PMH44

Costs and Outcomes of Atypical Antipsychotics for the Treatment of Acute Schizophrenia

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Introduction

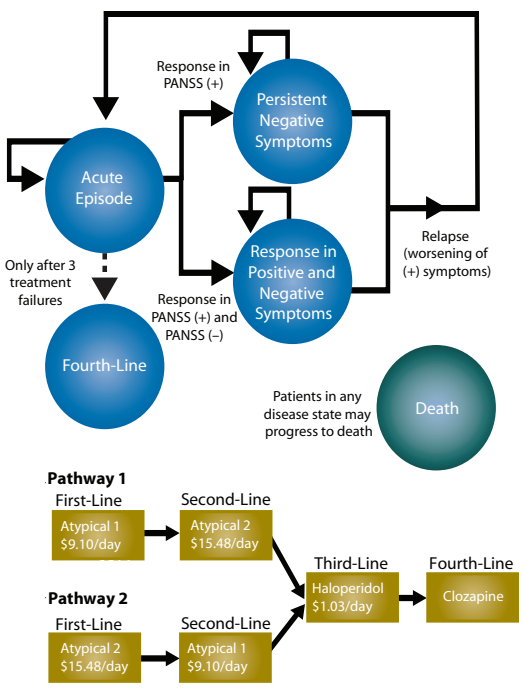
- Schizophrenia is a chronic condition that requires treatment over many years, and patients with schizophrenia frequently switch among treatments due to lack of efficacy, lack of tolerability, or other reasons.[1,2]
- Estimates of the costs and health outcomes associated with a new pharmacotherapy are frequently requested by healthcare decision makers before putting a new drug on a national or local formulary.
- Although the treatment of schizophrenia with atypical antipsychotics has been demonstrated to be cost effective,[3,4] the cost implications of initiating treatment with a later atypical antipsychotic rather than an earlier atypical antipsychotic remain unclear.

Objective

- To estimate the 1-year resource use and costs when starting treatment with an earlier atypical antipsychotic (Atypical 1) versus a later agent (Atypical 2), while taking into account switching patterns.

Methods

Markov Model



Average daily cost data sources: Verispan Physician & Diagnosis Audit and Wholesale Audit Costs.

- Schizophrenic patients experiencing acute psychotic episodes were followed through 4 health states (ie, acute episodes with positive symptoms and negative symptoms, response in positive and negative symptoms, response in positive symptoms but not in negative symptoms, and fourth-line treatment) and death.
  - Patients could move from the acute episode state to other health states.
  - Scores of the positive and negative subscales of the Positive and Negative Syndrome Scale (PANSS) were used to define the first 3 health states.
- The model used a 6-week cycle time, a 2-year maximum time horizon, a US societal perspective, and transition probabilities in each time period that varied by efficacy of treatment.
- Health state transition probabilities were based on baseline and changes in PANSS scores.
  - Transition probabilities were calculated assuming a normal distribution and by estimating the proportion of patients crossing the positive and/or negative PANSS score response thresholds.
  - Two treatment paths were defined: initiating therapy with an earlier atypical antipsychotic ("Atypical 1," based on data for risperidone) versus a later atypical antipsychotic ("Atypical 2," based on data for olanzapine).

Efficacy Parameters

Pooled Trial Data (mean ± SD) for PANSS Positive and Negative Scores at Baseline and End of Study by Treatment Pathway

Treatment	Positive Score at Baseline	End-of-Study Change in Positive Score	Negative Score at Baseline	End-of-Study Change in Negative Score
Atypical 1	21.76±5.97	–5.33±7.02	25.40±6.74	–4.64±7.11
Atypical 2	22.81±5.85	–6.16±7.10	24.03±6.50	–4.65±6.58
Haloperidol	21.71±5.88	–4.13±6.83	24.95±7.11	–3.55±6.44

- Negative symptoms were defined as PANSS negative subscale scores ≥20; positive or negative response was defined as 20% changes from baseline; efficacy data were obtained from all published clinical trials.
  - All patients started in the acute episode state and were assumed to be experiencing positive symptoms at baseline.
- Efficacy was assumed to be independent of position in the treatment pathway and no correlation was assumed between response in positive and negative symptoms.

Discontinuation and Adherence Rates

Discontinuation Rates by Treatment Pathway

Treatment	Discontinuation for Lack of Efficacy	Discontinuation for Lack of Tolerability	Discontinuation for Other Reasons
Atypical 1			
First 12 weeks	0.0670	0.0233	0.0821
Long-term	0.0306	0.0112	0.0267
Atypical 2			
First 12 weeks	0.0328	0.0571	0.0620
Long-term	0.0115	0.0153	0.0199
Haloperidol			
First 12 weeks	0.1284	0.1070	0.0300
Long-term	0.0350	0.0292	0.0082

- It was assumed that 60% of patients continuing therapy were ≥80% adherent.[5]
- Discontinuation rates were taken from published clinical trials,[6,7] and as in clinical practice, are higher for the first 12 weeks than for subsequent weeks.

Relapse Rates

Six-Week Relapse Rates in Patients With ≥80% Adherence by Treatment Pathway

Treatment	Six-Week Relapse Rate
Atypical 1	0.0233
Atypical 2	0.0223
Haloperidol	0.0448
Off drug treatment	0.1600

- Relapse risk at <80% adherence was assumed to be 2.4 times higher than risk at >80% adherence.[8]
- Relapse rates were taken from the Schizophrenia Outpatient Health Outcomes (SOHO) Study for individuals who are a ≥80% adherent to each of the 3 drugs,[9] and pooled placebo-arms from 3 clinical trials for those patients no longer on pharmacotherapy.[10-12]

Adverse Events

Adverse Event Rate by Treatment Pathway

Treatment	Extrapyramidal Symptoms (EPS)	Metabolic Dysfunction	Weight Gain (≥7% Increase)
Atypical 1	23.5%	1.8%	14.0%
Atypical 2	8.8%	9.2%	30.0%
Haloperidol	38.6%	1.2%	11.9%

- EPS rates were taken from the SOHO longitudinal study.[9]
- Metabolic syndrome and weight gain were taken from Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE).[7]

Mortality Rates

- Mortality from all other causes was assumed to be 2.32 times greater than the general US population.[13]
- Mortality was included for suicide as well as all other causes.

Resource Use and Costs

Six-Week Treatment Costs by Health State (in US Dollars)

Health State	Inpatient	Outpatient
Acute episode (cycle 1)	$17,167	$5,089
Acute episode (subsequent cycles)	$0	$6,383
Persistent negative symptoms	$0	$2,448
Response in positive and negative symptoms	$0	$1,224
Fourth-line	$4,292	$3,786

- Unit costs are in 2006 US dollars and are applied to all nondrug resource items.
- Resources included: inpatient and outpatient psychiatrist visits, hospital days, primary care visits, treatment programs (residential, partial residential, and outpatient), and group therapy; outpatient costs for persistent negative symptoms were assumed to be twice that of positive and negative symptom response states.[14]
- AE costs per 6-week period: $50 for EPS, $357 for metabolic syndrome, and $89 for weight gain.
- Fourth-line therapy costs are assumed to equal the mean value for other health states.
- Resource use and cost data were obtained from published sources[15-19] and from the National Association of Psychiatric Health Systems Annual Survey (2005).

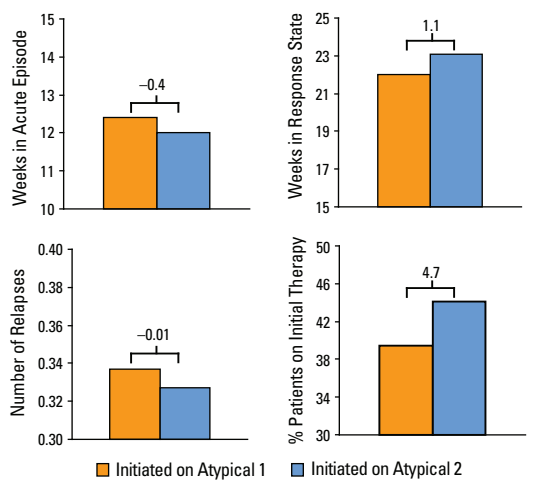
This research was supported by Organon International Inc and Pfizer Inc. This presentation was supported by Organon International Inc

International Society for Pharmacoeconomics and Outcomes Research
10th Annual European Congress
October 20–23, 2007
Dublin, Ireland

Results

Efficacy Implications of Therapeutic Strategies

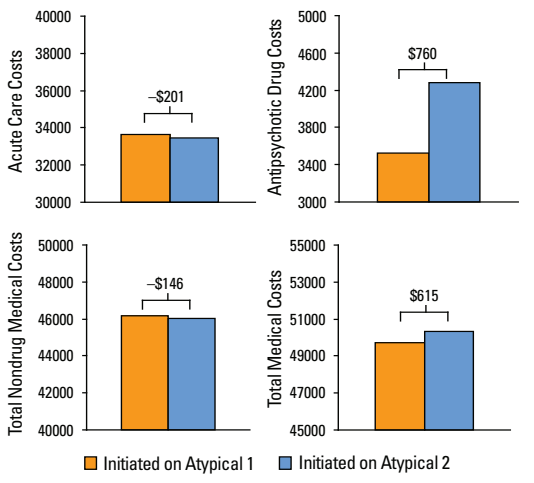
Initiating therapy with Atypical 2 was associated with more time without symptoms.



- Initiating therapy with Atypical 2 reduced time in the acute episode state (12.0 vs 12.4 wk) and lowered the number of relapses (0.327 vs 0.337) at 1 year.
- Initiating therapy with Atypical 2 increased time in the response state (23.1 vs 22.0 wk) and increased the percentage of patients remaining on their initial therapy (44.1% vs 39.4%) at 1 year.

Cost Implications of Therapeutic Strategies

Initiating therapy with Atypical 2 was associated with lower total nonmedical costs.



- Initiating therapy with Atypical 2 was associated with lower acute care costs ($33,445 vs $33,646) and lower annual total nondrug costs in all states ($46,041 vs $46,187).
- Initiating therapy with Atypical 2 was associated with higher antipsychotic drug costs ($4,279 vs $3,519) and higher total medical care costs ($50,321 vs $49,706).
- When taken together, the first year costs of initiating therapy with Atypical 2 exceeded the costs of initiating therapy with Atypical 1 by $615.

Conclusions

- **Starting treatment with a later atypical antipsychotic (represented by Atypical 2) rather than with an earlier atypical antipsychotic (represented by Atypical 1) may result in more time without symptoms and lower nondrug healthcare costs during the first year of treatment.**
- **Differences in nondrug healthcare costs are primarily due to differential efficacy. Differences in discontinuation and relapse rates are additional costs.**

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