

## **Original Research**

# **Are Antipsychotic Prescribing Patterns Different in Older and Younger Adults?: A Survey of 1357 Psychiatric Inpatients in Toronto**

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**Objective:** To compare antipsychotic prescribing patterns in younger (aged 59 years or younger) and older (aged 60 years or older) patients with psychotic or mood disorders.

**Method:** Pharmacy records of all patients discharged from the Centre for Addiction and Mental Health over a 21-month period were reviewed. A total of 1357 patients who were prescribed an antipsychotic at the time of their discharge were included in the analysis (956 with a primary psychotic disorder and 401 with a primary mood disorder). World Health Organization–defined daily doses were used as the standardized dosing unit.

**Results:** Both in patients with a primary psychotic disorder and in patients with a primary mood disorder, the prescribing patterns were similar in older and younger patients, with no statistical difference in the proportions receiving first-generation antipsychotics, second-generation antipsychotics (SGAs), multiple antipsychotics, or long-acting (depot) antipsychotics. Overall, the mean daily antipsychotic doses were lower only in the older group of patients with a primary mood disorder. However, the mean dose of SGAs was about 30% lower in older patients in both diagnostic groups. Regardless of age, patients with a mood disorder were prescribed lower doses of antipsychotics than those with a psychotic disorder.

**Conclusions:** Our data suggest that older patients are prescribed lower antipsychotic dosages primarily when using SGAs. This finding emphasizes the need for dose-finding studies assessing both the efficacy and the safety of antipsychotics in older patients with a psychotic or mood disorder.

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### **Clinical Implications**

- Older patients with a primary psychotic disorder or a mood disorder may be successfully treated with lower doses of antipsychotic drugs.
- Patients with mood disorders may need lower doses of antipsychotic drugs than those with primary psychotic disorders.
- Antipsychotic dose adjustment may be necessary as patients grow older irrespective of their diagnosis.

### **Limitations**

- The analysis is based on prescription data. Thus it reflects physician's prescribing behaviour, which may or may not be related to clinical effects.
- Some clinical characteristics, including duration of treatment, that are expected to impact prescribing behaviour were not available.

**Key Words:** *antipsychotics, prescribing patterns, elderly, aging*

Aging is associated with increased sensitivity to medications. This is thought to be due to a combination of a decreased ability of the body to eliminate drugs with aging, as well as increased sensitivity of the target organs.<sup>1,2</sup> The primary indication for antipsychotic medication is in the management of schizophrenia and bipolar disorder, both lifelong conditions that are associated with a high relapse rate on drug discontinuation. The literature on antipsychotic dosing in older adults is almost entirely restricted to practice guidelines that are largely guided by expert clinical opinion rather than empirical data. These guidelines recommend that elderly patients should be initiated and maintained on lower doses of antipsychotics<sup>3,4</sup> owing to greater sensitivity to adverse effects.<sup>1,2</sup> These recommendations imply that this increased sensitivity to drug adverse effects is associated with a parallel increased sensitivity to therapeutic effects resulting in lower dosing requirements in this older population. However, to date, this assertion has not been explicitly tested in prospective studies. Also, it is unclear whether these recommendations are routinely followed in clinical practice. Most pharmaco-epidemiologic studies of antipsychotic medications have not explicitly evaluated their use in elderly populations,<sup>5-8</sup> have not compared elderly populations with younger populations,<sup>9-11</sup> and have not provided specific dosing information.<sup>9,10,12</sup> One recent study<sup>13</sup> has evaluated the effect of age on antipsychotic dose in patients with psychotic disorders across a broad age range and settings in Japan. In this study, prescribed antipsychotic doses increased with age through the third decade, subsequently plateaued, and decreased after the fifth decade.<sup>13</sup> However, this survey did not include patients with mood disorders. Further, prescribed doses reflect various direct and indirect local influences such as training and local standard of care. This limits the extrapolation of results from one community to another.

We therefore sought to examine the pattern of use for antipsychotic medications in a large Canadian psychiatric hospital. The objectives of our study were to compare the antipsychotic prescribing patterns in younger (aged 59 years or younger) and older (aged 60 years or older) hospitalized patients with a psychotic disorder or a mood disorder. Given the higher sensitivity to adverse effects of older patients, we hypothesized that, compared with younger patients: they would be more likely to be prescribed SGAs and less likely to be prescribed multiple antipsychotics, clozapine, or depot

antipsychotic formulations; and they would be prescribed lower antipsychotic doses. Further, we hypothesized that, regardless of age, patients with a primary mood disorder would be less likely than patients with a primary psychotic disorder to be prescribed FGAs, multiple antipsychotics, clozapine, or depot antipsychotic formulations.

## Methods

### Setting and Subjects

CAMH is a large Canadian psychiatric hospital, fully affiliated with the University of Toronto, with more than 600 inpatient beds and about 120 psychiatrists. Patients discharged from January 2005 to September 2006 who were prescribed an antipsychotic medication at time of discharge were included in the analysis. Antipsychotic regimens at discharge were chosen as a proxy of the optimal regimen needed for therapeutic benefit based on the clinical judgment of the treating psychiatrists. Similarly, if a patient was discharged on an antipsychotic medication more than once in that period, only the data from the most recent discharge were included, under the assumption that this would be more likely to represent optimization of the antipsychotic regimen for the patient. Antipsychotics to be used as needed were excluded from the analysis.

Clozapine, olanzapine, quetiapine, and risperidone were the 4 SGAs available in Canada when our study was conducted. All other antipsychotics were classified as FGAs. The unit of measurement used for standardizing antipsychotic doses was the World Health Organization Collaborating Centre for Drug Statistics Methodology system of DDD. The DDD unit is the assumed average maintenance dose per day for a drug used for its main indication in adults. For example, 1 DDD unit is 300 mg/day for oral chlorpromazine, 5 mg/day for oral risperidone, and 10 mg/day for oral olanzapine. It is important to note that the DDD units do not imply recommended dosing in specific populations, but rather serves as a method of standardizing dosage units across agents for the purpose of pharmacoepidemiologic studies.

Primary diagnostic categories (that is, psychotic disorders and mood disorders) were based on diagnoses recorded in the standardized RAI administered at discharge.<sup>14</sup> Schizophrenia, schizoaffective disorder, and psychotic disorder not otherwise specified were classified as psychotic disorders. Major depressive disorder, bipolar disorder, and dysthymic disorder were classified as mood disorders. Younger patients were defined as aged 59 years or younger and older patients were defined as aged 60 years and older. This cut-off was chosen to reflect the dichotomous definitions commonly used in treatment guidelines.

### Data Analysis

SPSS version 15 (SPSS Inc, Chicago, IL) for Windows was used for the statistical analyses. Differences between groups were tested using a Student *t* test or one-way ANOVA for parametric data or chi-square test for categorical variables. A

### Abbreviations used in this article

CAMH	Centre for Addiction and Mental Health
DDD	defined daily dose
FGA	first-generation antipsychotic
PORT	Patient Outcomes Research Team
RAI-MH	Resident Assessment Instrument—Mental Health
SGA	second-generation antipsychotic

**Table 1 Antipsychotic prescription patterns at discharge in patients with a primary psychotic disorder diagnosis**

Prescription variable	Older group ≥60 years	Younger group <60 years	Statistics
All antipsychotics, <i>n</i> (%)	105 (100)	851 (100)	
DDD, mean (SD)	1.36 (1.93)	1.45 (0.86)	ns
Monotherapy, <i>n</i> (%)	92 (87.6)	717 (84.3)	ns
SGA, <i>n</i> (%)	75 (71.4)	589 (69.2)	ns
DDD, mean (SD)	0.96 (0.57)	1.37 (0.71)	$t = 5.63, df = 106, P < 0.001$
FGA, <i>n</i> (%)	17 (16.2)	128 (15.0)	ns
DDD, mean (SD)	1.74 (3.28)	1.05 (0.83)	ns
Polytherapy, <i>n</i> (%)	13 (12.4)	134 (15.7)	ns
Specific agents			
Clozapine, <i>n</i> (%)	14 (13.3)	137 (16.1)	ns
DDD, <sup>a</sup> mean (SD)	1.35 (0.4)	1.47 (0.65)	ns
Risperidone (oral), <i>n</i> (%)	37 (35.2)	230 (27.0)	ns
DDD, <sup>b</sup> mean (SD)	0.59 (0.39)	1.15 (0.71)	$t = 7.13, df = 82, P < 0.001$
Olanzapine (oral), <i>n</i> (%)	25 (23.8)	308 (36.2)	$\chi^2 = 6.31, df = 1, P = 0.01$
DDD, <sup>c</sup> mean (SD)	1.78 (1.26)	1.85 (0.86)	ns
Depot formulations, <i>n</i> (%)	25 (23.8)	184 (21.6)	ns
DDD, mean (SD)	2.48 (3.59)	1.76 (1.09)	ns

<sup>a</sup> 400 mg/day.  
<sup>b</sup> 5 mg/day.  
<sup>c</sup> 10 mg/day.  
ns = not significant

*P* value of 0.05 was considered statistically significant and all tests were 2-tailed. Our study was approved by the Research Ethics Board of the CAMH and exempted from the requirement for informed consent because the study involved de-identified data acquired during routine care.

## Results

During the study period, 2310 patients were prescribed an antipsychotic at time of discharge. RAI diagnostic information was available for 1549 of these patients, of whom 956 had a primary psychotic disorder diagnosis and 401 patients had a primary mood disorder diagnosis. The analyses are based on 1357 patients. Secondary diagnoses in these patients were highest for substance use disorders (17.4%), anxiety disorders (14.1%), and cognitive disorders (2.3%).

### Patients With a Primary Psychotic Disorder

In patients with a primary psychotic disorder, there were no differences between the 2 age groups in the proportion of those prescribed SGAs or FGAs (Table 1). Likewise, there were no significant differences between the proportion of patients in each age group prescribed multiple antipsychotics. Risperidone was the most commonly used antipsychotic in the older group, with olanzapine ranked second. Similar proportions of patients in the 2 groups were prescribed clozapine, as

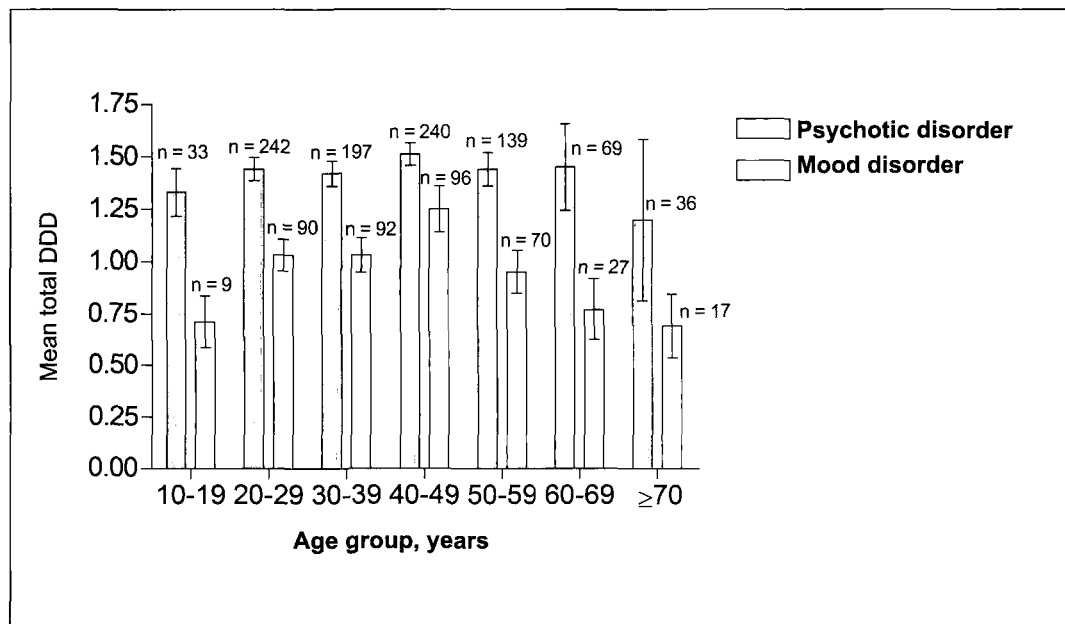
were the proportions prescribed depot formulations. Most depot formulations were FGAs, with risperidone prolonged-release suspension comprising 22.5%.

Overall, the prescribed antipsychotic doses did not differ significantly between younger and older patients (Table 1 and Figure 1). However, when comparing dosing of each antipsychotic category, the mean daily dose of SGAs was about 30% lower in the older group, compared with the younger group. Risperidone dosing in particular was lower in the elderly group, compared with the younger group. In patients prescribed FGAs, there was a large variability of doses in the older group (as reflected by the large SD) and the mean doses of the 2 groups did not differ significantly (Table 1).

### Patients With a Primary Mood Disorder

In patients with a primary mood disorder, there were similar proportions of patients in the older group and younger group prescribed FGAs, SGAs, or depot antipsychotic formulations (Table 2). None of the older patients with a primary mood disorder were prescribed multiple antipsychotics or clozapine. Overall, the mean antipsychotic dose was about 30% lower in the older group than in the younger group (Table 2). This was the case primarily with SGAs, whereas the dosing for the FGAs was similar between the groups (Table 2).

**Figure 1 Mean total DDD for antipsychotics by age group and diagnostic category**



The vertical bars represent standard errors. A significant difference in prescribed dose was not found among age decade groups in patients with a primary psychotic disorder ( $n = 956$ ;  $F = 0.59$ ,  $df = 6,949$ ,  $P = 0.73$ ) but was in patients with a primary mood disorder ( $n = 401$ ;  $F = 2.26$ ,  $df = 6,394$ ,  $P = 0.04$ ), using a 1-way ANOVA.

**Comparing Patients With a Primary Mood Disorder or a Primary Psychotic Disorder**

When comparing patients with a primary mood or psychotic disorder, only 7.7% of patients with a mood disorder were receiving an FGA, compared with 16.8% of those with a psychotic disorder ( $\chi^2 = 27.12$ ,  $df = 2$ ,  $P < 0.001$ ). Patients with a mood disorder were also less likely to be prescribed multiple antipsychotics (8.7%, compared with 15.4%;  $\chi^2 = 10.75$ ,  $df = 1$ ,  $P = 0.001$ ), clozapine (1.2%, compared with 15.8%;  $\chi^2 = 58.77$ ,  $df = 1$ ,  $P < 0.001$ ), and depot formulations (5.0%, compared with 21.9%;  $\chi^2 = 57.35$ ,  $df = 1$ ,  $P < 0.001$ ). As illustrated in Figure 1, regardless of age, significantly lower total daily doses of antipsychotics were prescribed to patients with a primary mood disorder than to patients with a psychotic disorder (mean [SD] DDD 1.03 [0.85], compared with 1.44 [1.03];  $t = 7.1$ ,  $df = 1355$ ,  $P < 0.001$ ).

**Discussion**

We examined the prescribing practices for antipsychotic medications at the time of discharge over a 21-month period in a large Canadian academic psychiatric hospital. Contrary to our hypothesis, our main findings are irrespective of diagnosis, older patients were as likely to receive FGAs, multiple antipsychotics, and long-acting injectable (depot) antipsychotics as younger patients. The mean daily antipsychotic doses were lower in the older group only in patients with a primary mood disorder. Consistent with our hypothesis, patients with a mood disorder were less likely to receive FGAs, multiple antipsychotics, clozapine, or depot formulations than those with a psychotic disorder. Also,

regardless of age, antipsychotic doses were lower in patients with mood disorders than in patients with psychotic disorders.

Very few published studies have specifically evaluated the pattern of antipsychotic prescriptions in elderly patients with schizophrenia or mood disorders. In one study<sup>12</sup> from the early 1990s (reflecting FGA usage) the prescribing patterns in 595 patients were analyzed. Patients with schizophrenia aged 56 years and older had reduced odds of receiving doses greater than 1000 mg chlorpromazine equivalents per day, defined as high antipsychotic doses according to the PORT recommendations (OR 0.43, 95% CI 0.24 to 0.76).<sup>12</sup> Another study also found differences in antipsychotic dosing in a group of patients with schizophrenia attending a depot neuroleptic clinic in 1998. In younger subjects (aged 44 years and younger,  $n = 79$ ) age and doses were not correlated, whereas, in subjects aged 45 years and older, they were negatively correlated ( $r = -0.25$ ,  $P = 0.02$ ,  $n = 86$ ). Further, subjects aged 60 years and older received lower daily doses, compared with those aged 20 to 40 years (mean [SD] dose, mg chlorpromazine equivalents per day: 275 [239], compared with 378 [346]).<sup>15</sup> A relation with age was also found in a large study that evaluated the quality of oral antipsychotic prescribing to patients with schizophrenia treated in the US Department of Veteran Affairs, over a 4-month period in 1999. Among 34 925 outpatients, 47% were receiving FGAs and 59% were receiving SGAs. Most patients (63.6%) were receiving doses within the range recommended by the PORT, with 23.3% receiving lower doses. With a mean age of 52 (SD 11) years, increasing age was associated with an increased likelihood of receiving a dose below the

**Table 2 Antipsychotic prescription patterns at discharge in patients with a primary mood disorder diagnosis**

Prescription variable	Older group ≥60 years	Younger group <60 years	Statistics
All antipsychotics, <i>n</i> (%)	44 (100)	357 (100)	
DDD, mean (SD)	0.74 (0.71)	1.07 (0.86)	$t = 2.4, df = 399, P = 0.02$
Monotherapy, <i>n</i> (%)	44 (100)	322 (90.2)	$\chi^2 = 4.73, df = 1, P = 0.02$
SGA, <i>n</i> (%)	39 (88.6)	298 (83.5)	ns
DDD, mean (SD)	0.72 (0.69)	1.00 (0.75)	$t = 2.19, df = 335, P = 0.03$
FGA, <i>n</i> (%)	5 (11.4)	24 (6.7)	ns
DDD, mean (SD)	0.89 (0.91)	1.05 (0.83)	ns
Polytherapy, <i>n</i> (%)	0	35 (9.8)	$\chi^2 = 4.73, df = 1, P = 0.02$
Specific agents			
Clozapine, <i>n</i> (%)	0	5 (1.4)	—
DDD <sup>a</sup> , mean (SD)	—	1.66 (0.88)	—
Depot formulations, <i>n</i> (%)	3 (6.8)	17 (4.8)	ns
DDD, mean (SD)	1.19 (1.07)	1.77 (0.77)	ns

<sup>a</sup> 400 mg/day.  
ns = not significant; — = not applicable

recommended range, and a decreased likelihood of receiving multiple antipsychotics (OR 1.3 and 0.93, respectively, for an age increment of 5 years).<sup>8</sup> In another large survey of antipsychotic dosing conducted in Japan, there was an inverted U-shaped relation between age and prescribed dose across the lifespan, with decreasing doses observed after the fifth decade.<sup>13</sup> Also, lower doses of antipsychotics were used in patients with late-onset schizophrenia and very late-onset schizophrenia (onset after age 60 years), compared with patients with early-onset schizophrenia.<sup>13</sup>

In contrast to these studies, and clinical practice guideline recommendations, patients with a primary psychotic disorder in our Canadian study did not demonstrate a clear relation between older age and lower dosing. As illustrated in Figure 1, presenting antipsychotic doses by decade, the dosing pattern for patients with a primary psychotic disorder appears quite level across the age ranges. Lower doses were only detected when specifically evaluating patients receiving SGAs, and risperidone in particular. This may reflect either clinical efficacy at lower doses or lower tolerability at higher doses. Although dosing information was not specified in previous studies based on class of antipsychotic, a significant proportion of the antipsychotics prescribed in these older surveys were FGAs. Since these studies were conducted, SGAs are used much more extensively: they were the predominant agents in our study. It is possible that the older patients receiving FGAs in our inpatient study are more difficult to treat (for example, they have failed to respond to SGAs) and require high doses. Thus the absence of a difference in the mean FGA

doses of older and younger patients may reflect this clinical complexity.

We had also hypothesized that given the reported enhanced sensitivity to adverse effects in older patients, these patients would be more likely to be prescribed SGAs and less likely to be prescribed multiple antipsychotics, clozapine, or depot antipsychotic formulations. However, this was not the case. The implication is that older patients treated as inpatients at a tertiary psychiatric care centre may be able to tolerate and benefit from similar prescribing approaches to those used in younger patients. If this is the case, then this observed prescribing practice may have some bearing on the neurobiology of the illness in treatment-refractory patients or long-term effects of antipsychotic drugs (for example, upregulation of dopamine receptors). It also may be that the overall very high rate of SGA use and low rate of prescribing multiple antipsychotics left little room for differences between the groups to emerge.

The use of SGAs in our patients is consistent with the trends in antipsychotic prescribing in the elderly for the entire province of Ontario as reported in a study examining the Ontario Drug Benefit prescription database for patients aged 65 years and older during the years from 1993 to 2002 (over 1.4 million people).<sup>8</sup> In addition to the overall increase in antipsychotic use (from 2.2% to 3% of the elderly population), the use of SGAs increased from no use in 1993 when they were not yet available to 82.5% of the antipsychotics prescribed in 2002 to this population. Risperidone and olanzapine were the most common SGAs prescribed in 2002

(accounting for 56.4% and 29.6% of SGA prescriptions, respectively).

Studies published to date have not focused on antipsychotic prescribing patterns in patients with primary mood disorders. In our study, the antipsychotic prescribing pattern is different for patients with mood disorders and for patients with psychotic disorders in that lower antipsychotic doses were prescribed to those with mood disorders (Figure 1 illustrates this difference across the entire age range). Further, in patients with mood disorders, doses peak during the fourth decade. Patients with mood disorders were also less likely to be prescribed FGAs, multiple antipsychotics, clozapine, or depot formulations. This appears to reflect a more cautious use of antipsychotic medications in patients who do not have a primary psychotic disorder. Alternatively, this finding may imply reduced requirements for antipsychotic drugs in patients with mood disorders. Despite a recent trend of using SGAs for mood disorders,<sup>16,17</sup> there are no published formal studies that compare therapeutic doses between psychotic and mood disorders. However, one recent systematic review shows that patients with bipolar disorder, especially bipolar depression, are more susceptible to extrapyramidal side effects than those with schizophrenia.<sup>18</sup> These findings, including ours, emphasize the need for further investigations to address the appropriate dosing of antipsychotics in younger and older patients with mood disorders.

Our study has both strengths and limitations. It has a relatively large sample in which we were able to compare antipsychotic prescribing patterns in different age and diagnostic groups, including class of antipsychotic (SGAs and FGAs) and use of depot antipsychotic preparations. However, as with most prescription database studies, we could not control for clinical variables other than age and diagnosis. Specifically, we could not link prescription patterns to clinical presentations and outcomes.

## Conclusions

Our data suggest that older patients are prescribed lower antipsychotic dosages primarily when using SGAs and that, regardless of age, patients with mood disorders are prescribed lower doses of antipsychotics than patients with psychotic disorders. These findings emphasize the need for dose-finding studies assessing both the efficacy and the safety of antipsychotics in older patients with psychotic or mood disorders.

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## **Résumé : Les modèles de prescription d'antipsychotiques sont-ils différents pour les jeunes adultes et les adultes âgés? Un sondage de 1357 patients psychiatriques hospitalisés à Toronto**

**Objectif :** Comparer les modèles de prescription d'antipsychotiques à des patients jeunes (de 59 ans ou moins) et des patients âgés (de 60 ans ou plus) souffrant de troubles psychotiques ou de l'humeur.

**Méthode :** Les dossiers pharmaceutiques de tous les patients ayant reçu leur congé du Centre de toxicomanie et de santé mentale sur une période de 21 mois ont été étudiés. Un total de 1357 patients à qui on avait prescrit un antipsychotique au moment de leur congé était inclus dans l'analyse (956 souffrant d'un trouble psychotique primaire et 401 souffrant d'un trouble de l'humeur primaire). Des doses quotidiennes définies par l'Organisation mondiale de la santé ont été utilisées comme unité de posologie normalisée.

**Résultats :** Tant chez les patients souffrant d'un trouble psychotique primaire que chez ceux souffrant d'un trouble de l'humeur primaire, les modèles de prescription étaient semblables pour les patients jeunes et âgés, et il n'y avait aucune différence statistique dans les proportions qui recevaient des antipsychotiques de la première génération, des antipsychotiques de la deuxième génération (ADG), des antipsychotiques multiples, ou des antipsychotiques à action prolongée. En général, les doses moyennes quotidiennes d'antipsychotiques étaient plus faibles seulement dans le groupe des patients âgés souffrant d'un trouble de l'humeur primaire. Toutefois, la dose moyenne d'ADG était environ 30 % plus faible pour les patients âgés des deux groupes diagnostiques. Sans égard à l'âge, on prescrivait aux patients souffrant d'un trouble de l'humeur des doses plus faibles d'antipsychotiques qu'à ceux souffrant d'un trouble psychotique.

**Conclusions :** Nos données suggèrent qu'on prescrit des doses plus faibles d'antipsychotiques aux patients âgés, surtout quand on utilise des ADG. Ce résultat souligne la nécessité d'études destinées à l'établissement de la posologie qui évaluent l'efficacité et l'innocuité des antipsychotiques pour les patients âgés souffrant d'un trouble psychotique ou de l'humeur.