



### Editor's key points

► There is a considerable concern about antidepressants and antipsychotics being prescribed to people with dementia who do not appear to suffer from relevant symptoms. This study provides an analysis of the prescribing of these medications to people with dementia for whom there was no documented evidence of depression or psychosis.

► This study found that family physicians usually prescribe antidepressants and antipsychotics appropriately; however, substantial numbers of people with dementia across Canada appear to be being prescribed these medications by their primary care providers without documented evidence of clinical need and despite being at risk of known adverse effects.

► Immediate, improved, and continued training and support in the management of people with dementia in primary care is of the utmost importance. Further research should focus both on estimating risks to patients with dementia associated with potentially inappropriate prescribing and on trialing and evaluating innovative deprescribing interventions, particularly in primary care.

# Antidepressant and antipsychotic prescribing in primary care for people with dementia

Neil Drummond PhD Lynn McCleary RN PhD Elizabeth Freiheit PhD  
Frank Molnar MD MSc MDCM FRCPC William Dalziel MD FRCPC Carole Cohen MD  
Diana Turner MD Rebecca Miyagishima MSc James Silvius MD

## Abstract

**Objective** To use data from the Canadian Primary Care Sentinel Surveillance Network (CPCSSN) to evaluate the prevalence of antidepressant and antipsychotic prescriptions among patients with no previous depression or psychosis diagnoses, and to identify the factors associated with the use of these drugs in this population.

**Design** Retrospective cohort study using data derived from CPCSSN.

**Setting** Primary care practices associated with CPCSSN.

**Participants** Patients who were born before 1949; who were associated with a CPCSSN primary care practitioner between October 1, 2007, and September 30, 2013; and whose electronic medical records contained data from at least 6 months before and 12 months after the date of dementia diagnosis.

**Main outcome measures** Prescription for an antidepressant or antipsychotic medication in the absence of a depression or psychosis diagnosis. Multivariable models were fitted to determine estimated odds ratios (ORs) and were adjusted for age and sex.

**Results** Of the 3252 patients without a depression diagnosis, 8.5% received a new prescription for an antidepressant in the 12 months following their diagnosis of dementia. Prescribing was reduced in association with older age (OR of 0.86 per 5-year age increase,  $P=.001$ ) and male sex (OR=0.77,  $P=.056$ ), and prescribing increased in association with prescription of cholinesterase inhibitor medications (OR=1.57,  $P=.003$ ). Of the 4262 patients without a diagnosis of psychosis, 6.1% received a new prescription for an antipsychotic in the 12 months following their diagnosis of dementia. Higher rates of antipsychotic prescriptions were reported in men (OR=1.31,  $P=.046$ ), those receiving a prescription for steroids (OR=1.90,  $P=.037$ ), and those diagnosed with Parkinson disease (OR 1.58,  $P=.051$ ).

**Conclusion** A substantial number of patients with dementia are being prescribed antidepressant or antipsychotic medications by their primary care practitioners without evidence of depression or psychosis in their electronic medical records.



# La prescription d'antidépresseurs et des antipsychotiques à des clients des soins primaires qui présentent une démence

Neil Drummond PhD Lynn McCleary RN PhD Elizabeth Freiheit PhD  
Frank Molnar MD MSc MDCM FRCPC William Dalziel MD FRCPC Carole Cohen MD  
Diana Turner MD Rebecca Miyagishima MSc James Silvius MD

## Résumé

**Objectif** À l'aide des données du Réseau canadien de surveillance sentinelle en soins primaires (RCSSSP), déterminer la prévalence de la prescription d'antidépresseurs et d'antipsychotiques à des patients qui n'ont pas encore de diagnostic de dépression ou de psychose, et identifier les facteurs associés à l'utilisation de ces médicaments chez ces patients.

**Type d'étude** Une étude de cohorte rétrospective à l'aide de données provenant du RCSSSP.

**Contexte** Des établissements de soins primaires associés au RCSSSP.

**Participants** Des patients nés avant 1949 qui ont reçu des soins primaires d'un médecin du RCSSSP entre le premier octobre 2007 et le 30 septembre 2013 et dont les dossiers médicaux électroniques contenaient des données couvrant au moins 6 mois précédant le diagnostic de démence et les 12 mois suivant ce diagnostic.

**Principaux paramètres à l'étude** La prescription d'antidépresseurs ou d'antipsychotiques à des patients n'ayant pas de diagnostic de dépression ou de psychose. Des modèles multivariés ont été adaptés pour déterminer les rapports de cotes (RC) et ajustés en fonction de l'âge et du sexe.

**Résultats** Une proportion de 8,5% des 3252 patients sans diagnostic de dépression s'est vu prescrire des antidépresseurs au cours des 12 mois suivant le diagnostic de démence. La fréquence de ces prescriptions diminuait avec l'âge (RC=0.86 pour chaque 5 ans d'augmentation, P=.001), et était moindre chez les hommes (RC=0.77, P=.003), alors qu'elle augmentait chez les personnes qui recevaient un inhibiteur de la cholinestérase (RC=1.57, P=.003). Parmi les 4262 patients sans diagnostic de psychose, 6,1% se sont vu prescrire un antipsychotique dans les 12 mois suivant le diagnostic de démence. On a observé que le taux de prescription d'antipsychotiques était plus élevé chez les hommes (RC=1.31, P=.046), chez les personnes qui prenaient des stéroïdes (RC=1.90, P=.037) et chez celles qui avaient un diagnostic de maladie de Parkinson (RC=1.58, P=.051).

**Conclusion** Un nombre important de patients souffrant de démence se voient prescrire des antidépresseurs ou des antipsychotiques par leurs médecins des soins primaires sans que leurs dossiers médicaux électroniques n'indiquent clairement l'existence d'une dépression ou d'une psychose.

## Points de repère du rédacteur

► La prescription d'antidépresseurs et d'antipsychotiques à des personnes qui souffrent de démence mais qui ne semblent pas présenter de symptômes importants soulève beaucoup de questions. Cette étude a procédé à une analyse de la prescription de ce type de médicaments à des personnes qui ne présentaient aucune preuve bien documentée d'une dépression ou d'une psychose.

► Cette étude a montré que les médecins de famille prescrivent des antidépresseurs et des antipsychotiques de façon appropriée; il semble toutefois qu'au Canada, un nombre appréciable de fournisseurs de premiers soins prescrivent ce type de médicaments à des patients souffrant de démence sans preuves bien documentées d'un tel besoin et malgré des risques d'effets indésirables bien prévisibles.

► Il est d'une importance primordiale d'assurer une formation et un soutien immédiats, améliorés et continus à la prise en charge des personnes souffrant de démence dans un contexte de soins primaires. Les études à venir devront porter d'abord sur les risques associés à la prescription de médicaments potentiellement inappropriés à des patients souffrant de démence, mais aussi sur des essais avec évaluation de certaines interventions innovatrices pour diminuer un tel comportement, notamment au niveau des soins primaires.

The fastest-growing age group in Canada is seniors older than 65 years of age.<sup>1</sup> Dementia affects around 8% of all Canadians in that age group and 7.3% of those older than age 65 who live in the community and are managed by primary care providers.<sup>2</sup> Prevalence is higher with increasing age and reaches 35% of those older than age 85.<sup>3,4</sup> An estimated 500 000 to 750 000 Canadians have Alzheimer disease or a related dementia, and it is predicted that by 2031 the number of cases will have risen to 940 000.<sup>5</sup> Future provision and organization of care will probably require a community-based, primary care focus with fundamental support from specialty services. Cholinesterase inhibitors and memantine constitute the main pharmacologic treatments of dementia.<sup>6</sup> The latest comprehensive Canadian clinical guidelines for dementia, including treatment of comorbid depression and psychosis, were issued in 2012.<sup>7,8</sup>

### Antidepressant medication in people with dementia

Depression is here identified according to the validated Canadian Primary Care Sentinel Surveillance Network (CPCSSN) case definition for the condition,<sup>9</sup> deriving from evidence for treatment or symptoms, whether major or minor, constant or episodic, in a patient's electronic medical record (EMR). Depression is often associated in dementia patients with symptoms including apathy, agitation, and anxiety, and is also often associated with distress in both the patient and his or her caregiver.<sup>10</sup> Research has demonstrated that patients with dementia have been treated with antidepressants when not associated with comorbid depression.<sup>11</sup> Studies of patients with any form of dementia have identified concurrent depression in "0% to 86%,"<sup>10</sup> the range of prevalence being attributed to factors including the setting of care, the diagnostic criteria for both dementia and depression, the specific type of dementia in question, and the severity of either condition.<sup>10</sup> About 40% of patients with Alzheimer disease, the most common form of dementia, are diagnosed with the condition.<sup>12</sup> Selective serotonin reuptake inhibitors (SSRIs) are among the most widely prescribed antidepressant agents.<sup>11</sup> There is some limited evidence that certain antidepressants might be effective in treating agitation and psychosis in people with dementia.<sup>11</sup>

Although many patients with depression and dementia are prescribed antidepressant medication, there is little evidence for the effectiveness and safety of the treatment in this population. For example, Bains et al,<sup>13</sup> Weintraub et al,<sup>14</sup> Banerjee et al,<sup>15</sup> and Nelson and Devanand<sup>16</sup> found no evidence for antidepressant effectiveness in people with dementia; however, Lyketsos et al<sup>17</sup> and Bergh et al<sup>18</sup> report positive outcomes. The Fourth Canadian Consensus Conference on the Treatment of Dementia<sup>19</sup> recommends a trial of antidepressant medication in the context of relevant symptoms or in the absence of response to nonpharmacologic treatment.

### Antipsychotic medication in people with dementia

Using data from the Health Improvement Network, a 2015 study in the United Kingdom reported that less than half of people prescribed an antipsychotic appeared to have a diagnosis of psychosis.<sup>20</sup> Many who had received an antipsychotic prescription were diagnosed with dementia. The Canadian Institutes of Health Information reported that in 2013, 32% of seniors in Canadian long-term care facilities had received an antipsychotic medication with no indication of psychosis in the relevant record.<sup>21</sup> Up to 20% of people with dementia are prescribed antipsychotic medication in any year,<sup>22</sup> typically in response to behavioural and psychiatric disorders such as agitation, aggression, wandering, shouting, sleep disturbance, and psychosis, of whom less than a quarter will receive clinical benefit.<sup>23</sup> Conventional antipsychotic medications such as chlorpromazine and haloperidol have now been generally superseded by atypical antipsychotic medications like risperidone, olanzapine, and quetiapine. However, only one antipsychotic is approved by Health Canada, and none is approved by the US Food and Drug Administration, for the treatment of dementia-related psychoses. Both conventional and atypical antipsychotics are associated with increased risk of mortality in elderly people treated for dementia-related psychoses.<sup>24,25</sup> Antipsychotics are associated with an increased risk of cerebrovascular adverse events in this population<sup>26</sup> and are associated with side effects, such as sedation, which can lead to confusion and intrinsic anticholinergic activity and contribute to cognitive impairment.<sup>27</sup> The family medicine-centric supplement to the Fourth Canadian Consensus Conference on the Treatment of Dementia<sup>19</sup> explicitly identifies nonpharmacologic treatments of agitation and aggression, and is selective in recommending antipsychotic medication in the context of symptoms.

### Canadian Primary Care Sentinel Surveillance Network

Canadian primary health care provides first-contact services through family physicians, nurses, nurse practitioners, and others, and coordinates continuity of management in specialized settings through referral.<sup>28</sup> A network of networks, CPCSSN is a collaboration of 11 community-based primary care research networks across the country hosted by university departments of family medicine.<sup>29</sup> Within CPCSSN are family physician and nurse practitioner "sentinels" who consent to allow routine extraction of deidentified data from their EMRs for the purposes of quality improvement studies, epidemiology, and health services research. The network's data are extracted quarterly, mapped to a common database structure, then cleaned and coded. As of September 30, 2013, data from 500 000 patients and 500 sentinels were housed in the secure CPCSSN

database at Queen's University in Kingston, Ont. The case definition for *dementia* by CPCSSN has been proven to have good sensitivity (97%), specificity (98%), positive predictive value (73%), and negative predictive value (99%) compared with direct study of EMR data by trained reviewers.<sup>9</sup> The case definition includes any patient with evidence of dementia in his or her EMR, including patients who have been diagnosed by a non-family physician specialist and are continuing to receive care from their family physician and those patients diagnosed and managed by their primary care physician without specialist consultation. It was both designed and proven to be valid in the context of primary care specifically; and while this might not be identical to validation by direct specialist assessment, the validation metrics associated with the CPCSSN definition are strong.

### Objective of the study

While there is justification for prescribing antidepressant and antipsychotic medication to people with depression or psychosis even if they have comorbid dementia, a considerable concern exists about these drugs being prescribed to people with dementia who do not appear to suffer from relevant symptoms. Data from CPCSSN were used to investigate the prevalence of antidepressant and antipsychotic prescribing in primary care in Canada for elderly community-dwelling people newly diagnosed with dementia in which there was no documented evidence for depression or psychosis, and to identify the factors associated with the use of these drugs in this population.

## — Methods —

### Study design

We implemented a retrospective cohort study in a sample of patients with dementia (according to the CPCSSN case definition<sup>9</sup>) who were born before 1949 (to ensure that all were older than age 65 by 2013), who were associated with a CPCSSN primary care practitioner between October 1, 2007, and September 30, 2013, and whose EMRs contained data from the 6 months before and 12 months after the date of dementia diagnosis. The dementia diagnosis date was used as the baseline for the analysis. Patients were excluded if they were not linked to a single provider, if their sex and age information was missing, or if their records did not have any medications recorded.

Research ethics approval was obtained from the University of Alberta Health Research Ethics Board in Edmonton and the University of Calgary Conjoint Health Research Ethics Board in Alberta.

### Participants

We first looked at persons who were not identified as having depression according to the CPCSSN case

definition at any point in their records over the period for which data were available<sup>9</sup> (but we excluded antidepressant prescription as a criterion). The outcome used for this analysis was a prescription (yes or no) of an antidepressant in the first 12 months after the dementia diagnosis date, with no previous prescription of an antidepressant in the 6 months before the dementia diagnosis date. Antidepressants were identified by the Anatomic Therapeutic Chemical (ATC) classification codes beginning with N06A (antidepressants) or with the code N06CA01, which comprises the group of antidepressants in combination with psycholeptics (amitriptyline and psycholeptics). The ATC codes classify medications according to the organ or system on which they act and their therapeutic and chemical characteristics.

We next studied persons who were not identified as having psychosis at any point in their EMRs, including typical behavioural and psychological symptoms of dementia. In the absence of a validated CPCSSN case definition, *psychosis* was defined as any EMR entry of certain ICD-9 codes (dementia with behavioural disturbance [294.11]; delirium [290.11, 290.3, 290.41, 291.0, 292.81, 293.0, 293.1, 297.1]; delusional disorder [290.12, 290.20, 290.42, 291.5, 292.11, 293.81]; schizophrenia [295]; and bipolar disorder [296.0, 296.4, 296.5, 296.6, 296.7, 296.80, 296.89]) as a documented "health condition," or associated with an encounter with a primary care provider and with a prescription within the following 6 months of a medication with the ATC code beginning with N05A (antipsychotics). The outcome for this analysis was a prescription (yes or no) for antipsychotic medication in the 12 months on or after the dementia diagnosis date with no previous prescription of an antipsychotic medication in the 6 months before the dementia diagnosis date.

Variables of interest were the following: patient age, sex, and residence (urban or rural); health care provider age, sex, and residence (urban or rural); and presence of chronic obstructive pulmonary disease, diabetes mellitus, osteoarthritis, hypertension, epilepsy, and Parkinson disease, all defined using CPCSSN validated algorithms.<sup>9</sup> For the antidepressant analysis, psychosis was used as a covariate, and for the antipsychotic analysis, depression was used as a covariate.

In addition, prescriptions for any of the following medications (ATC codes) were included if prescribing took place in the 6 months before the dementia diagnosis date: analgesics (N02),  $\beta$ -blockers (C07, S01ED), calcium channel blockers (C08, C09BB, C09DB), and systemic corticosteroids (H02). Digitalis glycosides (ATC code C01AA) were used as a covariate for the antidepressant outcome only. Polypharmacy was an indicator variable if, in the 6 months before the dementia diagnosis, a patient had had 5 or more prescriptions for different medications in any 30-day period. The definition of *polypharmacy* did not include antidepressants when



a new antidepressant prescription was the outcome, or include antipsychotics when a new antipsychotic prescription was the outcome. One additional covariate was whether one of the following anti-dementia medications (ATC code) was prescribed on the day of dementia diagnosis: memantine (N06DX01), donepezil (N06DA02), rivastigmine (N06DA03), and galantamine (N06DA04).

### Statistical analysis

To account for dependencies in the data due to patients clustering around the same health care providers, generalized linear mixed models were used to estimate odds ratios (ORs). The models had a random intercept with provider as the repeated variable. One-to-one associations were measured first, then multivariable models were fitted. A combination of backward and forward selection was used to determine the best-fitting multivariable model, using both the magnitude of the coefficient and statistical significance as criteria. Given our intention to develop a model predictive of prescribing, covariates were identified as explanatory variables rather than as confounders, including patient and physician characteristics, comorbidities for which validated case definitions were available within the CPCSSN data set, and prescriptions for particular drug categories associated with dementia treatment or known to be associated with side effects on mood or mental health. These were tested for associations with prescribing outcomes. Covariates were also tested for interactions with age and sex as potential modifiers of the association with prescribing outcomes. Analyses were performed using R, version 3.2.2. The “glmer” command from the lme4 1.1.10 package, with binomial distribution and random intercept, was used for the generalized linear mixed models.<sup>30</sup> The *P* values were based on the likelihood ratio test.

## — Results —

Of the 600565 patients in the database, 11777 had a diagnosis of dementia and were born before 1949. Of these patients, 8821 had medication data, 4500 also had data at least 6 months before and 12 months after dementia diagnosis, and 4343 were also associated with a single health care provider and had complete information on demographic characteristics. This resulted in 2 groups of patients: 3252 who had no depression diagnosis (of whom 33 had psychosis), and 4262 who had no psychosis diagnosis (of whom 1043 had depression) (Figure 1). These 2 groups were used in the analyses.

Tables 1 and 2 show the characteristics of the overall patient sample, as well as those without a depression diagnosis and those without a psychosis diagnosis. Of the entire patient sample, 38% were men with a mean (SD) age of 82 (8.2) years; 22.0% lived in a rural area. A little more than 60% of patients had a male health care provider; however, more than half of the health care providers

represented in this sample were female. The mean (SD) age of the health providers was 48.2 (10.7) years, and 14.8% of them practised in rural areas.

Of the 3252 patients with no depression diagnosis, 276 patients (8.5%) received a new prescription for an antidepressant within 12 months of their dementia diagnosis. Of the 4262 patients with no psychosis diagnosis, 258 (6.1%) were given a new prescription for an antipsychotic within 12 months of their dementia diagnosis.

Unadjusted univariable associations between a new antidepressant prescription and patient characteristics are presented in Table 3. Older age was protective against new prescriptions among those with no depression diagnosis (OR=0.92, *P*=.038 for each increase of 5 years). Increased odds of antidepressant prescription was associated with anti-dementia medication prescriptions (OR=1.61, *P*=.002).

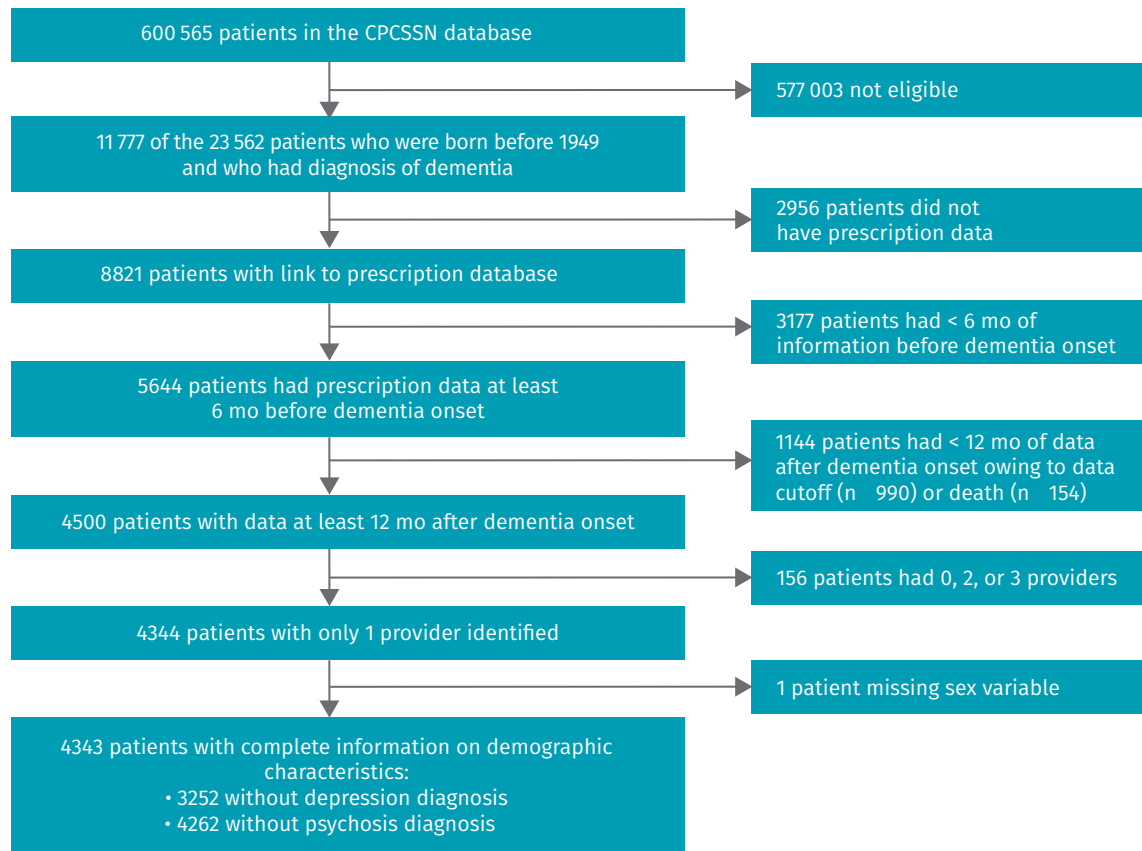
In the best multivariable model (Table 4), age and male sex were protective, with an OR of 0.86 per 5-year age increase (*P*=.001) and an OR of 0.77 for men compared with women (*P*=.056). The prescription of anti-dementia medications on the day of dementia diagnosis was associated with the prescription of antidepressants in the subsequent year (OR=1.57, *P*=.003) and with polypharmacy (OR=1.23, *P*=.155). In addition, a potential interaction was found, in which polypharmacy increased the ORs for antidepressant prescription by 1.21 times per 5-year increase in age (*P*=.037).

Unadjusted univariable associations between a new antipsychotic prescription and patient characteristics are presented in Table 5. Male sex (OR=1.31, *P*=.043) was associated with antipsychotic prescriptions.

In the best multivariable model (Table 6), male sex (OR=1.31, *P*=.046), a steroid prescription (OR=1.90, *P*=.037), and Parkinson disease (OR 1.58, *P*=.051) were all associated with increased odds of receiving an antipsychotic prescription among those without a psychosis diagnosis.

## — Discussion —

Our discussion is focused on the results of our multivariable analysis. The association we report between younger people with dementia and antidepressant prescription might be attributable to younger people expressing more worry about their diagnosis than older people do, being more likely to be informed of it themselves, and being more likely to be screened for depression or given a trial course of antidepressants. The tendency for women with dementia to receive more prescriptions for antidepressants might be reflective of the gendered distribution of prescriptions for these medications in the general population.<sup>31</sup> The associations between prescription of antidepressants with anti-dementia medication and with polypharmacy might indicate a tendency among physicians to treat aggressively in general, or reflect the observation that

**Figure 1. Derivation of analysis sample**

CPCSSN—Canadian Primary Care Sentinel Surveillance Network.

behavioural problems might respond to cholinesterase inhibitor treatment.<sup>32</sup> The interaction between polypharmacy and age in relation to antidepressant prescribing might be reflective of developing diagnostic or clinical complexity, increased patient burden, or concern for side effects in older people.

The higher rate of antipsychotic prescribing for men might be explained by the latter being thought to be more likely to become aggressive and difficult to provide care for than women. However, there appears to be no evidence in support of this interpretation in terms of the prevalence of behavioural disorders in association with sex.<sup>33</sup> Steroids are a known cause of mood symptoms and mental health problems, and Parkinson disease is often complicated by psychosis (as a symptom and as a medication side effect associated with dopaminergic treatment) and might be indicative of a non-Alzheimer dementia.

### Strengths and limitations

Longitudinal data on a large volume of community-based

patients and primary care physicians and nurse practitioners across the country is collected by CPCSSN. The data are based on physician or nurse practitioner diagnoses and contain an array of important clinical information. The CPCSSN denominator calculations and case definitions are proven by research and the patient and provider samples have been shown to be representative of the base populations of Canadian citizens and Canadian family physicians. Anonymization and data cleaning algorithms by CPCSSN are robust and effective.

The main limitations of the study derive from the quality of the data entered into the EMR. No enforceable EMR data entry standards exist in Canada and data quality can be highly variable despite the application of CPCSSN cleaning and coding algorithms. It is not possible to identify type and severity of dementia, which is an important factor in determining the medications received. People with even uncomplicated dementia are often referred to specialist geriatric psychiatrists, geriatricians, or neurologists<sup>34</sup> from whom communication about treatment, including prescribing,

might be uncertain and if conducted through non-electronic means (fax, mail, and telephone) might be entirely unrecorded in the primary care EMR. The observational window was restricted to 12 months postdiagnosis to increase the number of eligible cases available for analysis. One effect of this is to limit our study to the prescription of antidepressant and antipsychotic

medications in the “peri-diagnostic” period, in which the incidence of depression and psychosis might be lower than later in the course of the disease; however, in practice, many people are diagnosed with dementia late in the course of the disease anyway. In addition, analysis of a longer data series would help provide more definitive rates for “non-indicated” prescribing.

**Table 1. Characteristics of patients: Mean (SD) age of the entire patient sample, of those without depression diagnosis, and of those without psychosis diagnosis was 82.0 (8.2) years, 82.7 (7.9) years, and 82.1 (8.2) years, respectively.**

CHARACTERISTICS	ENTIRE PATIENT SAMPLE (N 4343), N (%)	THOSE WITHOUT DEPRESSION DIAGNOSIS (N 3252), N (%)	THOSE WITHOUT PSYCHOSIS DIAGNOSIS (N 4262), N (%)
Male sex	1653 (38.1)	1277 (39.3)	1627 (38.2)
Residence in rural area*	910 (22.1)	687 (22.3)	893 (22.1)
Antidepressant prescription before dementia diagnosis	764 (17.6)	365 (11.2)	746 (17.5)
Antipsychotic prescription before dementia diagnosis	127 (2.9)	70 (2.2)	112 (2.6)
Analgesic prescription before dementia diagnosis	671 (15.5)	447 (13.7)	658 (15.4)
β-blocker prescription before dementia diagnosis	606 (14.0)	454 (14.0)	597 (14.0)
Calcium channel blocker prescription before dementia diagnosis	540 (12.4)	405 (12.5)	532 (12.5)
Digoxin prescription before dementia diagnosis	89 (2.0)	69 (2.1)	NA
Steroid prescription before dementia diagnosis	125 (2.9)	88 (2.7)	125 (2.9)
Polypharmacy in 6 mo preceding dementia diagnosis	1257 (28.9)	876 (26.9)	1235 (29.0)
Polypharmacy (excluding antidepressants) in 6 mo preceding dementia diagnosis	1185 (27.3)	846 (26.0)	NA
Polypharmacy (excluding antipsychotics) in 6 mo preceding dementia diagnosis	1237 (28.5)	NA	1215 (28.5)
Anti-dementia medication prescribed on date of dementia diagnosis	766 (17.6)	613 (18.8)	757 (17.8)
COPD	749 (17.2)	521 (16.0)	729 (17.1)
Diabetes	1085 (25.0)	787 (24.2)	1062 (24.9)
Epilepsy	147 (3.4)	98 (3.0)	144 (3.4)
Hypertension	2768 (63.7)	2052 (63.1)	2714 (63.7)
Osteoarthritis	1704 (39.2)	1184 (36.4)	1671 (39.2)
Parkinson disease	253 (5.8)	161 (5.0)	243 (5.7)
Psychotic episodes	81 (1.9)	33 (1.0)	NA
Depression	1091 (25.1)	NA	1043 (24.5)

COPD—chronic obstructive pulmonary disease, NA—not applicable.  
 \*Residency information available for only 4117 patients among the entire sample, 3078 patients among those without depression diagnosis, and 4040 patients among those without psychosis diagnosis.

**Table 2. Characteristics of health care providers: A) Characteristics of patients' health care providers and B) characteristics of health care providers.**

A) PATIENTS HEALTH PROVIDERS	ENTIRE PATIENT SAMPLE (N 4343)	THOSE WITHOUT DEPRESSION DIAGNOSIS (N 3252)	THOSE WITHOUT PSYCHOSIS DIAGNOSIS (N 4262)
Patient's health provider is male, N (%)	2680 (61.7)	2025 (62.3)	2626 (61.6)
Patient's health provider practises in rural area, N (%)	768 (17.7)	587 (18.1)	756 (17.7)
Mean (SD) age of patient's health provider age,* y	51.4 (10.2)	51.7 (10.2)	51.4 (10.2)
B) HEALTH CARE PROVIDERS	ENTIRE HEALTH CARE PROVIDER SAMPLE (N 385)	HEALTH CARE PROVIDERS OF THOSE WITHOUT DEPRESSION DIAGNOSIS (N 365)	HEALTH CARE PROVIDERS OF THOSE WITHOUT PSYCHOSIS DIAGNOSIS (N 377)
Health care provider is male, N (%)	184 (47.8)	180 (49.3)	184 (48.8)
Health care provider practises in rural area, N (%)	57 (14.8)	55 (15.1)	57 (15.1)
Mean (SD) age of health care provider,* y	48.2 (10.7)	48.4 (10.7)	48.2 (10.7)

\*Information on health care provider's age was available for only 3994 patients and for 341 health care providers among the entire sample; 3009 patients and 321 health care providers among those without depression diagnosis; and 3920 patients and 341 health care providers among those without psychosis diagnosis.

## Conclusion

As the population of people with dementia in Canada grows through societal aging, the responsibility for providing diagnosis and care for them is likely to fall increasingly onto community-based primary care providers. This study provides the first analysis of the prescribing of antidepressant and antipsychotic

medication for people with dementia in primary care across the country, using clinical data derived directly from the sector of interest. In general our data indicate that family physicians are usually prescribing these medications appropriately, but we do find that small proportions across the country yet substantial numbers of people with dementia living in the community appear to be

**Table 3. Univariable associations between a new antidepressant prescription and characteristics of patients without depression diagnosis**

CHARACTERISTIC	NEW ANTIDEPRESSANT PRESCRIPTION		
	ESTIMATED OR	95% CI	P VALUE
Patient age (per 5-y increase)	0.92	0.85-0.99	.038
Male sex	0.80	0.61-1.04	.093
Residence in rural area*	1.17	0.84-1.63	.357
Health care provider age (per 5-y increase) <sup>†</sup>	1.05	0.97-1.13	.250
Male health care provider	0.76	0.57-1.02	.073
Analgesic prescription <sup>‡</sup>	0.96	0.66-1.38	.818
β-blocker prescription <sup>‡</sup>	0.94	0.64-1.36	.722
Calcium channel blocker prescription <sup>‡</sup>	0.83	0.55-1.24	.344
Digoxin prescription <sup>‡</sup>	1.19	0.53-2.69	.683
Steroid prescription <sup>‡</sup>	1.05	0.49-2.23	.907
Antipsychotic prescription <sup>‡</sup>	0.80	0.31-2.03	.623
Polypharmacy (not including antidepressants) <sup>§</sup>	1.28	0.97-1.70	.085
Anti-dementia medication prescription <sup>  </sup>	1.61	1.20-2.17	.002
Ever psychosis	1.61	0.54-4.74	.415
COPD	1.34	0.98-1.85	.077
Diabetes	1.00	0.75-1.34	.992
Epilepsy	0.95	0.45-2.01	.890
Hypertension	1.06	0.81-1.38	.669
Osteoarthritis	1.14	0.88-1.48	.321
Parkinson disease	1.09	0.63-1.91	.756

COPD—chronic obstructive pulmonary disease, OR—odds ratio.  
 \*Owing to missing patient residency information, this analysis is based on a sample of 3078 patients.  
 †Owing to missing information on health care provider age, this analysis is based on a sample of 3009 patients.  
 ‡Prescription of the medication in the 6 months before the dementia diagnosis.  
 §Prescription of 5 or more medications within a 30-day period in the 6 months before the dementia diagnosis.  
 ||Prescription of the medication on the day of dementia diagnosis.

**Table 4. Final multivariable model for a new antidepressant prescription for patients without depression diagnosis: Among the 3252 patients without depression diagnosis, 276 (8.5%) were given a new antidepressant prescription.**

CHARACTERISTIC	NEW ANTIDEPRESSANT PRESCRIPTION		
	ESTIMATED OR	95% CI	P VALUE
Male sex	0.77	0.59-1.01	.056
Age, per 5-y increase*	0.86	0.78-0.94	.001
Anti-dementia medication prescription <sup>†</sup>	1.57	1.16-2.12	.003
Polypharmacy <sup>‡</sup>	1.29	0.92-1.64	.058
Polypharmacy interaction with age increase <sup>§</sup>	1.21	1.01-1.46	.037

OR—odds ratio.  
 \*This OR would be valid for people with no polypharmacy.  
 †Prescription for anti-dementia medication on date of dementia diagnosis.  
 ‡At least 5 different prescriptions filled within a 30-day window, within 6 months of dementia diagnosis. This OR estimate valid for those aged 82.  
 §Change in OR for people with polypharmacy for each 5-year increase in age.



being prescribed antidepressant and antipsychotic medications by their primary care providers without documented evidence for clinical need and despite being at risk of known adverse effects. Immediate, improved, and continuing training and support in the management of people with dementia in primary care is of the utmost importance. Further research should focus both on estimating risks to patients with dementia associated with potentially inappropriate prescribing and on trialing and evaluating innovative deprescribing interventions, particularly in primary care. Examples of the latter include audit and feedback processes<sup>35</sup> and other mechanisms for facilitating deprescribing through systemic,

financial, clinical, or social factors,<sup>36</sup> including developing methods in clinical practice for identifying and estimating patient (or caregiver) expectations of physician prescribing behaviour.<sup>37-40</sup>

**Dr Drummond** is Professor and holds the Alberta Health Services Chair in Primary Care Research in the Department of Family Medicine at the University of Alberta in Calgary. **Dr McCleary** is Associate Professor in the Department of Nursing at Brock University in St Catharines, Ont. **Dr Freiheit** is Managing Director in the Statistical Analysis of Biomedical and Educational Research unit in the Department of Biostatistics at the University of Michigan School of Public Health in Ann Arbor. **Dr Molnar** is a specialist in geriatric medicine practising in Ottawa, Ont. **Dr Dalziel** is Professor of Geriatric Medicine in the Department of Medicine at the University of Ottawa. **Dr Cohen** is the Clinical Director of the Psychiatric Services for the Elderly at Sunnybrook Health Sciences Centre in Toronto, Ont. **Dr Turner** is Medical Director of Carewest of Alberta Health Services. **Ms Miyagishima** is Research Coordinator in the Department of Family Medicine at the University of Alberta in Edmonton. **Dr Silvius** is Clinical Associate Professor in the Cumming School of Medicine at the University of Calgary.

**Table 5. Univariable associations between a new antipsychotic prescription and characteristics of patients without psychosis diagnosis**

CHARACTERISTIC	NEW ANTIPSYCHOTIC PRESCRIPTION		
	ESTIMATED OR	95% CI	P VALUE
Patient age (per 5-y increase)	1.03	0.96-1.12	.409
Male sex	1.31	1.01-1.70	.043
Residence in rural area <sup>†</sup>	1.08	0.76-1.54	.669
Health care provider age (per 5-y increase) <sup>†</sup>	0.99	0.91-1.06	.708
Male health provider	1.32	0.98-1.80	.070
Analgesic prescription <sup>‡</sup>	1.11	0.79-1.57	.541
β-blocker prescription <sup>‡</sup>	1.12	0.78-1.61	.533
Calcium channel blocker prescription <sup>‡</sup>	0.85	0.57-1.29	.444
Steroid prescription <sup>‡</sup>	1.90	1.04-3.47	.053
Antidepressant prescription <sup>‡</sup>	1.11	0.80-1.54	.540
Polypharmacy (not including antipsychotics) <sup>§</sup>	1.14	0.86-1.51	.362
Anti-dementia medication prescription <sup>  </sup>	1.32	0.96-1.82	.091
Depression	1.13	0.85-1.52	.407
COPD	1.13	0.81-1.57	.478
Diabetes	1.06	0.79-1.42	.682
Epilepsy	1.21	0.62-2.35	.587
Hypertension	0.94	0.72-1.22	.242
Osteoarthritis	0.93	0.71-1.21	.577
Parkinson disease	1.62	1.02-2.56	.051

COPD—chronic obstructive pulmonary disease, OR—odds ratio.

<sup>\*</sup>Owing to missing patient residency information, this analysis is based on a sample of 4040 patients.

<sup>†</sup>Owing to missing information on health care provider age, this analysis is based on a sample of 3920 patients.

<sup>‡</sup>Prescription of the medication in 6 months before the dementia diagnosis.

<sup>§</sup>Prescription of 5 or more medications within a 30-day period in 6 months before the dementia diagnosis.

<sup>||</sup>Prescription for the medication on the day of diagnosis.

**Table 6. Final multivariable model for new antipsychotic prescriptions for patients without psychosis diagnoses: Among the 4262 patients without psychosis diagnosis, 258 (6.1%) were given a new antipsychotic prescription.**

CHARACTERISTIC	NEW ANTIPSYCHOTIC PRESCRIPTION		
	ESTIMATED OR	95% CI	P VALUE
Male sex	1.31	1.01-1.70	.046
Age (per 5-y increase)	1.05	0.97-1.14	.261
Steroid prescription <sup>*</sup>	1.90	1.04-3.48	.037
Parkinson disease	1.58	1.00-2.51	.051

OR—odds ratio.

<sup>\*</sup>A prescription for steroids in the 6 months preceding a dementia diagnosis.

**Contributors**

All authors contributed to the concept and design of the study; data gathering, analysis, and interpretation; and preparing the manuscript for submission.

**Competing interests**

None declared

**Correspondence**

Dr Neil Drummond; e-mail [ndrummon@ualberta.ca](mailto:ndrummon@ualberta.ca)

**References**

- Government of Canada [website]. *Canadians in context. Aging population/Indicators of well-being in Canada*. Ottawa, ON: Government of Canada; 2006. Available from: <http://www4.hrsdc.gc.ca/3ndic.1t4r@-eng.jsp?id=33>. Accessed 2014 Feb 10.
- Drummond N, Birtwhistle R, Williamson T, Khan S, Garies S, Molnar F. Prevalence and management of dementia in primary care practices with electronic medical records: a report from the Canadian Primary Care Sentinel Surveillance Network. *CMAJ Open* 2016;4(2):E177-84.
- Scott KR, Barrett AM. Dementia syndromes: evaluation and treatment. *Expert Rev Neurother* 2007;7(4):407-22.
- Whitfield K, Wismer S. Inclusivity and dementia: health services planning with individuals with dementia. *Healthc Policy* 2006;1(2):120-34.
- Alzheimer Society Canada [website]. *Latest information and statistics*. Toronto, ON: Alzheimer Society Canada; 2018. Available from: <http://alzheimer.ca/en/Home/Get-involved/Advocacy/Latest-info-stats>. Accessed 2018 Oct 22.
- Ellis JM. Cholinesterase inhibitors in the treatment of dementia. *J Am Osteopath Assoc* 2005;105(3):145-58.
- Gauthier S, Patterson C, Chertkow H, Gordon M, Herrmann N, Rockwood K, et al. 4th Canadian Consensus Conference on the Diagnosis and Treatment of Dementia. *Can J Neurol Sci* 2012;39(6 Suppl 5):S1-8.
- Herrmann N, Lanctôt KL, Hogan D. Pharmacological recommendations for the symptomatic treatment of dementia: the Canadian Consensus Conference on the Diagnosis and Treatment of Dementia. *Alzheimers Res Ther* 2013;5(Suppl 1):S5. Epub 2013 Jul 8.
- Williamson T, Green ME, Birtwhistle R, Khan S, Garies S, Wong ST, et al. Validating the 8 CPCSSN case definitions for chronic disease surveillance in a primary care database of electronic health records. *Ann Fam Med* 2014;12(4):367-72.
- Meyers BS. Depression and dementia: comorbidities, identification, and treatment. *J Geriatr Psychiatry Neurol* 1998;11(4):201-5.
- Seitz DP, Adunuri N, Gill SS, Gruneir A, Herrmann N, Rochon P. Antidepressants for agitation and psychosis in dementia. *Cochrane Database Syst Rev* 2011;(2):CD008191.
- Zubenko GS, Zubenko WN, McPherson S, Spoor E, Marin DB, Farlow MR, et al. A collaborative study of the emergence and clinical features of the major depressive syndrome of Alzheimer's disease. *Am J Psychiatry* 2003;160(5):857-66.
- Bains J, Birks JS, Denning TR. Antidepressants for treating depression in dementia. *Cochrane Database Syst Rev* 2002;(4):CD003944.
- Weintraub D, Rosenberg PB, Drye LT, Martin BK, Frangakis C, Mintzer JE, et al. Sertraline for the treatment of depression in Alzheimer disease: week-24 outcomes. *Am J Geriatr Psychiatry* 2010;18(4):332-40.
- Banerjee S, Hellier J, Romeo R, Dewey M, Knapp M, Ballard C, et al. Study of the use of antidepressants for depression in dementia: the HTA-SADD trial—a multicentre, randomised, double-blind, placebo-controlled trial of the clinical effectiveness and cost-effectiveness of sertraline and mirtazapine. *Health Technol Assess* 2013;17(7):1-166.
- Nelson JC, Devanand DP. A systematic review and meta-analysis of placebo-controlled antidepressant studies in people with depression and dementia. *J Am Geriatr Soc* 2011;59(4):577-85. Epub 2011 Mar 31.
- Lyketsos CG, DelCampo L, Steinberg M, Miles Q, Steele CD, Munro C, et al. Treating depression in Alzheimer disease: efficacy and safety of sertraline therapy, and the benefits of depression reduction: the DIADS. *Arch Gen Psychiatry* 2003;60(7):737-46.
- Bergh S, Selbæk G, Engedal K. Discontinuation of antidepressants in people with dementia and neuropsychiatric symptoms (DESEP study): double blind, randomised, parallel group, placebo controlled trial. *BMJ* 2012;344:e1566.
- Moore A, Patterson C, Lee L, Vedel I, Bergman H. Fourth Canadian Consensus Conference on the Diagnosis and Treatment of Dementia. Recommendations for family physicians. *Can Fam Physician* 2014;60:433-8 (Eng), e244-50 (Fr).
- Marston L, Nazareth I, Petersen I, Walters K, Osborn DP. Prescribing of antipsychotics in UK primary care: a cohort study. *BMJ Open* 2015;4(12):e006135.
- Canadian Institute for Health Information. *When a nursing home is home: how do Canadian nursing homes measure up on quality?* Ottawa, ON: Canadian Institute for Health Information; 2013. Available from: [https://secure.cihi.ca/free\\_products/CCRS\\_QualityinLongTermCare\\_EN.pdf](https://secure.cihi.ca/free_products/CCRS_QualityinLongTermCare_EN.pdf). Accessed 2018 Oct 10.
- Crugel M, Paton G, Singh P, Jeboda R, Treloar A. Antipsychotics in people with dementia: frequency of use and rationale for prescribing in a UK mental health service. *Psychiatrist* 2012;36(5):165-9.
- Banerjee S. *The use of antipsychotic medication for people with dementia: time for action*. London, Engl: Department of Health; 2009.
- Ballard C, Hanney ML, Theodoulou M, Douglas S, McShane R, Kossakowski K, et al. The dementia antipsychotic withdrawal trial (DART-AD): long-term follow-up of a randomised placebo-controlled trial. *Lancet Neurol* 2009;8(2):151-7. Epub 2009 Jan 8.
- Schneider LS, Dagerman KS, Insel P. Risk of death with atypical antipsychotic drug treatment for dementia: meta-analysis of randomized placebo-controlled trials. *JAMA* 2005;294(15):1934-43.
- Mittal V, Kurup L, Williamson D, Muralee S, Tampi RR. Risk of cerebrovascular adverse events and death in elderly patients with dementia when treated with antipsychotic medications: a literature review of evidence. *Am J Alzheimers Dis Other Demen* 2011;26(1):10-28.
- McShane R, Keene J, Gedling K, Fairburn C, Jacoby R, Hope T. Do neuroleptic drugs hasten cognitive decline in dementia? Prospective study with necropsy follow up. *BMJ* 1997;314(7076):266-70.
- Government of Canada [website]. *Primary health care*. Ottawa, ON: Government of Canada; 2015. Available from: [www.hc-sc.gc.ca/hcs-sss/prim/index-eng.php](http://www.hc-sc.gc.ca/hcs-sss/prim/index-eng.php). Accessed 2018 Oct 10.
- Canadian Primary Care Sentinel Surveillance Network [website]. Kingston, ON: 2016. Available from: <http://cpcssn.ca>. Accessed 2018 Oct 10.
- Bates D, Mächler M, Bolker B, Walker S. Fitting linear mixed-effects models using lme4. *J Stat Softw* 2015;67:1-48.
- Rotermann M, Sanmartin C, Hennessy D, Arthur M. Prescription medication use by Canadians aged 6 to 79. *Health Rep* 2014;25(6):3-9.
- Sadowsky CH, Galvin JE. Guidelines for the management of cognitive and behavioural problems in dementia. *J Am Board Fam Med* 2012;25(3):350-66.
- Teri L, Larson EB, Reifer BV. Behavioural disturbance in dementia of the Alzheimer's type. *J Am Geriatr Soc* 1988;36(1):1-6.
- Pimlott NG, Siegel K, Persaud M, Slaughter S, Cohen C, Hollingworth G, et al. Management of dementia by family physicians in academic settings. *Can Fam Physician* 2006;52:1108-9.e1-6. Available from: [www.cfp.ca/content/cfp/52/9/1108.full.pdf](http://www.cfp.ca/content/cfp/52/9/1108.full.pdf). Accessed 2018 Oct 10.
- Ivers N, Jamtvedt G, Flottorp S, Young JM, Odgaard-Jensen J, French SD, et al. Audit and feedback: effects on professional practice and healthcare outcomes. *Cochrane Database Syst Rev* 2012;(6):CD000259.
- Bolmsjö BB, Palagyi A, Keay L, Potter J, Lindley RI. Factors influencing deprescribing for residents in advanced care facilities: insights from general practitioners in Australia and Sweden. *BMC Fam Pract* 2016;17(1):152.
- Cockburn J, Pit S. Prescribing behaviour in clinical practice: patients' expectations and doctors' perceptions of patients' expectations - a questionnaire study. *BMJ* 1997;315(7107):520-3.
- Britten N, Ukoumunne O. The influence of patients' hopes of receiving a prescription on doctors' perceptions and the decision to prescribe: a questionnaire survey. *BMJ* 1997;315(7121):1506-10.
- Janzen JA, Silvius J, Jacobs S, Slaughter S, Dalziel W, Drummond N. What is a health expectation? Developing a pragmatic conceptual model from psychological theory. *Health Expect* 2006;9(1):37-48.
- Leung KK, Silvius JL, Pimlott N, Dalziel W, Drummond N. Why health expectations and hopes are different: the development of a conceptual model. *Health Expect* 2009;12(4):347-60. Epub 2009 Aug 18.

This article has been peer reviewed.

Cet article a fait l'objet d'une révision par des pairs.

*Can Fam Physician* 2018;64:e488-97