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CHEF DE DEPARTEMENT : PROFESSEUR Patrice GUEX

Off-Label Utilization of Antipsychotics

THESE

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Romain Bilancioni

Médecin diplômé de la Confédération Suisse

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RÉSUMÉ

Impact du diagnostic psychiatrique sur les prescriptions d'antipsychotiques

Ce travail s'inscrit dans un programme de recherche centré sur la pharmacovigilance en psychiatrie.

Buts de l'étude

Les nouveaux antipsychotiques atypiques sont prescrits avec beaucoup de succès, parce qu'ils présentent une sécurité dans leur emploi bien supérieure à celle des antipsychotiques classiques. Cette situation a conduit à une large prescription « off-label » (hors indication admise). Le but de ce travail a été d'étudier la pratique en matière de prescription des psychiatres hospitaliers en ce qui concerne les antipsychotiques en comparant des patients traités pour des psychoses ou d'autres indications officielles aux patients recevant un traitement antipsychotique « off-label ».

Méthode

Dans le cadre d'un programme de pharmacovigilance - pharmacoépidemiologie, tous les médicaments prescrits à 5 jours de référence (entre 1999 et 2001) à l'hôpital psychiatrique universitaire de Lausanne (98 lits) ont été enregistrés, avec des données sur l'âge, le sexe et le diagnostic des patients. Les prescriptions de 202 patients ont été évaluées.

Les patients ont été classés dans 3 groupes diagnostiques : (1) patient présentant des troubles psychotiques, (2) patient présentant des épisodes maniaques et des épisodes dépressifs avec des symptômes psychotiques, et (3) patient présentant d'autres troubles. Les groupes (1) et (2) forment une classe de patients recevant un antipsychotique pour une indication officielle, et les prescriptions dans le groupe (3) ont été considérées comme « off-label ».

Résultats principaux

Moins de patients psychotiques ont reçu un antidépresseur ($p<0.05$) ou des hypnotiques non-benzodiazepine ($p<0.001$) comparés aux patients des deux autres groupes. Les patients présentant des troubles affectifs recevaient seulement exceptionnellement une combinaison d'un antipsychotique atypique et conventionnel, tandis qu'un nombre inférieur de patients avec des indications « off-label » ont reçu moins souvent des antipsychotiques atypiques que ceux des deux groupes de comparaison ($p<0.05$). L'analyse statistique (stepwise logistic regression) a révélé que les patients présentant des troubles psychotiques avaient un risque plus élevé de recevoir un médicament antipsychotique d'une dose moyenne ou élevée, ($p<0.001$) en comparaison aux deux autres groupes.

Conclusion

Les nouveaux médicaments antipsychotiques semblent être prescrits avec moins d'hésitation principalement pour des indications admises. Les médecins prescrivent de nouveaux médicaments « off-label » seulement après avoir acquis une certaine expérience dans le domaine des indications approuvées, et ils étaient plus prudents en ce qui concerne la dose en traitant sur la base « off-label ».

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OFF-LABEL UTILIZATION OF ANTIPSYCHOTICS

[1]Daniele Fabio Zullino*
[2]Romain Bilancioni*
[2]Philippe Conus
[3]Bruno Schwartz
[2]Yasser Khazaal
[2]Pierre Baumann

* The contributions of these authors have to be considered as equivalent

[1]Division of substance abuse, University Hospitals, Geneva, Switzerland
[2]University Department of Adult Psychiatry, Prilly-Lausanne, Switzerland
[3]Private practice, Geneva, Switzerland

Corresponding author:
Dr. Daniele Zullino
Service d'abus de substances
Hôpitaux Universitaires de Genève
Rue Verte 2
1205 Genève
Switzerland
Daniele.Zullino@hcuge.ch
Tel +41 (22) 320 23 58 (from 01.11.2005 on : +41 (22) 372 55 50)
Fax +41 (22) 328 17 60

Abstract

Objective

The new brands of atypical antipsychotics are very successfully prescribed because of their enhanced safety profiles and their larger pharmacological profile in comparison to the conventional antipsychotic. This has led to broad off-label utilisation. The aim of the present survey was to study the prescription practice of hospital psychiatrists with regard to antipsychotic drugs, comparing patients treated for psychoses or other registered indications to patients receiving an off-label antipsychotic treatment.

Method

As part of a pharmacovigilance/pharmacoepidemiology program, all drugs given on 5 reference days (1999 – 2001) in the 98-bed psychiatric hospital of the University of Lausanne, Switzerland, were recorded along with age, sex and diagnosis. The prescriptions of 202 patients were assessed.

Patients were classified in 3 diagnostic groups: (1) patient with psychotic disorders, (2) patients with manic episodes and depressive episodes with psychotic symptoms, and (3) patients with other disorders. Group (1) and (2) formed the class of patients receiving an antipsychotic for a registered indication, and the prescriptions in group (3) were considered as off-label.

Main results

A lesser number of psychotic patients received antidepressant ($p<0.05$) and nonbenzodiazepine hypnotics ($p<0.001$) compared to the patients of the other two groups. The patients with affective disorders received only exceptionally a combination of an atypical and a conventional antipsychotic, whereas a lesser number of patients with off-label indications received less often atypical antipsychotics than those of the two comparison groups ($p<0.05$). Stepwise logistic regression revealed that patients with psychotic disorder were at higher risk of receiving an antipsychotic medication in medium or high dose ($p<0.001$), in comparison to the two other groups.

Conclusions

The new antipsychotic drugs seem to be prescribed with less hesitation mainly for approved indications. Physicians prescribe new drugs on off-label application only after having gained some experience in the field of the approved indications, and were more cautious with regard to dose when treating on an off-label basis.

Key words

Antipsychotic drugs, off-label use, prescription habits, psychotic disorders, affective disorders

OFF-LABEL UTILIZATION OF ANTIPSYCHOTICS

Introduction

There has been recently an increasing interest to understand the factors that influence the prescription of psychotropic drugs. Characteristics of the health care system, physician management style, physician specialty and training, public attitudes, drug cost and availability, patients preferences, local education tradition, marketing and formulary have been reported to have some impact on prescription habits [1-5]. On the other hand, it is reported that the patient' characteristics were taken less into consideration when physicians prescribe for adult patients [3, 4].

A major concern in studies on drug utilisation during the 70s and 80s was the appropriateness of the practices of psychotropic drug prescription [4]. Many articles on this topic pointed out the frequent lack of concordance between psychiatric diagnoses and the prescribed psychotropic medications [6, 7], i.e. and they revealed their off-label use.

This may be particularly true with antipsychotic medications, due in part to their sedative properties, frequently used without a need of antipsychotic effect [8].

The arrival of the newer atypical antipsychotics has achieved rapid acceptance by prescribers because of enhanced safety profiles, relative to those observed with conventional antipsychotics [9]. Besides their evident antipsychotic efficacy, they have been found to offer a larger pharmacological profile than conventional antipsychotic [10], with some efficacy in depressive and anxious symptoms as well as suicide prevention and in mood stabilization. This has, combined with the favourable tolerance profile, led to broad off-label utilizations.

Whereas several of the actual off-label utilizations are investigated with regard to their responsiveness to the newer antipsychotics, no conclusive data is often available with regard to the specific prescription modalities like dose, treatment duration, comedication, etc.

The aim of the present survey is to study the prescription habits of hospital psychiatrists with regard to antipsychotic drugs, comparing patients treated for psychoses or other registered indications with patients receiving off-label antipsychotic treatment.

Methods

The present study has been realized as part of the AMSP project (Arzneimittelsicherheit in der Psychiatrie = drug safety in psychiatry), which is a program for continuous assessment of adverse drug reactions in psychiatric inpatients under naturalistic conditions of routine clinical treatment. The methodology has been described elsewhere [11-13]. Currently, more than 35 German and Swiss sites are participating. Data on drug use in the participating hospitals are based on two reference days per year. All drugs given on a reference day are recorded along with age, sex, and diagnosis (ICD-10) for all patients under surveillance. The daily dosage is also recorded.

The data of the present study are drawn out of 5 reference days from 1999 to 2001 in the 98-bed psychiatric hospital of the University of Lausanne, Switzerland. Presently the mean hospitalisation duration is 20 days and the nurse/bed ratio is 0.95.

Definition of drug classes

The group of atypical antipsychotics was defined as including clozapine, olanzapine, risperidone, quetiapine and amisulpride. All other antipsychotics were classed as conventional antipsychotics.

Among the conventional antipsychotics, two subclasses were identified: "sedative" and "high potency". Sedative antipsychotics were levomepromazine, promazine, clotiapine, thioridazine, and chlorprotixen. High potency antipsychotics were zuclopentixol, haloperidol, penfluridol, flupentixol and fluphenazine.

Benzodiazepines were classified as one group, including sedative and hypnotic drugs. As sedative benzodiazepines were also often used as hypnotics, the different indications therefore being difficult to assess. Nonbenzodiazepine hypnotics formed a further drug class, including zolpidem, zopiclone and zaleplon. Further classified were anticonvulsants, lithium salts, anticholinergics, and somatic drugs.
Three antipsychotic drug dose ranges were defined (see Table I).

Wards

Data on prescriptions was collected in 5 different wards. Two of these wards are specialized in the treatment of patients presenting a diagnosis of the schizophrenia spectrum disorders and are supervised by the same senior physicians. Two wards are aimed of treating anxiety and affective disorders, both again run by the same team of physicians. The fifth ward treats particularly patients with cluster B and C personality disorders.

Analyses

In descriptive data analyses, means and standard deviations were calculated for numerical variables while frequency categories values and percentages are reported for nominal variables. In exploratory analyses, the differences between groups were tested with chi-square tests (for nominal variables) and analyses of variance for numerical ones.

Three predictive models were built with multivariate logistic regression analysis. Stepwise binary logistic regression analysis was used to determine factors predicting the prescription of atypical antipsychotics and the prescription of benzodiazepines. The forward stepwise method using likelihood-ratio statistic was performed. The third model, predicting the antipsychotic dose range used was analysed by stepwise multinominal logistic regression. Multinominal logistic regression broke the regression up into a series of binary regressions comparing each group to a baseline group, which we determined to be the low dose range group.

The data were analysed using the *SPSS for Windows* program, version 12.0.

Results

Characteristics of the sample

The prescriptions of 202 patients were assessed. The mean (± SD) age was 38.6 ± 12.2 (range 18 - 64). The proportion of women was 43.1%. There were no differences between index days with regard to age and sex distribution.

The distribution regarding their primary ICD-10 diagnosis was: Mental and behavioural disorders due to psychoactive substance use (F10): 9 (4.5 %); Schizophrenia, schizotypal and delusional disorders (F20): 122 (60.4 %); Mood disorders (F30): 39 (19.3 %); Behavioural syndromes associated with physiological disturbances and physical factors (F50): 6 (3.0 %); Disorders of adult personality and behaviour (F60): 24 (11.9 %).

Number of prescribed drugs per patient and comedications

The mean number of drugs administered was 4.0 ± 1.8 (range 1 – 10), and the mean number of prescribed antipsychotics was 1.3 ± 0.5 (range 1 – 3).
Fifty patients received nonbenzodiazepine hypnotics (24.8 %), 117 (57.9 %) had benzodiazepines prescribed, 70 (34.7 %) antidepressants, 38 (18.8 %) anticonvulsants, 28 (13.9 %) lithium, 54 (26.7 %) anticholinergics, and 83 (41.1 %) somatic drugs.

Atypical vs. conventional antipsychotics

Patients treated with atypical antipsychotics (n = 67) were compared to those receiving conventional antipsychotics (n = 99), subjects being prescribed drugs from both classes forming a third group (n = 36). There was no difference with regard to age and sex between the three groups. As expected, the mean number of drugs was different between the first two groups (atypical or conventional antipsychotic) and the third group (combination): 3.6 ± 1.7, 3.9 ± 1.7 and 4.8 ± 1.8 respectively ($p < 0.01$). The same was true for the mean number of antipsychotics per patient: for patients with atypical antipsychotics 1.0 ± 0.1, for those with conventional drugs 1.3 ± 0.5, and for those with a combination of both 2.1 ± 0.2 ($p < 0.001$). No differences were found with regard to number of comedications: atypical antipsychotics 2.6 ± 1.7, conventional antipsychotics 2.6 ± 1.8, combination 2.8 ± 1.8.

The proportion of patients treated concomitantly with different substance classes are shown in Table II. Patients treated with conventional antipsychotics received less antidepressants ($p < 0.05$), whereas patients under atypical antipsychotics were less likely to receive anticholinergics ($p < 0.01$). Two observations may be of particular interest: Twelve percent of patients under atypical antipsychotics had a concomitant anticholinergic treatment, and patients under an "atypical/conventional combination" treatment presented a similar proportion of anticholinergic treatment.

The distribution with regard to dose ranges showed significant differences between the three groups. Patients treated with atypical antipsychotics received mainly medium doses, patients treated with combination of both antipsychotic classes mostly high doses, whereas the group receiving conventional drugs was more evenly distributed ($p < 0.001$).

Diagnostic groups and prescription habits

Patients were classified in 3 diagnostic groups: (1) patient with F20 (psychotic disorders) diagnoses, (2) patients with manic episodes (F30.x, F31.1, F31.2) and depressive episodes with psychotic symptoms (F32.3, F33.3), and (3) patients with other disorders. Group (1) and (2) formed the class of patients receiving an antipsychotic for a registered indication, and the prescriptions in group (3) can be considered as off-label.

The 3 groups differed with regard to age [$F(2)=6.12$; $p=0.003$]: psychotic patients 37.7 ± 11.8 years, patients with affective disorders 44.4 ±13.9 years, patients with off-label indications 35.7 ± 9.9 years. The contrasts between patients with registered indication vs. patients with off-label indications was significant [$t(199)=2.45$; $p=0.015$], whereas the contrast between psychotic patients vs. the other two diagnostic categories was not [$F(199)=-1.38$; $p=0.169$].

As shown in Table III, the diagnostic groups differed with regard to number of prescribed drug per patient ($p<0.01$), number of prescribed antipsychotic per patient ($p<0.001$) and number of prescribed comedication drugs ($p<0.001$). Contrasting registered indications (groups 1 and 2) with off-label indications (group 3) revealed no significant differences with regard to these observations. Contrasting psychotic patients with the two other groups revealed significant differences for all 3 comparisons ($p<0.001$).

Several differences appeared between the diagnostic groups with regard to comedications: less psychotic patients received antidepressant ($p<0.05$) and nonbenzodiazepine hypnotics ($p<0.001$) than patients of the other two groups. More patients of the affective disorders group received anticonvulsants than subjects of the two comparative groups ($p<0.001$).

Patients with affective disorders received only exceptionally a combination of an atypical and a conventional antipsychotic, whereas patients with off-label indications received less often atypical antipsychotics than the two comparison groups ($p<0.05$).

Secular effects

Only one significant change over the 5 index days was observed. The percentage of patients treated with atypical antipsychotics increased over the observation period. The proportions for the 5 index days were 25.5%, 22.5%, 29.4%, 33.3% and 53.3% respectively, the differences being statistically significant ($p < 0.05$).
As shown in Figure 1, there is a secular trend which can be found for patients without psychosis, who were less often be treated with atypical antipsychotics than patients with the diagnosis of psychosis, at the beginning of the observation, the difference disappearing until the last observation.

Logistic regressions

Three predictive models were built with multivariate logistic regression analysis.

A first model was computed to determine factors predicting the prescription of atypical antipsychotics (Table IV). The following parameters were entered into the stepwise logistic regression model: index day, sex, age, diagnostic class, and use of

nonbenzodiazepine hypnotics, benzodiazepines, antidepressants, anticonvulsants, lithium and somatic drugs. The parameters diagnostic class and prescription of an antidepressant were retained. The positive predictive value was 57.8%.

The second model was aimed to determine factors predicting the prescription of concomitant benzodiazepines (Table V). The parameters entered into the stepwise logistic regression model were: index day, sex, age, diagnostic class, and use of an atypical antipsychotic, of nonbenzodiazepine hypnotics, antidepressants, anticonvulsants, lithium and somatic drugs. The parameters retained were the use of antidepressants and the use of nonbenzodiazepine hypnotics. The positive predictive value was 62.3%.

Stepwise multinominal logistic regression analysis was used to assess factors associated with the use of medium range and high range doses (Table VI). The group of individuals having received the antipsychotic medication at a low dose range were defined as the reference group. The following parameters were entered into the model: age, index day, sex, diagnostic class, use of nonbenzodiazepine hypnotics, benzodiazepines, antidepressants, anticonvulsants, lithium, antiparkinsonians, and somatic drugs. The parameters of the diagnostic class and the prescription of antiparkinsonian drugs were retained. The positive predictive value was 50.5%.

Presenting a primary diagnosis of a ICD-10:F20 disorder was associated with a 10-fold risk of having received the antipsychotic medication in the middle dosage range and not in the low dosage range ($p<0.001$), and a 20-fold risk of receiving antipsychotics in the high dose range ($p<0.001$). For patients with an affective disorder considered a registered indication for an antipsychotic treatment, the odds ratio of receiving a middle dose treatment was 4.75 ($p<0.05$), but the increased relative risk to receive a high dose therapy instead of a low-dose treatment was not significant. Whereas patients treated on an off-label basis did not have a significantly higher risk to receive a middle dose treatment compared to a low dose regimen, their odds ratio of receiving their antipsychotics in high doses was 7.77 higher than for low doses ($p<0.007$). When patients received an antiparkinsonian, the risk that they also were treated with high antipsychotic doses was increased 8.29-fold compared to low doses ($p<0.01$).

Discussion

Like in previous survey studies in psychiatric hospitals [14-18], polypharmacy was frequent in our sample, the mean number of prescribed drugs being 4 and ranging from 1 to 10 drugs per patient. Whereas polypharmacy has often been considered as malpractice in earlier studies [19-22], it has become increasingly apparent nowadays, that psychiatric polypharmacy can have some advantages, i.e. to further improve sleep, have a more potent anxiolytic or sedative effect and to overcome therapy resistances [17, 23, 24]. Such considerations may also have played a role for the prescription habits of the physicians in our study, as 58% of the patients in our sample received benzodiazepines concomitantly to the antipsychotic, and 25% a nonbenzodiazepine hypnotic. This seemed to be particularly true for patients with affective or other disorders, as psychotic patients received less comedications in general and especially less antidepressant and nonbenzodiazepine hypnotics.

Interestingly, conventional antipsychotics were more often associated with an antidepressant comedication. This may be due to differences between the two diagnostic classes with regard to secular trends. The use of newly introduced atypical antipsychotic drugs spread more rapidly in the treatment of psychoses (the primary indication), and with certain latency in pharmacotherapy of affective disorders (mania and psychotic depression) and off-label indications.
Whereas patients with the diagnosis of a psychosis were already treated in more than 50% of the cases with an atypical agent at the beginning of the observation period, the proportion was 25% in patients without psychosis. The difference vanished over the five index days, the proportion of prescribed atypical antipsychotics being near 65% in all diagnostic groups during the last index day. The most convincing hypothesis rationalizing these observations would be that the newer drugs were used with less hesitations firstly in approved indications, and that prescribing physicians used newer drugs off-label only after having accumulated some experience in approved indications. This effect may even have been reinforced by the fact, that our hospital wards are organized according to diagnostic groups (schizophrenia, affective disorders, personality disorders, triage unit). Therefore physicians working in the units with a high prevalence of psychotic patients had accumulated experiences with newer drugs more rapidly. One can, furthermore, hypothesize that due to the usual turn-over of the assistants (residents) the prescribing habits developed on the specialised wards was "exported" later on in the whole hospital.

Further interesting results are the dose differences between patients treated for an approved indication compared to off-label use. Whereas the proportion of patients being treated with antipsychotics at medium doses was similar, high doses were more frequent in patients with approved indications, low doses were more frequent for off-label use. Once again, physicians treating patients with approved indications seem to be less hesitant when using antipsychotics.

The observations made with regard to comedications confirmed what was expected. Antidepressants, nonbenzodiazepine hypnotics and mood stabilizers were more often given to patients without psychosis, most likely in order to treat their primary disease, using antipsychotics probably most often as sedatives.

The use of atypical antipsychotics itself seems to be associated with some particular prescribing habits. As could be expected, the use of anticholinergics was lower. Atypical drugs were particularly often been used in medium doses, whereas monotherapy with conventional drugs was also in more than one third of the cases been applied in higher doses. This last observation is difficult to interpret. One highly speculative hypothesis could be that the prescribing physicians were more confident in the effects of atypical antipsychotics, using them less often in high doses.

The results of this study need to be viewed against their methodological limitations. The data are based on five index day surveys, i.e. five crossover data samples. The secular trends found in this study should therefore be interpreted with particular caution. Furthermore, the measured data do not always reflect the intended medication for one given patient, which is a more dynamic process. This will be particularly the case in patients having been hospitalised only recently, whose medication is possibly not yet stabilized. The diagnoses were derived from the

medical records, could therefore not be considered as valid as diagnoses which would have been determined by structured interviews.

Whereas previous studies have stressed out that prescription habits are primarily influenced by doctors characteristics and contextual factors [1-5], less likely by patients characteristics [3, 4], our study suggests that, at least shortly after the introduction of newer therapeutic agents, patients diagnosis may influence drug choice, dose and comedications. While no analogous data on off label prescribing has been published, to our knowledge, in Africa, it seems likely that similar observation may be made in the South African context.

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Figure 1
Evolution of the proportion of atypical antipsychotics over the five index days of the study: comparison between the 3 diagnostic groups

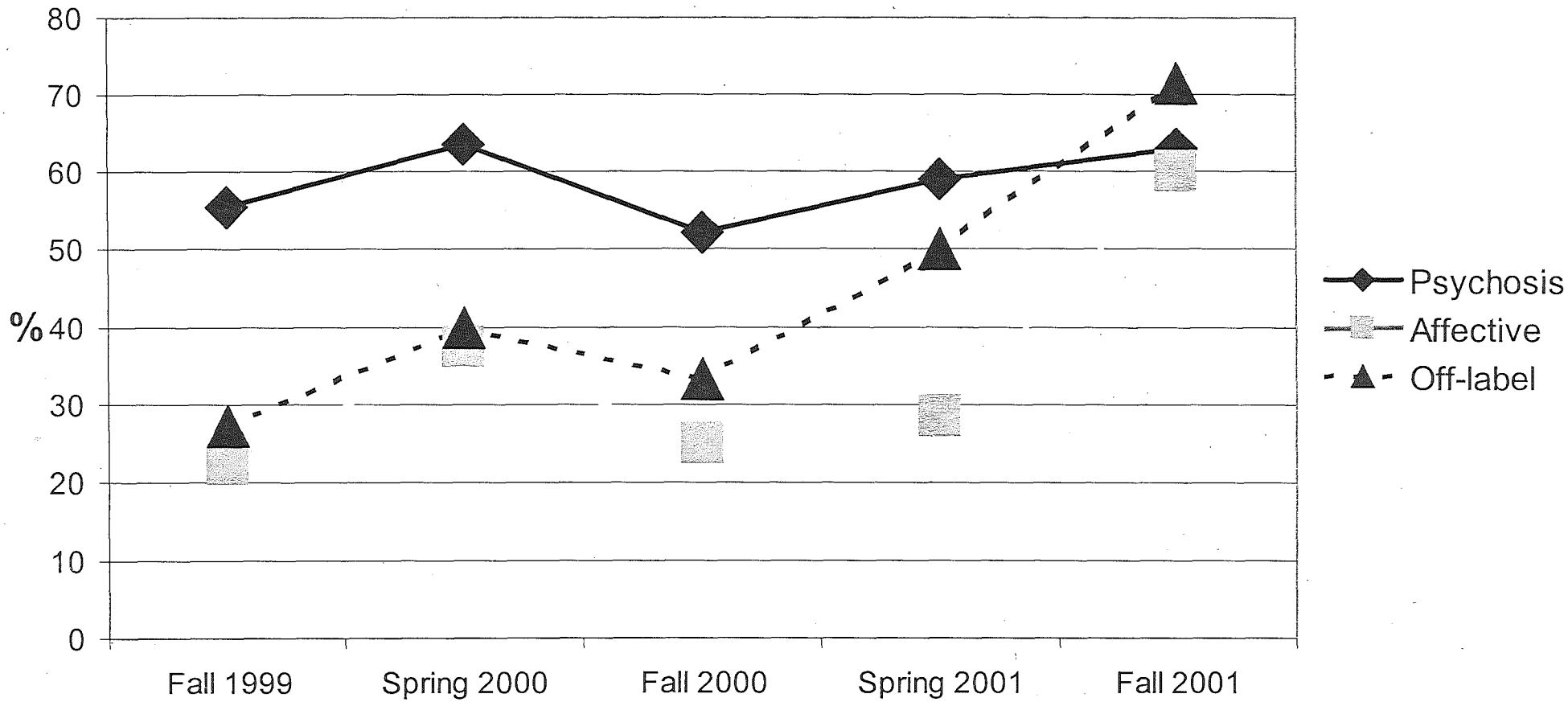

Table I
Defined dose ranges for antipsychotic drugs

	Dose		
	low	medium	high
Levomepromazine	< 100	100-200	>200
risperidone	<3	3-4	>4
olanzapine	<10	10-20	>20
clozapine	<200	200-400	>400
clotiapine	<80	80-120	>120
clopentixol	<20	20-40	>40
haloperidol	<6	6-10	>10
penfluridol	<20/week	21-40	>40
chlorprothixen	<45	45-90	>90
flupentixol	<4	4-6	>6
quetiapine	<300	300-600	>600
fluphenazin	<20	20-50	>50
thioridazin	<100	100-200	>200
amisulprid	<300	300-600	>600

Table II
Comparison of patients treated with atypical antipsychotics with those treated with conventional antipsychotics

	Atypical (n = 67)	Conventional (n = 99)	Both (n = 36)		
Comedication (drug class)					
Antidepressants	40.3 %	26.3 %	47.2 %	Ch^{i2} (2)=6.55	*
Benzodiazepines	64.2 %	51.5 %	63.9 %	Ch^{i2} (2)=3.27	ns
Hypnotics	20.9 %	26.3 %	27.8 %	Ch^{i2} (2)=0.83	ns
Anticonvulsants	17.9 %	22.2 %	11.1 %	Ch^{i2} (2)=2.19	ns
Lithium	14.9 %	15.2 %	8.3 %	Ch^{i2} (2)=1.12	ns
Anticholinergics	11.9 %	34.3 %	33.3 %	Ch^{i2} (2)=11.21	**
Somatic drugs	43.3 %	38.4 %	44.4 %	Ch^{i2} (2)=0.60	ns
Antipsychotic dose received					
Dose range					
Low	16.4 %	22.2 %	2.8 %	Ch^{i2} (4)=60.92	***
Medium	71.6 %	42.4 %	11.1 %		
High	11.9 %	35.4 %	86.1 %		

Table III
Diagnostic groups and prescription habits

	Psychosis (n = 80)		Labelled affective disorder (n = 122)		Off label indication (n = 51)				Contrast registered indications vs off-label use		Contrast Psychosis vs others	
								p	t	p	t	p
	mean	SD	mean	SD	mean	SD						
Number drugs	3.54	1.61	4.79	1.64	4.39	1.95	F(2)=9.84	0.003	t(199)=-0.726	0.469	t(199)=-4.324	<0.001
Number Antipsychotics	1.43	0.56	1.05	0.32	1.22	0.47	F(2)=9.01	<0.001	t(199)=0.210	0.834	t(199)=-4.002	<0.001
Number Comedication	2.11	1.53	3.74	1.63	3.17	1.82	F(2)=17.89	<0.001	t(199)=-0.828	0.409	t(199)=-5.706	<0.001
Comedication (drug class)												
Antidepressants	27.9	%	41.0	%	48.8	%	$Ch^{i2}(2)=6.79$	0.034				
Benzodiazepines	54.9	%	64.1	%	61.0	%	$Ch^{i2}(2)=1.22$	0.543				
Hypnotics	18.0	%	38.5	%	31.7	%	$Ch^{i2}(2)=7.96$	0.019				
Anticonvulsants	11.5	%	41.0	%	19.5	%	$Ch^{i2}(2)=16.91$	<0.001				
Lithium	7.4	%	41.0	%	7.3	%	$Ch^{i2}(2)=29.87$	<0.001				
Anticholinergics	30.3	%	30.8	%	12.2	%	$Ch^{i2}(2)=5.55$	0.062				
Somatic drugs	36.1	%	51.3	%	46.3	%	$Ch^{i2}(2)=3.41$	0.182				
Class of antipsychotics												
Atypical	35.2	%	35.9	%	24.4	%	$Ch^{i2}(4)=11.41$	0.022				
Conventional	41.8	%	61.5	%	58.5	%						
Both	23.0	%	2.6	%	17.1	%						
Proportion hifh-potency (N Conventionals = 133)	65.4	%	72.0	%	20.0	%	$Ch^{i2}(2)=21.20$	<0.001				
Proportion low-potency (N Conventionals = 133)	56.4	%	32.0	%	83.3	%	$Ch^{i2}(2)=14.91$	<0.001				
Dose range												
Low	9.2	%	28.0	%	30.0	%	$Ch^{i2}(4)=15.54$	0.004				
Medium	28.9	%	48.0	%	30.0	%						
High	61.8	%	24.0	%	40.0	%						

Table IV
Stepwise logistic regression model for use of atypical antipsychotics

	Atypical antipsychotics		
	OR[a]	p	CI
Diagnostic class			
Psychosis	1	0.007	
Registered affective disorder	0.38	0.010	0.18 - 0.79
Off-label use	0.45	0.029	0.22 - 0.92
Use of an antidepressant	2.73	0.001	1.51 - 4.92

[a] Odds ration for the probability of receiving an atypical antipsychotic

Table V
Stepwise logistic regression model for use of benzodiazepines

	Benzodiazepines		
	OR[a]	p	CI
Use of an antidepressant	2.50	0.002	1.40 - 4.44
Use of a nonbenzodiazepine hypnotic	1.97	0.049	1.00 - 3.85

[a] Odds ration for the probability of receiving a benzodiazepine

Table VI
Logistic regression model for choice of antipsychotic dose range

	Medium dosis			High dosis		
	OR	p	CI	OR	p	CI
Diagnostic class						
Psychotic	10.11	0.001	2.69 -38.08	20.66	<0.001	5.49 - 77.84
Registered affective disorder	4.75	0.020	1.27 - 17.69	2.40	0.239	0.56 - 10.27
Off-label indication	3.94	0.068	0.91 - 17.10	7.77	0.007	1.74 - 34.69
Antiparkinsonian	2.89	0.113	0.78 - 10.72	8.29	0.002	2.18 - 31.46