Effectiveness of Antipsychotic Therapy in a Naturalistic Setting: A Comparison Between Risperidone, Perphenazine, and Haloperidol

Kim C. Coley, Pharm.D.; Cameron S. Carter, M.D.; Stacey V. DaPos, M.S.; RaeAnn Maxwell, Ph.D.; John W. Wilson, Ph.D.; and Robert A. Branch, M.D.

Background: Therapeutic ineffectiveness and noncompliance with antipsychotic agents are major contributors to rehospitalization in patients with psychotic disorders. It is unknown whether risperidone's favorable side effect profile compared with that of the conventional antipsychotics results in improved compliance and reduced hospitalizations in a naturalistic setting. The purpose of this study was to test the hypothesis that treatment with risperidone reduces readmission rates and associated costs when compared with treatment with perphenazine or haloperidol.

Method: Inpatients prescribed either risperidone, perphenazine, or haloperidol between January 1, 1995, and December 31, 1995, as a single oral antipsychotic at discharge were retrospectively identified. Data were collected for that index hospitalization and for a 1-year follow-up period. Primary outcome measures included readmission rates, changes in antipsychotic therapy, anticholinergic drug use, and costs.

Results: There were 202 evaluable patients (81 treated with risperidone, 78 with perphenazine, and 43 with haloperidol). Baseline demographics were similar between groups except that more patients in the risperidone group had a primary diagnosis of psychotic disorder or had been hospitalized in the year prior to study. The percentage of patients readmitted during the 1-year follow-up period was similar among drug groups (41% risperidone, 26% perphenazine, and 35% haloperidol) when controlled for baseline differences in diagnosis and hospitalization history ($p = .32$). Anticholinergic drug use was more common in the haloperidol group ($p = .004$). Mean yearly cost (drug + hospitalization) in the risperidone group was $20,317, nearly double that in the other treatment groups ($p < .001$).

Conclusion: The results from this naturalistic study indicate that the high cost of risperidone is not offset by a reduction in readmission rates when compared with conventional antipsychotics.

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Received Dec. 1, 1998; accepted May 26, 1999. From the Center for Clinical Pharmacology (Drs. Coley, Wilson, and Branch), the Department of Psychiatry (Dr. Carter), Medical Archival Systems, (Ms. DaPos), and the Department of Pharmacy (Dr. Maxwell), University of Pittsburgh Medical Center, Pittsburgh, Pa.

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Reprint requests to: Kim C. Coley, Pharm.D., Center for Clinical Pharmacology, 623 Scaife Hall, University of Pittsburgh, Pittsburgh, PA 15213.

Although adults with schizophrenia account for only 1% of the population, the resultant economic burden on the health care system is tremendous. Despite an increasing shift toward outpatient management, it is estimated that over 80% of the direct costs of treating schizophrenia are due to hospitalization and nursing home care.[1] Maintenance on antipsychotic therapy is considered to be the single most important factor in preventing rehospitalization in this population.[2,3]

Antipsychotic drugs such as haloperidol are associated with many side effects that often necessitate treatment changes or lead to noncompliance. The most troublesome of these effects are extrapyramidal symptoms (EPS), which include akathisia, pseudoparkinsonism, and dystonia. Tardive dyskinesia is another disturbing side effect that is associated with long-term use of antipsychotic agents. It can be irreversible in some patients and continues to be a medical and legal challenge to practitioners.

It was not until the first atypical antipsychotic, clozapine, was introduced that physicians had an effective agent with a low propensity to cause EPS and tardive dyskinesia. However, the risk of agranulocytosis with clozapine (1%–2%) has limited its use to treatment-resistant patients.[4] Several new atypical antipsychotics have recently been introduced that offer efficacy similar to that of the conventional antipsychotic agents with a low incidence of EPS. The first of these agents, risperidone, was marketed in 1994 and rapidly became one of the most commonly prescribed antipsychotics at Western Psychiatric Institute and Clinics (WPIC) at the University of Pittsburgh Medical Center (UPMC).[5]

Risperidone has been shown to have efficacy similar to that of the conventional antipsychotics in controlled clinical trials.[6–8] These studies also demonstrate that risperi-

done has a low propensity for inducing EPS at doses less than 6 mg/day. The improved side effect profile of risperidone has not come at a low price. Risperidone costs over 100 times that of an equivalent dose of haloperidol. During its first year of availability, risperidone accounted for 77% of the total cost of antipsychotics purchased at WPIC, and its total cost to the institution exceeded that for the entire antipsychotic budget in the previous year.[5] Drug costs alone, however, cannot be the only consideration when choosing the most efficient therapy. If a drug such as risperidone can reduce hospitalization rates, it might prove to be the most cost-effective treatment.

Only a few studies have been published that evaluate the financial impact of risperidone.[9–12] Although these trials provide some insight into the cost-effectiveness profile of the drug, they are limited in several aspects. Some studies evaluate only patients who are treatment responders or patients enrolled in controlled clinical trials. This patient sample does not accurately reflect medication use in the real-world setting, where patients may not respond to treatment or may be noncompliant. Other studies only evaluate the impact of risperidone in treatment-intolerant or treatment-resistant patients. An important limitation of many of these studies is that they compare patients in a pretreatmemt to posttreatment fashion. Although the threshold for admission to the hospital has probably not changed over time, many institutions continue to decrease overall length of stay as part of cost-cutting measures. As a result, a drug could appear to shift resource utilization from an inpatient to outpatient setting when in fact the change was due to changes in clinical practice. Providing an active control population as a comparison would account for these changes in hospitalization patterns. Therefore, we set out to determine whether risperidone could reduce hospitalization rates and subsequent costs compared with 2 conventional antipsychotics in patients treated in a naturalistic setting.

METHOD

This was a retrospective study of inpatients at WPIC, a 279-bed psychiatric hospital that is part of the UPMC Health System. WPIC provides psychiatric care to the Pittsburgh metropolitan area and serves as a referral center for patients throughout southwestern Pennsylvania. This study was approved by the institution review board.

Patients were included if they were admitted to WPIC between January 1, 1995, and December 31, 1995, and were discharged on treatment with either risperidone, haloperidol, or perphenazine as a single oral antipsychotic agent (index hospitalization). Patients were excluded if they received more than one antipsychotic agent at discharge or were receiving decanoate injections. Patients who did not have electronic medical abstracts or discharge summaries for their index hospitalization were excluded from the analysis. No patients were excluded based on the indication for which these drugs were prescribed or on their past antipsychotic drug use history. This study was designed as an intent-to-treat protocol. Once a patient was discharged on his/her index drug, all clinical outcomes and costs were attributed to that index drug.

Patients were identified using the Medical Archival System (MARS) at the UPMC. MARS is a large-scale medical data archiving system that integrates patient data from various inpatient and outpatient UPMC information systems.[13] Data from central transcription, laboratory, pharmacy, radiology, and other departmental systems in the UPMC hospitals and clinics are contained in a comprehensive whole-text–indexed relational database. Demographic data were extracted from each patient's medical abstract (Medipac), history, and physical and discharge summary for the index hospitalization.

The primary efficacy outcomes were readmission rates in the 1 year following the index hospitalization and changes in index antipsychotic treatment on readmission. Subset analyses were conducted for patients with a primary diagnosis of psychotic disorder, for those patients with a history of hospitalization in the year prior to study entry, and for patients in the WPIC catchment area. The number of admissions in the year prior to study was collected as a surrogate marker for the severity of illness. *Catchment* is a term that describes the area of permanent residence of the patient. Patients living in the WPIC catchment who require hospitalization would most likely receive subsequent psychiatric care at WPIC.

Safety and side effects were measured by EPS reports during the index hospitalization and anticholinergic drug use at discharge. Anticholinergic drug prescriptions were used as surrogate markers for the occurrence of EPS in study patients. Actual EPS were identified by reviewing the UPMC adverse drug reaction monitoring database as well as conducting chart reviews of patients receiving injectable anticholinergics.

Cost Analysis

An assessment of the economic impact of treatment selection was based on the cost associated with index antipsychotic selection, readmissions to WPIC, and lengths of stay during 1 year after the index hospitalization. Antipsychotic costs were estimated based on the 1995 Health Care Financing Administration federal upper price limit for multisource products (perphenazine, haloperidol) or the average wholesale price (risperidone) of the discharge antipsychotic and the dose at discharge from the index hospitalization. The daily cost of the discharge dosing regimen was multiplied by 365 to determine the yearly drug cost. Hospital costs were calculated based on the UPMC Medicare per diem cost in 1995, which was $813 per day. This rate was multiplied by the actual lengths of stay for readmissions during the 1-year follow-up period.

Table 1. Patient Demographics[a]

Variable	Risperidone N = 81	Perphenazine N = 78	Haloperidol N = 43	p Value[b]
Age, y				
Mean	40.6	42.3	42.7	.92
Range	11–82	12–94	8–94	
Gender, % M/F	43/57	42/58	49/51	.78
Race, % white	63	71	53	.18
Highest mean GAF score from previous year	53	51	51	.76
Mean discharge GAF score from index hospitalization	57	55	55	.42
≥ 2 previous antipsychotics other than index, N (%)	13 (16)	5 (6)	3 (7)	.13
Patients hospitalized in the year prior to index hospitalization, N (%)	27 (33)	14 (18)	8 (19)	.05
Mean hospitalization days in the year prior to index hospitalization	21	26	30	.45
Median dose at discharge from index hospitalization, mg/d	4	10	4	...

[a]Abbreviation: GAF = Global Assessment of Functioning scale.
[b]p Values are from Kruskal-Wallis or Fisher exact test (2-tailed).

Table 2. Primary DSM-IV Diagnosis

	Risperidone N = 81		Perphenazine N = 78		Haloperidol N = 43	
Diagnosis	N	%	N	%	N	%
Psychotic disorder[a]	35	43	19	24	16	37
Mood disorder	35	43	41	53	15	35
Dementia	4	5	12	15	5	12
Childhood disorder	1	1	1	1	4	9
Other	6	7	5	6	3	7

[a]p =.04, 2-tailed chi-square.

Data Analysis

Associations between baseline factors and drug groups were tested using the Fisher exact test and the Wilcoxon rank sum test. Associations between drug groups and readmission (yes/no) and time to first readmission were examined using logistic regression and proportional hazards regression, respectively. A plot of readmission-free period by drug group was prepared using the Kaplan-Meier approach. Associations between drug group and cost were analyzed using a median test. Each patient was coded as above or below the median cost over all 3 drug groups. This binary outcome was then used as the response variable in logistic regression models.

All regression analyses (including the cost analysis) were adjusted for differences between the baseline populations. First, models were fit allowing confounding variables (e.g., admission during the year prior to the index admission, history of prior antipsychotic use, primary diagnosis) to predict outcome (e.g., readmission). Then, drug group was added to the model and was assessed for statistical significance using a likelihood ratio test. Thus, drug group was not considered significant in the adjusted analysis unless it provided substantial additional predictive power for the outcome beyond that provided by the confounding variable alone.

RESULTS

Patient Population

There were 226 patients who met inclusion criteria. Medical abstracts were not available on 24 patients, and they were dropped from the analysis. Of the 202 evaluable patients, 81 received risperidone, 78 received perphenazine, and 43 received haloperidol. The groups were similar with respect to age, gender, race, and Global Assessment of Functioning (GAF) scores (Table 1). More patients in the risperidone group were hospitalized during the 1 year prior to the index hospitalization (p = .05). Although not statistically significant, there were more patients in the risperidone group who had been treated with 2 or more antipsychotics (other than the index agent) prior to the index admission (p = .13). The antipsychotic doses at discharge from the index hospitalization were at the low end of the dose-response curve for all 3 agents. The median doses were 4 mg/day for risperidone, 10 mg/day for perphenazine, and 4 mg/day for haloperidol.

Table 2 lists the primary DSM-IV psychiatric diagnosis of patients in the study. More patients in the risperidone group had a primary diagnosis of psychotic disorder (p = .04). Perphenazine was prescribed slightly more often in patients with mood disorder (p = .16). The numbers of patients with a history of substance abuse anywhere in their diagnosis fields were evaluated, and the numbers were found to be similar among the 3 treatment groups (36% risperidone, 28% perphenazine, 37% haloperidol; p = .48).

Response to Treatment

Table 3 describes treatment outcomes in the 3 groups. There were more patients in the risperidone group who were readmitted during the 1-year follow-up period. Forty-one percent of all risperidone-treated patients were readmitted compared with 26% of perphenazine patients and 35% of haloperidol patients. This difference, however, did not reach statistical significance when controlled for differences in the baseline characteristics. Figure 1 represents the time to first readmission for each treatment group. There was no difference between groups with respect to time to first readmission when adjusted for baseline characteristics (p > .26, proportional hazards regression). The mean number of hospitalization days during the 1-year follow-up was slightly higher in the risperidone group at 22 days compared with perphenazine and haloperidol at 12 and 14 days, respectively (p = .13). Treatment switches from the index antipsychotic to a different antipsychotic agent were compared for those patients who were readmitted (see Table 3). Thirty-three percent of risperidone patients were switched to a different antipsy-

Table 3. Outcomes for 1-Year Follow-Up

Outcome	Risperidone N = 81	Perphenazine N = 78	Haloperidol N = 43	p Value
Readmissions				
Unique patients, N (%)	33 (41)	20 (26)	15 (35)	.32[a]
Total readmissions	73	49	26	
Mean (SE) hospitalization days during 1-year follow-up	22 (4.2)	12 (2.9)	14 (3.4)	.13[b]
Change of therapy on readmission, N (%)	10/33 (33)	5/20 (25)	5/15 (33)	.86[c]

[a]p Value is from logistic regression controlled for differences in baseline characteristics.
[b]p Value is from Wilcoxon rank sum test.
[c]p Value is from 2-tailed chi-square test.

Figure 1. Time to First Readmission by Index Drug

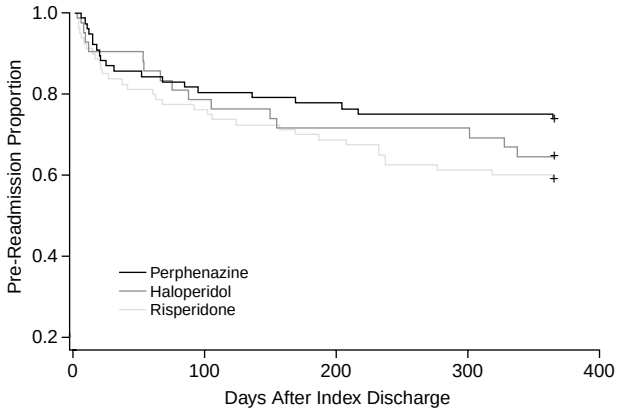


Table 4. Overall Treatment Success

Drug	N	Never Readmitted	Readmitted Treatment Success	Overall Treatment Success[a]
Risperidone	81	48	17	65 (80%)
Perphenazine	78	58	10	68 (87%)
Haloperidol	43	28	10	38 (88%)

[a]p = .40, Fisher exact test.

Table 5. Response to Treatment: Subset Populations[a]

Variable	Risperidone	Perphenazine	Haloperidol	p Value[b]
No prior hospitalizations, N	54	64	35	
Readmissions, N (%)	16 (30)	16 (25)	11 (31)	.68
Prior hospitalizations, N	27	14	8	
Readmissions, N (%)	17 (63)	4 (29)	4 (50)	.05
Primary psychotic disorder, N	35	19	16	
Readmissions, N (%)	16 (46)	5 (26)	6 (38)	.24
WPIC catchment area, N	27	21	10	
Readmissions, N (%)	13 (48)	7 (33)	4 (40)	.38

[a]Abbreviation: WPIC = Western Psychiatric Institute and Clinics.
[b]p Values are for risperidone vs. perphenazine, 2-tailed Fisher exact test.

Table 6. Safety Data From Index Hospitalization[a]

Variable	Risperidone N = 81	Perphenazine N = 78	Haloperidol N = 43
Patients receiving anticholinergic agents, N (%)[b]	16 (20)	23 (30)	21 (49)
EPS during index admission, N (%)	7 (8)	4 (5)	5 (12)
Mean daily dose at which EPS occurred	4.5 mg	11.5 mg	5.6 mg

[a]Abbreviation: EPS = extrapyramidal symptoms.
[b]p = .004, Fisher exact test.

chotic on readmission. This rate was similar to that observed in the perphenazine and haloperidol treatment groups (p = .86).

Although any readmission can be considered a treatment failure, we evaluated the rationale for changes in antipsychotic therapy at readmission. If patients continued on treatment with their index antipsychotic agent during the year follow-up period despite being readmitted, we classified them as a treatment success. If patients were taken off their index antipsychotic for reasons other than treatment failure or an adverse drug reaction and no other antipsychotic was instituted, they were also classified as a treatment success. No differences in overall treatment success among the 3 treatment groups were found when these criteria were utilized (Table 4).

Subset analyses were conducted based on previous hospitalization history, primary diagnosis of psychotic disorder, and residence in the WPIC catchment area (Table 5). Readmission rates were similar among groups for patients who were not hospitalized at WPIC during the previous year. However, for patients with a history of hospitalization during the previous year, risperidone-treated patients had a higher readmission rate compared with perphenazine patients (p = .05). Readmission rates were similar between risperidone- and haloperidol-treated patients. When comparing those patients with a primary diagnosis of psychotic disorder, more patients in the risperidone group were readmitted compared with the perphenazine group. However, this difference did not reach statistical significance (p = .24). These findings demonstrate that risperidone-treated patients did not have better outcomes with respect to hospitalization rates when compared with similar patients treated with conventional antipsychotics.

Anticholinergic Use and EPS

Table 6 describes anticholinergic drug use and EPS occurrences in the study population during the index hospitalization. Concomitant use of anticholinergic drugs was significantly lower in the risperidone and perphenazine patients (20% and 30%, respectively) compared with the patients receiving haloperidol (p = .004). Nearly half of the haloperidol-treated patients received a prescription for an anticholinergic agent. The number of EPS reported dur-

Figure 2. Drug Therapy Mean Yearly Cost

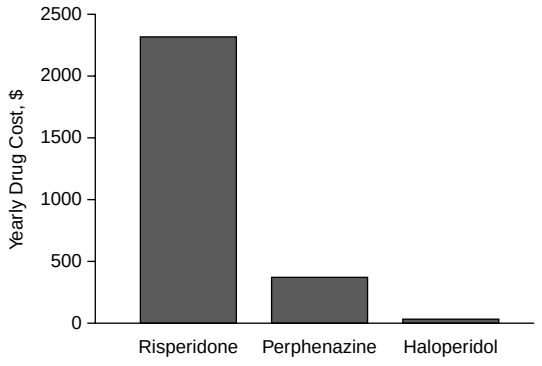
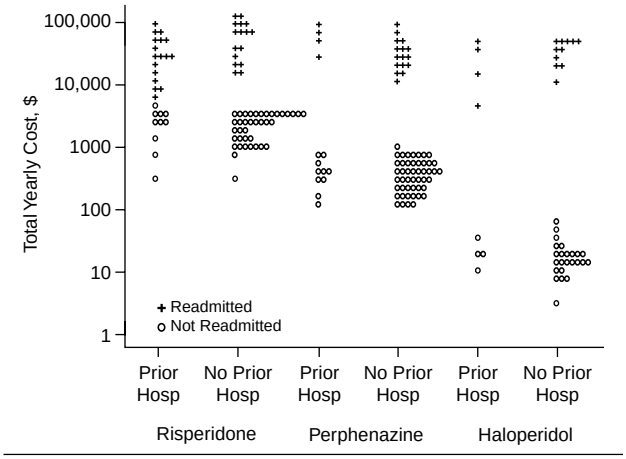


Figure 3. Total Estimated Cost by Prior Hospitalization (Hosp) History



ing the index admission was similar between the 3 treatment groups ($p = .42$). The mean antipsychotic doses at which EPS occurred were low for all 3 agents. The mean daily dose for which EPS occurred in the risperidone-treated patients was 4.5 mg (range, 2–8 mg). EPS occurred in the perphenazine- and haloperidol-treated patients at mean doses of 11.5 mg and 5.6 mg, respectively.

Costs

The cost associated with drug therapy alone was significantly higher for risperidone than the other agents (Figure 2). The estimated yearly mean cost of risperidone based on average wholesale price was $2321 per patient, compared with $364 for perphenazine and $21 for haloperidol. The high drug cost of risperidone was not offset by a reduction in readmission days and their associated costs. The total costs of treatment (drug cost plus readmission cost) in the risperidone group were higher than in the other treatment groups ($p < .001$) when controlled for prior admission history and previous antipsychotic use (Figure 3). The mean cost of treatment with risperidone was $20,317 per patient during the year following the index hospitalization. This cost was nearly double that of perphenazine at $10,298 and haloperidol at $11,459.

CONCLUSION

The atypical antipsychotics are rapidly becoming the treatment of choice for the management of psychotic disorders. Several prospective studies have been published that demonstrate their equal efficacy and improved side effect profiles compared with the conventional antipsychotics.[6–8,14–16] Since these agents are significantly more expensive than older agents such as haloperidol, it is necessary to determine whether they are cost-effective. Only a few trials have been published that attempt to evaluate the cost-effectiveness of the atypical antipsychotics.[9–12]

To evaluate the clinical and economic outcomes of treatment in a real-world setting, we tested the hypothesis that risperidone was more efficacious than either perphenazine or haloperidol. The results of this naturalistic study demonstrate that treatment with risperidone does not improve patient outcomes as measured by hospitalization rates when compared with conventional antipsychotics. Indeed, the higher readmission rates and subsequent hospitalization days resulted in significantly higher costs in the risperidone population.

Analysis of the baseline characteristics of our 3 treatment groups demonstrated that they were similar with the exception that more patients in the risperidone group had been hospitalized in the year prior to the study period. In addition, slightly more risperidone patients had received 2 or more antipsychotics previously. These data suggest that more patients in the risperidone group were treatment resistant. When analyzing the primary outcome measures of readmissions and cost, we controlled statistically for this difference in the 3 treatment groups. Despite this, risperidone offered no advantage to the conventional agents with respect to hospitalization rates and was associated with significantly higher costs. Indeed, of patients who were hospitalized prior to the study period, those treated with risperidone were readmitted more frequently than patients receiving perphenazine.

Our findings differ from those of other published reports that have evaluated outcomes and costs of treating patients with risperidone.[9–12] Addington and colleagues[9] conducted a retrospective analysis to determine whether treatment with risperidone resulted in a reduction in hospitalization days during a 1-year follow-up period. They report a 20% reduction in hospitalization days after the initiation of risperidone. One limitation of that study was that only patients who were successfully maintained on risperidone treatment during the follow-up were included in the analysis. Sixty-four percent of the patients who were initiated on risperidone treatment were not eligible

for analysis. Reasons for withdrawal included insufficient treatment response, adverse drug effects, and noncompliance. In addition, only patients with a primary diagnosis of schizophrenia were included. Since that study compared hospitalization days pretreatment and posttreatment, reduction in hospitalization days due to factors other than drug therapy could not be controlled. Our study evaluated a broad range of patients with multiple diagnoses and included those who were treatment resistant as well as patients with no prior history of antipsychotic use.

Albright and colleagues[10] described the economic impact of risperidone in a retrospective cohort of 146 patients with treatment-resistant schizophrenia who resided in Saskatchewan, Canada. A 60% reduction in hospital admissions and a 58% decrease in length of stay was observed after approximately 10 months of treatment. Although the annual cost of drug treatment was increased by Can $1172/patient/year, the overall cost of treatment decreased by Can $7925/patient/year based on cost savings achieved with reduced hospitalization, physician services, and mental health services. Those results clearly conflict with the present study. However, as with the Addington et al. study, the evaluation by Albright et al. did not account for reductions in length of stay that may occur over time.

Only 2 studies have been published that include patients who failed treatment with risperidone in their analyses.[11,12] The first was a 2-year retrospective cohort of 50 patients who were either treatment intolerant or treatment resistant to other antipsychotics who were then treated with risperidone.[11] This intent-to-treat analysis found that responders to risperidone, with response defined as successful treatment with risperidone during the entire 12-month follow-up, had a reduction in hospitalization days compared with their baseline period. There was no difference in hospitalization days in patients who were nonresponders. The overall reduction in inpatient days resulted in a net annual savings of $147,962. The second study evaluated 139 patients initiated with risperidone who were either treatment intolerant or treatment resistant to other antipsychotics.[12] This retrospective study demonstrated a shift in resource utilization from provider-delivered services (e.g., acute inpatient care stays, skilled nursing facility) to ambulatory services such as community living and residential treatment. However, the costs of treatment with risperidone in this study were not offset by savings associated with the shift to lower cost services.

Although our study was also designed as an intent-to-treat protocol, it differs from the other published trials primarily in that we compared risperidone with 2 active controls during the same time frame. Hospitalization rates were compared between groups instead of with the period prior to antipsychotic initiation. This design allowed us to control for overall reductions in length of stays that occurred at our institution as a result of increasing pressure to control costs. Our goal in selecting an intent-to-treat study design was to account for the outcomes of all patients, including those who may be noncompliant or treatment resistant. We did not restrict our sample to patients with a primary diagnosis of psychotic disorder since it was apparent that physicians were prescribing these agents in patients with multiple psychiatric conditions.

One limitation to our study is that we did not evaluate outpatient services in our cost analysis since these services are not captured in our database. Based on our findings, however, if risperidone use was also associated with an increase in the use of outpatient services, this would have only had a more adverse effect on overall costs. Another limitation to our study, inherent to the naturalistic design, was that physician selection of drug could have introduced bias. We considered that such bias could have been based on illness severity. We did, therefore, control for illness severity (as measured by prior hospitalization history, prior antipsychotic use, and diagnosis) in our analysis both statistically and by evaluating comparable subset populations between groups. Despite these measures, patients receiving risperidone did not have better outcomes than those patients receiving the conventional agents.

We also set out to determine the relative safety with respect to EPS between risperidone and the other antipsychotics. Anticholinergic drug prescriptions were used to assess the EPS risk in our patient population. Twenty percent of risperidone-treated patients received a prescription for an anticholinergic drug at discharge from their index hospitalization. This incidence is similar to that reported in prospective studies.[6,17] Patients receiving risperidone or perphenazine were less likely to be prescribed anticholinergics than those patients receiving haloperidol. There was no difference in anticholinergic drug use between the risperidone- and perphenazine-treated patients. These findings are consistent with those in a prospective study by Hoyberg et al.[8] comparing risperidone and perphenazine. That study reported similar use of antiparkinsonian drugs as well as EPS ratings between treatment groups. Conversely, our findings differ with those of a recently published study,[18] which found risperidone to be superior to conventional antipsychotics in causing EPS. That study, however, groups all the conventional antipsychotics together in the analysis, and the majority of patients were receiving antipsychotics with a high propensity to induce EPS. The number of EPS reported in our study for all 3 agents was low. This is most likely due to a number of factors, including the relatively low doses of antipsychotics used as well as a high threshold for EPS reporting in our referral psychiatric center.

One issue not addressed in this study is the risk of tardive dyskinesia in patients treated with these agents. Our safety data raise the issue of whether risperidone would be less likely to cause tardive dyskinesia compared with perphenazine since anticholinergic drug use in our evalu-

ation was similar between risperidone- and perphenazine-treated patients. Prospective studies with long-term follow-up are necessary to determine whether risperidone has a lower propensity to induce tardive dyskinesia.

Despite the high cost of the atypical antipsychotics, their use is increasing and will continue to grow with the arrival of new agents to the marketplace. Our study does not support the hypothesis that the cost of these agents is offset by improved patient outcomes as measured by a reduction in inpatient stays.

Drug names: clozapine (Clozaril and others), haloperidol (Haldol and others), perphenazine (Trilafon and others), risperidone (Risperdal).

REFERENCES

1. Rupp A, Keith SJ. The costs of schizophrenia. Psychiatr Clin North Am 1993;16:413–423
2. Doering S, Muller E, Kopcke W, et al. Predictors of relapse and rehospitalization in schizophrenia and schizoaffective disorder. Schizophr Bull 1998;24:87–98
3. Schooler NR, Keith SJ, Severe JB, et al. Relapse and rehospitalization during maintenance treatment of schizophrenia: the effects of dose reduction and family treatment. Arch Gen Psychiatry 1997;54:453–463
4. Fitton A, Heel RC. Clozapine: a review of its pharmacological properties and therapeutic use in schizophrenia. Drugs 1990;40:722–747
5. Carter CS, Mulsant BH, Sweet RA, et al. Risperidone use in a teaching hospital during its first year after market approval: economic and clinical implications. Psychopharmacol Bull 1995;31:719–725
6. Marder SR, Meibach RC. Risperidone in the treatment of schizophrenia. Am J Psychiatry 1994;151:825–835
7. Chouinard G, Jones B, Remington G, et al. A Canadian multicenter placebo-controlled study of fixed doses of risperidone and haloperidol in the treatment of chronic schizophrenic patients. J Clin Psychopharmacol 1993;13:25–40
8. Hoyberg OJ, Fensbo C, Remvig J, et al. Risperidone versus perphenazine in the treatment of chronic schizophrenia patients with acute exacerbations. Acta Psychiatr Scand 1993;88:395–402
9. Addington DE, Jones B, Bloom D, et al. Reduction of hospital days in chronic schizophrenic patients treated with risperidone: a retrospective study. Clin Ther 1993;15:917–926
10. Albright PS, Livingstone S, Keegan DL, et al. Reduction of healthcare resource utilization and costs following the use of risperidone for patients with schizophrenia previously treated with standard antipsychotic therapy. Clin Drug Invest 1996;11:289–299
11. Finley PR, Sommer BR, Corbitt JL, et al. Risperidone: clinical outcome predictors and cost-effectiveness in a naturalistic setting. Psychopharmacol Bull 1998;34:75–81
12. Viale G, Mechling L, Maislin G, et al. Impact of risperidone on the use of mental health care resources. Psychiatr Serv 1997;48:1153–1159
13. Yount RJ, Vries JK, Councill CD. The Medical Archival System: an information retrieval system based on distributed parallel processing. Information Process Manage 1991;27:379–389
14. Tollefson G, Beasley CM, Tran P, et al. Olanzapine versus haloperidol in the treatment of schizophrenia and schizoaffective disorders: results of an international collaborative trial. Am J Psychiatry 1997;154:457–465
15. Peuskens J, Link CGG. A comparison of quetiapine and chlorpromazine in the treatment of schizophrenia. Acta Psychiatr Scand 1997;96:265–273
16. Arvanitis LA, Miller BG, and the Seroquel Trial 13 Study Group. Multiple fixed doses of Seroquel (quetiapine) in patients with acute exacerbation of schizophrenia: a comparison with haloperidol and placebo. Biol Psychiatry 1997;42:233–246
17. Simpson GM, Lindenmayer JP. Extrapyramidal symptoms in patients treated with risperidone. J Clin Psychopharmacol 1997;17:194–201
18. Miller CH, Mohr F, Umbricht D, et al. Prevalence of acute extrapyramidal signs and symptoms in patients treated with clozapine, risperidone, and conventional antipsychotics. J Clin Psychiatry 1998;59:69–75