.</td>
<td>St typical</td>
<td>2.82%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>94.14%</td>
<td>0.00%</td>
<td>3.04%</td>
</tr>
<tr>
<td>Risp.</td>
<td>St typical</td>
<td>2.04%</td>
<td>4.45%</td>
<td>2.71%</td>
<td>0.90%</td>
<td>83.61%</td>
<td>6.29%</td>
</tr>
<tr>
<td>Olan.</td>
<td>St typical</td>
<td>2.14%</td>
<td>3.09%</td>
<td>2.97%</td>
<td>0.54%</td>
<td>6.35%</td>
<td>84.91%</td>
</tr>
</tbody>
</table>

85% of the patients with olanzapine as their principal treatment will remain under this treatment the next year (no switch).
# Sensitivity Analysis

→ 50,000 samples of each distribution:

<table>
<thead>
<tr>
<th>Variables</th>
<th>Distribution</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transition probabilities</td>
<td>Dirichlet</td>
<td>Detailed survey</td>
</tr>
<tr>
<td>Initial market shares</td>
<td></td>
<td>Registry</td>
</tr>
<tr>
<td>Age &lt; 42 in 2003</td>
<td>Beta</td>
<td>Detailed survey</td>
</tr>
<tr>
<td>Private practice prescription</td>
<td></td>
<td></td>
</tr>
<tr>
<td>New onset schizophrenia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean daily treatment costs</td>
<td>Normal</td>
<td></td>
</tr>
</tbody>
</table>

→ Model recalculation for each sample vector.
RESULTS
Simulation Results

<table>
<thead>
<tr>
<th>Time (years)</th>
<th>Standard Typicals</th>
<th>Depot Typicals</th>
<th>Amisulpride</th>
<th>Risperidone</th>
<th>Olanzapine</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>27.1%</td>
<td>22.0%</td>
<td>16.5%</td>
<td>18.2%</td>
<td>27.1%</td>
</tr>
<tr>
<td>2004</td>
<td>32.3%</td>
<td>21.4%</td>
<td>12.4%</td>
<td>20.9%</td>
<td>18.2%</td>
</tr>
<tr>
<td>2005</td>
<td></td>
<td></td>
<td>9.6%</td>
<td>11.4%</td>
<td>22.0%</td>
</tr>
<tr>
<td>2006</td>
<td></td>
<td></td>
<td>3.8%</td>
<td>4.4%</td>
<td>32.3%</td>
</tr>
</tbody>
</table>
Sensitivity Analysis

Time (years)

Patient percentage

2003 2004 2005 2006

OLAN
DT'S
RISP
ST'S
Amis
Cloz
Risp
## Antipsychotics Daily Treatment Cost

Weighted average DTC, ex-factory price

<table>
<thead>
<tr>
<th>Year</th>
<th>DTC (€/day)</th>
<th>Estimated CI$_{95%}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>2.25</td>
<td>[2.149 – 2.352]</td>
</tr>
<tr>
<td>2004</td>
<td>2.38</td>
<td>[2.281 – 2.496]</td>
</tr>
<tr>
<td>2005</td>
<td>2.47</td>
<td>[2.363 – 2.606]</td>
</tr>
<tr>
<td>2006</td>
<td>2.53</td>
<td>[2.413 – 2.689]</td>
</tr>
</tbody>
</table>

Cost of principal antipsychotic taken (cost of co-prescriptions not included).

- **Budget increase from 2003 to 2006: +12.3%**
- **Estimated confidence interval: [8.3% - 18.6%]**
CONCLUSION

Schizophrenia treatment patterns are not stationary;

Simple Markov-based models can help understand the evolution of prescriptions;

Average daily treatment cost is expected to increase in the next years.