Current Research in Diabetes & Obesity Journal
ISSN: 2476-1435

Juniper Publishers
key to the Researchers

Research Article
Volume 2 Issue 4 – June 2017
DOI: 10.19080/CRDOJ.2017.2.555593

Curre Res Diabetes & Obes J

Antidepressant Prescription Practices among Primary Health Care Providers for Patients with Diabetes Mellitus

Gagnon J, Lussier MT, Daskalopoulou SS, MacGibbon B, Bartlett G

[1]*Department of Family Medicine, McGill University, Canada*

[2]*Department of Family Medicine and Emergency Medicine, Université de Montréal, Canada*

[3]*Department of Medicine, McGill University, Canada*

[4]*Department of Mathematics, Université du Québec à Montréal, Canada*

[5]*Department of Family Medicine, McGill University, Canada*

Submission: June 13, 2017; **Published:** June 27, 2017

***Corresponding author:** Gillian Bartlett, Department of Family Medicine, McGill University, Canada, Tel: +1 514 399 9100; Fax: +1 514 398 4202; Email: gillian.bartlett@mcgill.ca

Abstract

Purpose: Depression is a common comorbidity in people with diabetes that increases the risk of poor diabetes control and diabetes-related complications. While treatment of depression is expected to help, some antidepressants have been associated with impaired glucose metabolism. Evidence is lacking in the scope of this problem for people with diabetes. The objective of this study is to describe the prescription of antidepressants for diabetic patients with a focus on medications suspected to impair glucose control.

Methods: A cross-sectional study of electronic medical record data from 115 primary care practices in the Canadian Primary Care Sentinel Surveillance Network was conducted. Descriptive statistics were used to describe the prescription of antidepressants for people with diabetes between 2009 and 2014.

Results: From the sample, 17,258 diabetic patients were prescribed at least one antidepressant (AD) between 2009 and 2014. In terms of pharmacological class, the greatest proportion of people were prescribed selective serotonin reuptake inhibitors (46.2%), followed by serotonin-norepinephrine reuptake inhibitors (24.3%) and tricyclic antidepressants (23.8%). The most frequently prescribed medications were Citalopram (16.6%), Amitriptyline (16.2%), Venlafaxine (15.7%), Trazodone (14.2%), Escitalopram (12.4%) and Bupropion (9.2%). Almost half of diabetics were prescribed ADs potentially associated with impaired glucose metabolism (SNRIs or TCAs).

Conclusion: The present study provides a description of AD prescription in primary care for people with diabetes by class and medication. The findings indicate that the issue of glucose impairment has little impact on selection of ADs for people with diabetes. Further research is needed to determine the health impact of these practices.

Keywords: Diabetes; Antidepressants; Depression; Primary care; Electronic health records; Pharmacoepidemiology

Abbreviations: AD: Antidepressant; ATC: Anatomical Therapeutic Chemical; CPCSSN: Canadian Primary Care Sentinel Surveillance Network; COPD: Chronic Obstructive Pulmonary Disease; EMR: Electronic Medical Records; MAOI: Monoamine Oxidase Inhibitor Noradrenergic; NaSSA: Specific Serotonergic Antidepressant; NDRI: Norepinephrine-dopamine Reuptake Inhibitors; SARI: Serotonin Antagonist and Reuptake Inhibitor; SSRI: Selective Serotonin Reuptake Inhibitor; SNRI: Serotonin-Norepinephrine Reuptake Inhibitor; T1DM: Type 1 diabetes mellitus; T2DM: Type 2 Diabetes Mellitus; WHO: World Health Organization

Introduction

Depression is a common comorbidity in people with diabetes mellitus which increases the risk of macrovascular and microvascular complications [1-3]. The relationship between depression and diabetes is bi-directional. People with diabetes are more likely to suffer from depression compared to those without diabetes [4] and depression is associated with poor glycemic control in people with diabetes [5,6]. Treatment of depression is expected to break this cycle, but recent evidence suggests that some classes of antidepressants (AD) are associated with impaired glucose metabolism, increasing the risk of poor

glycemic control [7,8]. Specifically, clinical trials suggest that Tricyclic antidepressants and Serotonin and norepinephrine reuptake inhibitors may be associated with poor glucose control [8-10]. Given the risk ADs may pose, especially for people with diabetes, knowledge about the prescription of ADs for people with diabetes is needed.

At present, there is a lack of observational research describing the prescription frequency of ADs for people with diabetes [11]. In a recent cross-sectional study, Wong et al. [12] describe the prescription of ADs in a pan-Canadian primary care population with a history of depression [12]; however, AD prescription is grouped by pharmacological class. As ADs within the same pharmacological class may differ in terms of their impact on glucose metabolism [13], information on the prescription of individual AD agents is needed. The prescription frequency of individual ADs is reported for the province of Quebec [14], but it is unknown whether AD Whether AD prescription in a general Canadian population or a smaller provincial study is the same as prescription of ADs for people with diabetes. The purpose of this study, therefore, is to describe the prescription of ADs for people with diabetes, which particularly focus on medications that may impact blood glucose control.

Methods

Data source and study population

The present cross-sectional study was conducted using primary care data extracted for public health surveillance and research purposes by the Canadian Primary Care Sentinel Surveillance Network (CPCSSN). At the time of the extraction, (September 30 2014), the CPCSSN database comprised health records from 115 primary care practices in 7 Canadian provinces and 1 territory. The electronic medical records (EMR) of 985,176 patients were extracted, anonymized, cleaned, coded and centralized by the CPCSSN [15]. The present study sample comprises all adult (18 years of age and over) patients (n=66,617) with diabetes in the CPCSSN database at the time of extraction. From this sample, 5 annual cross-sections of diabetic patients prescribed ADs between October 1, 2009 and September 30, 2014 (n=17,258) were generated. This was further reduced to the 2014 cross-section (n=10,152) to reflect current prescription practices.

Diabetes

Diabetes cases were identified using the validated CPCSSN algorithm that detects cases using a combination of information from patients' problem list, medication prescription records, laboratory results and billing [16]. The diabetes case definition includes both type 1 diabetes (T1DM) and type 2 diabetes (T2DM). The case definition for diabetes has a sensitivity of 95.6 95% CI: 93.4-97.9 and a specificity of 97.1 95% CI (96.3-97.9) [16]. The study sample comprises patients identified as having diabetes at the time of data extraction.

Depression

Cases of depression were identified using a validated case detection algorithm developed by the CPCSSN which combines information from patients' problem list, prescription records and billing. The case definition for depression includes depressive, bipolar and manic disorders. The algorithm detects lifetime depression-at least one occurrence of one of the above mood disorders (hereafter "history of depression"). The CPCSSN case definition for depression has a sensitivity of 81.1 95% CI: (77.2–85.0) and a specificity of 94.8 95% CI: (93.7–95.9) [16].

Antidepressants

Medications in the patient health records were assigned World Health Organization (WHO) Anatomical Therapeutic Chemical (ATC) codes. Medications classed as antidepressants (ATC N06A) by the WHO Collaborating Centre for Drug Statistics Methodology [17] were included. The pharmacological classes reported here are: tricyclics (TCA); selective serotonin reuptake inhibitors (SSRI); serotonin-norepinephrine reuptake inhibitors (SNRI); serotonin antagonist reuptake inhibitors (SARI)-comprising only Trazodone; monoamine oxidase inhibitors (MAOI); norepinephrine-dopamine reuptake inhibitors (NDRI) and noradrenergic and specific serotonergic antidepressants (NaSSA). ADs are classified according to the drug's molecular structure and/or the way they interfere with the serotonergic and norepinephrine neurotransmitter systems, rather than in terms of their receptor affinity and mechanisms of action [13]. Therefore, the action of AD agents within the same pharmacological class can differ greatly and their impact on glucose metabolism may be distinct. AD prescription is therefore reported in terms of individual medication as well as by pharmacological class.

Other variables of interest

Patients are characterized in terms of age, sex, body mass index (BMI), concurrent health conditions, and diabetes medication prescription. Age at the date of extraction was computed using patients' dates of birth. A median BMI was computed for each patient using all BMI measures listed in their files. The median BMI was selected as a more reliable value (less susceptible to outliers) than the most recent measure or mean, given that a number of measures were suspected to be in error (outside the expected range and/or computed using weight in pounds rather than kilograms). Since BMI does not generally change a great deal over time [18], use of a fixed BMI measure is justifiable. The concurrent health conditions reported consist of conditions for which validated case definitions were developed by the CPCSSN: hypertension, depression, osteoarthritis, and chronic obstructive pulmonary disease (COPD). Diabetes medication prescription was identified using ATC classification. This information was categorically transformed to approximate diabetes type and severity: insulin only (T1DM), oral diabetes medications only (non-insulin-dependent T2DM), and both

How to cite this article: Gagnon J, Lussier MT, Daskalopoulou SS, MacGibbon B, Bartlett G. Antidepressant Prescription Practices among Primary Health Care Providers for Patients with Diabetes Mellitus. Curre Res Diabetes & Obes J. 2017; 2(4): 555593. DOI: 10.19080/CRDOJ.2017.2.555593.

insulin and oral diabetes medications (insulin-dependent T2DM).

Statistical analyses

The sample population is described using frequencies and proportions, and means and standard deviations, as appropriate. First, the characteristics of the sample of patients with diabetes and prescribed ADs in 2014 (n=10,152), stratified by sex, are reported. Second, AD prescription frequencies and proportions (by pharmacological class and individual AD agent) for the 2014 cross-section, stratified by sex and history of depression, are reported. Finally, as a sensitivity analysis, the frequencies and proportions of AD prescriptions are described through a 5-year comparison of annual cross-sections of patients prescribed ADs between 2009 and 2014. Analyses were performed using SAS version 9.4.

Ethics

The CPCSSN received ethics approval from the research ethics boards of all host Universities for all participating networks and from the Health Canada Research Ethics Boards. The present study received ethics approval from the McGill University Faculty of Medicine Institutional Research Board.

Results

Population characteristics

Table 1 provides description of characteristics of diabetic patients prescribed ADs in 2014 (n=10,152), stratified by sex. This sample is described according to age, BMI, presence of co-morbidities and anti-diabetic medication prescription. In the cohort of diabetic patients prescribed ADs in 2014, more of the patients were female than male. Among those with BMI measurements (n=7, 387; 27.2% missing), almost all were overweight and nearly two thirds were obese (BMI>30kg/m^2). History of depression was identified in over half of the sample. With regard to other comorbidities, hypertension was most frequent, followed by osteoarthritis and COPD. Regarding prescription of anti-diabetic medication, most were prescribed oral medications, followed by a combination of oral medications and insulin, and less than 10% were prescribed insulin alone. In over ¼ of the diabetic patients, no prescription of diabetes medications was identified.

Table 1: Characteristics of adult patients with diabetes mellitus prescribed an antidepressant in 2014. (October 1st 2013 to September 20th 2014).

	Male (n=3920, 38.6%)	Female (n=6232, 61.4%)	Total (N=10152)
	n (%)	n (%)	n (%)
Age - mean (sd)	63.3 (13.10)	62.7 (14.60)	63.0 (14.03)
18-35	96 (2.5)	288 (4.6)	384 (3.8)
36-55	945 (24.2)	1531 (24.7)	2476 (24.5)
>55	2861 (73.3)	4384 (70.7)	7245 (71.7)
BMI – mean* (sd)	32.5 (6.59)	33.9 (7.89)	33.4 (7.44)
Underweight (<18.5)	4 (0.1)	13 (0.3)	17 (0.2)
Normal (18.5-24.9)	259 (9.0)	484 (10.7)	743 (10.1)
Overweight (25-29.9)	846 (29.5)	1053 (23.3)	1899 (25.7)
Obese (>30.0)	1764 (61.4)	2964 (65.7)	4728 (64.0)
Multimorbidity			
No comorbidity**	619 (15.8)	815 (13.1)	1434 (14.1)
Hypertension	2241 (57.2)	3529 (56.6)	5770 (56.8)
History of depression	2044 (52.1)	3661 (58.8)	5705 (56.2)
COPD	649 (16.6)	865 (13.9)	1514 (14.9)
Osteoarthritis	942 (24.0)	1997 (32.0)	2939 (29.0)
Antidiabetic medication classes			
No diabetes medication	1014 (25.9)	1744 (28.0)	2758 (27.2)
Insulin only	276 (7.0)	408 (6.5)	684 (6.7)
Oral medication only	1907 (48.7)	3025 (48.5)	4932 (48.6)
Both oral and insulin	723 (18.4)	1055 (16.9)	1778 (17.5)

*Group mean of individuals' median BMI values

**None of the conditions for which CPCSSN case definitions were developed

Characteristics of males and females in the sample were generally comparable, with a few exceptions. Mean age and mean BMI (group mean of the individuals' median values) were comparable between the sexes. Males were only slightly older than females, and slightly more females were obese than males. Very slight differences in diabetes medication prescription were observed, with more males than females prescribed insulin (either alone or in combination with oral medications).

Antidepressant prescription

Table 2 presents the frequency and proportion of ADs prescribed for the 2014 cross-section of diabetic patients, in terms of pharmacological class and individual medication, stratified by sex and history of depression. The most frequently prescribed AD classes given to people with diabetes were SSRI, followed by SNRI, TCA, SARI, NDRI, NaSSA and MAOI. A trend was observed in which the prescription of certain ADs for patients with a history of depression differed from those without. For diabetics with a history of depression, the most commonly prescribed classes were SSRI, followed by SNRI, TCA, SARI, NDRI and NaSSA. The most frequently prescribed classes of AD given to diabetic patients without depression were TCAs, followed by SSRIs, SNRIs, SARIs, NDRI and NaSSA.

How to cite this article: Gagnon J, Lussier MT, Daskalopoulou SS, MacGibbon B, Bartlett G. Antidepressant Prescription Practices among Primary Health Care Providers for Patients with Diabetes Mellitus. Curre Res Diabetes & Obes J. 2017; 2(4): 555593. DOI: 10.19080/CRDOJ.2017.2.555593.

Table 2: Number and proportion of patients prescribed antidepressants in 2014 (October 1st 2013 to September 30th 2014) by pharmacological class and agent, stratified by history of depression and sex.

	History of depression (n=5705)			No history of depression (n=4447)	Total (n=10152)
	Male (n=2044)	Female (n=3661)	Male (n=1876)	Female (n=2571)	n (%)
	n (%)	n (%)	n (%)	n (%)	
Tricyclic antipderessants	219 (10.7)	561 (15.3)	675 (36.0)	965 (37.5)	2420 (23.8)
Amitriptyline	145 (7.1)	386 (10.5)	440 (23.5)	672 (26.1)	1643 (16.2)
Nortriptyline	60 (2.9)	120 (3.3)	199 (10.6)	216 (8.4)	595 (5.9)
Doxepin	6 (0.3)	29 (0.8)	20 (1.1)	45 (1.8)	100 (1.0)
Imipramine	3 (0.2)	15 (0.4)	12 (0.6)	25 (1.0)	55 (0.5)
Desipramine	3 (0.2)	5 (0.1)	9 (0.5)	10 (0.4)	27 (0.3)
Trimipramine	2 (0.1)	9 (0.2)	4 (0.2)	6 (0.2)	21 (0.2)
Clomipramine	8 (0.4)	5 (0.1)	4 (0.2)	4 (0.2)	21 (0.2)
Amoxapine	0 (0.0)	1 (0.0)	0 (0.0)	0 (0.0)	1 (0.0)
Maprotiline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Selective serotonin reuptake inhibitors	1236 (60.5)	2209 (60.3)	473 (25.2)	768 (29.9)	4686 (46.2)
Citalopram	473 (23.1)	852 (23.3)	142 (7.6)	222 (8.6)	1689 (16.6)
scitalopram	363 (17.8)	588 (16.1)	115 (6.1)	188 (7.3)	1254 (12.4)
Sertraline	208 (10.2)	408 (11.1)	63 (3.4)	110 (4.3)	789 (7.8)
Paroxetine	104 (5.1)	215 (5.9)	127 (6.8)	202 (7.9)	648 (6.4)
Fluoxetine	96 (5.0)	176 (4.8)	26 (1.4)	66 (2.6)	364 (3.6)
Fluvoxamine	32 (1.6)	41 (1.1)	9 (0.5)	8 (0.3)	90 (0.9)
Selective serotonin reuptake inhibitors	262 (12.8)	425 (11.6)	344 (18.3)	412 (16.0)	1443 (14.2)
Trazodone	262 (12.8)	425 (11.6)	344 (18.3)	412 (16.0)	1443 (14.2)
Serotonin-norepinephrine reuptake inhibitors	442 (21.6)	948 (25.9)	405 (21.6)	667 (25.9)	2462 (24.3)
Venlafaxine	289 (14.1)	641 (17.5)	234 (12.5)	427 (16.6)	1591 (15.7)
Duloxetine	141 (6.9)	289 (7.9)	159 (8.5)	225 (8.8)	814 (8.0)
Desvenlafaxine	24 (1.2)	46 (1.3)	13 (0.7)	23 (0.9)	106 (1.0)
Monoamine oxidase inhibitors	7 (0.3)	6 (0.2)	1 (0.1)	4 (0.2)	18 (0.2)
Phenelzine	0 (0)	1 (0.0)	1 (0.1)	0 (0.0)	2 (0.0)
Tranylcypromine	1 (0.1)	2 (0.1)	0 (0.0)	0 (0.0)	3 (0.0)
Moclobemide	6 (0.3)	3 (0.1)	0 (0.0)	4 (0.0)	13 (0.1)
Norepinephrine-dopamine reuptakeinhibitors	244 (11.9)	375 (10.2)	171 (9.1)	145 (5.6)	935 (9.2)
Bupropion	244 (11.9)	375 (10.2)	171 (9.1)	145 (5.6)	935 (9.2)
Norepinephrine and specific serotonergic antidepressants	207 (10.1)	290 (7.9)	60 (3.2)	65 (2.5)	622 (6.1)
Mirtazapine	207 (10.1)	290 (7.9)	60 (3.2)	65 (2.5)	622 (6.1)

How to cite this article: Gagnon J, Lussier MT, Daskalopoulou SS, MacGibbon B, Bartlett G. Antidepressant Prescription Practices among Primary Health Care Providers for Patients with Diabetes Mellitus. Curre Res Diabetes & Obes J. 2017; 2(4): 555593. DOI: 10.19080/CRDOJ.2017.2.555593.

The most frequently prescribed AD agents given to diabetic patients with a history of depression were Citalopram, Escitalopram, Venlafaxine, Trazodone, Bupropion, Amitriptyline and Sertraline. For diabetic patients without a history of depression, the most frequently prescribed ADs were Amitriptyline, Trazodone, Venlafaxine, Nortriptyline, Duloxetine, Citalopram and Bupropion. In people with diabetes and a history of depression, more females than males were prescribed ADs in general. The proportion with which individual ADs were prescribed were generally comparable between the sexes, with a few exceptions. Amitriptyline and Venlafaxine were more often prescribed for females than males, and Mirtazapine was more often prescribed for males than females.

Table 3: Number and proportion of patients prescribed antidepressants by pharmacological class and agent– 5-year comparison (2009-2014).

	2009-2010 (n=6474)	2010-2011 (n=7590)	2011-2012 (n=8501)	2012-2013 (n=9368)	2013-2014 (n=10152)
	n (%)	n (%)	n (%)	n (%)	n (%)
Tricyclic antidepressants	1540 (23.8)	1774 (23.4)	1876 (22.1)	2225 (23.8)	2420 (23.8)
Amitriptyline	1129 (17.4)	1281 (16.9)	1319 (15.5)	1487 (15.9)	1643 (16.2)
Nortriptyline	286 (4.4)	344 (4.5)	388 (4.6)	564 (6.0)	595 (5.9)
Doxepin	75 (1.2)	73 (1.0)	79 (0.9)	81 (0.9)	100 (1.0)
Imipramine	48 (0.7)	50 (0.7)	62 (0.7)	53 (0.6)	55 (0.5)
Desipramine	22 (0.3)	17 (0.2)	15 (0.2)	27 (0.3)	27 (0.3)
Trimipramine	27 (0.4)	23 (0.3)	18 (0.2)	21 (0.2)	21 (0.2)
Clomipramine	18 (0.3)	19 (0.3)	24 (0.3)	21 (0.2)	21 (0.2)
Amoxapine	0 (0.0)	1 (0.0)	0 (0.0)	0 (0.0)	1 (0.0)
Maprotiline	2 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Selective serotonin reuptake inhibitors	3062 (47.3)	3689 (48.6)	4096 (48.2)	4362 (46.6)	4686 (46.2)
Citalopram	1407 (21.7)	1627 (21.4)	1664 (21.4)	1662 (17.7)	1689 (16.6)
Escitalopram	457 (7.1)	654 (8.6)	943 (11.1)	1086 (11.6)	1254 (12.4)
Sertraline	388 (6.0)	502 (6.6)	603 (7.1)	690 (7.4)	789 (7.8)
Paroxetine	560 (8.6)	626 (8.6)	640 (7.5)	652 (7.0)	648 (6.4)
Fluoxetine	272 (4.2)	312 (4.1)	324 (3.8)	330 (3.5)	364 (3.6)
Fluvoxamine	69 (1.1)	79 (1.0)	77 (0.9)	82 (0.9)	90 (0.9)
Serotonin antagonist reuptake inhibitors	775 (12.0)	893 (11.8)	1093 (12.9)	1300 (13.9)	1443 (14.2)
Trazodone	775 (12.0)	893 (11.8)	1093 (12.9)	1300 (13.9)	1443 (14.2)
Serotonin-nor epinephrine reuptake inhibitors	1515 (23.4)	1706 (22.5)	2056 (24.2)	2244 (24.0)	2462 (24.3)
Venlafaxine	1209 (18.7)	1285 (16.9)	1464 (17.2)	1520 (16.2)	1591 (15.7)
Duloxetine	304 (4.7)	396 (5.2)	551 (6.5)	687 (7.3)	814 (8.0)
Desvenlafaxine	40 (0.6)	72 (0.9)	94 (1.1)	90 (1.0)	106 (1.0)
Monoamine oxidase inhibitors	10 (0.2)	15 (0.2)	12 (0.1)	18 (0.2)	18 (0.2)
Phenelzine	1 (0.0)	0 (0.0)	0 (0.0)	1 (0.0)	2 (0.0)
Tranylcypromine	1 (0.0)	3 (0.0)	2 (0.0)	4 (0.0)	3 (0.0)
Moclobemide	8 (0.1)	12 (0.2)	10 (0.1)	13 (0.1)	13 (0.1)
Norepinephrine-dopamine reuptake inhibitors	619 (6.9)	703 (9.3)	828(9.7)	866 (9.2)	935 (9.2)
Bupropion	619 (6.9)	703 (9.3)	828 (9.7)	866 (9.2)	935 (9.2)
Norepinephrine and specific serotonergic antidepressants	302 (4.7)	363 (4.8)	452 (5.3)	561 (6.0)	622 (6.1)
Mirtazapine	302 (4.7)	363 (4.8)	452 (5.3)	561 (6.0)	622 (6.1)

How to cite this article: Gagnon J, Lussier MT, Daskalopoulou SS, MacGibbon B, Bartlett G. Antidepressant Prescription Practices among Primary Health Care Providers for Patients with Diabetes Mellitus. Curre Res Diabetes & Obes J. 2017; 2(4): 555593. DOI: 10.19080/CRDOJ.2017.2.555593.

For diabetic patients without a history of depression, larger differences were observed. The prescription frequency was higher for females than males for each of the individual SSRIs; Amitriptyline, Nortriptyline and Venlafaxine were more frequently prescribed for females than males; and Bupropion was more prescribed for males than females. Table 3 provides a comparison of 5 annual cross-sections of diabetic patients prescribed ADs between 2009 and 2014. Across the 5-year span, the relative proportions with which the pharmacological classes were prescribed remained stable. Changes in proportions were observed for individual medications within the classes, however. Increases in relative prescription frequency was observed for Escitalopram, Duloxetine, Bupropion, Mirtazapine and Trazodone. A decrease was observed for Citalopram, Paroxetine, Venlafaxine and Amitriptyline.

Discussion

Interpretation

The present study provides a description of AD prescription in Canada for people with diabetes. This appears to be the first epidemiological study of primary care practices describing the prescription of ADs for people with diabetes in Canada. Additionally, very few studies to date have described the prescription of ADs in terms of individual medication.

This study's findings regarding the proportion with which the different classes of ADs were prescribed for people with diabetes and a history of depression are consistent with other research using CPCSSN data but described the prescription of ADs in a Canadian primary care population with a history of depression (with and without diabetes) [12]. The finding that SSRIs are most frequently prescribed class of AD is consistent with literature suggesting SSRIs are the standard of care for depression [19]. Evidence from clinical trials suggests SSRIs and NDRIs may be associated with improved glucose metabolism [7,20,21] and that TCAs and SNRIs may be associated with impaired glucose metabolism [8-10]. The mechanisms explaining these findings are inconclusive, but research suggests that the ADs binding profiles (the transporter and receptor affinity) play an important role [13,22,23]. The present study shows that almost half of diabetics prescribed ADs were given SNRIs or TCAs. While evidence so far is inconclusive, the frequency with which these ADs are prescribed may be cause for concern as it appears that primary healthcare providers are not aware of the negative impact of these medications with regard to glucose metabolism. Given the similarity in prescription patterns for the general primary care population with a history of depression [12] and diabetic patients with a history of depression, it appears that health care providers' AD prescription choices are not affected by current evidence regarding the risks certain ADs pose for people with diabetes.

This study found that over half of the diabetic patients prescribed ADs had a history of depression. History of depression was used to define those for whom ADs were prescribed for the treatment of depression. The prescription of ADs for people with depression tended to differ from those without. This is to be expected as ADs are prescribed for a number of other conditions than depression, including: general anxiety or panic disorders, obsessive-compulsive disorder, and eating disorders; and clinically accepted off-label indications include insomnia, tobacco-cessation, headaches, neuropathic pain and chronic pain [24]. In patients without a history of depression (and those with a history of depression but were prescribed an AD for the treatment of another condition), the ADs were more likely prescribed for other conditions. The trend of differing prescription frequencies between males and females for specific ADs is largely related to the frequency with which these conditions are presented and treated in primary care.

Between 2009 and 2014, an increase in AD prescription frequency was observed; however, this may be a reflection of gradual increases participating clinics as well as their data capture. Increases in relative prescription frequency were observed for Trazodone, Bupropion and Mirtazapine, for which little research on their effect on glycemic control has been published. Citalopram and Paroxetine (SSRIs) decreased in frequency, while Escitalopram, an alternate SSRI, increased; and Duloxetine (SNRI) decreased while Venlafaxine, an alternate SNRI, increased. A slight decrease in prescription frequency was observed for Amitriptyline (TCA), relative to an increase in the prescription of Nortriptyline, an alternate TCA. Despite growing evidence that TCAs are associated with impaired glucose metabolism [7,8,25,26] no change in proportional frequency was observed over the course of the five-year observation period.

Limitations

One limitation is that the sample is only somewhat representative of the general Canadian population. In comparison with 2011 Canadian census data, the CPCSSN population in 2013 over-represented older adults and under-represented younger adults; and the CPCSSN population comprised significantly fewer young adult males than the general Canadian population [27]. Furthermore, given that the practices participating in the CPCSSN were not randomly selected, the population may not be generalizable to the Canadian primary care population [27]. Participating practices tended to be those affiliated with the practice-based research networks involved in the project and those more engaged in chronic disease surveillance. Nevertheless, the trends observed with this sample are expected to compare to those in a wider population. Future research should seek to confirm this hypothesis.

Second, the case detection algorithms for depression has a relatively high false positive rate. The case definition for depression detects lifetime depression, and includes manic disorders and bipolar mood disorders. Lifetime depression was used in this study to approximate the prescription of ADs for the treatment of depression as AD dose and reason for prescription

How to cite this article: Gagnon J, Lussier MT, Daskalopoulou SS, MacGibbon B, Bartlett G. Antidepressant Prescription Practices among Primary Health Care Providers for Patients with Diabetes Mellitus. Curre Res Diabetes & Obes J. 2017; 2(4): 555593. DOI: 10.19080/CRDOJ.2017.2.555593.

were not consistently recorded or could not be coded. Patients with a history of depression may be given ADs for other conditions. For instance, TCAs are more commonly prescribed insomnia and chronic pain, Mirtazapine is more commonly prescribed for smoking cessation and Trazodone is more often prescribed in low doses as a hypnotic [28,29]. Given the number of ADs prescribed to people with depression, use of lifetime depression as an approximation over-estimates the number of ADs prescribed for the treatment of depression.

A third limitation of this study pertains to the use of health records for research. While primary care EMRs permit the naturalistic examination of prescriptions and health conditions over time, some values may be missing (not entered or could not be coded) and some fields may differ between EMR products or may not be used in a standardized manner by primary health care providers. Were the data available, AD dose, refer to psychotherapy and diagnoses for other health conditions for which ADs are prescribed would have been included to better describe depression treatment practices in primary care patients living with diabetes.

Conclusion

The present research study provides information on the prescription of ADs for people with diabetes in primary care practices. This information is valuable as it provides insight into the implications of research evaluating the impact of ADs on glycemic control in people with diabetes. As new and more conclusive evidence on the effects of ADs on blood sugar emerges, or as new clinical recommendations are introduced, this study provides the means of estimating the number of patients that will be affected.

Acknowledgement

JG received a travel award for this research from the Canadian Institutes for Health Research (CIHR) and a travel award from the McGill University Department of Family Medicine. SSD is Chercheur-BoursierClinicien, supported by a Fonds de Recherche Québec Santé award. This research was part of the CPCSSN initiative, which is funded by the Public Health Agency of Canada (PHAC) under a contribution agreement with the College of Family Physicians of Canada on behalf of 9 practice-based research networks associated with departments of family medicine across Canada. The views expressed herein do not necessarily represent the views of the PHAC.

References

1. Hofmann M, Köhler B, Leichsenring F, Kruse J (2013) Depression as a risk factor for mortality in individuals with diabetes: A meta-analysis of prospective studies. PLoS One 8(11): e79809.
2. Dooren FEP, Nefs G, Schram MT, Verhey FRJ, Denollet J, et al. (2013) Depression and risk of mortality in people with diabetes mellitus: a systematic review and meta-analysis. PLoS One 8(3): e57058-e57059.
3. Groot M, Anderson R, Freedland KE, Clouse RE, Lustman PJ (2001) Association of depression and diabetes complications: a meta-analysis. Psychosom Med 63(4): 619-630.
4. Mezuk B, Eaton WW, Albrecht S, Golden SH (2008) Depression and Type 2 Diabetes Over the Lifespan A meta-analysis. Diabetes Care 31(12): 2383-2390.
5. American Diabetes Association (2010) Diagnosis and classification of diabetes mellitus. Diabetes Care 33 (Suppl 1): S62-S69.
6. Egede LE, Ellis C (2010) Diabetes and depression: Global perspectives. Diabetes Res Clin Pract 87(3): 302-312.
7. McIntyre RS, Soczynska JK, Konarski JZ, Kennedy SH (2006) The effect of antidepressants on glucose homeostasis and insulin sensitivity: synthesis and mechanisms. Expert Opin Drug Saf 5(1): 157-168.
8. Hennings JM, Schaaf L, Fulda S (2012) Glucose metabolism and antidepressant medication. Curr Pharm Des 18(36): 5900-5919.
9. Hall JA, Wang FJ, Oakes TMM, Utterback BG, Crucitti A, et al. (2010) Safety and tolerability of duloxetine in the acute management of diabetic peripheral neuropathic pain: analysis of pooled data from three placebo-controlled clinical trials. Expert Opin Drug Saf 9(4): 525-537.
10. Ghaeli P, Shahsavand E, Mesbahi M, Kamkar MZ, Sadeghi M, et al. (2004) Comparing the effects of 8-week treatment with fluoxetine and imipramine on fasting blood glucose of patients with major depressive disorder. J Clin Psychopharmacol 24(4): 386-388.
11. Ivanova A, Nitka D, Schmitz N (2010) Epidemiology of antidepressant medication use in the Canadian diabetes population. Soc Psychiatry Psychiatr Epidemiol 45(9): 911-999.
12. Wong ST, Manca D, Barber D, Morkem R, Khan S, Kotecha J, et al. (2014) The diagnosis of depression and its treatment in Canadian primary care practices: an epidemiological study. CMAJ Open 2(4): E337-E342.
13. Derijks HJ, Heerdink ER, Janknegt R, De Koning FHP, Olivier B, et al. (2008) Visualizing pharmacological activities of antidepressants: A novel approach. The Open Pharmacology Journal 2: 54-62.
14. Conseil du medicament (2016) Portrait de l'usage des antidépresseurs chez les adultes assurés par le régime public d'assurance médicaments du Québec Québec (QC): Gouvernement du Québ.
15. Birtwhistle RV (2011) Canadian Primary Care Sentinel Surveillance Network: A developing resource for family medicine and public health. Can Fam Physicia 57(10): 1219-1220.
16. Williamson T, Green ME, Birtwhistle R, Khan S, Garies S, et al. (2014) Validating the 8 CPCSSN case definitions for chronic disease surveillance in a primary care database of electronic health records. Ann Fam Med 12(4): 367-372.
17. WHO (2015) Collaborating Centre for Drug Statistics Methodology. Guidelines for ATC classification and DDD assignment. Oslo, Norway.
18. Hopman WM, Leroux C, Berger C, Joseph L, Barr SI, et al. (2007) Changes in body mass index in Canadians over a five-year period: Results of a prospective, population-based study. BMC Public Health 7(1): 1-11.
19. Ables AZ, Baughman OL (2003) Antidepressants: update on new agents and indications. Am Fam Physician 67(3): 547-554.
20. Khazaie H, Rahimi M, Tatari F, Rezaei M, Najafi F, Tahmasian M (2011) Treatment of depression in type 2 diabetes with Fluoxetine or Citalopram? Neurosciences (Riyadh) 16(1): 42-45.
21. Anderson JW, Greenway FL, Fujioka K, Gadde KM, McKenney J, et al. (2002) Bupropion SR enhances weight loss: a 48-week double-blind, placebo- controlled trial. Obes Res 10(7): 633-641.
22. Mulder H, Franke B, van der-BAA, Arends J, Wilmink FW, et al. (2007) The association between HTR2C polymorphisms and obesity in psychiatric patients using antipsychotics: a cross-sectional study. Pharmacogenomics J 7(5): 318-324.

How to cite this article: Gagnon J, Lussier MT, Daskalopoulou SS, MacGibbon B, Bartlett G. Antidepressant Prescription Practices among Primary Health Care Providers for Patients with Diabetes Mellitus. Curre Res Diabetes & Obes J. 2017; 2(4): 555593. DOI: 10.19080/CRDOJ.2017.2.555593.

23. Reed Larsen P, Henry M. Kronenberg, Shlomo Melmed, Polonsky KS (2003) Williams Textbook of Endocrinology. (10th edn.) Elsevier Science.

24. CPA (2016) Compendium of Pharmaceuticals and Specialties. Int J Health Serv 13(10).

25. Yoon JM, Cho EG, Lee HK, Park SM (2013) Antidepressant use and diabetes mellitus risk: a meta-analysis. Korean J Fam Med 34(4): 228-240.

26. Bhattacharjee S, Bhattacharya R, Kelley GA, Sambamoorthi U (2013) Antidepressant use and new-onset diabetes: a systematic review and meta-analysis. Diabetes Metab Res Rev 29(4): 273-284.

27. Queenan JA, Williamson T, Khan S, Drummond N, Garies S, et al. (2016) Representativeness of patients and providers in the Canadian Primary Care Sentinel Surveillance Network: a cross-sectional study. CMAJ Open 4(1): E28-E32.

28. Jenna Wong, Aude Motulsky, Tewodros Eguale, Dadvid L Buckeridge, Michal Abrahamowicz, et al. (2016) Treatment Indications for Antidepressants Prescribed in Primary Care in Quebec, Canada, 2006-2015. JAMA 315(20): 2230-2232.

29. Wong J, Motulsky A, Abrahamowicz M, Eguale T, Buckeridge DL, et al. (2017) Off-label indications for antidepressants in primary care: descriptive study of prescriptions from an indication based electronic prescribing system. BMJ 356-603.

DOI: 10.19080/CRDOJ.2017.2.555593

How to cite this article: Gagnon J, Lussier MT, Daskalopoulou SS, MacGibbon B, Bartlett G. Antidepressant Prescription Practices among Primary Health Care Providers for Patients with Diabetes Mellitus. Curre Res Diabetes & Obes J. 2017; 2(4): 555593. DOI: 10.19080/CRDOJ.2017.2.555593.