The place of subjectivity in the French system (HAS): a good thing or an archaism?

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The French system

- **Efficacy**: EMA
- **Effectiveness** : HAS (Transparency Committee)
  - Dossier (firm)
  - Vote of an SMR (level of reimbursement)
  - Vote of an ASMR (added value) : 5 to 1
  - Quick
  - And “dirty” (subjective)
- **Efficiency** : CEPS (Economic Committee)
  - Bargain

The place of subjectivity

- Science and statistics are supposed to help us to get rid of subjectivity
- NICE (≠ HAS / TC)
- But…
  - We have no data
  - We have no models (Utilities ? EQ5D ?)
  - We have experts
  - We have a growing literature on complex systems

A proposal

Comparative effectiveness

=

Comparative efficacy

+

Effect model (elicited from experts)

Effect model

- The relative efficacy of B versus A is given by a log(OR)
- If p_A and p_B are success rates :
  $\log(OR_{RCT}) = \log[(p_B/q_B)/(p_A/q_A)]$
- → $E[\log(OR_{RL})] = a + E[\log(OR_{RCT})]$
- → $Var[\log(OR_{RL})] = b \times Var[\log(OR_{RCT})]$ $(b \geq 1)$

- Question 1: Give a number between 0 and 100 that reflects best your confidence in the relative efficacy (Re) of the drug because of the potential methodological flaws of the trial. (this number is equivalent to a cut in the sample size of the trial: 0 means 100% of cut so that there is no more data and thus no confidence at all in the results, 100 means 0% of cut so that there is no loss in confidence)

- Question 2: Give a number between 0 and 100 that reflects best your confidence in the relative effectiveness (Rr) of the drug under real-life conditions because of the problems of transposing trial results into real life. (this number is also equivalent to a cut in the sample size of the trial)

- Question 3: By which number can be multiplied OR_{RCT} (relative efficacy) to obtain OR_{RL} (relative effectiveness that might be observed under real-life conditions after *short-term* administration, a few months, a few years). Base your answer on your clinical experience and knowledge of clinical trials.

- Question 4: By which number can be multiplied OR_{RCT} (relative efficacy) to obtain OR_{RL} (relative effectiveness that might be observed under real-life conditions in the *long term* (patient's life expectancy)).

Effect model

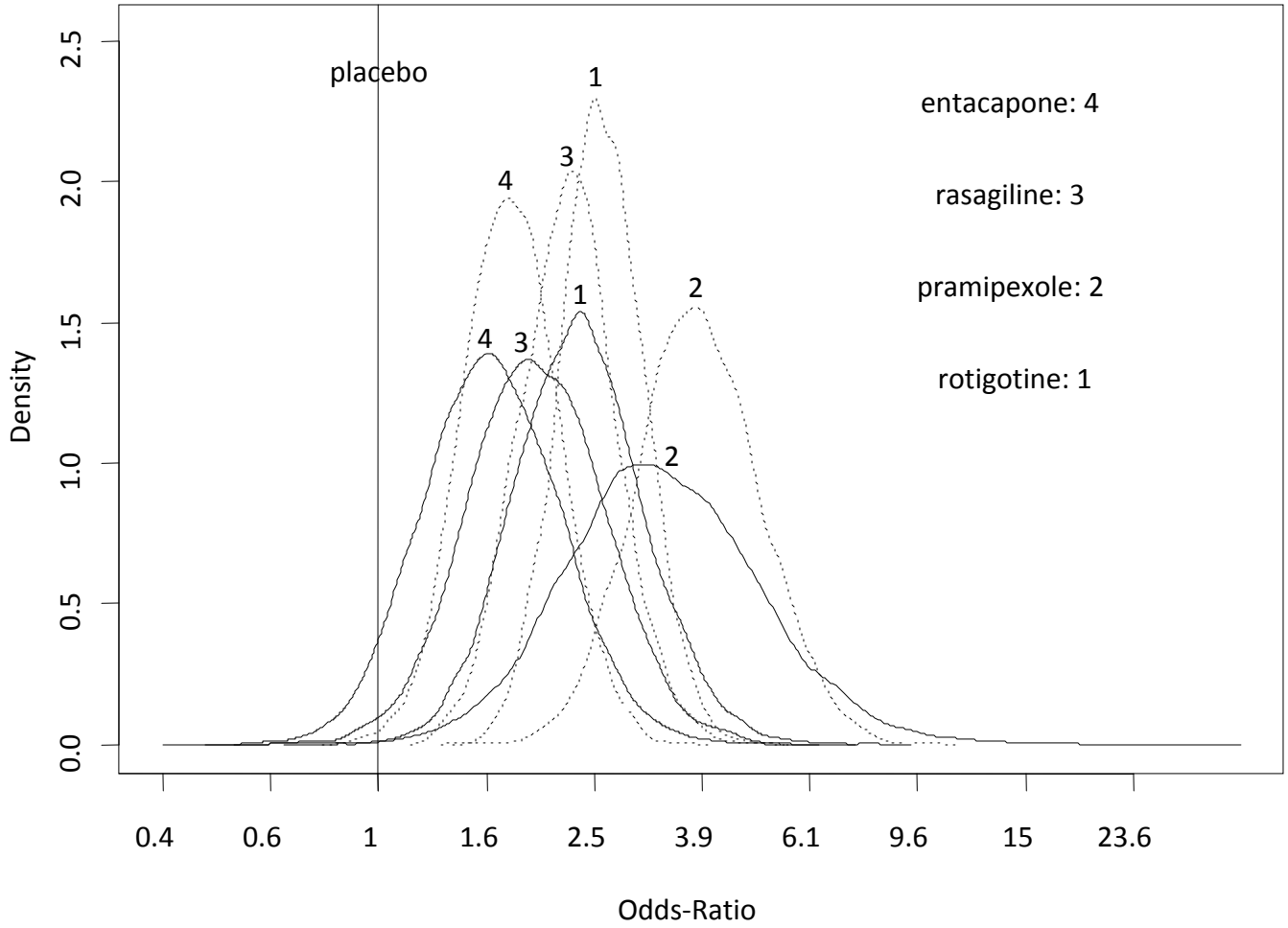
- $E[\log(OR_{RL})] = a + E[\log(OR_{RCT})]$
- $Var[\log(OR_{RL})] = b \times Var[\log(OR_{RCT})]$ $(b \geq 1)$
- $a = \log(a_1 \times a_2)$
- $b = 1/(b_1 \times b_2)$

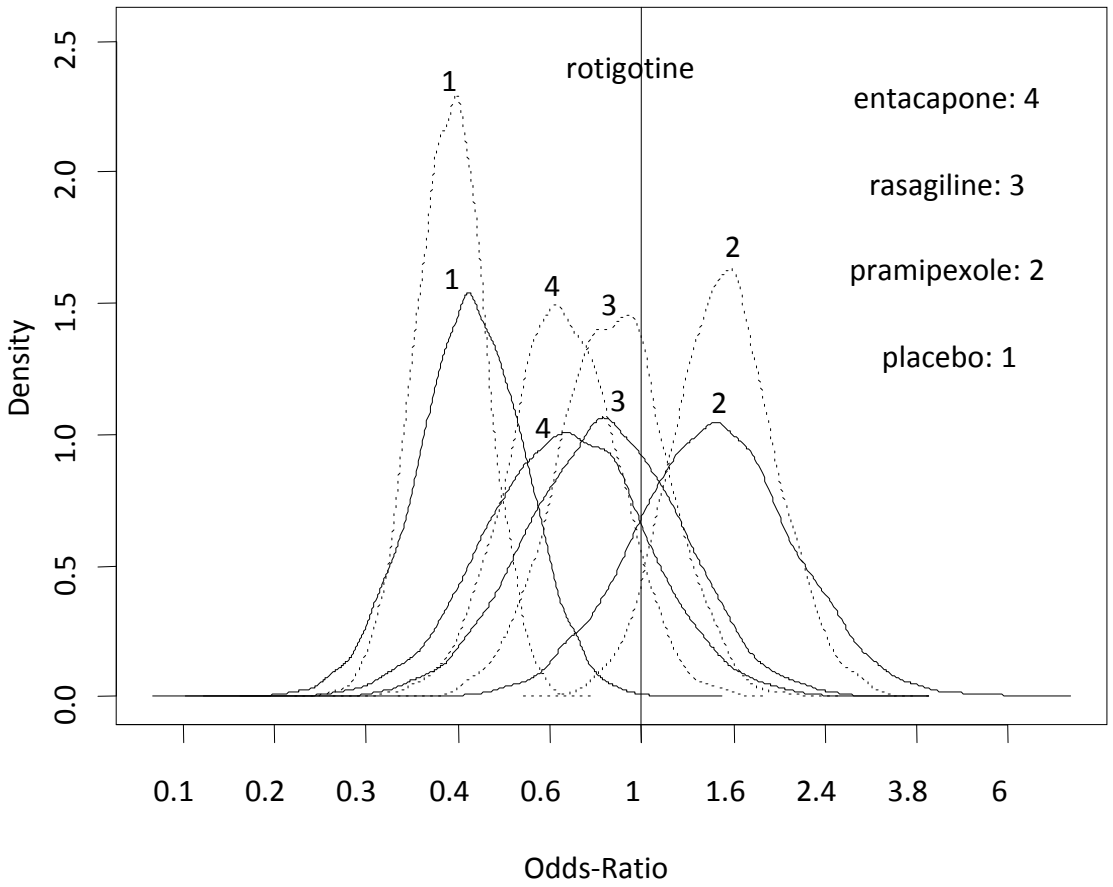
(if a_1 or a_2 are negative then

a_1 or a_2 is changed in $-1/a_1$ or $-1/a_2$)

Pooling of $\log(OR_{RL})$, uncertainty

- Network analysis: unidimensional scaling
- Uncertainty: bootstrap
- Example
  - Rotigotine in Parkinson disease
  - Placebo, pramipexole, entacapone and rasagiline
  - Ro-Pcb, Ro-P-Pcb, E-Ra-Pcb


placebo
entacapone: 4
rasagiline: 3
pramipexole: 2
rotigotine: 1
Density
0.0
0.5
1.0
1.5
2.0
2.5
0.4
0.6
1
1.6
2.5
3.9
6.1
9.6
15
23.6
Odds-Ratio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0.6
1
1.6
2.4
3.8
6
Odds-Ratio

Conclusion

- Effectiveness is a complex concept, there is even perhaps no “true” effectiveness of a drug
- Experts have (often unconsciously) a valuable insight of the clinical aspects of effectiveness
- Statistics can synthetize different sources of data in a transparent way
- This is a crucial point in a democracy
- The Bayesian perspective is not the only framework that can deal with subjectivity

Conclusion

- Is the method used in practice ?

Conclusion

- Is the method used in practice ?
  - No !
  - Because transparency is not always welcome
  - Changes and progresses are more dependent of power and politics than from statistics