Antipsychotic Therapy and Short-term Serious Events in Older Adults With Dementia

Paula A. Rochon, MD, MPH, FRCPC; Sharon-Lise Normand, PhD; Tara Gomes, MHSc; Sudeep S. Gill, MD, MSc; Geoffrey M. Anderson, MD, PhD; Magda Melo, MSc; Kathy Sykora, MSc; Lorraine Lipscombe, MD, MSc; Chaim M. Bell, MD, PhD; Jerry H. Gurwitz, MD

Background: Antipsychotic therapy is widely used to treat behavioral problems in older adults with dementia. Cohort studies evaluating the safety of antipsychotic therapy generally focus on a single adverse event. We compared the rate of developing any serious event, a composite outcome defined as an event serious enough to lead to an acute care hospital admission or death within 30 days of initiating antipsychotic therapy, to better estimate the overall burden of short-term harm associated with these agents.

Methods: In this population-based, retrospective cohort study, we identified 20 682 matched older adults with dementia living in the community and 20 559 matched individuals living in a nursing home between April 1, 1997, and March 31, 2004. Propensity-based matching was used to balance differences between the drug exposure groups in each setting. To examine the effects of antipsychotic drug use on the composite outcome of any serious event we used a conditional logistic regression model. We also estimated adjusted odds ratios using models that included all covariates with a standard difference greater than 0.10.

Results: Relative to those who received no antipsychotic therapy, community-dwelling older adults newly dispensed an atypical antipsychotic therapy were 3.2 times more likely (95% confidence interval, 2.77-3.68) and those who received conventional antipsychotic therapy were 3.8 times more likely (95% confidence interval, 3.31-4.39) to develop any serious event during the 30 days of follow-up. The pattern of serious events was similar but less pronounced among older adults living in a nursing home.

Conclusions: Serious events, as indicated by a hospital admission or death, are frequent following the short-term use of antipsychotic drugs in older adults with dementia. Antipsychotic drugs should be used with caution even when short-term therapy is being prescribed.

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NEWER ANTIPSYCHOTIC drugs (olanzapine, quetiapine fumarate, and risperidone) have been on the market for more than a decade and are commonly used to treat the behavioral and psychological symptoms of dementia. They have largely replaced the older conventional antipsychotic medications.[1] Cohort studies examining safety concerns have individually explored the association between the use of antipsychotic drugs and adverse events such as extrapyramidal symptoms (EPS),[2,3] falls,[4] hip fractures,[5] cerebrovascular events,[6,7] or death.[8,9] Cohort studies have not simultaneously assessed the risk of developing any one of these or other serious events.

Antipsychotic drugs are often used for short periods to treat agitation in clinical practice. They are frequently prescribed around the time of nursing home admission. Of residents newly admitted to a nursing home, 17% are started on antipsychotic drug within 100 days of their admission, and 10% receive only a single antipsychotic prescription.[10] In some guidelines, antipsychotic drugs are recommended for short-term use as part of the pharmacologic treatment of delirium,[11] although there is no randomized controlled trial evidence to support this practice.[12] Given the frequency of the short-term use of these agents, it is important to evaluate their safety.

We examined serious adverse events associated with the use of antipsychotic drugs in a population-based cohort to characterize the full effect of short-term harm associated with these agents. Specifically, we determined the risk of developing the composite outcome of *any serious event* among older adults with dementia dispensed an atypical antipsychotic drug relative to those dispensed a conventional antipsychotic drug and to a matched control group. Because the severity of serious adverse events differ, we also describe the distribution of individual outcomes.

Author Affiliations are listed at the end of this article.

METHODS

DATA SOURCES

We conducted a population-based retrospective cohort study using Ontario, Canada, administrative health care data between April 1, 1997, and March 31, 2004. During the study period, Ontario had a population of approximately 1.4 million older adults. Provincial health coverage for these individuals includes most physician services, hospital admissions, and prescription drugs that are listed on the Ontario Drug Benefit formulary. This study used 4 linkable administrative health care databases that contain demographic data for eligible claimants, diagnostic information from the physician claims and hospital discharge abstracts, and drug information from the drug benefit claims. The study was approved by the Ethics Review Board of Sunnybrook Health Sciences Centre.

COHORT DEFINITION

Dementia Cohort

We created a cohort of all Ontario residents 66 years and older who received a diagnosis of dementia and a prescription for an antipsychotic drug between April 1, 1997, and March 31, 2004. *International Classification of Diseases, Ninth Revision*, and *International Statistical Classification of Diseases, 10th Revision*, diagnosis codes and drug therapies were used to define the cohort, outcome definitions, and exclusion criteria.

Cohort entry was the date of the first claim for an atypical or conventional antipsychotic drug. We excluded individuals with a history of schizophrenia, tics, Huntington disease, and dialysis during the previous 5 years because antipsychotic therapy is used differently in these contexts.

To ensure that all individuals were at risk for one of the serious adverse events, we excluded individuals with a history of parkinsonism or other EPS during the previous 5 years. We also excluded individuals with a history of brain tumor because this condition may predispose individuals to develop parkinsonism and has been used as an exclusion criterion in previous studies.[2,3] Similarly, as has been done in previous work,[13] we also excluded individuals with a diagnosis of epilepsy or trauma or a history of pathological fractures or hip fractures because these conditions may predispose patients to develop a subsequent hip fracture. To ensure that death was likely related to antipsychotic therapy, we excluded deaths among individuals receiving palliative care because, although antipsychotic drugs may be used in this setting, death is an expected outcome.

We divided our population into 2 groups: a community-dwelling cohort and a nursing home cohort. Individuals were included in the nursing home cohort if their index drug claim was submitted by a long-term care facility. Otherwise, they were assumed to be community dwellers. Nursing home residents were evaluated separately because prescription rates for antipsychotic drugs are substantial in nursing homes,[10,14] and they are generally more vulnerable to experiencing an adverse event because of advanced age, multiple medical problems, and use of multiple drug therapies.

For each cohort, we identified 3 groups based on antipsychotic drug exposure: none, atypical, or conventional. The latter 2 groups included individuals who received a new prescription for atypical or conventional antipsychotic drugs. New use of antipsychotic drugs was identified if any atypical (olanzapine, quetiapine, and risperidone) or conventional (eg, haloperidol, loxapine) agents were dispensed following cohort entry. Clozapine was almost never used in this patient population and therefore was not included in the analysis. The "none" group was a control group that included older adults with dementia who had not been given prescriptions for antipsychotic drugs but had been given at least 1 other medication. This ensured recent physician contact and additional homogeneity across cohorts. Cohort entry for the control group was defined as the most recent medication claim on or before a date chosen randomly from the accrual period. If the most recent claim took place more than 6 months before that date, or if it took place before the start of the accrual period, the subject was excluded from the analysis.

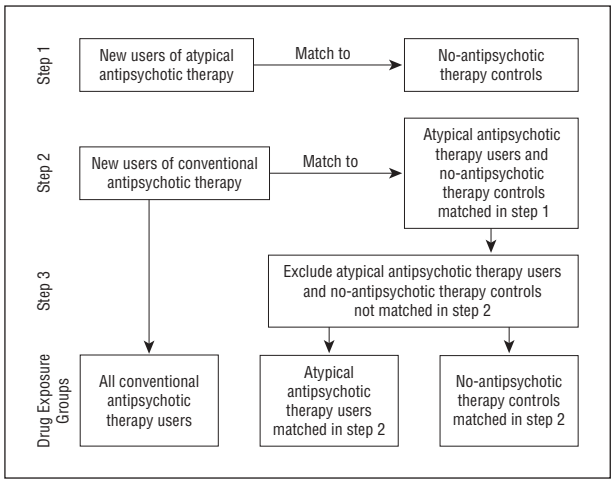

Figure 1. Propensity-based matching process to identify 3 drug exposure groups of equal size. Since users of conventional antipsychotic therapy made up the smallest group, no additional exclusions from that group were necessary.

Cohort Matching

Propensity-based matching was used to create 3 drug exposure groups for community dwellers and nursing home residents. The goal was to create homogeneous groups that differed only by their exposure to antipsychotic therapy. We used logistic regression to compute 2 sets of propensity scores for (1) the probability of receiving an atypical antipsychotic drug vs none; and (2) the probability of receiving atypical vs conventional antipsychotic drugs. The propensity score analysis was performed separately for the community and nursing home groups. Comorbidity was measured using the Charlson comorbidity index,[15] based on hospital admissions in the previous 5 years and the number of distinct drug therapies dispensed in the year before the index date.

The matching process was executed in 3 steps (**Figure 1**). First, new users of atypical antipsychotic drugs were matched to controls. Second, new users of conventional antipsychotic drugs (the smallest group) were matched to users of atypical drugs who were successfully matched in the first step. Finally, we excluded any users of atypical antipsychotic drugs and the corresponding controls if they were not matched to a conventional antipsychotic drug user in the second step. All matching was 1:1 and used a greedy matching algorithm with a caliper width of 0.6 of the standard deviation of the logit of the propensity score.[16] Using this approach, we identified 3 similar drug exposure groups of equal size.

OUTCOMES

The primary outcome was the composite category of any serious event. All events were identified in the 30 days following cohort entry. Our definition of any serious event was based on the International Conference on Harmonization *Clinical Safety*

Data Management: Definitions and Standards for Expedited Reporting[17] guidelines. A serious adverse event is one that results in death, is life threatening, requires inpatient hospital admission or prolongation of existing hospital stay, or results in persistent or significant disability/incapacity. Individuals in our cohort were all living in the community or in a nursing home setting at the time of cohort entry and therefore prolongation of an existing hospital stay was not relevant. Congenital anomalies and birth defects did not apply to our older population.

The composite outcome included only adverse events resulting in hospital admission or death that occurred within 30 days of initiating antipsychotic therapy. Acute care hospital admissions were divided into 2 categories: known serious events (ie, EPS, falls or hip fractures, and cerebrovascular events) or other events. The EPS, including parkinsonism[3] and other drug-induced movement disorders,[2] as well as falls[4] or hip fractures,[5,18] were classified as known serious events because these adverse events have been associated with antipsychotic drug use in previous studies. Hospital admissions for a cerebrovascular event were classified as a known serious event because warnings issued to physicians by Health Canada starting in 2002[19] stated that there was an increased risk of cerebrovascular events and transient ischemic attacks associated with use of antipsychotic drugs. Similar warnings were issued by the US Food and Drug Administration starting in 2003.[20] We defined other hospital admissions as acute care hospital admissions that were not for one of these known events.

We defined death as a serious event for 3 reasons. First, this is consistent with the International Conference on Harmonization definition. Second, large cohort studies[8,9] and a systematic review[21] reported a link between antipsychotic drug use and death. Finally, warnings linking death to the use of antipsychotic therapy were first issued by the US Food and Drug Administration in 2005.[20]

STATISTICAL ANALYSES

We examined the distribution of all baseline covariates across our groups after matching using standard differences. We used a 0.10 cutoff, or a 10% difference, to reflect an imbalance between groups.

To examine the effects of antipsychotic drug use on the composite outcome of any serious event we used a conditional logistic regression model adjusted by propensity-based matching. For all analyses, the no antipsychotic therapy group was the reference. We also estimated adjusted odds ratios that included all covariates with a standard difference greater than 0.10. In the community model, the covariates were use of anxiolytics, sedatives, or hypnotics; cholinesterase inhibitor use; number of physician contacts in the previous year; number of visits to any specialist (ie, psychiatrist, neurologist, or geriatrician); number of visits to a psychiatrist; number of hospital admissions; recent hospital admission; hospital admission for delirium; and computed tomographic scan of the head. In the nursing home model the covariates were number of drugs used in the previous year (identified by number of drug identification numbers); antidepressant use; cholinesterase inhibitor use; number of visits to a psychiatrist; and computed tomographic scan of the head. Analyses were performed using SAS statistical software, version 9.1.3 (SAS Institute, Cary, North Carolina).

RESULTS

The cohort included 20 682 community-dwelling older adults and 20 559 nursing home residents with dementia, all aged 66 years or older. The community-dwelling cohort included 3 propensity-matched groups of 6894 individuals, and the nursing home cohort included 3 propensity-matched groups of 6853 individuals. The characteristics of these groups were similar (**Table 1**).

The most frequently prescribed atypical antipsychotic drug at cohort entry was risperidone (community group, 5051 individuals [72.0%]; nursing home group, 5310 individuals [73.1%]) followed by olanzapine (1405 [20.0%]; 1469 [20.2%]) and quetiapine (564 [8.0%]; 486 [6.7%]). The most frequently prescribed conventional antipsychotic drugs were haloperidol (community group, 4087 individuals [58.6%]; nursing home group, 3780 individuals [52.9%]) followed by loxapine (1242 [17.8%]; 1726 [24.2%]) and thioridazine hydrochloride (745 individuals [10.7%]; 830 [11.6%]).

COMMUNITY GROUP

In the community cohort, we matched all 6894 individuals who were given an atypical antipsychotic drug to individuals in the control group. We matched 6894 (99.2%) of those who were given a conventional antipsychotic drug to individuals in the atypical antipsychotic therapy group.

The 30-day distribution of the frequency of serious adverse events in the community cohort is outlined in **Figure 2**A. Among 6894 community-dwelling older adults in the atypical antipsychotic therapy group, 960 individuals (13.9%) were classified as having experienced any serious event. This included 140 individuals (2.0%) with a hospital admission for known serious events (20 [0.3%] for EPS, 82 [1.2%)] for a fall or hip fracture, and 47 [0.7%] for a cerebrovascular event) and 760 individuals (11.0%) in the other hospital admissions category. Furthermore, 186 individuals (2.7%) in this group died. The pattern of serious adverse events was similar among drug exposure groups, but events were more frequent among individuals who received a conventional antipsychotic drug (Figure 2A).

Relative to those in the control group, individuals in the conventional antipsychotic therapy group were 3.8 times more likely to have experienced any serious event at 30 days' follow-up (95% confidence interval, 3.31-4.39) (**Table 2**). Those in the atypical antipsychotic therapy group were 3.2 times more likely to have experienced any serious event leading to a hospital visit or death during the 30 days of follow-up (95% confidence interval, 2.77-3.68).

NURSING HOME GROUP

In the nursing home group, we matched 6853 of the individuals (68.8%) who received a prescription for an atypical antipsychotic drug to those in the control group. We matched 6853 of the individuals (89.1%) in the conventional antipsychotic therapy group to those in the atypical antipsychotic therapy group.

The 30-day frequency of serious adverse events among nursing home residents is outlined in Figure 2B. Among 6853 older adults who received a prescription for an atypical antipsychotic drug, 645 individuals (9.4%) experienced any serious event. This included more than 80 individuals (1.2%) with a hospital admission for a known

Table 1. Characteristics of Older Adults With Dementia by Antipsychotic Drug Exposure[a]

Characteristic	Antipsychotic Therapy in the Community Group (n=20 682)			Antipsychotic Therapy in the Nursing Home Group (n=20 559)		
	None (n=6894)	Atypical (n=6894)	Conventional (n=6894)	None (n=6853)	Atypical (n=6853)	Conventional (n=6853)
Demographic characteristic						
Age, mean (SD), y	81.6 (7.0)	81.9 (7.0)	81.5 (7.0)	85.2 (6.9)	84.9 (7.0)	84.8 (7.0)
Women	4400 (63.8)	4208 (61.0)	4187 (60.7)	4922 (71.8)	4825 (70.0)	4734 (69.1)
Rural residence	944 (13.7)	991 (14.4)	1009 (14.6)	941 (13.7)	1025 (15.0)	1033 (15.1)
Low income	2307 (33.5)	2510 (36.4)	2507 (36.5)	3116 (45.5)	3029 (44.2)	3008 (43.9)
Comorbidity, mean (SD)						
Charlson score	0.9 (1.5)	1.1 (1.6)	1.2 (1.7)	1.2 (1.6)	1.2 (1.6)	1.2 (1.6)
No. of DINs used in past year	9.9 (6.2)	9.3 (6.8)	9.3 (7.0)	10.8 (6.6)	8.9 (6.6)	9.2 (6.9)
Psychotropic medication use in past 120 d						
Antidepressants	1611 (23.4)	1623 (23.5)	1633 (23.7)	2358 (34.4)	1776 (25.9)	1765 (25.8)
Anxiolytics, sedatives, and hypnotics	1703 (24.7)	2227 (32.3)	2220 (32.2)	2730 (39.8)	2535 (37.0)	2587 (37.7)
Anticonvulsants	174 (2.5)	222 (3.2)	240 (3.5)	305 (4.5)	272 (4.0)	267 (3.9)
Antimanic agents	12 (0.2)	17 (0.2)	16 (0.2)	19 (0.3)	11 (0.2)	11 (0.2)
Cholinesterase inhibitors	1195 (17.3)	331 (4.8)	336 (4.9)	439 (6.4)	183 (2.7)	185 (2.7)
Physician contacts in past year						
Any physician, mean (SD)	24.4 (22.6)	29.0 (27.2)	29.0 (27.3)	39.6 (27.5)	40.1 (30.3)	40.9 (30.5)
Any specialist mean (SD)	1.0 (3.2)	1.4 (4.6)	1.4 (4.3)	0.8 (4.1)	1.0 (4.6)	1.2 (4.9)
Mean (SD) No. of visits to						
Geriatrician	0.41 (1.9)	0.42 (2.1)	0.39 (2.0)	0.29 (2.2)	0.33 (2.3)	0.41 (2.9)
Neurologist	0.30 (1.1)	0.38 (2.2)	0.39 (1.6)	0.19 (1.8)	0.25 (2.6)	0.28 (2.3)
Psychiatrist	0.28 (2.1)	0.62 (2.9)	0.63 (3.2)	0.32 (2.9)	0.43 (2.6)	0.47 (2.7)
Hospital admissions before cohort entry						
No. of admissions in past 5 y, mean (SD)	1.4 (1.8)	1.7 (2.2)	1.7 (2.3)	1.7 (2.0)	1.7 (2.3)	1.8 (2.0)
Admitted in past 3 mo	1191 (17.3)	1822 (26.4)	1797 (26.1)	1057 (15.4)	1303 (19.0)	1489 (21.7)
Admitted for delirium in past year	134 (1.9)	257 (3.7)	257 (3.7)	116 (1.7)	173 (2.5)	203 (3.0)
Computed tomographic scan in past year	1648 (23.9)	2032 (29.5)	2026 (29.4)	850 (12.4)	1099 (16.0)	1230 (17.9)

Abbreviation: DINs, drug identification numbers.
[a]Data are given as the number (percentage) of individuals, unless otherwise indicated.

serious adverse event (less than 6 for EPS, 67 [1.0%] for a fall or hip fracture, and 11 [0.2%] for a cerebrovascular event) and 311 (4.5%) in the other hospital admission category. In addition, 355 nursing home residents (5.2%) died within 30 days of receiving a prescription for an atypical antipsychotic drug. The pattern of hospital admissions and deaths was similar among drug exposure groups but serious adverse events were more frequent in the conventional antipsychotic therapy group.

Relative to nursing home residents in the control group, individuals in the conventional antipsychotic therapy group were 2.4 times more likely to experience a serious adverse event leading to an acute care hospital admission or death (95% confidence interval, 2.08-2.72). Those in the atypical antipsychotic group were 1.9 times more likely to experience a serious adverse event during 30 days of follow-up (95% confidence interval, 1.68-2.21) (Table 2).

COMMENT

We examined the composite outcome of any serious event and its association with antipsychotic therapy to gain a better appreciation of the short-term spectrum of harm associated with use of these drugs. Our data indicate that serious adverse events occur frequently within 30 days of initiating antipsychotic therapy as indicated by an acute care hospital admission or death. Relative to community-dwelling older adults with dementia who did not receive a prescription for antipsychotic drugs, similar older adults who did receive atypical antipsychotic drugs were 3 times more likely and those who received a conventional antipsychotic drug were almost 4 times more likely to experience a serious adverse event within 30 days of starting therapy.

Our findings also demonstrate that these serious adverse events are more common among those who receive a prescription for a conventional antipsychotic drug relative to those who receive a prescription for a newer atypical drug. These findings are consistent with other studies demonstrating that, although the pattern of serious adverse events is similar for the 2 types of antipsychotic therapy, these events are more frequent in the conventional antipsychotic therapy group. This same pattern was identified in studies evaluating the relationship between antipsychotic therapy and parkinsonism,[3] drug-induced movement disorders,[2] hip fractures,[18] and death.[8,9] A meta-analysis of short-term randomized controlled trials (ie, 6- to 12-week duration)[21] and a recent observational study[9] have demonstrated that the risk of death with antipsychotic therapy emerges within weeks, justifying our use of a 30-day end point in the present study. This

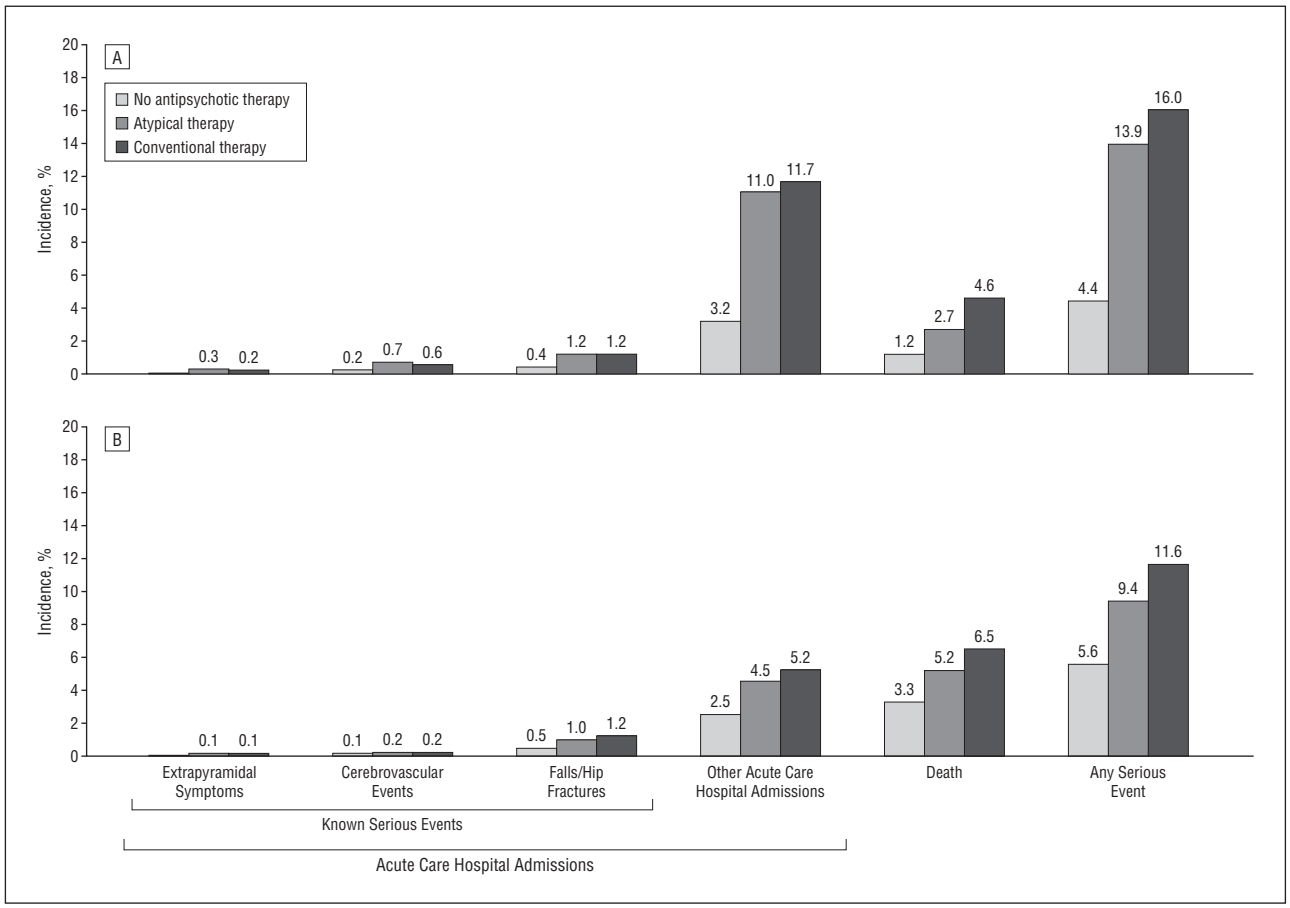

Figure 2. The distribution of any serious event within 30 days of cohort entry among community-dwelling older adults (A) and nursing home residents (B) by type of antipsychotic therapy. The figure describes the composite outcome "Any Serious Event." This outcome was considered present if an individual had a hospital admission for a known serious event, or a hospital admission for another reason, or if the individual died.

close temporal relationship between exposure and outcomes, and the consistency with previous studies, are strengths of our study.

The pattern of serious adverse events was similar for the community and nursing home groups, although it was less pronounced among nursing home residents. It is particularly important to fully understand the short-term effect of the use of antipsychotic drugs in nursing homes because these drugs are so widely used in this setting. A recent study of nursing homes in Ontario demonstrated that more than a third of nursing home residents receive prescriptions for antipsychotic drugs.[14] Moreover, antipsychotic drugs are 1 of 3 types of medications responsible for the most adverse events in nursing homes.[22]

Cohort studies can play an important role in postmarketing surveillance of medications. Data on serious adverse events can be difficult to obtain from published trial data. Some information on the spectrum of adverse events associated with antipsychotic drugs has been obtained from a systematic review[23] and a meta-analysis,[21] but these studies were limited by the poor reporting of adverse events in the individual trials included in their samples.[23] For example, Schneider et al[20] found it difficult to obtain counts of adverse events because published trials did not report less frequent events. Furthermore, not all randomized controlled trials were published, which excludes important data from the public domain. Data on the occurrence of cerebrovascular events and death associated with antipsychotic therapy were obtained from warnings issued to the public by federal agencies in Canada and the United States that were in turn based on unpublished data.[20] In addition, data obtained from randomized controlled trials may not fully represent the true risk in frail older adults with dementia who are not the subjects of these trials.

Our study is unique in that it uses population-based data to explore the range of serious adverse events associated with antipsychotic drugs. Knowing the risk of developing a single adverse event (ie, EPS, a fall or hip fracture, a cerebrovascular event, or death) is important, but when a drug causes multiple adverse events, it is important to know the risk of developing *any* of these serious events. Our study provides patients and physicians with this important clinical information. We used the International Conference on Harmonization definition of serious adverse events as a base from which to identify serious events in our cohort. Relative to clinical trials, we studied serious events in a real-world setting, in which individuals are often more frail[24,25] and more likely to experience an adverse event than those enrolled in trials.

Our study likely underestimates the prevalence of adverse events associated with antipsychotic therapy for 2 reasons. First, we focus only on serious adverse

Table 2. Risk of Any Serious Event Within 30 Days of Beginning Antipsychotic Therapy

	Community Group (n=20 682)		Nursing Home Group (n=20 559)	
Antipsychotic Therapy	OR (95% CI)[a]	Adjusted OR (95% CI)[b]	OR (95% CI)[a]	Adjusted OR (95% CI)[b]
None	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Atypical	3.54 (3.09-4.05)	3.19 (2.77-3.68)	1.76 (1.54-2.01)	1.92 (1.68-2.21)
Conventional	4.19 (3.66-4.79)	3.81 (3.31-4.39)	2.23 (1.96-2.53)	2.38 (2.08-2.72)

Abbreviations: CI, confidence interval; OR, odds ratio.
[a] The ORs were obtained using a conditional logistic regression model that was adjusted by propensity-based matching.
[b] Adjusted ORs were obtained using a conditional logistic regression model that was adjusted by propensity-based matching and for all covariates with a standard difference greater than 0.10. For a description of the covariates, please see the "Statistical Analyses" subsection of the "Methods" section.

events and therefore evaluate only those EPS or falls severe enough to result in an acute care hospital admission. Many physicians who observe the early signs of such problems (eg, mild EPS or unstable gait) would discontinue the antipsychotic therapy and likely avert a more serious adverse event. In the CATIE-AD (Clinical Antipsychotic Trials of Intervention Effectiveness–Alzheimer's Disease) study,[26] EPS were the adverse event most commonly responsible for discontinuation of antipsychotic therapy. Furthermore, nursing home residents often have their medical problems managed in the home, thereby avoiding the need for admission to an acute care hospital. Serious adverse events that are managed outside the acute care hospital are not included in our analyses. Second, our follow-up time was short, so we cannot account for adverse events that took longer to develop or to be recognized by the physician. For example, one type of EPS known as tardive dyskinesia generally develops after months or years of drug use and would likely not have been identified during the short follow-up period in this study. Our results exploring serious adverse events likely identify only the "tip of the iceberg." Nonetheless, we demonstrated that the frequency of the serious adverse events we do identify is substantial. As with all observational cohort studies, there is the potential risk for selection bias when choosing a comparable group and of confounding in the estimation of risks associated with serious adverse events in this population. To limit the potential for selection bias, we used a propensity-based matching technique. This strategy results in treatment groups that are well balanced across several important measured covariates. However, it is still possible that our results may have been influenced by unmeasured confounders.

CONCLUSIONS

Serious adverse events, as indicated by a hospital admission or death, are frequent following the short-term use of antipsychotic therapy in older adults with dementia. Serious adverse events were more common among those who received a prescription for conventional vs atypical antipsychotic drugs. Antipsychotic drugs should be prescribed with caution even for short-term therapy.

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Author Affiliations: Departments of Medicine (Drs Rochon, Lipscombe, and Bell) and Health Policy, Management, and Evaluation (Drs Rochon, Anderson, and Bell), University of Toronto; Institute for Clinical Evaluative Sciences (Drs Rochon, Gill, Anderson, Lipscombe, and Bell and Mss Gomes, Melo, and Sykora); Kunin-Lunenfeld Applied Research Unit, Baycrest (Dr Rochon); Department of Medicine, Women's College Hospital (Dr Lipscombe); and Department of Medicine and Keenan Research Centre (Dr Bell), Li Ka Shing Knowledge Institute (Ms Melo), St Michael's Hospital, Toronto, Ontario, Canada; Department of Health Care Policy, Harvard Medical School, and Department of Biostatistics, Harvard School of Public Health, Boston, Massachusetts (Dr Normand); Queen's University, Kingston, Ontario, Canada (Dr Gill); and Meyers Primary Care Institute, University of Massachusetts Medical School, Worcester (Dr Gurwitz).
Correspondence: Paula A. Rochon, MD, MPH, FRCPC, Kunin-Lunenfeld Applied Research Unit, Baycrest, 3560 Bathurst St, Room 732, Toronto, ON M6A 2E1, Canada.
Author Contributions: Drs Rochon, Normand, Anderson, Bell, and Gurwitz had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Rochon, Normand, Anderson, Melo, Sykora, and Bell. *Acquisition of data:* Gomes. *Analysis and interpretation of data:* Rochon, Normand, Gomes, Gill, Anderson, Sykora, Lipscombe, Bell, and Gurwitz. *Drafting of the manuscript:* Rochon, Normand, Gomes, and Bell. *Critical revision of the manuscript for important intellectual content:* Rochon, Normand, Gill, Anderson, Melo, Sykora, Lipscombe, Bell, and Gurwitz. *Statistical analysis:* Normand, Gomes, Gill, Sykora, and Bell. *Obtained funding:* Rochon and Anderson. *Administrative, technical, and material support:* Gill and Anderson. *Study supervision:* Rochon.
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Correction

Errors in Table. In the Original Investigation titled "Lipoprotein(a) Levels and Risk of Future Coronary Heart Disease: Large-Scale Prospective Data," by Bennet et al, published in the March 24 issue of the *Archives* (2008; 168[6]:598-608), errors occurred in Table 1 on page 599. In the lipid factors section of that table, the mean (SD) log triglyceride and log lipoprotein(a) values for cases should have been given as 4.63 (0.45) mg/dL and 2.07 (1.61) mg/dL, respectively, and the values for controls should have been given as 4.51 (0.44) mg/dL and 1.74 (1.73) mg/dL, respectively. In addition, the last footnote should have read as follows: "[c]Median (interquartile range) values for C-reactive protein, triglycerides, and lipoprotein(a) were 1.41 mg/L (0.67-3.05 mg/L), 93 mg/dL (67-128 mg/dL), and 9.4 mg/dL (3.0-23.2 mg/dL), respectively."