Cost and Outcome Implications of Using Typical and Atypical Antipsychotics in Ordinary Practice in Italy

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Background: It is uncertain whether atypical antipsychotic agents, as prescribed in ordinary practice, are a cost-effective alternative to conventional agents. This study examined the financial and clinical implications of using atypical antipsychotics in the context of community psychiatric care in Italy.

Method: Service costs and outcome data over a 24-month period (June–November 1999 to June–November 2001) were compared between 2 cohorts of ICD-10–diagnosed subjects, the first including patients receiving atypical and the second typical antipsychotics, according to the type of treatment received at the beginning of the study.

Results: At baseline, 183 subjects were under treatment with antipsychotic drugs, of whom 73 were treated with atypical agents. Most patients had a diagnosis of schizophrenia and only a minority were first-contact patients. Conventional antipsychotics were used in more chronic and elderly patients, while atypicals were prescribed in more severe and recently diagnosed cases. After background group differences were controlled for, the use of atypical agents was neither predictive of higher total health care costs nor of better patient outcome. Predictors of higher costs and better outcome were severity of illness at baseline and first-contact patients.

Conclusions: The introduction of atypical agents had a small impact in terms of total health care costs and outcome, and more important than the agent prescribed was the severity of illness.

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Over the last 10 years, second-generation antipsychotic agents, also known as atypical antipsychotics, have been licensed in several countries on the basis of evidence derived from experimental studies conducted in patients with schizophrenia and related disorders.[1] These studies have suggested that atypical agents induce fewer extrapyramidal adverse effects than conventional antipsychotic drugs, improve patient compliance, and reduce the number of hospital admissions and hospital length of stay. As a consequence, despite the increased acquisition costs, atypical agents appear no more expensive for the health care system. Clozapine is considered as a cost-effective tool for managing patients with treatment-refractory schizophrenia, while the other atypicals are considered cost neutral.[2–4]

However, it is still under debate whether atypical agents, as prescribed in ordinary practice, represent a cost-effective alternative to conventional agents. In fact, research findings from highly selected patients, followed-up over short periods, are hardly applicable to heterogeneous populations of everyday patients who receive antipsychotic treatment, and many other psychotropic drugs, for long periods.[5–7] The present study was therefore carried out to evaluate the cost and outcome implications of using atypical agents, as prescribed in the context of community psychiatric care in Italy. The following research questions were addressed: Are there differences in terms of sociodemographic and clinical characteristics between patients receiving typical and atypical drugs? Is the use of atypical agents cost neutral or cost saving? Is the use of atypical agents associated with better patient outcome in comparison with typical agents? Are there predictors of total health care costs and clinical outcome in patients treated with typical and atypical antipsychotic drugs?

METHOD

Study Area

This study was carried out in the Department of Mental Health of Legnano, a town located in northern Italy. The department is in charge of managing all public psychiatric services provided to residents in this area (390,000 persons). These services include 2 psychiatric wards provid-

ing inpatient care and 5 community mental health centers providing outpatient, domiciliary, and rehabilitative care. All but emergency cases are expected to have their first contact with these facilities. A network of psychiatric residential facilities provides long-term residential care. A more detailed description of the study area is presented elsewhere.[8]

Study Sample

During a 6-month recruitment period (June–November 1999), 3 community mental health centers enrolled all first-contact patients and a randomly chosen sample of 20% of ongoing patients with the ICD-10 diagnoses of schizophrenia and related disorders (F2 categories), bipolar affective disorder (F31), and recurrent depressive disorder (F33).[9] Patients who were receiving antipsychotic treatment at enrollment were selected from the whole sample. Two cohorts of subjects were defined, the first including patients on atypical and the second on typical drugs, according to the type of treatment received at the beginning of the study. At the time of recruitment, the atypical agents available in Italy were clozapine, olanzapine, and risperidone. Patients receiving at baseline both typical and atypical antipsychotics were allocated to the atypical agent cohort. The 2 cohorts were prospectively followed for 2 years (through June–November 2001).

Outcome Measures

A clinical and psychosocial assessment was carried out by means of the Brief Psychiatric Rating Scale (BPRS),[10] Global Assessment of Functioning Scale (GAF),[11] Disability Assessment Schedule (WHODAS II),[12] and Health of the Nation Outcome Scale (HoNOS),[13] a simple tool that has been found to be useful as a present state profile in the context of everyday clinical practice. Patients were assessed at baseline and at the end of the second year of follow-up.

Cost Evaluation

Cost estimation followed a 2-step procedure.[14] First, information on all health care services provided to patients during the 2-year period was gathered from the local Psychiatric Information Computerized System. According to this system, each service is recorded at the time it is provided to patients. Second, a monetary value was assigned to each service. Total costs for each patient were determined by multiplying the units of resources consumed by the specific unit costs. Average costs per patient per year were then calculated. The following service units were used in the study: days spent in hospital, days spent in residential facilities, and number of interventions provided by the community mental health centers. Costs were calculated according to a full cost accounting procedure based on information collected from the Department of Mental Health and from the administrative sections of the Legnano Health Authority.[14] Full cost refers to a methodology of cost accounting that identifies and measures in monetary terms all resources used to achieve an objective (e.g., hospital days, psychiatric visits, rehabilitative group interventions). This methodology comprises costs directly attributable to the provision of services and a "fair" share of overheads. Costs per hospital day accounted for 210 euro; psychiatric visits and psychologist consultations accounted for 54 euro and 55 euro, respectively. Nurse domiciliary interventions cost 40 euro, while the unit cost of social worker services ranged from 20 euro to 111 euro. On average, rehabilitation group therapies had a total cost of 103 euro per intervention (17 euro per client). Italian lire were converted into euro according to the rates that went into effect in January 1999 (1,936.27 Italian lire for 1 euro). Other details on the unit costs of services provided by the local community mental health centers have been previously reported.[14]

Information on psychotropic drug use, including drug names, dosages, and length of therapy, was collected from clinical records. This source of information was in addition used to gather detailed information on laboratory tests and general practitioner (GP) visits during the study period. Unit costs for laboratory tests and GP consultations were derived from the Italian National Health Service fee schedule,[15] and drug costs were taken from the price list of the Italian National Formulary. At the time of the study, the costs per tablet of atypicals were as follow: risperidone 1-mg tablet = 0.91 euro, olanzapine 10-mg tablet = 5.68 euro, clozapine 100-mg tablet = 1695 euro, haloperidol 5 mg-tablet = 0.17 euro.

Statistical Analyses

Categorical data were analyzed by chi-square statistics, and Mann-Whitney 2-sample statistics were used to analyze continuous data that were not normally distributed. When assessing the magnitude of difference between baseline and follow-up assessments, an estimate of the effect size (ES) was calculated. Operationally, the magnitude of change was calculated as the ratio of the difference between baseline and follow-up scores to the standard deviation (SD) of the score at baseline [mean baseline – mean follow-up/SD].[16] An effect size of 0 indicates no improvement; an effect size of 0.2 is considered a small, 0.5 a medium, and 0.8 a large improvement.

Costs were calculated by multiplying the resources consumed during the 2 years by their unit costs as identified above. Since some patients remained in the study for less than 2 years, service use and costs were normalized to 12 months. Costs are presented in euro (at the time of the study X1 = US $0.893).

Linear regression analysis was run to assess the association between the dependent variables total health care costs and effect size of improvement on the BPRS and the following independent variables: age (years),

gender (female = 0, male = 1), unemployment (no = 0, yes = 1), living alone (no = 0, yes = 1), first-contact patient (no = 0, yes = 1), diagnosis (other = 0, schizophrenia = 1), BPRS at baseline (score), risperidone (no = 0, yes = 1), clozapine (no = 0, yes = 1), olanzapine (no = 0, yes = 1). A nonparametric bootstrap method of statistical accuracy was used, assuming that the observed distribution of the present sample was a good estimate of the true population distribution.[17]

RESULTS

Sociodemographic Information and Psychiatric History

During the 6-month recruitment period, 248 subjects were enrolled. Of these, 183 were under treatment with antipsychotic drugs and represented the sample of the present analysis. The distribution of subjects receiving typical and atypical agents by sociodemographic and clinical variables showed that the 2 groups were similar in gender but not age distribution: one third of patients treated with atypical drugs were 30 years of age or younger, versus only 10% of those treated with typical agents (Table 1). Most patients in both groups were single or married, less than 20% received more than 8 years of education, and only 30% were employed. Subjects receiving typical agents had a longer psychiatric history in comparison with those treated with atypical drugs, although differences were statistically nonsignificant (Table 1). Most patients in both groups had a diagnosis of schizophrenia and only a minority were first-contact patients. The median length of follow-up was 730 days in both groups (mean = 671, SD = 140 in subjects receiving atypical agents; mean = 673, SD = 138 in those receiving typical agents). The median dose of clozapine during the study period was 250 mg/day (mean = 227.5, SD = 153.8), the median dose of olanzapine was 10 mg/day (mean = 10.3, SD = 3.8), and that of risperidone was 3 mg/day (mean = 3.14, SD = 1.61). Chlorpromazine was administered during the study period at a median dose of 40 mg/day (mean = 54.4, SD = 36.6) and haloperidol at a median dose of 3 mg/day (mean = 3.51, SD = 2.81).

Table 1. Distribution of Patients' Sociodemographic and Clinical Characteristics by Antipsychotic Drug Class

	Typical Antipsychotics (N = 110)		Atypical Antipsychotics (N = 73)			
Characteristic	N	%	N	%	χ^2	p
Sex					0.11	.740
Male	57	51.8	36	49.3		
Female	53	48.2	37	50.7		
Age, y					13.8	.019
22–30	11	10.0	22	30.1		
31–40	22	20.0	16	21.9		
41–50	25	22.7	13	17.8		
51–60	27	24.6	10	13.7		
61–86	25	22.7	12	16.4		
Marital status					1.79	.616
Single	57	51.8	41	56.2		
Married	34	30.9	22	30.1		
Widowed	9	8.2	7	9.6		
Separated	10	9.1	3	4.1		
Education					0.86	.647
5 y	49	44.6	28	38.4		
8 y	43	39.1	30	41.1		
> 8 y	18	16.4	15	20.6		
Living conditions					2.12	.145
Alone	19	17.3	7	9.6		
Not alone	91	82.7	66	90.4		
Employment					7.14	.210
Unemployed	19	17.3	13	17.8		
Homemaker	7	6.4	12	16.4		
Student	0	0	1	1.4		
Retired	19	17.3	9	12.3		
Sheltered	29	26.4	15	20.6		
Regular	36	32.7	23	31.5		
Length of illness					3.88	.143
0–3 y	17	15.4	20	27.4		
4–10 y	34	30.9	19	26.0		
> 10 y	59	53.6	34	46.6		
ICD-10 diagnosis					0.35	.553
F2	93	84.6	64	87.7		
F3	17	15.4	9	12.3		
First-contact patients					1.17	.278
Yes	12	10.9	12	16.4		
No	98	89.1	61	83.6		

Clinical and Psychosocial Information and Patient Outcomes

At baseline, the group of patients receiving atypical antipsychotic drugs showed a mean BPRS score higher than those receiving typical agents, but this difference was of borderline statistical significance (z = –1.80, p = .070). The 2 groups did not differ at baseline according to the GAF, HoNOS, and DAS scales (Table 2). At follow-up, the effect size of improvement showed that patients treated with atypical agents improved on the BPRS significantly more than those treated with typical agents (Table 2). A similar finding emerged for the GAF, although this comparison yielded a figure of uncertain statistical significance. Finally, the effect size of improvement for the HoNOS and DAS was similar in the 2 groups of patients.

Service Utilization

The average number of days spent in hospital per year was higher in those receiving atypical agents, while the average number of days spent in residential facilities and the average number of community interventions were similar in the 2 groups (Table 3). In addition, patients treated with atypical agents underwent more GP consultations and laboratory tests (Table 3).

The use of psychotropic drugs during the 2-year period is presented in Table 4. Subjects receiving atypical agents at baseline were prescribed during the 2-year follow-up period more antipsychotic drugs, more antidepressive agents, and more benzodiazepines. No differences emerged with respect to the use of mood stabilizers and anticholinergic agents.

Table 2. Clinical and Psychosocial Outcome of Patients Treated With Typical (N = 110) and Atypical (N = 73) Antipsychotic Drugs After the 2-Year Follow-Up Period

	Typical Antipsychotics			Atypical Antipsychotics			Comparison of Mean Effect Sizes	
Assessment	Mean	SD	Mean Effect Size	Mean	SD	Mean Effect Size	z	p
BPRS								
Baseline	38.0	10.7	0.21	42.3	13.7	0.45	2.57	.010
Endpoint	35.4	9.6		37.5	12.2			
GAF								
Baseline	59.3	14.8	0.14	56.5	17.0	0.25	–1.85	.063
Endpoint	61.4	14.6		59.6	15.5			
HoNOS								
Baseline	9.08	5.43	0.13	9.66	6.28	0.24	–0.61	.536
Endpoint	8.40	5.55		8.71	5.67			
DAS								
Baseline	1.24	0.90	0.11	1.17	1.07	0.10	0.305	.760
Endpoint	1.13	0.91		1.10	1.04			

Abbreviations: BPRS = Brief Psychiatric Rating Scale, DAS = Disability Assessment Scale, GAF = Global Assessment of Functioning Scale, HoNOS = Health of the Nation Outcome Scale.

Table 3. Service Use per Year in Patients Treated With Typical and Atypical Antipsychotic Drugs

	Typical Antipsychotics (N = 110)	Atypical Antipsychotics (N = 73)		
Service Use	Mean (Range)	Mean (Range)	z	p
Days spent in the hospital	5.77 (0–193)	9.71 (0–162)	–2.47	.013
Days spent in residential facilities	6.76 (0–226)	5.93 (0–153)	–1.19	.232
No. of community interventions	23.7 (0.5–241)	25.6 (0–201)	0.35	.719
No. of other interventions (GP visits, laboratory tests)	0.6 (0–11)	1.1 (0–7)	–2.77	.005

Abbreviation: GP = general practitioner.

Service Costs

Total health care costs were nearly double in patients receiving atypical compared with typical antipsychotic agents (Table 5). This difference was explained by the costs associated with the inpatient admissions and by the costs associated with the use of psychotropic drugs, which accounted for 9% and 29% of total health care costs in patients receiving typical and atypical agents, respectively (Table 5).

The ratio between the cost of patients treated with clozapine, risperidone, or olanzapine and typical drugs is presented in Table 6. The use of clozapine increased the costs correlated with psychotropic drugs more than 7-fold, and the total health care costs were 3 times higher. The use of olanzapine increased the costs associated with psychotropic drugs nearly 7-fold, and the total health care costs increased around 30%. The use of risperidone increased the costs associated with psychotropic drugs 3.8-fold, and the total health care costs increased about 60%.

Linear Regression Analysis

The results of the linear regression analyses are shown in Table 7. In the first model, total health care costs were the dependent variable, while in the second model, the dependent variable was the effect size of improvement. In both models, the only independent variables predictive of higher costs and a better clinical outcome were being a first-contact patient and having a greater severity of illness at baseline.

DISCUSSION

These findings should be interpreted bearing in mind the naturalistic design adopted, which was not used to draw any conclusion of cost efficacy in absolute terms, but to explore the consequences of introducing atypical agents into the clinical practice. This naturalistic design had 2 consequences. First, in the group of those receiving the atypicals, there were patients who were concomitantly receiving conventional antipsychotic agents. Concomitant treatment might imply that these patients were more ill. Although we acknowledge that the selection of patients on atypical monotherapy would have certainly simplified the comparison between the 2 groups, surely it would have introduced a distortion to the naturalistic approach. In fact, it has been reported that in real life atypical antipsychotics are frequently added to conventional agents to switch medication; however, in a relevant proportion of cases, patients become "stuck" on the combina-

Table 4. Psychotropic Drug Use During the 2-Year Follow-Up Period

Category	Typical Antipsychotics (N = 110) N	%	Atypical Antipsychotics (N = 73) N	%	χ^2	p
Antipsychotic drugs					19.7	< .001
One	89	80.91	38	52.05		
Two	18	16.36	26	35.62		
Three	3	2.73	5	6.85		
Four	0	0	4	5.48		
Antidepressant drugs					4.03	.045
No	87	79.09	48	65.75		
Yes	23	20.91	25	34.25		
Benzodiazepines					3.22	.073
No	46	41.82	21	28.77		
Yes	64	58.18	52	71.23		
Mood stabilizers					0.03	.849
No	96	87.27	63	86.30		
Yes	14	12.73	10	13.70		
Anticholinergic drugs					0.60	.437
No	84	76.36	52	71.23		
Yes	26	23.64	21	28.77		

Table 5. Average Costs per Year per Patient Treated With Typical and Atypical Antipsychotic Drugs

Variable	Typical Antipsychotics X Per Year[a] Mean (Range)	Atypical Antipsychotics X Per Year[a] Mean (Range)	z	p
Psychotropic drugs				
Antipsychotics	100.1 (2.41–357)	1341.1 (14–4833)	–9.63	< .001
Antidepressants	73.8 (0–1553)	63.4 (0–742)	–1.69	.089
Benzodiazepines	85.7 (0–1055)	106.5 (0–574)	–1.81	.069
Mood stabilizers	11.7 (0–140)	12.4 (0–278)	0.08	.929
Anticholinergic drugs	7.1 (0–77)	7.5 (0–88.9)	–0.67	.497
Total psychotropic drugs	278.4 (3.4–2372)	1530.9 (25–5344)	–9.41	< .001
Days spent in the hospital	1223.6 (0–41,059)	2056.1 (0–34,303)	–2.47	.013
Days spent in residential facilities	488.9 (0–19,968)	481.9 (0–16,356)	–1.18	.236
Community interventions	1047.2 (21–10,603)	1137.1 (0–7902)	–0.50	.610
Other costs (laboratory, GP visits)	10.9 (0–265)	11.4 (0–96.9)	–2.22	.026
Total health care costs	3049 (177–50,372)	5217 (417–49,270)	–6.24	< .001

[a]At the time of the study, X1 = US $ 0.893.
Abbreviation: GP = general practitioner.

tion.[18] Excluding these patients from the analysis, therefore, would have disregarded some important consequences of the introduction of atypical agents in ordinary practice. Second, the 2 groups of subjects receiving atypical and typical agents were not balanced for sociodemographic and clinical characteristics. Those on atypicals were younger, with a shorter length of illness and with slightly more psychopathology, as shown by the BPRS scores at baseline. Although in the multivariate model the overall comparison was adjusted by these independent variables, the possibility that other patient characteristics, not included in the model, could have hampered the comparison cannot be completely ruled out.

It might be surprising that quite low antipsychotic doses were administered in comparison with the U.S. standards. These data, similarly reported in other Italian surveys,[19] confirm a common prescribing behavior of giving doses of antipsychotic drugs as low as possible and of using some antipsychotics, for example chlorpromazine, as sedative agents. It might be surprising, in addition, that in the Italian context of psychiatric care those receiving atypical agents were only slightly younger and had only a slightly shorter length of illness than those receiving old compounds. In other countries, atypical agents are dispensed to patients with first-episode schizophrenia, while conventional agents are reserved for patients stabilized on antipsychotic treatment for a long time. In Italy, the prescribing behavior is different because specific regulatory policies stated that olanzapine and risperidone could be reimbursed by the Italian National Health Service only when prescribed to nonresponders to typical agents.[20] This policy strongly supported the use of conventional agents as first-line treatment and that of atypicals as a second-line strategy. Although this regulation has recently been revised, and currently these 2 compounds are reimbursed as first-line

Table 6. Ratio Between the Cost of Patients Treated With Atypical and Typical Antipsychotic Drugs[a]

Cost Category	Clozapine/Typical Antipsychotics	Olanzapine/Typical Antipsychotics	Risperidone/Typical Antipsychotics	Atypical/Typical Antipsychotics
Antipsychotics	18.0	17.5	8.3	13.4
Antidepressants	1.3	0.6	1.0	0.8
Benzodiazepines	0.9	1.2	1.4	1.2
Mood stabilizers	0.7	0.5	1.8	1.0
Anticholinergic drugs	1.7	1.3	0.8	1.1
Total psychotropics	7.2	6.9	3.8	5.5
Total health care costs	3.0	1.3	1.6	1.7

[a]Clozapine, N = 11; olanzapine, N = 30; risperidone, N = 39.

Table 7. Determinants of Total Health Care Costs and Clinical Outcome: Linear Regression Analysis

	Health Care Costs (Euro)		Brief Psychiatric Rating Scale (Effect Size of Improvement)	
Explanatory Variable	Coefficient	BC 95% CI[a]	Coefficient	BC 95% CI[a]
Age (years)	–52.6	–138.2 to 14.0	0.001	–0.006 to 0.009
Gender (female = 0, male = 1)	–1008.2	–3241 to 801.9	–0.124	–0.310 to 0.084
Unemployment (no = 0, yes = 1)	1971.2	–1616 to 6108.1	0.231	–0.022 to 0.539
Living alone (no = 0, yes = 1)	2418.7	–1410 to 6855.4	–0.041	–0.325 to 0.200
First-contact patient (no = 0, yes = 1)	5049.6	633.9 to 11,650*	0.288	0.029 to 0.540*
Diagnosis (other = 0, schizophrenia = 1)	–2979.9	–7566 to 365.3	–0.118	–0.437 to 0.189
BPRS at baseline (score)	140.4	32.0 to 278.0*	0.026	0.014 to 0.040*
Risperidone (no = 0, yes = 1)	1007.2	–1456 to 3343.8	0.189	–0.033 to 0.423
Clozapine (no = 0, yes = 1)	4321.4	–608.2 to 12,930	–0.157	–0.888 to 0.327
Olanzapine (no = 0, yes = 1)	–231.7	–3060.0 to 1497	0.106	–0.148 to 0.362
Constant term	2173	–3404.5 to 8801	–0.778	–1.318 to –0.277
R^2	0.2085		0.3383	

[a]Bias-corrected, 95% confidence interval, bootstrap method, 5000 repetitions.
*Significant at $p < .05$. Positive coefficients indicate that explanatory variables included in the model were correlated with higher total health care costs and a more favorable treatment outcome; positive upper and lower limits of confidence intervals indicate a statistically significant positive association. Negative coefficients indicate that explanatory variables included in the model were correlated with lower total health care costs and a less favorable treatment outcome; negative upper and lower limits of confidence intervals indicate a statistically significant negative association.

treatments, the general prescribing behavior still remains to try conventional agents first.[21] Clozapine, in contrast, may be prescribed only to patients with schizophrenia who do not respond to typical antipsychotics. No dose restrictions are imposed by the Italian National Health Service. Despite these policies, data have consistently shown, in Italy[21] and in other countries,[22] that a significant proportion of antipsychotic prescriptions does not follow National Health Service restrictions, that is, they are for off-label indications. It is likely, therefore, in the present study, that the differences in sociodemographic and clinical characteristics of those receiving atypical and conventional agents were the result of a combination of both factors, National Health Service regulations and physicians' prescribing behaviors.

The difference in symptom severity, although not very marked at baseline, was responsible for the differences in the pattern of subsequent service use, costs, and clinical improvement. Those receiving atypicals had more frequent hospital admissions, received more psychotropic drugs, incurred more costs, and improved more than those receiving conventional compounds. In the multivariate model, where symptom severity at baseline was included as a covariate, these differences disappeared, and no association was found between atypicals and increased total health care costs nor between atypicals and better clinical outcome. The only 2 predictors of cost and outcome were severity at baseline and the fact of being a first case. Similar findings were reported by Lewis and colleagues,[23] who prospectively followed a cohort of patients receiving atypical agents in South London. Although no attempt was made to evaluate the patients' clinical outcome, the regression of costs on background characteristics demonstrated that symptomatology a baseline was predictive of future costs, as was the number of days spent in the hospital during the previous 2 years. In contrast, Amaddeo and colleagues[24] showed that first-ever patients were less costly than longer-term patients, but this study did not consider costs attributable to drug treatments.

From a clinical viewpoint, the implication of the present analysis is that the introduction of atypical antipsychotic agents had a minor impact in terms of cost and outcome, and that the severity of illness is more important

than the agent prescribed. Obviously, it is worth noting that in absolute terms the proportion of total health care costs attributable to psychotropic drugs was less than 10% in those receiving conventional compounds and nearly 30% in those receiving atypical agents. This could have different implications in the various health care systems. In Italy, for example, for some years the National Health Service had the pressing need to decrease drug expenditure, and therefore it reimbursed the costs of purchase of atypical agents only when prescribed to nonresponding patients, as certified by the treating clinician. Patients had to pay the full cost if they had not been treated with conventional agents first. In other contexts of care, the first-line use of atypical compounds could be more reasonable, for example, in those services with high costs associated with inpatient and outpatient care.

The implications of using atypical agents were studied with respect to service use, costs, and patient outcome, as measured by a number of instruments that have been extensively employed to describe the clinical and psychosocial status of psychiatric patients. However, no specific attempt was made to directly measure the burden of side effects associated with typical and atypical agents. This is a study limitation, since a finding that has consistently emerged from experimental studies is the safer adverse event profile of newer agents, especially in terms of extrapyramidal side effects, leading to better compliance, satisfaction, and, according to some studies, better quality of life.[1–4] Although this study measured neither the side effects nor the quality of life, indirect measures have been considered. The use of anticholinergic agents, for example, could be considered as a proxy indicator of extrapyramidal side effects, as well as the use of inpatient facilities, which is frequently motivated by the need to change or modify the psychopharmacologic treatment in those experiencing troublesome adverse events. Moreover, another proxy indicator of the burden of side effects is the length of therapy, since in many cases patients discontinue their drug treatment because of the emergence of these effects, and this parameter has been included into the calculation of costs attributable to antipsychotic agents.

In conclusion, the availability of atypical antipsychotic agents has undoubtedly extended the treatment options available for patients with severe mental disorders, but evidence from everyday clinical practice of advantages over conventional drugs in terms of cost and outcome has still to be generated.

Drug names: chlorpromazine (Thorazine, Sonazine, and others), clozapine (Clozaril and others), haloperidol (Haldol and others), olanzapine (Zyprexa), risperidone (Risperdal).

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