Age comparison of treatment adherence with antipsychotic medications among individuals with bipolar disorder

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SUMMARY

Background   Few studies have evaluated medication adherence among older *vs* younger individuals with bipolar disorder (BPD). We compared adherence with antipsychotic medication among older (age 60 and older) and younger individuals using a large case registry ($n = 73,964$).
Methods   Adherence was evaluated using the medication possession ratio (MPR) for patients receiving antipsychotic medication.
Results   Twenty six thousand five hundred and thirty younger individuals (mean age 46.9) and 6,461 older individuals (mean age 69.2) were prescribed antipsychotic medication. Among older individuals, 61.0% ($n = 3,350$) were fully adherent, while 19.0% ($n = 1,043$) were partially adherent and 20.0% ($n = 1,098$) were non-adherent. Among younger individuals, 49.5% ($n = 10,644$) were fully adherent, while 21.8% ($n = 4,680$) were partially adherent, and 28.7% ($n = 6,170$) were non-adherent. As with younger patients, comorbid substance abuse and homelessness predicted non-adherence among older patients with BPD.
Conclusion   Older individuals with BPD were more adherent with antipsychotic medications compared to younger individuals. However, a substantial proportion (approximately 39%) of older patients with BPD still have difficulties with adherence. Copyright © 2007 John Wiley & Sons, Ltd.

KEY WORDS — treatment adherence; antipsychotic medications; bipolar disorder; elderly; geriatric

INTRODUCTION:

An emerging literature has identified treatment non-adherence as a pervasive problem that leads to illness relapse, hospitalization and other negative sequelae (Perlick *et al*., 2004). Studies evaluating medication non-adherence among patients with BPD found median rates of 41% (Lingam and Scott, 2002)

and 42% (Perlick *et al*., 2004). Medication adherence is a complex phenomenon that appears to be influenced by a number of patient, provider, and environmental factors (Aagaard *et al*., 1988; Aagaard and Vestergaard, 1990; Colom and Vieta, 2002; Berk *et al*., 2004). Patient characteristics that appear to be associated with adherence in BPD include age, marital status, gender, and educational level (Aagard *et al*., 1988; Lingam and Scott, 2002; Berk *et al*., 2004). Concurrent psychiatric disorders also appear to influence adherence (Aagaard and Vestergaard, 1990; Keck *et al*., 1997; Perlick *et al*.,

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2004). However, few studies have evaluated older *vs* younger individuals with BPD with respect to treatment adherence. Additionally, there is limited information on adherence with antipsychotic medications, a class of drugs that is being used with increasing frequency to treat bipolar illness. Using a large case registry ($n = 73,964$), we examined adherence with antipsychotic medication among veterans with BPD within a one-year period [Federal Fiscal Year 2003 (FY03), 1 October 2002–30 September 2003]. The aim of the study was to compare treatment adherence among older individuals (age 60 and older) with younger individuals.

METHODS

Subjects

Registry patients were identified using the VA's National Psychosis Registry (NPR), which regularly incorporates data from the VA Patient Treatment File (PTF), census data files, and Outpatient Care Files (OPC) and the VA Pharmacy Benefits Management Group. We identified patients with bipolar diagnosis in the NPR using ICD9-CM codes 296.0, 296.1, 296.4, 296.5, 296.6, 296.7, and 296.8. Individuals were included if they had at least one qualifying diagnosis during Federal Fscal Year 2003 (FY03). In the event that patients received more than one diagnosis over time, individuals were assigned to the diagnosis which appeared in the greatest number of episodes of care. Ties were resolved using a rank ordering of: (1) schizophrenia; (2) bipolar disorder; and (3) other psychosis. A full report of the Psychosis Registry may be viewed at: http://www.va.gov/annarbor-hsrd.

Measurement of adherence

Medication adherence was evaluated using the medication possession ratio (MPR) for patients receiving any antipsychotic medication. The MPR is the ratio of the 'number of days supply of medication that a patient has received' to the 'number of days supply that they should have received' had they been taking medication as prescribed. An MPR of 1 or 100% indicates that the patient has received all the medication needed to take their antipsychotic medication as prescribed, whereas an MPR of 0.5% or 50% indicates that the patient has received medication sufficient to take only half of the prescribed dose.

The MPR was calculated among patients with at least 90 outpatient days of observation during the fiscal year. The MPR was calculated for the time period of FY03 following the date of the patient's first antipsychotic medication fill of the year. Days spent in institutional settings were subtracted from the numbers of days supply the patient 'should have received' in order to take their medication as prescribed. MPR calculations were limited to individuals who were taking no more than two antipsychotic medications during the fiscal year. In cases where an individual was on two antipsychotic medications, a weighted average of the two MPRs was calculated. The MPR, a measure of prescription refills, has been widely utilized in both medical and psychiatric settings as a proxy measure of treatment adherence (Al-Zakwani *et al.*, 2003; Hertz *et al.*, 2005; Patel *et al.*, 2005; Sanchez *et al.*, 2005; Yu *et al.*, 2005), including assessment of adherence in populations with serious mental illness, and in bipolar populations specifically (Valenstein *et al.*, 2002; Gianfrancesco *et al.*, 2006).

Antipsychotics prescribed in the VA during FY03 were conventional antipsychotic agents as well as the atypical agents clozapine, risperidone, olanzapine, quetiapine, ziprasidone and aripiprazole. Long-acting injectable medications and medications prescribed for use in inpatient settings were not included in analysis.

Adherence intensity

Patients' degree of adherence was evaluated in three clinically relevant categories. Individuals who were fully adherent with antipsychotic medication had MPRs greater than 0.8. Individuals who were partially adherent with antipsychotic medication had MPRs of more than 0.5 and less than or equal to 0.8. Individuals who were considered to be non-adherent with medication had MPRs of less than or equal to 0.5. Unlike some other previous reports (Al-Zakwani *et al.*, 2003), a maximum ratio of 1 was not applied, as this would bias comparisons against agents with a relatively high adherence intensity. While MPRs greater than 1 may also reflect over-prescribers (Gilmer *et al.*, 2004) this cannot be determined solely from claims data. For example, MPRs greater than 1 were possible in cases where prescriptions may not have been completely used due to interim changes in dosage.

Statistical analysis

Descriptive statistics were used to characterize demographic and clinical characteristics of all patients with BPD. A multiple logistic model was used to compare characteristics of older *vs* younger patients

with BPD. Multinomial multiple logistic regression models compared characteristics of patients with full or partial adherence to patients who were non-adherent to antipsychotic medication, controlling for the effects of gender, age, race/ethnicity, marital status, previous psychiatric hospitalization, post-traumatic stress disorder (PTSD), homelessness, and concurrent substance abuse. PTSD and substance abuse were selected as covariates of particular relevance given the overwhelmingly male sample and the fact that relatively high rates of combat-related PTSD are seen in veteran populations. Characteristics associated with adherence were examined separately for the younger and older age groups. In addition, a model including both age groups was analyzed to examine interactions between age group and demographic and clinical variables, adjusting the significance tests for multiple comparisons. Wilcoxon tests were used to compare mean MPRs for patients receiving one *vs* two antipsychotics, for patients

receiving atypical *vs* conventional antipsychotics, for patients receiving clozapine *vs* other atypical antipsychotics, and for older *vs* younger patients.

RESULTS

There were 56,572 (76.5% of the total bipolar group) individuals under age 60 and 17,388 (23.5%) individuals age 60 or older. Compared to younger individuals, older individuals were more likely to be Caucasian (Wald $\chi^2 = 128.6$, df $= 1$, $p < 0.0001$) and married (Wald $\chi^2 = 149.7$, df $= 1$, $p < 0.0001$). Younger individuals were more likely to have comorbid substance abuse (Wald $\chi^2 = 511.5$, df $= 1$, $p < 0.0001$), comorbid PTSD (Wald $\chi^2 = 420.2$, df $= 1$, $p < 0.0001$) and be homeless (Wald $\chi^2 = 95.6$, df $= 1$, $p < 0.0001$) compared to older individuals (Table 1). There were 26,530 (46.9%) individuals prescribed antipsychotic medications among the younger group (mean age 46.9, SD ± 8.1 years) compared to 6,461 (37.2%) among the

Table 1. Characteristics of veterans with bipolar disorder in FY03, stratified by age group

Characteristic	All veterans with bipolar disorder n (%)	All veterans with bipolar disorder Age <60 years n (%)	All veterans with bipolar disorder Age ≥60 years n (%)	Test of significance between groups (controlling for other covariates)
Number of patients	73,964	56,572 (76.5)	17,388 (23.5)	
Mean age (SD)	52.3 (12.5)	47.0 (8.3)	69.5 (7.1)	Wilcoxon Test $Z = 199.8$, $p < 0.0001*$
Gender				
Male	65,212 (88.2)	48,559 (85.8)	16,650 (95.8)	Wald $\chi^2 = 300.3$, $p < 0.0001$, df $= 11$
Female	8,752 (11.8)	8,013 (14.2)	738 (4.2)	
Ethnicity				
White	46,251 (62.5)	34,395 (60.8)	11,856 (68.2)	Wald $\chi^2 = 128.6$, $p < 0.0001$, df $= 1$
Black	7,694 (10.4)	6,904 (12.2)	790 (4.5)	
Hispanic	2,249 (3.0)	1,814 (3.2)	435 (2.5)	
American Indian	239 (0.3)	216 (0.4)	23 (0.1)	
Asian	172 (0.2)	142 (0.3)	30 (0.2)	
Unknown	17,359 (23.5)	13,101 (23.2)	4,254 (24.5)	
Marital status				
Never married	15,386 (21.0)	13,637 (24.3)	1,748 (10.1)	Wald $\chi^2 = 149.7$, $p < 0.0001$, df $= 1$
Married	27,651 (37.7)	18,813 (33.6)	8,838 (51.2)	
Divorced/separated	27,751(37.9)	22,619 (40.4)	5,131 (29.7)	
Widowed	2,497 (3.4)	949 (1.7)	1,548 (9.0)	
Substance use disorder				
Yes	23,484 (31.8)	21,152 (37.4)	2,331 (13.4)	Wald $\chi^2 = 511.5$, $p < 0.0001$, df $= 11$
No	50,480 (68.3)	35,420 (62.6)	15,057 (86.6)	
PTSD diagnosis				
Yes	15,721 (21.3)	13,921 (24.6)	1,800 (10.4)	Wald $\chi^2 = 420.2$, $p < 0.0001$, df $= 1$
No	58,243 (78.8)	42,651 (75.4)	15,588 (89.7)	
Homelessness				
Yes	10,176 (13.8)	9,447 (16.7)	729 (4.2)	Wald $\chi^2 = 95.6$, $p < 0.0001$, df $= 1$
No	63,788 (86.2)	47,125 (83.3)	16,659 (95.8)	
Psychiatric hospitalization in FY02				
Yes	10,236 (13.8)	8,689 (15.4)	1,547 (8.9)	Wald $\chi^2 = 0.6$, $p = 0.4333$, df $= 1$
No	63,724 (86.2)	47,883 (84.6)	15,841 (91.1)	

*Comparing mean age between groups: 47.0 *vs* 69.5.

older group (mean age 69.2 ± 7.0 years) ($\chi^2 = 510.4$, df $= 1$, $p < 0.0001$).

Among younger adults prescribed antipsychotics, 49.5% ($n = 10,644$) were fully adherent, while 21.8% ($n = 4,680$) were partially adherent, and 28.7% ($n = 6,170$) were non-adherent (Table 2). Among older adults prescribed antipsychotics, 61.0% ($n = 3,350$) were fully adherent, while 19.0% ($n = 1,043$) were partially adherent and 20.0% ($n = 1,098$) were non-adherent (Table 3). Non-adherent older adults were more likely to have substance abuse [Odds Ratio (OR) $= 1.38$, 95% Confidence Intervals (CI):1.13, 1.68] and be homeless (OR $= 1.44$, 95% CI:1.05, 1.97) compared to older adults who were fully or partially adherent, while non-adherent younger adults were more likely to be of minority ethnicity (OR $= 1.49$, 95% CI:1.38, 1.61), have comorbid substance abuse (OR $= 1.30$ 95% CI:1.20, 1.40) and be homeless (OR $= 1.53$, 95% CI:1.39, 1.67) compared to younger adults who were fully or partially adherent. The

interaction effects on adherence between age group and gender, race/ethnicity, marital status, previous psychiatric hospitalization, homelessness, comorbid PTSD, and substance abuse were also examined. With the exception of race/ethnicity, these interactions were non-significant, suggesting that demographic and clinical factors have similar associations with adherence across age groups. However, the race/ethnicity and age-group interaction was significant (Wald $\chi^2 = 22.0$, df $= 2$, $p < 0.0001$). This indicates that being in the older age group was associated with a greater increase in antipsychotic adherence among African Americans than among white patients (OR $= 1.58$, 95% CI:1.17, 2.14).

Table 4 demonstrates adherence intensity for individuals with BPD. Younger individuals had a mean MPR on any antipsychotic of 0.74 (± 0.37), while older individuals had a mean MPR of 0.82 (± 0.34) (Wilcoxon Test, $Z = 14.4$, $p < 0.0001$). The majority of individuals prescribed antipsychotics in

Table 2. Intensity of adherence among individuals with bipolar disorder, age <60 years

	Fully adherent[a] n (%)	Partially adherent[b] n (%)	Non-adherent[c] n (%)	Test of significance between groups (controlling for other covariates)
Number of patients	10,644 (49.5)	4,680 (21.8)	6,170 (28.7)	
Mean age (SD)	48.0 (7.6)	46.9 (8.0)	45.6 (8.6)	Wald $\chi^2 = 150.4$, $p < 0.0001$, df $= 1$
Gender				
Male	9,137 (85.8)	4,011 (85.7)	5,287 (85.7)	Wald $\chi^2 = 3.2$, $p = 0.0726$, df $= 1$
Female	1,507 (14.2)	669 (14.3)	883 (14.3)	
Ethnicity				
White	7,509 (70.6)	3,027 (64.7)	3,621 (58.7)	Wald $\chi^2 = 97.3$, $p < 0.0001$, df $= 1$
Black	1,000 (9.4)	706 (15.1)	1,051 (17.0)	
Hispanic	372 (3.5)	168 (3.6)	237 (3.8)	
American Indian	49 (0.5)	16 (0.3)	21 (0.3)	
Asian	26 (0.2)	8 (0.2)	15 (0.2)	
Unknown	1,688 (15.9)	755 (16.1)	1,225 (19.9)	
Marital status				
Never married	2,555 (24.2)	1,118 (24.0)	1,604 (26.2)	Wald $\chi^2 = 0.5$, $p = 0.4971$, df $= 1$
Married	3,735 (35.3)	1,538 (33.0)	1,872 (30.6)	
Divorced/separated	4,111 (38.9)	1,921 (41.3)	2,546 (41.6)	
Widowed	168 (1.6)	80 (1.7)	95 (1.6)	
Substance use disorder				
Yes	3,554 (33.4)	1,921 (41.1)	2,742 (44.4)	Wald $\chi^2 = 46.7$, $p < 0.0001$, df $= 1$
No	7,090 (66.6)	2,759 (59.0)	3,428 (55.6)	
PTSD diagnosis				
Yes	2,905 (27.3)	1,390 (29.7)	1,776 (28.8)	Wald $\chi^2 = 3.5$, $p = 0.0629$, df $= 1$
No	7,739 (72.7)	3,290 (70.3)	4,394 (71.2)	
Homelessness				
Yes	1,213 (11.4)	782 (16.7)	1,286 (20.8)	Wald $\chi^2 = 81.1$, $p < 0.0001$, df $= 1$
No	9,431 (88.6)	3,898 (83.3)	4,884 (79.2)	
Psychiatric hospitalization in FY02				
Yes	2,071 (19.5)	1,027 (21.9)	1,354 (21.9)	Wald $\chi^2 = 0.3$, $p = 0.5674$, df $= 1$
No	8,573 (80.5)	3,653 (78.1)	4,816 (78.1)	

[a]Adherent with >80% of medication.
[b]Adherent with >50–80% of medication.
[c]Adherent with less than or equal to 50% of medication.

Table 3. Intensity of adherence among individuals with bipolar disorder, age ≥ 60 years

	Fully adherent[a] n (%)	Partially adherent[b] n (%)	Non-adherent[c] n (%)	Test of significance between groups (controlling for other covariates)
Number of patients	3,350 (61.0)	1,043 (19.0)	1,098 (20.0)	
Mean age (SD)	69.2 (6.9)	69.2 (7.0)	69.0 (7.3)	Wald $\chi^2 = 0.1$, $p = 0.8108$, df $= 1$
Gender				
Male	3,181 (95.0)	993 (95.2)	1,042 (94.9)	Wald $\chi^2 = 0.1$, $p = 0.7089$, df $= 1$
Female	169 (5.0)	50 (4.8)	56 (5.1)	
Ethnicity				
White	2,473 (73.8)	718 (68.8)	800 (72.9)	Wald $\chi^2 = 0.4$, $p = 0.5029$, df $= 1$
Black	168 (5.0)	65 (6.2)	64 (5.8)	
Hispanic	110 (3.3)	47 (4.5)	29 (2.6)	
American Indian	5 (0.2)	2 (0.2)	0	
Asian	4 (0.1)	2 (0.2)	3 (0.3)	
Unknown	590 (17.6)	209 (20.0)	202 (18.4)	
Marital status				
Never married	368 (11.0)	92 (8.9)	106 (9.7)	Wald $\chi^2 = 0.6$, $p = 0.4581$, df $= 1$
Married	1,673 (50.2)	508 (49.2)	512 (46.9)	
Divorced/separated	973 (29.2)	332 (32.2)	384 (35.2)	
Widowed	318 (9.5)	100 (9.7)	89 (8.2)	
Substance use disorder				
Yes	459 (13.7)	154 (14.8)	215 (19.6)	Wald $\chi^2 = 10.1$, $p = 0.0015$, df $= 1$
No	2,891 (86.3)	889 (85.2)	883 (80.4)	
PTSD diagnosis				
Yes	404 (12.1)	113 (10.8)	139 (12.7)	Wald $\chi^2 = 0.3$, $p = 0.5914$, df $= 1$
No	2,946 (87.9)	930 (89.2)	959 (87.3)	
Homelessness				
Yes	114 (3.4)	56 (5.4)	75 (6.8)	Wald $\chi^2 = 5.2$, $p = 0.0225$, df $= 1$
No	3,236 (96.6)	987 (94.6)	1,023 (93.2)	
Psychiatric hospitalization in FY02				
Yes	493 (14.7)	151 (14.5)	180 (16.4)	Wald $\chi^2 = 0.3$, $p = 0.5693$, df $= 1$
No	2,857 (85.3)	892 (85.5)	918 (83.6)	

[a]Adherent with >80% of medication.
[b]Adherent with >50–80% of medication.
[c]Adherent with less than or equal to 50% of medication.

both older (91.9%) and younger (95.4%) groups received atypical antipsychotics. MPRs were higher for patients on two antipsychotics compared to those taking single antipsychotics for both younger individuals ($Z = 6.1$, $p < 0.0001$) and older individuals ($Z = 2.6$, $p = 0.0082$). For individuals on only one antipsychotic, MPRs were higher for conventional antipsychotics compared to atypical antipsychotics for both younger ($Z = 5.7$, $p < 0.0001$) and older ($Z = 2.6$, $p = 0.0094$) individuals.

DISCUSSION

In this large sample, antipsychotic medications were prescribed less often to treat older individuals with BPD (37.2%), compared to younger individuals with BPD (46.9%). In common with earlier reports on treatment adherence with traditional mood stabilizers, older adults with BPD were more adherent with antipsychotic medications compared to younger adults with BPD (Perlick *et al.*, 2004). Preliminary work by this group of investigators (Valenstein and Sajatovic, in press) suggests that non-adherence rates among bipolar populations appear rather similar across compounds including lithium, anticonvulsants and antipsychotic drugs. However, approximately 39% of older adults had adherence difficulties, indicating that this remains a pressing clinical issue for geriatric populations. As with younger adults, substance abuse and being homeless predicted non-adherence among older adults with BPD. It has been reported that younger and older bipolar populations have cognitive impairments (Nehra *et al.*, 2006; Robinson *et al.*, 2006; Young *et al.*, 2006) that potentially could impact treatment adherence. Older adults may be more likely than younger individuals to have other individuals such as family re-filling their medications, thus contributing at least in part, to their slightly greater adherence rates.

The majority of bipolar patients prescribed antipsychotic medications received atypical agents. Clearly, atypical antipsychotic medications have

Table 4. Adherence with antipsychotic medication among individuals with bipolar disorder

	<60 years		≥60 years		Wilcoxon Test of significance between age groups
	Number of individuals n (%)	MPR Mean (SD)	Number of individuals n (%)	MPR Mean (SD)	
All veterans with bipolar disorder on any antipsychotic with MPR	21,494 (38.0)	0.74 (0.37)	5,491 (31.6)	0.82 (0.34)	$Z = 14.4$, $p < 0.0001$
Individuals on conventional antipsychotic	1,700 (7.9)	0.81 (0.34)	657 (12.0)	0.87 (0.31)	$Z = 4.2$, $p < 0.0001$
Individuals on atypical antipsychotics	20,514 (95.4)	0.74 (0.37)	5,044 (91.9)	0.81 (0.35)	$Z = 13.6$, $p < 0.0001$
Clozapine	29	0.85 (0.24)	9	0.81 (0.32)	$Z = -0.2$, $p = 0.8637$
Risperidone	6,720	0.73 (0.36)	1,622	0.79 (0.35)	$Z = 6.2$, $p < 0.0001$
Olanzapine	8,776	0.73 (0.36)	2,508	0.82 (0.33)	$Z = 11.9$, $p < 0.0001$
Quetiapine	7,410	0.76 (0.38)	1,400	0.83 (0.37)	$Z = 6.2$, $p < 0.0001$
Ziprasidone	965	0.76 (0.38)	104	0.85 (0.34)	$Z = 2.2$, $p = 0.0293$
Aripiprazole	114	0.79 (0.39)	22	0.75 (0.33)	$Z = -0.6$, $p = 0.5349$
Individuals on a single antipsychotic medication	17,261 (80.3)	0.73 (0.37)[a]	4,655 (84.7)	0.81 (0.34)[b]	$Z = 13.6$, $p < 0.0001$
Individuals on two antipsychotic medications	4,233 (19.7)	0.77 (0.36)	836 (15.2)	0.85 (0.34)	$Z = 5.6$, $p < 0.0001$
For individuals on only one AP:					
Atypical	16,294 (94.4)	0.73 (0.37)[c]	4213 (90.5)	0.81 (0.35)[d]	$Z = 12.8$, $p < 0.0001$
Conventional	967 (5.6)	0.80 (0.33)	442 (9.5)	0.86 (0.31)	$Z = 12.8$, $p = 0.0010$
Clozapine	19 (0.12)	0.90 (0.15)[e]	7 (0.17)	0.90 (0.14)[f]	$Z = 0.1$, $p = 0.9539$
Other atypicals	16,275 (99.9)	0.73 (0.37)	4206 (99.8)	0.81 (0.35)	$Z = 12.8$, $p < 0.0001$

[a]single antipsychotic vs two antipsychotics: Wilcoxon Test, $Z = 6.1$, $p < 0.0001$.
[b]single antipsychotic vs two antipsychotics: Wilcoxon Test, $Z = 2.6$, $p = 0.0082$.
[c]atypical vs conventional APs: Wilcoxon Test, $Z = 5.7$, $p < 0.0001$.
[d]atypical vs conventional APs: Wilcoxon Test, $Z = 2.6$, $p = 0.0094$.
[e]clozapine vs other atypicals: Wilcoxon Test, $Z = 1.9$, $p = 0.0545$.
[f]clozapine vs other atypicals: Wilcoxon Test, $Z = 0.4$, $p = 0.6681$.

assumed an important place in the treatment of individuals with bipolar illness across the age span. Individuals prescribed a single atypical antipsychotic agent in both older and younger groups were less adherent with treatment compared to individuals prescribed a single typical agent. However, the group of individuals on typical agent monotherapy represented a small proportion (approximately 5% of younger patients, and 10% of older patients) of all patients. Possibly, individuals on typical antipsychotics represent a sub-group of individuals who have both good response and tolerance to these older agents. Clinicians and patients may be reluctant to switch from therapies that appear to be working well. Interestingly, treatment adherence appears better with two antipsychotic agents compared to monotherapy in both older and younger individuals. This has been observed in other bipolar populations (Sajatovic et al., 2006) in a prospective mixed-age study. It is not clear if more adherent patients are being more aggressively treated, or alternatively, if more aggressive use of atypical antipsychotic agents actually promotes better treatment adherence among patients with bipolar disorder. Clinicians may treat patients with two agents only if they are convinced that patients are adherent with monotherapy, while at the same time avoiding use of complicated (multi-drug) regimens for individuals with a history of non-adherence.

Limitations of this study include the fact that prescription refills may not actually reflect medication ingestion, and that the elderly group may represent a survivor cohort characterized by long-term adherence. The 'younger' sample in this analysis averaged 48 years of age. Differences among older vs younger bipolar groups might be more pronounced among bipolar adults in their 20s and 30s vs an older population. Additionally, since this was a VA sample, results cannot necessarily be extrapolated to a more gender heterogenous bipolar population.

It has been suggested that focused attention to treatment adherence may improve adherence (Scott and Tacchi, 2002). Interventions to enhance treatment adherence among older adults with BPD should consider those who are at greatest risk of non-adherence—individuals with comorbid substance use,

and those with poor psychosocial supports. Additionally, older individuals with BPD are noted to have substantial deficits in knowledge regarding medications and treatment (Schaub *et al.*, 2001) and are likely to benefit from interventions that will improve illness understanding.

REFERENCES

Aagaard J, Vestergaard P, Maarbjerg K. 1988. Adherence to lithium prophylaxis: II. Multivariate analysis of clinical, social, and psychosocial predictors of nonadherence. *Pharmacopsychiatry* **21**: 166–170.

Aagaard J, Vestergaard P. 1990. Predictors of outcome in prophylactic lithium treatment: a 2-year prospective study. *J Affect Disord* **18**: 259–266.

Al-Zakwani IS, Barron JJ, Bullano MF, *et al.* 2003. Analysis of healthcare utilization patterns and adherence in patients receiving typical and atypical antipsychotic medications. *Curr Medical Res Opin* **19**: 619–626.

Berk M, Berk L, Castle D. 2004. A collaborative approach to the treatment alliance in bipolar disorder. *Bipolar Disord* **6**: 504–518.

Colom F, Vieta E. 2002. Treatment adherence in bipolar patients. *Clin Approaches Bipolar Disord* **1**: 49–56.

Gianfrancesco FD, Rajagopalan K, Sajatovic M, Wang RH. 2006. Treatment adherence among patients with bipolar or manic disorder taking atypical and typical antipsychotics. *J Clin Psychiatry* **67**: 222–232.

Gilmer TP, Dolder CR, Lacro JP, *et al.* 2004. Adherence to treatment with antipsychotic medication and health care costs among Medicaid beneficiaries with schizophrenia. *Am J Psychiatry* **161**: 692–699.

Hertz RP, Unger AN, Lustik MB. 2005. Adherence with pharmacotherapy for type 2 diabetes: a retrospective cohort study of adults with employer-sponsored health insurance. *Clin Therapeut* **27**: 1064–1073.

Keck PE Jr, McElroy SL, Strakowski SM, *et al.* 1997. Compliance with maintenance treatment in bipolar disorder. *Psychopharmacol Bull* **33**: 87–91.

Lingam R, Scott J. 2002. Treatment non-adherence in affective disorders. *Acta Psychiatr Scand* **105**: 164–172.

Nehra R, Chakrabarti S, Pradhan BK, Khera N. 2006. Comparison of congitive functions between first-and multi-episode bipolar affective disorders. *J Affect Disord* **93**: 185–192.

Patel NC, Crismon ML, Miller AL, Johnsrud MT. 2005. Drug adherence: effects of decreased visit frequency on adherence to clozapine therapy. *Pharmacotherapy* **25**: 1242–1247.

Perlick DA, Rosenheck RA, Kaczynski R, Kozma L. 2004. Medication non-adherence in bipolar disorder: a patient centered review of research findings. *Clin Approaches Bipolar Disord* **3**: 56–64.

Robinson LJ, Thompson JM, Gallagher P, *et al.* 2006. A meta-analysis of congitive deficits in euthymic patients with bipoalr disorder. *J Affect Disord* **93**: 105–115.

Sajatovic M, Bauer MS, Kilbourne AM, *et al.* 2006. Self-reported medication treatment adherence among veterans with bipolar disorder. *Psychiatric Serv* **57**(1): 56–62.

Sanchez RJ, Crismon ML, Barner JC, *et al.* 2005. Assessment of adherence measures with different stimulants among children and adolescents. *Pharmacotherapy* **25**: 909–917.

Schaub RT, Berghoefer A, Muller-Oerlinghausen B. 2001. What do patients in a lithium outpatient clinic know about lithium therapy? *J Psychiatry Neurosci* **26**: 319–324.

Scott J, Tacchi MJ. 2002. A pilot study of concordance therapy for individuals with bipolar disorders who are non-adherent with lithium prophylaxis. *Bipolar Disord* **4**: 386–392.

Valenstein M, Copeland LA, Blow FC, *et al.* 2002. Pharmacy data identify poorly adherent patients with schizophrenia at increased risk for admission. *Med Care* **40**: 630–639.

Valenstein M, Sajatovic M. Adherence to treatment: a lifecourse perspective. In *Bipolar Disorders in Later Life*, Sajatovic M, Blow F (eds). Johns Hopkins Press: Baltimore, MD.

Young RC, Murphy CF, Heo M, *et al.* 2006. Cognitive impairment in bipolar disorder in old age: literature review and findigs in manic patients. *J Affect Disord* **92**: 125–131.

Yu YF, Nichol MB, Yu AP, Ahn J. 2005. Persistence and adherence of medications for chronic overactive bladder/urinary incontinence in the California Medicaid Program. *Value Health* **8**: 495–505.