

COST-EFFECTIVENESS OF ATYPICAL AND TYPICAL ANTIPSYCHOTICS : A COMPLIANCE MARKOV MODEL

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ABSTRACT

New compounds (Sertindole and Olanzapine) have been introduced to treat schizophrenic patients in the last 4 years. Their safety and efficacy with respect to conventional treatments are well documented, but their economic impact in a naturalistic context is still pending.

Objective: Comparison of costs and effectiveness of Sertindole with respect to Haloperidol and Olanzapine in usual practice with a pragmatic Markov Model of patients compliance under treatment.

Methods: Four databases are analysed; two French cohorts (2 747 patients), a German cohort (459 patients), a British cross sectional study (1 051 patients) and a randomised clinical trial (92 patients). The model is based on a 6 month Markov cycle tree divided into 4 sub-trees; the simulation is conducted over 10 years.

Results: The relative risk of relapse of Haloperidol and Olanzapine with respect to Sertindole is respectively equal to 1.4 and 1.2. Not only is Sertindole self-financing because of saved hospital admissions (- 16 000 \$ compared with Haloperidol and - 8 000 \$ compared with Olanzapine), but it produces net savings compared with the two components. The additional expenses due to mild and intensive health care management in community care is less than the decrease in hospitalisation costs. Olanzapine and Haloperidol are dominated strategies with a lower effectiveness and a greater cost. A sensitivity analysis carried out on toxicity, compliance, relapse and drop-out rates confirms the robustness of the results.

Conclusion: In schizophrenia, Sertindole brings a benefit of 5 months without relapse compared with Olanzapine and 13.5 months with respect to Haloperidol. In terms of cost effectiveness, our study clearly shows the interest of Sertindole.

DATA SOURCES

Four files are analysed:

- 1 - **Germany:** Fixed cohort: 294 patients with a 6 year follow-up (1978-1983).
- 2 - **Great Britain:** Cross-sectional survey: 1 051 patients in 340 facilities across 8 districts (1997).
- 3 - **France: Site 1:** Dynamic cohort: 884 patients.
Fixed cohort: 400 patients (1993-1995).
- 4 - **France: Site 2:** Dynamic cohort: 1 863 patients.
3 fixed cohort: 405 patients (1993-1995); 238 patients (1990-1992) and 171 patients (1990-1995).

CARE MANAGEMENT CATEGORIES AND CLINICAL STATES

- IPC: personal collective care
- MPC: mild personal care
- HOSP: hospital
- ICC: intensive collective care
- MCC: mild collective care

The clinical states are defined according to the relative variation of an intensity of care index based upon the number of hospitalisation days (i.e. full hospitalisation, day and overnight hospitalisations) and the number of ambulatory encounters (visits to psychiatrists, psychologists, nurses or social workers).

Three clinical states are identified: relapse patients (R⁺), non relapse patients (R⁻) and chronically hospitalised patients.

Average resources utilisation per patient and per 6 months

Catchment Areas	Hospit.	Intensive Personal Care	Intensive Collective Care	Mild Personal Care	Milds Collective Care
FRANCE (2) - RELAPSE					
Full inpatient hospitalisation (days)	163.54	39.63	40.85	4.03	2.60
Day hospitalisation (days)	0.62	14.37	13.16	0.21	0.00
Overnight hospitalisation (nights)	0.00	0.00	0.00	0.00	0.00
Ambulatory encounters	43.85	83.17	137.56	33.52	34.15
FRANCE (2) - NON RELAPSE					
Full inpatient hospitalisation (days)	141.50	17.31	13.87	0.44	0.28
Day hospitalisation (days)	0.00	23.79	2.61	0.05	0.00
Overnight hospitalisation (nights)	0.00	0.20	0.00	0.00	0.00
Ambulatory encounters	23.50	138.00	203.37	19.52	24.31

Adverse events (short term studies)

	Sertindole (%)	Olanzapine (%)	Haloperidol (%)
EPS	15	21	48
Somnolence	10	26	20
Weight gain	20	30	11
Sexual disturbance	2.5	1	2
Total	47.5	78	81

RESULTS

The compliance and relapse rates are extracted from the literature. The relative risk of relapse is respectively 1.4 and 1.2 for Haloperidol and Olanzapine with regards to Sertindole. Comparing sertindole and haloperidol by clinical status shows that the 10 year cost per patient of non relapse time on sertindole was higher than that for haloperidol : + 20,000 US \$. Conversely, time in relapse on haloperidol incurred higher costs than sertindole (27,000 US \$). Breaking the costs down

Compliance and effectiveness: annual relapse rate

Authors	n	Non-compliant Annual rate	n	Compliant Annual rate
Baldessarini	1260	72%	-	-
Davis - 1995	278	46%	249	29%
Gilbert - 1993	1224	61%	3114	20%
Glaser - 1996	-	55%	-	10%
Hogarty - 1984	141	68%	841	41%
Kissling - 1992	270	73%	-	-
Weiden - 1995	373	76%	285	35% - 22%

THE MARKOV MODEL

The model studied is based on a 6 month cycle and takes into consideration treatments used, adverse events, compliance to treatment and clinical states (i.e. relapse R⁺, non relapse R⁻ and chronically hospitalised), as well as drop-outs and deaths. The model is divided into 4 sub-trees: M1, M2, M3 and M4. 1) M1 identifies the drug strategies in schizophrenia: sertindole versus olanzapine versus haloperidol. 2) M2 enumerates the care structures. 3) M3 identifies the clinical events. Each of the treatments has side effects determining the compliance or non compliance and the frequency of relapses. 4) M4 shows the patients paths in the health care system. The model runs over 10 years.

- 17 Markov states (R⁺, R⁻, Chro, DO, Death)
- Cycle length: 6 months
- Time frame: 10 years
- End points: survival without relapse and costs

INCREMENTAL COST-EFFECTIVENESS RATIO

$$\frac{\Delta C}{\Delta E} = \frac{(\Delta CMC + \Delta CIC + \Delta CH)}{\Delta Q}$$

- C: Total medical cost per patient
- E: Total efficacy
- CMC: Cost of mild care
- CIC: Cost of intensive care
- CH: Cost of inpatient hospitalisation care
- Q: Survival without relapse
- Δ: Difference in cost or effectiveness

by professional service shows that the net savings achieved with sertindole are a result of a reduced expenditure in the hospital in-patient setting. saving a 16,000 US \$ (France Site 1) and 8,000 US \$ (France Site 1) for sertindole versus haloperidol and olanzapine, respectively. These savings more than offset the increased cost of outpatient/community care and the drug itself.

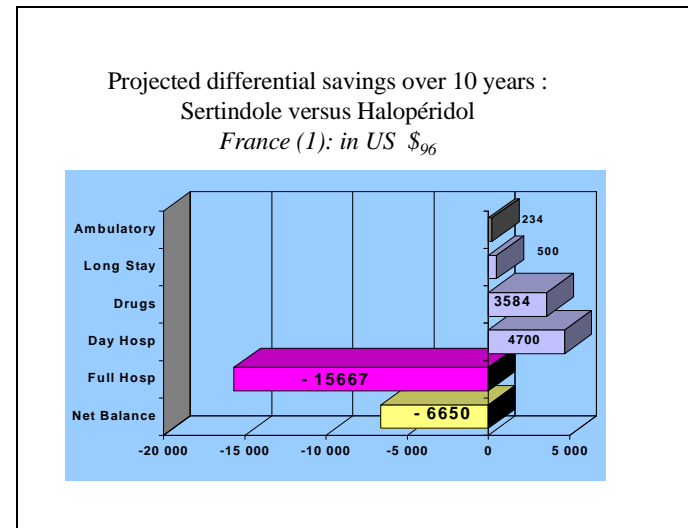
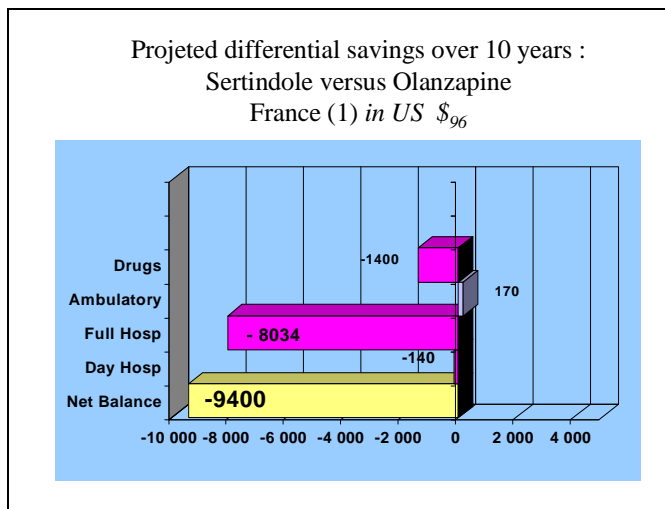
**Standard average six months mental health care costs (US \$)
across categories of care**

Relapse cases

	MPC	MCC	IPC	ICC	HOSP
Great-Britain	10 000	19 000	11 500	20 000	-
Germany	7 300	14 400	7 400	27 800	18 500
France site 1	2 600	1 700	17 400	15 700	39 000
France site 2	2 000	1 500	13 500	17 500	39 300

Non Relapse Cases

	MPC	MCC	IPC	ICC	HOSP
Great-Britain	6 100	13 000	9 900	18 000	-
Germany	1 000	27 000	1 200	11 000	-
France site 1	900	500	17 100	18 100	33 800
France site 2	700	800	10 400	10 500	33 900



Relative Risk of Relapse

◆ Haloperidol vs Sertindole :

1.40

◆ Olanzapine vs Sertindole :

1.20

**Incremental Cost-Effectiveness Ratio
Baseline Assumptions**

	STRATEGIES	
	Sertindole vs Olanzapine	Sertindole vs Haloperidol
Incremental effectiveness		
All countries	5.7 months	13.5 months
Incremental cost (US \$)		
France: Site 1	-9 400	-6 650
Germany	-7 467	-1 984
France: Site 2	-4 917	-34
Great Britain		
Medical Services	-4667	-2667
Services + Accommodation	-3500	5000
Incremental Cost-Effectiveness		
France: Site 1	Sertindole dominant	Sertindole dominant
Germany	Sertindole dominant	Sertindole dominant
France: Site 2	Sertindole dominant	Sertindole dominant
Great Britain	Sertindole dominant	Sertindole dominant

Conclusion

- ▼ Sertindole brings a benefit of 5 months without relapse compared with Olanzapine and 13,5 with respect to Haloperidol.
- ▼ Sertindole is self-financing because of saved hospital admissions. The medical management cost is lower across all the European countries where the study was carried out despite the fact that the drug costs are higher.
- ▼ Sertindole has a better cost effectiveness ratio, the other drugs are less effective and as or more

