

## Cost-effectiveness of sertindole versus olanzapine or haloperidol: A comprehensive model

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*The safety and efficacy of second generation antipsychotics relative to conventional treatment are well documented in schizophrenia, although their economic impact has not yet been evaluated. The aim of this study was to evaluate antipsychotics in normal practice using a 10-year cost-effectiveness model based on a 6-month Markov cycle tree. The model incorporated three competing drug strategies (sertindole, olanzapine and haloperidol); five care management strategies, defined by place of residence (hospital, residential or private home) and intensity of care (intensive or mild); clinical events (extrapyramidal symptoms, sedation, weight gain, sexual dysfunction, and relapse); and direct medical costs associated with each. Adverse-event rates were estimated from integrated safety reports; compliance and relapse rates were obtained from meta-analysis of the literature. The model comprised 15 discrete health states; transition probabilities among these were derived from local patient cohorts. The model computed that the relative risks of relapse on haloperidol or olanzapine compared with sertindole are 1.4 and 1.2, respectively, corresponding to an additional 5.7 and 13.5 months without relapse over 10 years. Furthermore, in most scenarios, sertindole is self-financing because less time is spent in hospital and indeed shows modest net savings compared with these drugs. These results clearly show the cost-effectiveness of sertindole. (Int J Psych Clin Pract 1998; 2(Suppl 2): S79–S86)*

### Keywords

schizophrenia  
sertindole  
olanzapine

cost-effectiveness model  
haloperidol

### INTRODUCTION

With increasing pressures on healthcare resources, doctors and healthcare purchasers have to make more and more medical and economic choices among the expanding range of available treatments. Drugs are often the first targets for rationalization, although they actually represent only approximately 13% of total health expenditure. However, an economic evaluation cannot be limited to drug acquisition costs. Non-drug costs such as those associated with staff time, equipment and hospitalization and, from a broader perspective, non-medical costs to patients, families and society, may need to be considered, and must be evaluated alongside treatment outcomes (efficacy, side-effects, quality of life, survival) before rational choices can be made to extract

the maximum benefit from available resources. Thus, health economic evaluation is not straightforward, and it is impossible to avoid using special techniques<sup>1</sup> which are becoming increasingly precise and sophisticated.

The present study uses one such analysis to compare the cost-effectiveness of three treatments for patients with schizophrenia. The safety and efficacy of the second generation antipsychotics relative to conventional agents is well documented, but the economics of their use in practice have not, to date, been evaluated prospectively. In the absence of prospective data, cost-effectiveness modelling is a useful and sophisticated method for estimating these data, using available results from a variety of sources. Indeed, this approach has a number of advantages. For example, a single model, with slight modifications, can easily be adapted to estimate the cost-effectiveness of

treatments in a number of different scenarios, by taking into account local costs and healthcare structures. Furthermore, the model can simulate a follow-up period that is much longer than that covered by most randomized clinical trials, thereby providing an objective measure of long-term outcome.

This study was designed to evaluate the clinical and economic consequences of recommended doses of haloperidol, olanzapine and sertindole in the management of schizophrenia in four different healthcare scenarios—France (two sites), Germany and the UK—using a computerized Markov model. The study was conducted from a psychiatric healthcare perspective and consisted of several stages: estimation of efficacy and adverse event rates for the three treatment strategies; measurement of benefits to patients (relapse-free survival); quantitative estimation of resources consumed, calculating costs associated with each of the treatments; and, finally, calculation of the cost/effectiveness ratio.

This paper focuses largely on the data and results for the French model. A summary of the final results for Germany and the UK is also presented.

## METHODS

In summary, the model defined the various paths through the healthcare system for schizophrenic patients on treatment, depending on whether or not they respond to treatment and as a function of the different management options available. The clinical benefits of treatment were measured by the time spent without relapse. Costs were calculated from the sum of the charges associated with medical services in each of the management situations over time. The contribution of each of the clinical states to overall health costs and to the individual benefit gained by a patient was estimated over a period of 10 years.

Three cohorts of patients were to be evaluated, each receiving a different treatment schedule: sertindole 12–24 mg/day as a single dose; haloperidol 10–20 mg/day in two divided doses; and olanzapine 10–20 mg/day in two divided doses.

## MODEL DESIGN

A Markov model was used to simulate patients' outcomes on each of the treatments and to calculate projected costs of care. To illustrate the Markov process simply, it may be considered as a series of probability trees—labelled A, B, C and D (Figure 1)—the branches of which are linked together over time, conventionally described as a Markov cycle tree. Each of the branches represents a health state or 'Markov state', defined from clinical factors characterizing the course of the disease, from the intensity of care required to manage the disease and from the premises in which the care is administered.

The model spans from the start of treatment and over

10 years, and is subdivided into 6-month time periods or 'cycles'. The decision to use a 6-month cycle was justified on clinical grounds: it is currently accepted that any schizophrenic deterioration which occurs within 6 months following a relapse should be considered as being part of that relapse (criterion D of the DSM-III-R).<sup>2</sup>

This type of decisional analysis records the distribution of a cohort of patients on treatment across different states of health associated with the clinical course of the disease, at 6-month intervals. Whether or not a patient passes from one state of health to another over time is determined by a 'transition probability'. Transition probabilities for this model were calculated from observed frequencies in two large-scale, longitudinal cohorts, and from published clinical findings.<sup>3–7</sup> A basic feature of the Markov process is that it has no memory. Regardless of the patient's past history when he passes into a given state of health in the model, all patients in that state of health are assumed to be subject to the same likelihood of developing potential subsequent events.

## HEALTH STATES

### Clinical states

Three clinical states were defined: relapse, non-relapse and chronic disease. In the published literature, the criteria used to define relapse vary, depending on the author.<sup>8–15</sup> Following Davis and colleagues' recommendations,<sup>5</sup> we used published comparative rates to calculate the probabilities of relapse in different clinical settings. We defined a chronic patient as any patient who has spent more than 120 days as a full inpatient during a 6-month follow-up period, and in whom there has been no significant change in consumption of resource from one 6-month period to the next.

### Intensity of care

Three care groups were identified: *hospitalization* (patients who were admitted to hospital for >4 months, regardless of their clinical state); *intensive management* (patients admitted to hospital for >30 days in a 6-month period); normal practice, or *mild care* (<30 days hospitalization during a 6-month period). Outpatient management (either intensive or mild) was differentiated by the place in which the patient lives—either in a family home or in community care. There were therefore five patient treatment groups: high-dependency hospital management (*hospital*), intensive home (*personal*) or residential (*collective*) care (IPC, ICC), and mild home or residential care (MPC, MCC) (Figure 1,B). Combining the clinical factors and intensity of care categories defined above produced 3 × 5 Markov states. Two other states were then added, one for patients lost to follow-up (*drop-out*), and one for death, making a total of 17 potentially usable Markov states. However, because patients with chronic disease were considered to require at least intensive care, the mild care group, either at home or

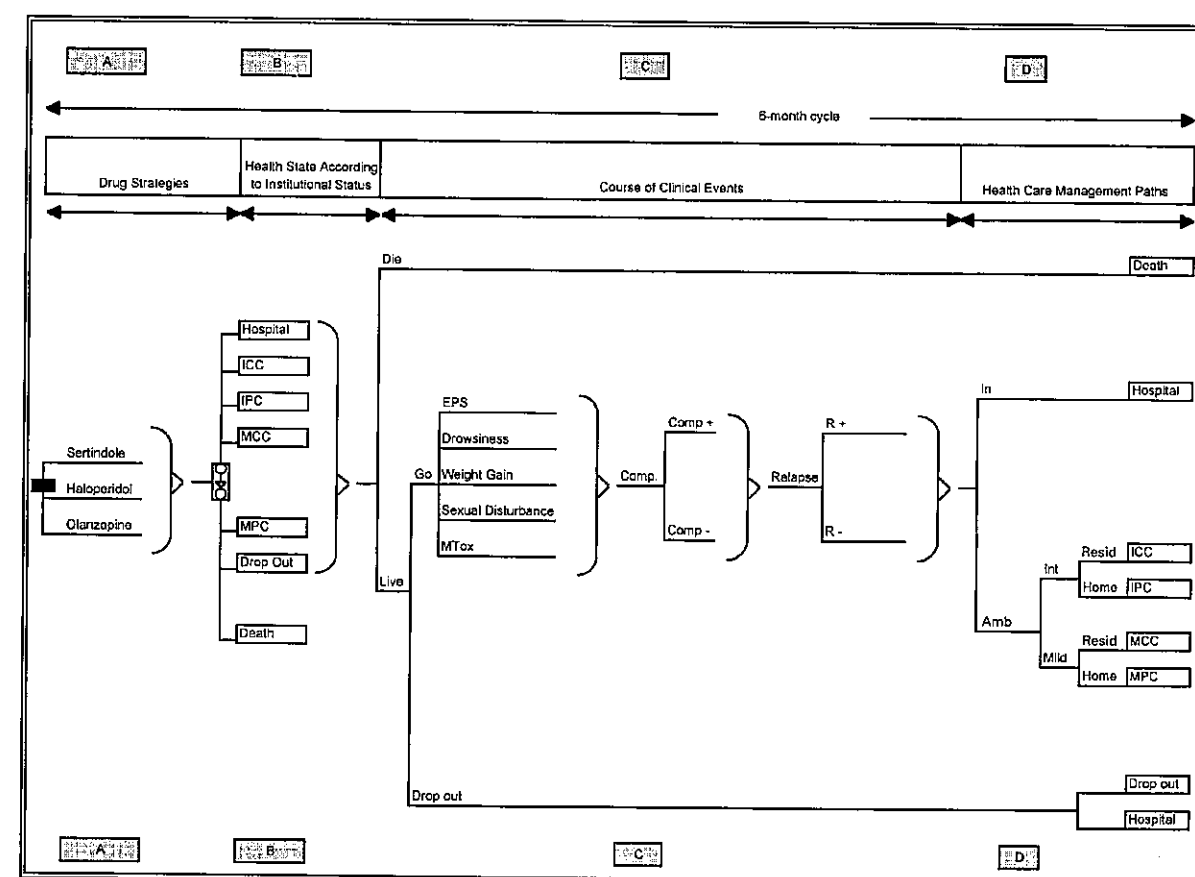


Figure 1

Cost-effectiveness model to assess the impact of antipsychotic treatment in patients with schizophrenia. The model is based on a 6-month Markov cycle tree. The tree starts at a decision node, the point at which the patients enter the model. The three branches coming out of this node represent the three competing management possibilities: sertindole versus haloperidol versus olanzapine. The bracket signifies that the same sub-tree is being used to evaluate the effects of the three treatments. The Markov node shown on the right of the bracket (B) indicates that the Markov process has been used. Each of the branches attached to the Markov node represents a health state or 'Markov state'.

Abbreviations: EPS=extrapyramidal symptoms; MTax=minor toxicity; Comp+=compliance; Comp-=non compliance; R+=relapse; R-=non relapse; In=inpatient; amb=ambulatory care; Int=intensive care; Mild=conventional care; Resid=residential care; Home=domiciliary care; ICC=intensive collective care; IPC=intensive personal care; MCC=mild collective care; MPC=mild personal care.

in community care, was not used for this type of patient. Fifteen Markov states were, therefore, finally used (Figure 2).

## CLINICAL EVENTS

The likelihood of patients finding themselves in any one of the 15 states described above is governed by side-effects, compliance and relapse (Figure 1,C). Patients on treatment may either survive or die. In the former situation, treatment may be stopped (*drop-out*) either because it is ineffective (for example, because a patient is resistant), or because the patient refuses to take the treatment. In all other cases treatment is continued.

### Data sources for adverse events

The list of potential side-effects associated with antipsychotic agents is extensive.<sup>16</sup> Most pertinent to this study

were those side-effects that occur with long-term treatment, and which have an impact on treatment decisions. Four main adverse events, extrapyramidal symptoms (EPS), sedation, weight gain (defined as  $\geq 7\%$  increase from baseline) and sexual dysfunction, were considered, as these were the ones most likely to influence compliance.

Adverse event rates were taken from registration dossiers for the three compounds studied. We used the frequencies obtained from the pooled short-term trials (>60 days), all doses combined, i.e. haloperidol 4–16 mg/day, sertindole 4–24 mg/day and olanzapine 5–20 mg/day. The incidence of EPS was far lower for sertindole (15% [177/1197]) than for haloperidol (48% [237/489]) or olanzapine (21% [52/248]). Similarly, sertindole was the least sedating of the three drugs studied (incidence of sedation: 10%, 20% and 26%, respectively). Weight gain (>7% of initial body weight) with sertindole (20%) occurred less frequently than with

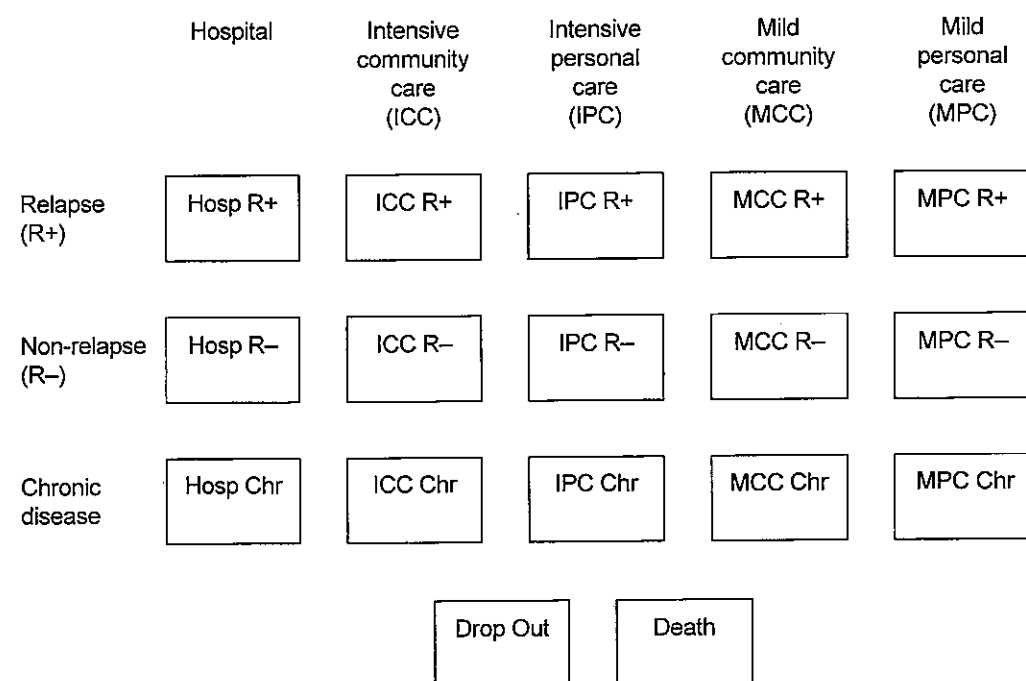


Figure 2 Potential Markov states defined by clinical factors and intensity of care categories included in the model. The shaded boxes represent states that were not actually used (see text), leaving a total of 15 usable states

olanzapine (29%), but more frequently than with haloperidol (11%). The incidence of sexual dysfunction was 2.5%, 2% and 1% for sertindole, haloperidol and olanzapine respectively. The majority of sexual dysfunction reports in sertindole-treated patients are decreased ejaculatory volume in male patients, which is generally not associated with decreased libido or impaired sexual performance.

**Compliance**

These adverse events will influence compliance, and patients in the model were defined as compliant (*comp+*) or non-compliant (*comp-*). The risk of relapse (*R+*) increased with decreasing compliance with treatment. Conversely, the probability of stabilization (*R-*) increased with increasing compliance. However, there was no systematic relationship between these findings: patients who complied strictly with their medication could still relapse.

**Data sources for relapse rates**

Estimated rates of relapse were derived from a survey of published meta-analyses. For non-compliant patients, relapse rates of 55–76% after 10–12 months have been reported.<sup>4,7,17</sup> Based on these findings, a 76% relapse rate 1 year after symptoms of schizophrenia have worsened appears to be the upper limit of the confidence interval in non-compliant patients. We used this worst-case assumption in the model by applying a 6-month probability of relapse of 0.51.

For compliant patients, we used results of comparative trials of patients treated with an optimal dose, in particular by depot injection of long-acting antipsychotics, or by continuous treatment, compared with those on conventional treatment or in whom treatment was interrupted. Gilbert and colleagues analysed 66 trials and found that the relapse rate in patients who received the optimal treatment dose was only 15.6% at 9.7 months.<sup>6</sup> However, Weiden and Olfson reported a relapse rate in compliant patients of 35% for conventional antipsychotics and 22% for second generation drugs.<sup>7</sup> These latter figures were conservatively selected as the 1-year relapse rates in the model, corresponding to 6-month relapse probabilities of 0.1937 and 0.1168, respectively.

**PATIENT TRANSITION PROBABILITIES**

Transitions of patients from one care group to another were calculated from two French cohorts.<sup>18</sup> Only those patients who had had at least one contact per 6 months with professionals or services in the care sector were included in the analysis. A total of 400 patients were followed up in Site 1 and 405 in Site 2 over the 3-year period spanning 1993 to 1995. The relative distributions of these populations across the 15 health states defined above (see Figure 2) over four 6-month periods were used to calculate the mean transition probabilities between care groups (hospital, ICC, IPC, MCC, MPC) for each clinical state.

Equivalent transition probability calculations were made for the German and UK models, based on data from

a German cohort of 294 patients and from a cross-sectional English study (1051 patients).<sup>19</sup> Local medical attitudes and the type of accommodation strongly influenced the probabilities, and there were considerable differences in the transitional probabilities calculated for different sites.

**COSTS**

**Resources consumed**

The two fixed French databases were also used to estimate the range and amount of resources consumed, by care group, per 6-month period. For each of the five patient care groups, the numbers of full inpatient hospitalization days, partial hospitalization (day hospitalization, overnight hospitalization) and the number of outpatient visits for each professional category (doctors, nurses, psychologists and social workers) were calculated for each category of care.

**Sources of cost data**

Three sources were used to obtain estimates of the unit costs of resources consumed in the model:

- daily tariff charges (social security system) for full inpatient hospitalization, and for partial hospitalization, day hospitalization or overnight hospitalization
- actual costs of professional procedures performed within the community on the two sites studied, calculated from the financial accounting structures within the establishments
- the public prices of antipsychotic drugs used within the sector.

All costs were adjusted to 1996 prices, and presented in US dollars (\$). Daily costs for full inpatient hospitalization, day hospitalization and overnight hospitalization were \$232, \$162 and \$81, respectively. The average unit cost of a medical procedure (all combined) was \$36 and the cost of a nursing procedure was \$52. The cost per visit of a consultation with a psychologist was \$21 and with a social worker, \$66. The costs of outpatient antipsychotic treatment were based on a daily hospital cost for haloperidol 15 mg/day of \$69 for 6 months.

In France, the costs of sertindole (12–24 mg/day) and of olanzapine (15 mg/day) were provisionally assumed to be identical and equal to \$1000 for a 6-month treatment period. At this time, no official price is available.

The actual 6-month cost associated with each Markov state was calculated by combining the resource use estimates and unit costs. The weighted cost of clinical states was obtained by calculating the product of actual costs and the probabilities associated with the patient's transitions within the care system. These are summarized in Table 1.

**INCREMENTAL COST-EFFECTIVENESS RATIO**

By definition, the three treatments being studied are mutually exclusive. Replacing one strategy with another results in a cost difference and in a difference in effectiveness. Together, these produce a *net increment in mean value* ('increment' because only differences between the strategies are measured; 'mean value' because it is a

Table 1 Mean 6-month average costs per care management group (US\$<sub>96</sub>)

Site/Population	Hospital	Intensive Care	Mild Care
<b>France (1)</b>			
Relapse	38 996	17 289	2472
full inpatient hospitalization	(97.7%)	(57.1%)	(55.5%)
day and overnight hospitalization	(0.8%)	(40.6%)	(29.0%)
outpatient visits	(1.5%)	(2.3%)	(15.5%)
Non-relapse	33 843	17 103	820
full inpatient hospitalization	(98.3%)	(21.9%)	(4.0%)
day and overnight hospitalization	(0.7%)	(76.1%)	(45.2%)
outpatient visits	(1.0%)	(2.0%)	(50.8%)
<b>France (2)</b>			
Relapse	39 254	14 473	1958
full inpatient hospitalization	(97.0%)	(64.2%)	(46.3%)
day and overnight hospitalization	(0.3%)	(15.8%)	(1.6%)
outpatient visits	(2.7%)	(20.0%)	(52.1%)
Non-relapse	33 883	10 421	742
full inpatient hospitalization	(97.2%)	(36.4%)	(13.2%)
day and overnight hospitalization	(0.0%)	(27.6%)	(1.0%)
outpatient visits	(2.8%)	(36.0%)	(85.8%)

mathematical calculation of expectation, defined as the sum of the probabilities of events, weighted by costs and associated effectiveness). The incremental cost is the algebraic sum of the positive and negative cost differences, linked to the expenditure associated with the treatments in each of the care groups: mild, intensive or hospital. The additional effectiveness of one treatment compared with another is measured in terms of gained months without relapse. The incremental cost-effectiveness ratio is defined as the quotient of these differences.

The calculation is represented by the following equation:

$$\Delta C/\Delta E = (\Delta CMC + \Delta CIC - \Delta CH)/\Delta Q$$

where C = total net medical cost per patient; E = total effectiveness; CMC = cost of mild care; CIC = cost of intensive care; CH = cost of inpatient hospitalization care; Q = survival without relapse;  $\Delta$  = difference.

A strategy is said to 'dominate' another if it is more effective (or equally as effective) and cheaper than the other. The strategy is said to be 'efficient' or 'cost-effective' if no procedure can produce a better result at lower cost.

## RESULTS

Sertindole, haloperidol and olanzapine were compared in the two different scenarios in the French model: one using data from Site 1, the second from Site 2. In each analysis, the model was run three times—once for each of the three treatment strategies—using the calculated probabilities specific to that drug (as described above).

### DESCRIPTION OF THE POPULATION

The initial distribution between different states in the model was the same as the distribution of the population by clinical state and by categories of care in the two French databases. Accordingly, the distribution of these patients' clinical states differed between the two models, reflecting the different approaches to care at the two sites: at Site 1, 18% of patients were chronically hospitalized and 22% of patients who relapsed stayed in hospital for >4 months, while Site 2 favoured community care services (1% chronic hospitalization and 6% of relapsed patients admitted for >4 months).

### ESTIMATION OF COMPLIANCE AND EFFICACY

The efficacy results (time in relapse/non-relapse) presented below apply to both of the French cohorts, as they are dependent on drug-specific parameters rather than local care management practices.

The model predicted that, during the 10-year study period, 72% of sertindole-treated patients would remain on treatment, 18% would be lost to follow-up and 10% would die. Of those patients maintained on treatment (comple-

ters), 2% were chronically hospitalized, 32% relapsed and 66% stabilized. The likelihood of relapse on treatment was therefore 0.32.

The estimation for haloperidol-treated patients during the same period revealed a higher risk of relapse, although the proportion of patients who died was the same as for sertindole (10%). Of 68% of patients who remained on treatment, 2% were chronically hospitalized, 45% relapsed and 53% stabilized. The probability of relapsing on treatment was therefore 0.45. The relative risk of relapse on haloperidol compared with sertindole is therefore 0.45 compared with 0.32, or 1.4, i.e. the risk of relapse on haloperidol is >40% higher than on sertindole.

Using similar calculations, the relative risk of relapse on olanzapine compared with sertindole is 1.2.

The mean time without relapse was 57 months for sertindole compared with 51.3 months for olanzapine and 43.5 months for haloperidol. Patients on sertindole benefited by 5.7 months compared with olanzapine and by 13.5 months compared with haloperidol.

### MEASUREMENT OF PROJECTED COSTS

Total medical costs are defined as the sum of all of the management costs for each of the categories of care involved, multiplied by the probability of requiring this category of care during the 10 years of the model.

The results for the France Site 1 cohort are presented in detail below (Table 2). The cost-effectiveness analyses were performed in a similar way for France Site 2, Germany and the UK (data not shown) to produce incremental cost-effectiveness ratios for sertindole vs haloperidol, and sertindole vs olanzapine, in each of the four systems (summarized later).

The projected mean total cost per patient over the 10-year model period, based on the Site 1 cohort, was \$198 800 for sertindole, \$205 300 for haloperidol and \$205 484 for olanzapine. Table 2 shows the break-down of these costs by clinical status, professional service and category of care.

Comparing sertindole and haloperidol by clinical status (Table 2a) shows that the 10-year cost per patient of non-relapse time on sertindole was higher than that for haloperidol (\$98 833 vs \$78 950: +\$19 883). Conversely, time in relapse on haloperidol incurred higher costs than on sertindole (\$117 033 vs \$90 150: +\$26 883), equivalent to a net difference in mean cost per acute patient of \$7000 between the two drugs. The fact that more of the haloperidol patients dropped out of the study reduced the cost of managing chronic patients by \$500 per patient compared with sertindole. The overall difference in cost was therefore \$6500 per patient in favour of sertindole.

A similar analysis of sertindole versus olanzapine shows a higher total mean 10-year cost associated with non-relapse for sertindole, but again, this is more than offset by the savings in costs associated with relapse, producing a net saving of \$6683 per patient treated with sertindole.

Breaking the costs down by professional service (Table 2a) and category of care (Table 2b), it is apparent that, compared with haloperidol or olanzapine, the net savings achieved with sertindole are a result of reduced expenditure in the hospital inpatient setting. Mean 10-year costs associated with full inpatient hospitalization (whether in relapse or non-relapse) were \$122 017 per patient for sertindole, compared with \$137 683 for haloperidol and \$130 050 for olanzapine, a saving of \$15 666 and \$8033 for sertindole versus haloperidol and olanzapine, respectively. These savings more than offset the increased costs of outpatient/community care and the drug itself.

### INCREMENTAL COST-EFFECTIVENESS RATIO

The results of the incremental cost-effectiveness calculation for all four patient cohorts are shown in Table 3.

Table 2

Results of the model (France Site 1): predicted 10-year mean costs per patient (US\$<sub>96</sub>)

Table 2a

by clinical status and professional service

Site/Population	Sertindole	Haloperidol	Olanzapine
Relapse total	90 150	117 033	105 017
full inpatient			
hospitalization	69 567	92 233	80 733
day and overnight			
hospitalization	18 367	22 433	21 867
outpatient visits	1783	2367	2133
incremental drug cost	433	0	284
Non-relapse total	98 833	78 950	90 650
full inpatient			
hospitalization	52 450	45 450	49 317
day and overnight			
hospitalization	39 850	31 083	36 500
outpatient visits	3233	2417	2700
incremental drug costs	3300	0	2133
Chronic	9817	9317	9817
Total	198 800	205 300	205 484

Table 2b

by category of care

Site/Population	Sertindole	Haloperidol	Olanzapine
Mild care	6383	4117	5317
Intensive care	95 733	92 217	99 383
Hospital	96 684	108 966	100 783
Total	198 800	205 300	205 484

The denominator shows a benefit of 5 months and 20 days without relapse in favour of sertindole compared with olanzapine and 13.5 months compared with haloperidol, for all countries. For France Site 1, the numerator reveals a

Table 3

Incremental cost-effectiveness ratios. Baseline assumptions

	Treatment strategy	
	Sertindole vs haloperidol	Sertindole vs olanzapine
Incremental effectiveness*		
All countries	13.5 months	5.7 months
Incremental cost (\$US, 1996)		
France (1)	-6500	-6683
France (2)	125	-2066
Germany	-4753	-4912
Great Britain	2735	-1846
Incremental cost-effectiveness ratio		
France (1)	Sertindole dominates	Sertindole dominates
France (2)	Sertindole more effective, but more costly	Sertindole dominates
Germany	Sertindole dominates	Sertindole dominates
Great Britain	Sertindole more effective, but more costly	Sertindole dominates

\*Time without relapse, months

### KEY POINTS

- The low level of EPS and minimal sedation reported with sertindole are likely to be responsible for the improved compliance shown in the model, compared with haloperidol or olanzapine
- Time without relapse is the most important determinant of cost-effectiveness of antipsychotics in schizophrenia
- Compared with sertindole, there is over 20% risk of relapse with olanzapine, and over 40% higher risk of relapse with haloperidol
- As a result, sertindole results in substantial savings in costs associated with hospital admissions
- In most scenarios, sertindole is more cost-effective than olanzapine or haloperidol; long-term treatment of schizophrenia with sertindole is predicted to produce net savings in the psychiatric healthcare budget

saving of \$6683 compared with olanzapine and \$6500 compared with haloperidol. As sertindole was both more effective and less costly than either olanzapine or haloperidol, it dominates both treatments in cost-effectiveness terms. Using data from France Site 2, however, produced less favourable results for sertindole versus haloperidol, most likely reflecting the different spread of medical services at the two sites.

Sensitivity analyses carried out on adverse events, compliance, relapse and drop-out rates confirmed the robustness of these results.

## CONCLUSIONS

The results of our model show that, compared with haloperidol or olanzapine, long-term treatment of schizophrenic patients with sertindole improves compliance, reduces the number of relapses and results in net savings to psychiatric healthcare services. First-line treatment of a

schizophrenic patient with sertindole produced a benefit of 13.5 months without relapse compared with treatment with haloperidol, and 5 months and 20 days compared with olanzapine. Results of the costs analysis varied from country to country, but were generally in favour of sertindole. The results of the analysis are dependent on local systems of healthcare provision, and for more accurate predictions the analysis should be performed site by site. Furthermore, the savings made in one sector may be absorbed by another, and it is important to consider local budgeting systems and transfer of funds between sectors when interpreting the results of such studies. Nevertheless, the results of the present study indicate that sertindole is self-financing as a result of savings in hospital admissions, and provides greater effectiveness at lower cost compared with haloperidol and olanzapine in the French (Site 1) and German models. The results demonstrate clear potential for sertindole as a cost-effective, long-term treatment in patients with schizophrenia.

## REFERENCES

1. Launois R (1997) Exemple d'étude medico-économique: dépistage du cancer de la prostate. In: *Dépistage des cancers* (ed Sancho-Garnier) 57-70. Editions INSERM, Paris.
2. American Psychiatric Association (1987) *Diagnostic and Statistical Manual of Mental Disorders*. Third edition (revised). (DSM-III-R). American Psychiatric Association, Washington DC.
3. Johnson DAW, Pasterski G, Ludlow JM et al (1983) The discontinuance of maintenance neuroleptic therapy in chronic schizophrenic patients: drug and social consequences. *Acta Psychiatr Scand* 67: 339-52.
4. Baldessarini RJ, Cohen BM, Teicher MH (1990) Pharmacological treatment. In: *Schizophrenia treatment of acute psychotic episodes* (eds Levy ST, Ninan PT) 61-118. American Psychiatric Press, Washington DC.
5. Davis JM, Matalon L, Watanabe MD, Blake L (1994) Depot antipsychotic drugs. *Drugs* 47: 741-73.
6. Gilbert P, Harris J, McAdams A, Jeste DV (1995) Neuroleptic withdrawal in schizophrenic patients. A review of the literature. *Arch Gen Psychiatry* 52: 173-88.
7. Weiden PJ, Olfson M (1995) Cost of relapse in schizophrenia. *Schizophr Bull* 21: 419-29.
8. Crawford R, Forrest D (1974) Control trial of depot fluphenazine in outpatient schizophrenics. *Br J Psychiatry* 124: 285-91.
9. Del Giudice J, Clark WG, Gocka EF (1975) Prevention of recidivism of schizophrenics treated with fluphenazine enanthate. *Psychosomatics* 16: 32-6.
10. Rifkin A, Quitkin F, Rabiner CJ, Klein DF (1977) Fluphenazine decanoate, fluphenazine hydrochloride given orally, and placebo in remitted schizophrenics. Relapse rates after one year. *Arch Gen Psychiatry* 34: 43-7.
11. Hogarty GE, Schooler N, Ulrich RF et al (1979) Fluphenazine and social therapy in the aftercare of schizophrenic patients: relapse analyses of a two year controlled study of fluphenazine decanoate and fluphenazine hydrochloride. *Arch Gen Psychiatry* 36: 1283-94.
12. Schooler N, Levine J, Severe JB (1979) NIMH-PRB collaborative fluphenazine study group. Depot fluphenazine in the prevention of relapse in schizophrenia: evaluation of a treatment regimen. *Psychopharmacol Bull* 15: 44-7.
13. Johnson DAW, Ludlow JM, Street K, Taylor RDW (1987) Double blind comparison of half-dose and standard dose flupentixol decanoate in the maintenance treatment of stabilised out-patients with schizophrenia. *Br J Psychiatry* 151: 634-8.
14. Hogarty GE, McEvoy JP, Munez M et al (1988) Dose of fluphenazine, familial expressed emotion, and outcome in schizophrenia. Results of a two year controlled study. *Arch Gen Psychiatry* 45: 797-805.
15. Davis JM, Kane JM, Marder SR et al (1993) Dose response of prophylactic antipsychotics. *J Clin Psychiatry* 54 (suppl 3): 24-30.
16. Cohen D (1994) Quelles sont les conséquences sociales et psychologiques en terme de qualité de vie des neuroleptiques et de leurs effets secondaires. In: *Conférence de consensus: stratégies thérapeutiques à long terme dans les psychoses schizophréniques*. (eds Kovess V, Caroli F, Durocher A et al) 149-84. Editions Frison Roche, Paris.
17. Kissling W (1992) Ideal and reality of neuroleptic relapse prevention. *Br J Psychiatry* 161 (suppl): 133-9.
18. Launois R, Schulenburg JM, Knapp M, et al (1998) Cost-effectiveness analysis of new neuroleptics. In: *Control of Health Complexity*, AEA proceedings, Lyon, July 1998.
19. Chisholm D, Knapp M, Astin J et al (1997) The mental health residential care study: the cost of provision. *J Mental Health* 6: 85-99.

# What is the experience with sertindole in clinical practice?

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*The use of conventional antipsychotics in the treatment of schizophrenia is well established. However, these drugs are not very effective in controlling the negative symptoms of schizophrenia (emotional flatness, lack of initiative and impaired communication). Their anticholinergic activity may also cause secondary negative symptoms such as emotional rigidity and sedation, and impair cognitive functioning, which is further exacerbated by the anticholinergic agents used to overcome motor side-effects. These problems, combined with side-effects such as weight gain and sexual disturbances, contribute to the poor compliance and high relapse rates observed with conventional antipsychotics. Second generation antipsychotics, including risperidone, olanzapine and sertindole, have shown promising results in the treatment of both negative and positive symptoms of schizophrenia. Moreover, sertindole lacks the motor and anticholinergic side-effects of conventional antipsychotics. In this open-label study of sertindole in clinical practice, patients improved substantially after their treatment was switched from conventional antipsychotics to sertindole. Patients and doctors both reported high levels of satisfaction. Compliance with sertindole was high, and the observed side-effects were mild and acceptable. Sertindole proved to be an effective, safe, well-tolerated and non-sedative antipsychotic agent. In our clinical experience, sertindole is commendable as an effective treatment in first-episode schizophrenia. (Int J Psych Clin Pract 1998; 2(Suppl 2): S87-S91)*

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## INTRODUCTION

The negative symptoms of schizophrenia (emotional flatness, lack of initiative and impaired communication) have a devastating effect on a patient's long-term functioning in the community.<sup>1</sup> Conventional antipsychotics are not very effective in the control of negative symptoms, and often even cause secondary negative symptoms, such as emotional rigidity and sedation.<sup>2</sup>

Impairment of cognitive skills is apparent in 40-60% of patients with schizophrenia,<sup>3</sup> and is most noticeable in tasks involving attention, memory and executive function. These symptoms are strongly associated with a loss of social and vocational functioning and, accordingly, predict the likelihood of social reintegration for patients with schizophrenia. The anticholinergic activity of conventional antipsychotics adds to existing impairment of cognitive

functioning, by reducing attention span and memory, and inducing thought disturbances. Also, cognitive functioning is further impaired by the anticholinergic medications that are prescribed to overcome motor side-effects such as dystonia, akathisia, and Parkinsonism.

Low efficacy against negative symptoms, impaired cognitive functioning, motor disturbances, and other side-effects such as weight gain and sexual disturbances, all contribute significantly to the serious clinical problems of low compliance and high relapse rates observed in schizophrenia.

## GOALS OF TREATMENT FOR SCHIZOPHRENIA

Most psychiatrists agree that preventing the relapse of symptoms is the key objective of treatment for schizo-