ORIGINAL ARTICLE

Trends in Antipsychotic Use in Dementia 1999-2007

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Context: Use of atypical antipsychotics for neuropsychiatric symptoms of dementia increased markedly in the 1990s. Concerns about their use began to emerge in 2002, and in 2005, the US Food and Drug Administration warned that use of atypical antipsychotics in dementia was associated with increased mortality.

Objective: To examine changes in atypical and conventional antipsychotic use in outpatients with dementia from 1999 through 2007.

Design: Time-series analyses estimated the effect of the various warnings on atypical and conventional antipsychotic usage using national Veterans Affairs data across 3 periods: no warning (1999-2003), early warning (2003-2005), and black box warning (2005-2007).

Subjects: Patients aged 65 years or older with dementia (n=254 564).

Main Outcome Measures: Outpatient antipsychotic use (percentage of patients, percentage of quarterly change, and difference between consecutive study periods).

Results: In 1999, 17.7% (95% confidence interval [CI], 17.2-18.1) of patients with dementia were using atypical or conventional antipsychotics. Overall use began to decline during the no-warning period (rate per quarter, −0.12%; 95% CI, −0.16 to −0.07; $P<.001$). Following the black box warning, the decline continued (rate, −0.26%; 95% CI, −0.34 to −0.18; $P<.001$), with a significant difference between the early and black box warning periods ($P=.006$). Use of atypical antipsychotics as a group increased during the no-warning period (rate, 0.23; 95% CI, 0.17-0.30; $P<.001$), started to decline during the early-warning period (rate, −0.012; 95% CI, −0.14 to 0.11; $P=.85$), and more sharply declined during the black box warning period (rate, −0.27; 95% CI, −0.36 to −0.18; $P<.001$). Olanzapine and risperidone showed declining rates and quetiapine showed an increase during the early-warning period, but rates of use for all 3 antipsychotics declined during the black box warning period. In the black box warning period, there was a small but significant increase in anticonvulsant prescriptions (rate, 0.117; 95% CI, 0.08-0.16; $P<.001$).

Conclusions: Use of atypical antipsychotics began to decline significantly in 2003, and the Food and Drug Administration advisory was temporally associated with a significant acceleration in the decline.

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ALTHOUGH COGNITIVE IMPAIRMENT is the clinical hallmark of dementia, noncognitive neuropsychiatric symptoms such as aggression, agitation, depression, and delusions are common and often dominate disease presentation.[1] Conventional antipsychotics had long been used to treat neuropsychiatric symptoms, and their overuse in nursing homes led to federal oversight regulations in 1987.[2] In the 1990s, there was a significant shift from conventional to atypical antipsychotics given the latter's lower reported rates of parkinsonism and tardive dyskinesia.[3] In 2001, more than 70% of US atypical antipsychotic prescriptions were written for off-label indications such as dementia,[4] and atypical antipsychotics accounted for 82% of antipsychotic prescriptions written for older patients in Canada in 2002.[5] Some pharmaceutical companies may have aided this growth by promoting the use of atypical antipsychotics for off-label purposes.[6]

However, starting in 2002, worries began to arise about atypical antipsychotic safety including concerns about diabetes[7] and cerebrovascular events[8,9] (the latter emerging from randomized placebo-controlled trials of patients with dementia). In 2005, the Food and Drug Administration (FDA) issued a black box warning that stated, "Treatment of behavioral disorders in elderly patients with dementia with atypical antipsychotic medications is associated with increased mortality."[10] In these analyses, atypical antipsychotics were associated with increased mortality (approximately 1.7-fold) compared with placebo-treated patients. Subsequently, a number of research articles confirmed the concern about mortality risks associated with both conventional and atypical antipsychotic use in patients with dementia.[11-13] A similar warning for conventional antipsychotics followed in June 2008.[14]

Although the black box warning is the strongest warning the FDA issues, there

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have been somewhat mixed results described in studies examining prescription rates in the wake of black box warnings for various medications.[15] In some cases, antipsychotics may be viewed as the only option for patients with harmful behaviors, given that there is little clinical trial data supporting the use of nonantipsychotic medications for treatment of neuropsychiatric symptoms in patients with dementia.[1] We sought to examine trends in antipsychotic use from 1999 through 2007, encompassing (1) a no-warning period (April 1999-June 2003); (2) an early-warning period (July 2003-March 2005), during which there were a number of early consensus statements, "Dear Doctor" letters, health system communications, and pharmaceutical company actions; and (3) a black box warning period (April 2005-September 2007). We hypothesized that, while the regulatory warnings would contribute to a decline in antipsychotic use over the study period, we thought a substantial minority of patients would continue to receive these medications following the warnings. In addition, we sought to examine concomitant trends in nonantipsychotic psychotropic use in the same time period to ascertain potential compensatory changes in other psychotropics.

METHODS

STUDY COHORT

The data used came from national veterans affairs (VA) registries maintained by the Serious Mental Illness Treatment, Resource, and Evaluation Center in Ann Arbor, Michigan, for veterans who received a dementia diagnosis (*International Classification of Diseases, Ninth Revision [ICD-9]* diagnoses 290.0, 290.1x, 290.2x, 290.3, 290.4x, 291.2, 294.10, 294.11, 331.0, 331.1, and 331.82) in a VA inpatient or outpatient setting. Patients included were aged 65 years or older and had a dementia diagnosis between April 1, 1999, and September 30, 2007. The final study sample included 254 564 patients. This study was approved by the VA Ann Arbor Healthcare System institutional review board.

To understand changes in psychotropic medication use and prescription rates, it is critical to determine and adjust for the number of patients with dementia over time. Thus, differences due to population changes are not conflated with those due to regulatory changes. The main analyses express the percentage of patients who used antipsychotic medication during the study period in which the denominator is all VA patients with dementia, so changes in the population with dementia over time are considered.

MEASURES OF ANTIPSYCHOTIC AND OTHER PSYCHIATRIC MEDICATION USE

Atypical and conventional antipsychotics, antidepressant and anticonvulsant medications, medications approved to treat the cognitive symptoms of dementia, and anxiolytic/hypnotics included in the analyses are listed in the eAppendix (http://archgenpsychiatry.com). We examined the number of patients with dementia in a given quarter who received the medications of interest in an outpatient setting.

STATISTICAL ANALYSIS

We used interrupted time-series analysis, a strong quasiexperimental design,[16,17] to examine the effect of the regulatory warnings on the percentage of patients with dementia who used antipsychotic medications. The interrupted time-series design produces more valid evidence of a policy effect than a simple pre/post design because it controls for preregulatory trends in study outcomes.[18,19]

For the main analyses, we identified all patients who had dementia during the study period. Once a patient was identified as having a dementia diagnosis, the patient remained in the cohort, regardless of their medication status, until their last day of VA service use or the end of the study period, whichever came first. We then grouped the data into sequential 3-month intervals and determined whether each patient received at least 1 prescription for each of the psychotropic medications of interest during each interval. This allowed us to calculate the outcome of interest on a quarterly basis.

We examined trends in conventional and atypical antipsychotic use during 3 time periods: (1) a no-warning period (April 1999-June 2003), (2) an early-warning period (July 2003-March 2005), and (3) a post–black box warning period (April 2005-September 2007). In addition, our analyses included a linear time-trend variable and 3 terms indicating changes in the mean level of prescribing during each time period. Finally, we included terms for changes in the linear time trend (slope) between periods 1 and 2 and between periods 2 and 3. Because the data are categorized based on 3-month intervals, all rates are expressed as quarterly. We used 2-tailed *t* tests to test the statistical significance of the black box warning policy and controlled for autocorrelation by assuming a first-order regressive process.

Statistical power will vary by each agent, as their base rates of use differ greatly. We considered the power to detect a change in rates of use of atypical antipsychotics, the medication category of our primary interest. At each 3-month interval, the number of patients with dementia aged 65 or older ranged from approximately 30 000 to 95 000. We based our power estimate on simulated data. In this simulation, we conservatively assumed a sample size of 30 000 patients at each time, 10.7% use as observed for atypical antipsychotics at first quarter, 0.2% increase in use per quarter during the prewarning period; and a first-order autocorrelation of 0.85. With these assumptions, the study would have 80% power to detect a decrease in the quarterly rate of use of 0.07% or larger from the no-warning to the early-warning period using an interrupted time-series model. Similarly, the study would have 80% power to detect a drop in the quarterly use rate of 0.07% or greater from the prewarning to the black box warning period.

We also performed 3 subanalyses to examine antipsychotic prescribing practices by age (80 years and older vs younger than 80), type of dementia (Alzheimer vs other types), and medical comorbidity (Charlson score > 1 vs ≤ 1). For the dementia type analyses, the following codes were used to indicate Alzheimer disease: 290.0, 290.3, 290.10-290.13, 290.20, 290.21, 294.10, 294.11, and 331.0.

RESULTS

The study population included 254 564 veterans aged 65 or older with a dementia diagnosis. Demographics and key characteristics of the study population are found in **Table 1**. Within the study population, 28.8% received a conventional or atypical antipsychotic during the study period. Use of any psychotropic medication (including antipsychotics, antidepressants, anxiolytics, and anticonvulsants but excluding cholinesterase inhibitors and memantine) was stable during the study period at approximately 40% of the study population at any given time point.

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Table 1. Characteristics of Patients With Dementia

Characteristic	Patients, % (n=254 564)
Female sex	3.0
Age, y	
65-74	27.4
75-84	58.1
≥85	14.5
Race	
White	69.4
Black	10.9
Other	1.2
Unknown	18.5
Marital status	
Married	64.5
Never married	6.4
Divorced	11.1
Widowed	16.2
Separated	0.5
Unknown	1.3
Comorbid diagnoses	
Depression	22.2
Psychosis	16.4
Schizophrenia	3.4
Bipolar	2.1
Parkinson disease	7.7
Substance abuse	5.7
Posttraumatic stress disorder	3.7
Other anxiety	6.9
Personality disorder	0.6
Comorbidity, Charlson index[a]	
0	37.6
1	23.2
>1	39.2

[a] Based on original Charlson weights, excluding dementia.

CASES OF DEMENTIA IN THE VA ELDERLY POPULATION

Figure 1 represents the total number of dementia cases in the VA inpatient or outpatient population aged 65 years or older during the study period (at any measurement time, this number serves as the denominator for the main analyses).

PERCENTAGE OF PATIENTS WITH DEMENTIA WITH OUTPATIENT ANTIPSYCHOTIC PRESCRIPTIONS

Figure 2A demonstrates the percentage patients with dementia who received outpatient antipsychotic medication (conventional or atypical) during the study period. **Table 2** depicts rates and trends in outpatient antipsychotic use (conventional or atypical) during the 3 study periods.

At the beginning of the study period (Spring 1999), 17.7% (95% confidence interval [CI], 17.2 to 18.1) of patients with dementia were using antipsychotics (conventional and atypical considered 1 group). Overall use began to decline in the no-warning period (rate per quarter, –0.12%; 95% CI, –0.16 to –0.07; $P<.001$). Following the black box warning, the decline continued (rate, –0.26%; 95% CI, –0.34 to –0.18; $P<.001$), with a significant difference between the preceding and black box warning periods ($P=.006$).

Use of atypical antipsychotics as a group increased during the no-warning period (rate, 0.23; 95% CI, 0.17 to 0.30; $P<.001$), started to decline during the early-warning period (rate, –0.012; 95% CI, –0.14 to 0.11; $P=.85$), and more sharply declined during the black box warning period (rate, –0.27; 95% CI, –0.36 to –0.18; $P<.001$). Rates of change were significantly different between the no-warning and early-warning periods (slope change, –0.246; 95% CI, –0.41 to –0.09; $P<.001$) as well as between the early-warning and black box warning periods (slope change, –0.261; 95% CI, –0.43 to –0.10; $P=.004$).

The main decrease in conventional antipsychotic use occurred during the no-warning period (rate, –0.38%; 95% CI, –0.50 to –0.27; $P<.001$). Subsequently, use of conventional antipsychotics in the study population was minimal at less than 2%.

In terms of individual antipsychotics (Figure 2B), olanzapine (rate, –0.22; 95% CI, –0.30 to –0.15; $P<.001$) and risperidone (rate, –0.13; 95% CI, –0.24 to –0.03; $P=.02$) showed declines, and quetiapine (rate, 0.27; 95% CI, 0.22 to 0.32; $P<.001$) showed an increase during the early-warning period. All 3 individual antipsychotics declined during the black box warning period (olanzapine rate, –0.12; 95% CI, –0.18 to –0.06; $P<001$; risperidone rate, –0.15; 95% CI, –0.22 to –0.08; $P<.001$; quetiapine rate, –0.04; 95% CI, –0.07 to –0.001; $P=.05$). Rates of change for olanzapine were significantly different between the no-warning and early-warning periods (slope change, –0.28; 95% CI, –0.38 to –0.18; $P<.001$) but not between the early-warning and black box warning periods. Rates of change for risperidone were not significantly different between the 3 study periods. Quetiapine rates of change were significantly different only between the early-warning and black box warning periods (slope change, –0.31; 95% CI, –0.38 to –0.24; $P<.001$).

Aripiprazole, clozapine, and ziprasidone are not presented in Figure 2B owing to low (<1%) rates of use.

USE OF NONANTIPSYCHOTIC PSYCHOTROPICS OR MEDICATIONS APPROVED TO TREAT THE COGNITIVE SYMPTOMS OF DEMENTIA

Figure 3 depicts trends in nonantipsychotic psychotropic use during the study period. While the rates of use of nonantipsychotic psychotropics as a group increased significantly after the black box warning (from 20% to 25%, not shown in Figure 3), there appeared to be no major compensatory increases in any individual nonantipsychotic psychotropic drug classes in the black box warning period. However, there was a small but significant increase in anticonvulsant prescriptions (rate, 0.117; 95% CI, 0.08-0.16; $P<.001$) during the black box warning period.

Regarding the medications approved to treat the cognitive symptoms of dementia, cholinesterase inhibitors showed a decreased rate from the early-warning period (rate, 0.70; 95% CI, 0.54 to 0.87; $P<.001$) and black box warning periods (rate, –0.09; 95% CI, –0.20 to 0.02; $P=.13$), with a significant difference between the 2 pe-

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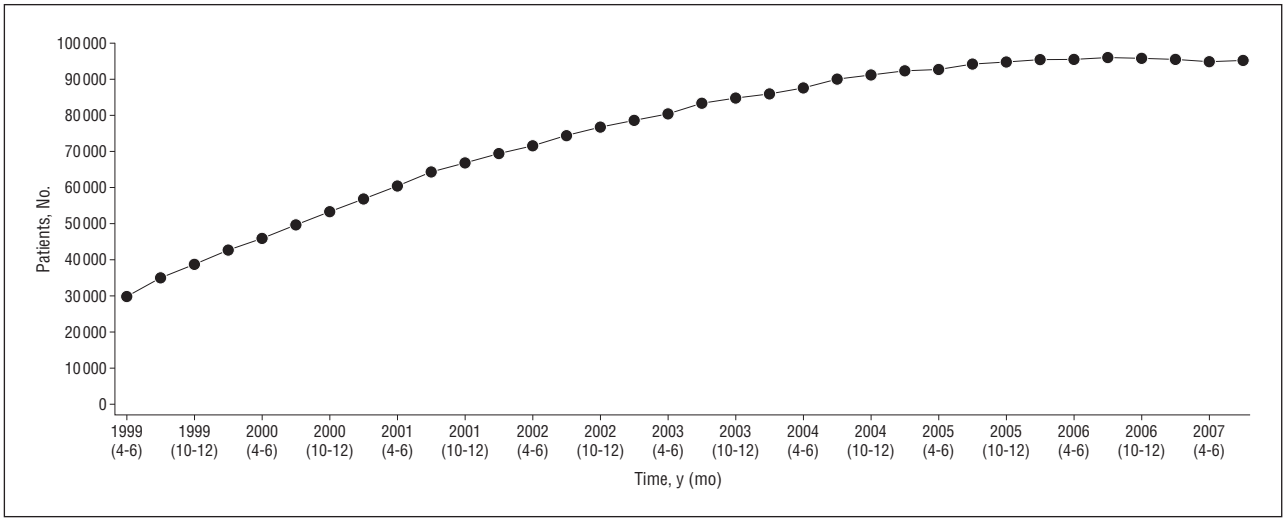

Figure 1. Total number of cases of dementia in the Veterans Affairs inpatient and outpatient population.

riods (slope change, –0.79; 95% CI, –1.01 to –0.56; $P < .001$). Memantine exhibited an increased rate in the early-warning period (rate, 1.43; 95% CI, 1.34 to 1.52, $P < .001$) and a decreased rate in the black box warning period (rate, 0.41; 95% CI, 0.36 to 0.46; $P < .001$) with a significant difference between the 2 periods (slope change, –1.02; 95% CI, –1.12 to –0.92; $P < .001$).

SENSITIVITY ANALYSES

Three additional analyses were performed to examine antipsychotic prescribing practices by age (80 years and older vs younger than 80 years), type of dementia (Alzheimer vs other types), and medical comorbidity (Charlson score greater than 1 vs 1 or less). While overall antipsychotic use was significantly lower for older patients and for those with greater medical comorbidity, the changes in rate during the 3 study time periods were not significantly different from those of younger patients or those with less medical comorbidity (eg, the increases in atypical antipsychotic use during the no-warning period and the decreases in use in the early-warning and black box warning periods were similar between subgroups). Interestingly, however, the use of atypical antipsychotics in patients with Alzheimer dementia rose more quickly during the no-warning period and declined more rapidly in the early and black box warning periods compared with those with other types of dementia.

COMMENT

In this national VA sample, we found that use of both conventional and atypical antipsychotics for patients with dementia began to decline significantly well before implementation of the black box warning. The 2005 FDA advisory was temporally associated with a significant acceleration in the decline of atypical antipsychotic use. A small but significant increase was seen for anticonvulsant scripts in the post–black box warning period.

There were substantial increases in absolute number of patients with dementia, from 30 000 cases in 1999 to 100 000 in 2007. The number of dementia cases (as well as increases over time) in our sample is similar to official VA projections from 2004.[20] Increases in the absolute number of veterans over time in older age groups can be expected owing to the aging of World War 2 and Korean War cohorts and the commonplace shift to use of VA health care by older veterans for favorable pharmacy and other (eg, respite care, home health aides) benefits.[21,22]

Similar to prior studies,[3,5] we found a rapid decline in the use of conventional antipsychotics as well as a rise in the use of atypical antipsychotics during the no-warning period. The shift from conventional to atypical antipsychotics in the elderly population during this period has been hypothesized to be due to several factors including efficacy evidence from early clinical trials, perceived safety advantages at that time, and published expert consensus guidelines.[23]

What contributed to overall decreases in antipsychotic use and prescriptions in the early-warning period? It is difficult to attribute causality, but temporally, there were the emergence of a number of early consensus statements, "Dear Doctor" letters, health system communications, and pharmaceutical company actions. Articles regarding cerebrovascular events associated with use of atypical antipsychotics in patients with dementia began to emerge in 2002, so the timing of the early-warning decreases in antipsychotic use is consistent with a relationship between such decreases and concern about these risks. Additionally, in May 2003, the Office of the Inspector General[24] issued compliance guidelines restricting the ability of pharmaceutical companies to market off-label uses of medications. This mandate led to the discontinuation of marketing, advertising, and detailing for atypical antipsychotics for use in patients with dementia, all prior to the 2005 black box warning. To the extent that drug company marketing activities influence physician prescribing patterns, the Office of the Inspector General mandate may have contributed to the decline in antipsychotic prescribing. The Office of the Inspector General mandate and emergence of adverse effect data were also coincident with the end of pharmaceutical industry efficacy studies of antipsychotics in patients with

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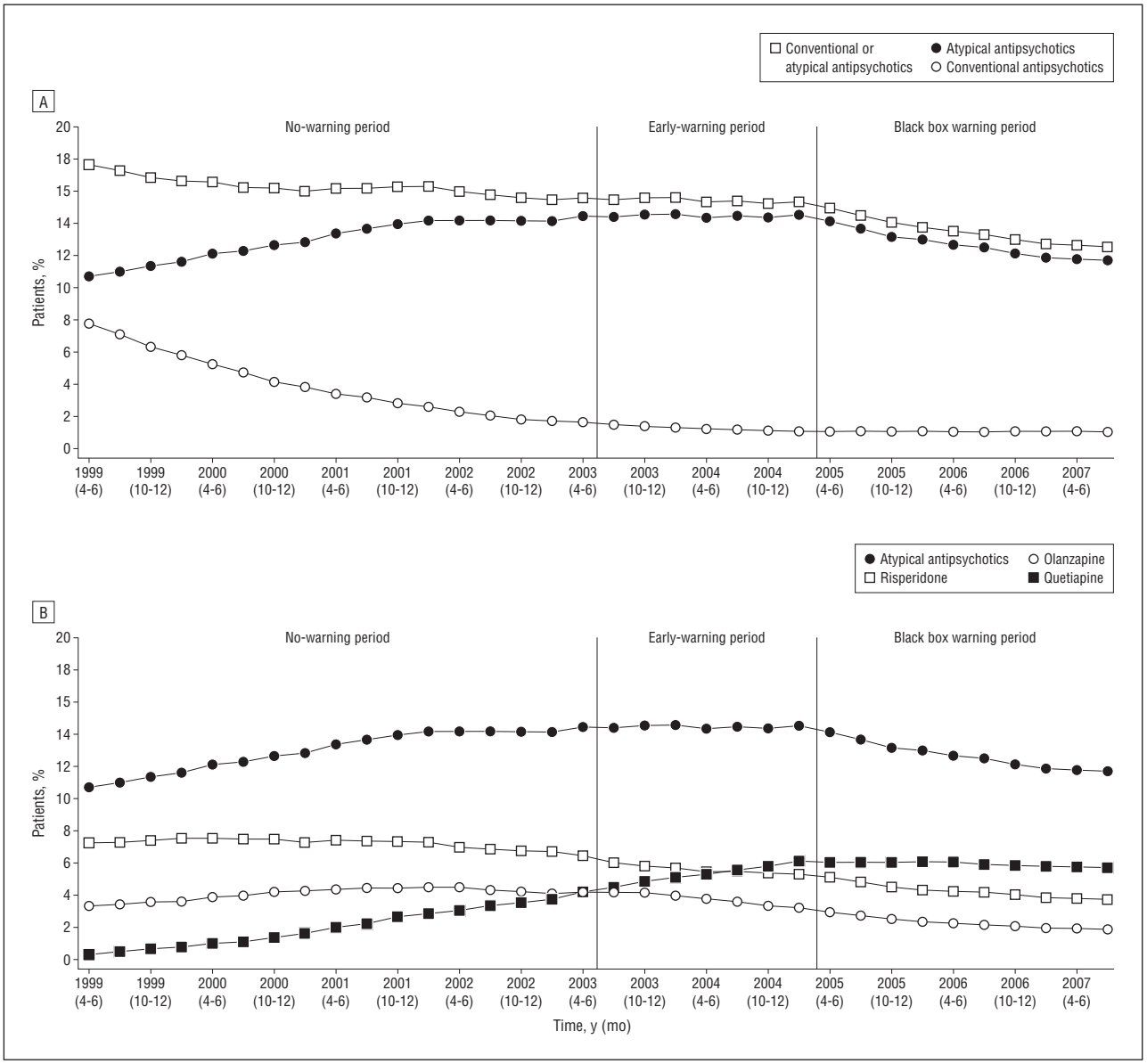

Figure 2. Percentage of patients with dementia with outpatient antipsychotic (A) and atypical antipsychotic (B) prescriptions.

Table 2. Rates and Trends of Outpatient Antipsychotic Use per 100 Patients With Dementia Aged 65 and Older

	Period 1[a]			Period 2[a]					Period 3[a]				
Antipsychotic	Use, %[b]	Slope	*P* Value	Use, %[b]	Slope	*P* Value	Slope Change[c]	*P* Value	Use, %[b]	Slope	*P* Value	Slope Change[d]	*P* Value
All	17.67	−.115	.001	15.51	−.021	.70	0.094	.17	14.93	−.262	.001	−.241	.006
Atypical	10.72	0.234	<.001	14.40	−.012	.85	−.246	.006	14.15	−.273	.001	−.261	.004
Conventional	7.80	−.384	<.001	1.50	−.055	.44	0.329	.008	1.09	0.003	.96	0.058	.48
Aripiprazole	0.00	0.001	.17	0.04	0.041	.001	0.040	.001	0.32	0.018	.001	−.023	.001
Clozapine	0.05	−.002	<.001	0.01	0.0004	.71	0.002	.05	0.01	0.003	.001	0.002	.04
Olanzapine	3.33	0.058	<.001	4.19	−.223	.001	−.281	.001	2.94	−.115	.001	0.108	.10
Quetiapine	0.35	0.246	<.001	4.57	0.272	.001	0.026	.44	6.09	−.037	.05	−.309	.001
Risperidone	7.24	−.053	.09	6.01	−.132	.02	−.079	.30	5.13	−.153	.001	−.021	.74
Ziprasidone	0.00	0.009	<.001	0.16	0.006	.19	−.003	.68	0.19	0.002	.60	−.005	.50

[a] Periods defined as: 1, no-warning period, April 1999 to June 2003; 2, early-warning period, July 2003 to March 2005; and 3, post–black box warning period, April 2005 to September 2007.
[b] During first quarter of the period.
[c] Slope change from period 1 to period 2.
[d] Slope change from period 2 to period 3.

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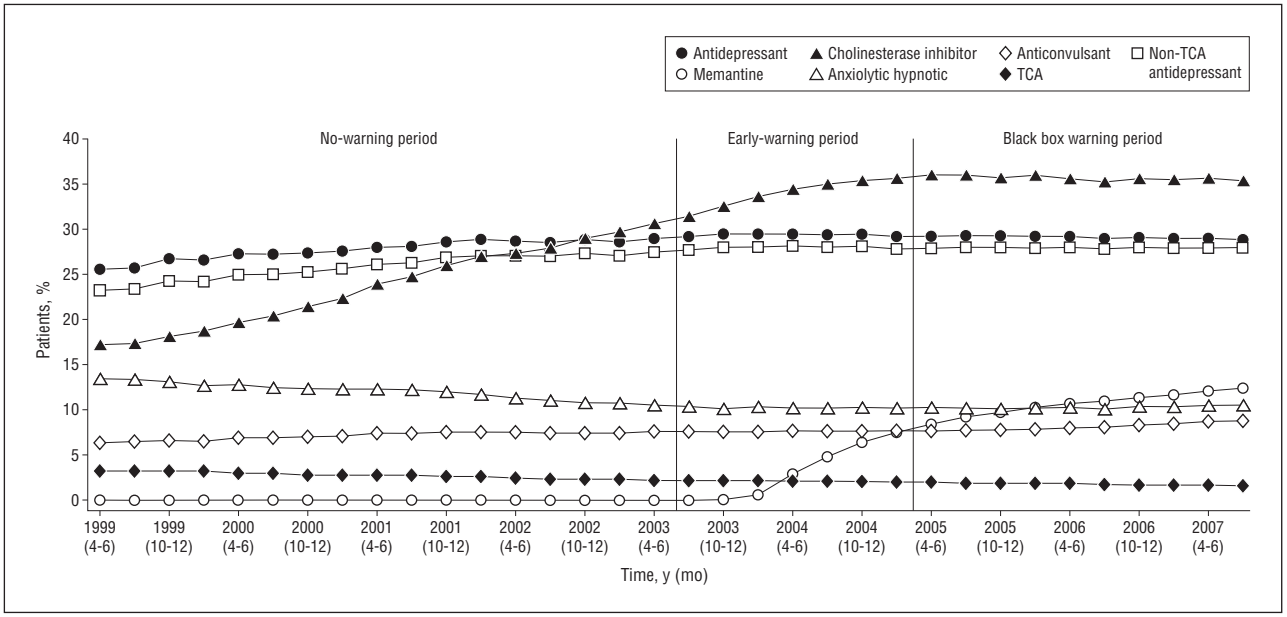

Figure 3. Percentage of patients with dementia with prescriptions for outpatient nonantipsychotic psychotropic medication or medications approved to treat the cognitive symptoms of dementia. TCA indicates tricyclic antidepressant.

dementia. Prior to the FDA warning, in the spring of 2003, VA Pharmacy Benefits Management performed internal analyses and found a possible stroke signal related to risperidone, olanzapine, and conventional antipsychotic agents.[25] These findings were communicated during the next few months to the regional pharmacy managers who, in turn, communicated with individual VA mental health chiefs who were asked to disseminate this information to VA mental health providers.

After the 2005 black box warning, we found a significant acceleration of the decline in use of atypical antipsychotics for patients with dementia. In addition to the potential effect of the FDA's warning about the association between mortality and the use of atypical agents in dementia, some of the factors that may have contributed to the decline in atypical prescriptions in the early warning period (worry about adverse effects, sharp decline in drug company promotion, and detailing of physicians) may have continued to have an influence during the postwarning period. Finally, increasingly negative media reports regarding the use of antipsychotics for elderly individuals[26] may have also had an effect on the decline. Within the VA, communications through Pharmacy Benefits Management to the field underscored the black box warning to providers.

Patterns of use between individual atypical antipsychotics are potentially revealing. At a health system level, the VA recommended risperidone and quetiapine in favor of other antipsychotics based on lack of identified efficacy differences between atypical agents as well as cost during the early-warning period.[27] Notably, during the prewarning period, there was a lack of safety warnings for cerebrovascular adverse events for quetiapine; this agent was the only individual atypical antipsychotic that continued to increase in use during the early-warning period. Quetiapine may have also been continued to be prescribed in low doses by providers for sedation and hypnotic purposes.

By 2007, overall use of antipsychotics in patients with dementia in the VA achieved somewhat of a steady state, leveling off to approximately 12% of patients with dementia. The percentage of psychotropic use (antipsychotics plus antidepressants, anxiolytics, and anticonvulsants) among VA patients with dementia remained fairly constant during the study period at 40% (and conversely, the percentage of patients not receiving was stable at 60%); therefore, we can state that there was no large shift to not giving patients medication after the black box warning. While the rates of use of nonantipsychotic psychotropics as a group increased significantly after the black box warning (from 20% to 25% of patients with dementia), there did not appear to be any major compensatory increases in individual nonantipsychotic psychotropic drug classes. In the black box warning period, there was a small but significant increase in anticonvulsant (rate, 0.117; $P < .001$) prescriptions. Though the cholinesterase inhibitors and memantine have been described as having behaviorally stabilizing effects,[28] their rate of growth actually slowed during the black box warning period, so there did not appear to be a major compensatory shift to these agents.

The limited efficacy and adverse effect issues with antipsychotics leave clinicians in a difficult situation given the prevalence of neuropsychiatric symptoms of dementia, desperation of families, and lack of true pharmacological alternatives. In addition to concerns about morbidity and mortality in dementia, the National Institute of Mental Health–sponsored Clinical Antipsychotic Trial of Intervention Effectiveness–Alzheimer Disease showed limited efficacy for atypical antipsychotic medications in favor of placebo.[29] A subsequent Clinical Antipsychotic Trial of Intervention Effectiveness–Alzheimer Disease study indicated that antipsychotics may be effective for management of particular symptoms such as anger, aggression, and paranoid ideation but do not appear to improve patient functioning, care needs, or quality of life.[30]

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However, at present, there is little research evidence documenting alternative pharmacologic or behavioral approaches that are effective. The only individual nonantipsychotic psychotropic class that we found to increase in the wake of the black box warning was anticonvulsants; however, studies have noted limited efficacy with these agents as well as a number of concerning adverse events.[31,32]

Both the American Association for Geriatric Psychiatry[33] and the FDA[10] have urged clinicians and families to adopt a risk-benefit approach to determining when to use antipsychotic medications in dementia that includes use of antipsychotics only for psychotic symptoms (eg, hallucinations, paranoia, delusions) that potentially endanger the patient or family (eg, patient has a delusion that family is poisoning him and won't eat); targeted treatment for neuropsychiatric symptom clusters (eg, use antidepressants for a depression symptom cluster; use anticonvulsants for agitated/labile cluster); and use of behavioral measures and thorough evaluation of behavioral antecedents. Recently, 2 groups have published more detailed discussions of suggested clinical approaches for patients with dementia and neuropsychiatric symptoms that may be helpful to physicians facing these treatment challenges.[34,35]

A key strength of our study is that we controlled for the large increase in the dementia population within the overall VA population during the study period. Our data indicate that the number of elderly patients diagnosed with dementia steadily increased from 1999 through 2007, similar to but somewhat less than official 2004 VA projections.[20] While a prior study using Health Canada data from Ontario found that regulatory warnings slowed the growth of atypical antipsychotic prescriptions, the Canadian study did not adjust for changes in the number of patients with dementia.[36] Similarly, a recent study using nationally representative data examining "drug mentions" (primary unit of analysis is a physician/patient interaction during which an antipsychotic is "mentioned as a therapy") in office-based prescribing in older adults with dementia reported decreases in the use of atypical antipsychotics but did not appear to adjust for changes in numbers of patients with dementia.[37] Such adjustment is important because it affects estimates of the effect of regulatory warnings. The large growth of the dementia population in the last decade is a phenomenon that is now well documented[38]; the results of these prior studies would have likely been more pronounced and more accurately reflect trends in prescribing practices had they controlled for the denominator. We note that it is possible that we were able to detect the slowing of antipsychotic prescribing prior to the black box warning, while the other 2 studies did not, because we controlled for the denominator of the increasing dementia population. Three other major strengths of this study are the examination of actual prescription rates in a US national sample, the examination of nonantipsychotic psychotropic use, and the assessment of prescription patterns during an 8-year period; the latter allowed us to discover the significant decrease in use during the early-warning period.

Inherent in the use of administrative data for pharmacoepidemiologic work are several limitations. Consistent with the demographic characteristics of the VA patient population, the study cohort was primarily male, and thus the results may not be completely generalizable to other clinical populations. In terms of pharmacy data, prescriptions filled can be an imprecise measure of actual drug exposure; medication filling may not reflect day-to-day use. Information on how changes in antipsychotic renewal and discontinuation rates might have changed during the study period was beyond the scope of this study but would be of interest to future research on the effect of the black box warning. Data on dementia severity were also lacking. Finally, while the large integrated VA health system offers us the opportunity to examine pharmacoepidemiologic changes, the findings may not be completely generalizable to other health care systems. However, in terms of comparison with other national data, we note that there are striking similarities on many key variables that might affect provider antipsychotic prescribing practices (eg, race mix, prevalence of key psychiatric and medical conditions) between our data and data from the Aging, Demographics, and Memory Study[39,40] (Ken Langa, MD, PhD, written communication, June 2010).

In conclusion, use of atypical antipsychotics for patients with dementia began to decline significantly in 2003, and the FDA advisory was temporally associated with a significant acceleration in the decline.

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Correction

Errors in Degree, Name, Honorific, Affiliations, and Funding/Support. In the Original Article titled "Trends in Antipsychotic Use in Dementia 1999-2007" by Kales et al, published in the February 2011 issue of the *Archives* (2011;68(2):190-197), an author's degree, another author's name, another author's honorific, an affiliation, and the Funding/Support line contained errors. Dr Claire Chiang's degree should be PhD, not MD; Rosalindo Ignacio should be Rosalinda V. Ignacio; and Ms Cunningham should be Dr Cunningham. The first affiliation should read Veterans Affairs Health Services Research and Development Center for Clinical Management Research, Serious Mental Illness Treatment, Resource, and Evaluation Center, Ann Arbor, Michigan. In the "Methods: Study Cohort" section, the data source should be listed as the Serious Mental Illness Treatment, Resource, and Evaluation Center. In addition, the Funding/Support line should read: This study was supported by grant R01-MH081070-01 from the National Institute of Mental Health; and the Serious Mental Illness Treatment, Resource, and Evaluation Center, Ann Arbor, Michigan. This article was corrected online.

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