Impact of the Diabetes Canada Guideline Dissemination Strategy on the Prescription of Vascular Protective Medications: A Retrospective Cohort Study, 2010–2015

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OBJECTIVE

The 2013 Diabetes Canada guidelines launched targeted dissemination tools and a simple assessment for vascular protection. We aimed to *1*) examine changes associated with the launch of the 2013 guidelines and additional dissemination efforts in the rates of vascular protective medications prescribed in primary care for older patients with diabetes and *2*) examine differences in the rates of prescriptions of vascular protective medications by patient and provider characteristics.

RESEARCH DESIGN AND METHODS

The study population included patients (≥40 years of age) from the Canadian Primary Care Sentinel Surveillance Network (CPCSSN) with type 2 diabetes and at least one clinic visit from April 2010 to December 2015. An interrupted time series analysis was used to assess the proportion of eligible patients prescribed a statin, ACE inhibitor (ACEI)/angiotensin receptor blocker (ARB), or antiplatelet prescription in each quarter. Proton pump inhibitor (PPI) prescriptions were the reference control.

RESULTS

A dynamic cohort was used where participants were enrolled each quarter using a prespecified set of conditions (range 25,985–70,693 per quarter). There were no significant changes in statin ($P = 0.43$), ACEI/ARB ($P = 0.42$), antiplatelet ($P = 0.39$), or PPI ($P = 0.16$) prescriptions at baseline (guideline intervention). After guideline publication, there was a significant change in slope for statin (−0.52% per quarter, SE 0.15, $P < 0.05$), ACEI/ARB (−0.38% per quarter, SE 0.13, $P < 0.05$), and reference PPI (−0.18% per quarter, SE 0.05, $P < 0.05$) prescriptions.

CONCLUSIONS

There was a decrease in prescribing trends over time that was not specific to vascular protective medications. More effective knowledge translation strategies are needed to improve vascular protection in diabetes in order for patients to receive the most effective interventions.

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The World Health Organization describes the "rule of halves" whereby half of the people with long-term conditions are not known, half of those conditions known are not treated, and half of those conditions treated are not controlled (1). As a result of these failures, patients with diabetes are at increased risk of developing significant morbidity and mortality related to atherosclerotic cardiovascular complications including coronary heart disease, stroke, and peripheral vascular disease (2). The lifetime 10-year cardiovascular disease (CVD) risk is >20% for patients aged >40 years and living with diabetes (3). Effective risk factor modification with vascular protective medications, including statins, antihypertension agents, and antiplatelet agents, is an essential component of diabetes management to improve both quantity and quality of life-years (3,4). Clinical trial data show a 22–37% risk reduction in CVD for patients age >40 years on statin therapy and a 25% risk reduction for patients age >55 years taking ACE inhibitors (ACEIs) (4–6). Despite evidence-based support for these therapies, a national physician survey in 2012 estimated that 43% of patients with diabetes do not meet guideline-recommended LDL targets (≤2 mmol/L) and 64% fail to meet blood pressure (BP) targets (<130/80 mmHg), suggesting suboptimal vascular protection management (7).

For bridging of this evidence-to-practice gap for vascular protection in patients with diabetes, dissemination tools were launched with the 2013 Diabetes Canada (previously Canadian Diabetes Association) evidence-based guidelines. Compared with previous (2008) guidelines, the 2013 Diabetes Canada guidelines no longer require providers to stratify patients into different risk categories prior to recommending vascular protective therapy, thereby simplifying the assessment for vascular protection (Supplementary Table 1). Statin use is recommended for all patients ≥40 years old and living with diabetes; ACEIs or angiotensin receptor blockers (ARBs) are recommended for patients ≥55 years old with diabetes. Antiplatelet medications are no longer recommended for routine use in the primary prevention of CVD for patients with diabetes (3). Diabetes Canada also expanded on its patient- and provider-directed dissemination and implementation strategy, which was based on the Knowledge-to-Action Cycle and included a variety of new dissemination tools (8). The nationwide dissemination strategy launched in April 2013 and targeted multiple national and provincial systems-level groups (e.g., government agencies, nongovernmental agencies, disease advocacy groups, and professional associations), as well as health care providers and people living with diabetes across Canada via large-scale communications campaigns (e.g., television, radio, digital and print media) (9) (Supplementary Table 2). Interventions including in-person lecture series, conferences, webinars, web-based professional and patient resources such as flow sheets, electronic point of care decision support, a mobile application, and electronic medical record (EMR) templates were rolled out over 24 months. An evaluation of the effectiveness of this dissemination strategy has been published elsewhere (9).

Multiple studies examining vascular protective agents in Canada have shown an increase in statins and ACEIs/ARBs prescribed and used over the past two decades (10–12). Estimates from one Canadian province (Ontario) suggest that statin prescriptions in patients with diabetes aged >65 years have increased 53% from 1996 to 2010 and ACEI/ARB prescriptions have increased by 22% over a 6-year period (1995–2001) (11,12). These studies used data from provincial drug registries, which failed to capture nonprescription medications including antiplatelets and typically involved smaller geographic areas (i.e., city- or province-level data), making it difficult to determine whether dissemination and implementation of the Diabetes Canada guidelines achieved a population-level impact across Canada. Drug registry data also exclude the population of patients with diabetes age <65 years who may be eligible for vascular protective therapy. In addition, there are no studies that examined the prescription of these medications before and after the 2013 Diabetes Canada guidelines were released and disseminated, leaving the impact of the guidelines unknown.

Successful guideline evaluation is critical in assessing whether suggested recommendations have been adopted into practice at a population level. The current study used data from the Canadian Primary Care Sentinel Surveillance Network (CPCSSN), a pan-Canadian EMR surveillance system, to capture longitudinal trends in vascular protective agent prescriptions. The specific aims were to *1*) examine changes associated with the launch of the 2013 Diabetes Canada Guidelines and additional dissemination efforts in the rates of vascular protective medications prescribed in primary care for older patients with diabetes and *2*) examine differences in the rates of vascular protective medication prescriptions according to provider and patient characteristics.

RESEARCH DESIGN AND METHODS

Study Design and Population

We used a retrospective cohort design and followed the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines (13). We included patients living with diabetes whose data were in the CPCSSN database from April 2010 to December 2015. Diabetes was defined according to the CPCSSN-validated case definition (14) (Supplementary Table 3). The study cohort was dynamic, and patients were enrolled quarterly when the following three temporal conditions were met: *1*) onset of diabetes recorded in the EMR prior to or during each quarter of interest, *2*) first patient visit recorded within a given quarter or any quarter preceding it, and *3*) patient met eligibility criteria for the medication being analyzed defined as per the 2013 Diabetes Canada guideline criteria: patients age ≥40 years for statins and age ≥55 years for ACEI/ARBs. For antiplatelet agents, patients age ≥40 years with no cardiovascular event were included, as guideline changes suggest that these medications should no longer be used for primary prevention in this group. Priorities set were based on well-accepted guideline recommendations and framed such that in our defined cohorts, those prescribed the agent are "controlled" and those not prescribed the agent are "uncontrolled." Achievement of LDL targets (≤2 mmol/L) and BP targets (<130/80 mmHg) was assessed in patients in the following age categories: age ≥40 years for LDL and age ≥55 years for BP. We employed a censoring point whereby patients were removed from the cohort using the last encounter date if they had not seen their family

doctor as indicated by an encounter in the EMR in the last 2 years. The study was approved by the University of Toronto's Research Ethics Board (REB#33127).

CPCSSN Database

CPCSSN, established in 2008, is an EMR-based information system designed for chronic disease surveillance. Every 3 months, EMR data from primary care practices in 10 practice-based research networks (PBRNs) across Canada are extracted, cleaned, and merged into a single database housed at the Centre for Advanced Computing at Queen's University in Kingston, Ontario, Canada (15). Contributing PBRNs are located in Alberta (two), British Columbia (one), Manitoba (one), Newfoundland and Labrador (one), Nova Scotia (one), Ontario (three), and Quebec (one), Canada. The network is composed of >1,100 family physicians contributing data for >1,500,000 patients. Information contained in the database includes network and provider identifiers, de-identified patient demographic information, date and type of each patient's encounters, patient health conditions, risk factors, referrals, laboratory investigations, procedures, and medications (15). CPCSSN captures all medications recorded in the EMR, including medications prescribed by primary care providers or specialists and those purchased over the counter.

Data Collection and Processing

Data from 1 January 2010 to 31 December 2015 were used for this project. The project data included patient demographic variables (year and month of birth, sex, and neighborhood-level socioeconomic status [SES] indicators derived from residential postal codes), physical measurements (height, weight, BMI, systolic BP, and diastolic BP), diabetes-related laboratory records (i.e., total cholesterol, LDL, HDL, triglycerides, and urine albumin-to-creatinine ratio), comorbidities/risk factors (i.e., hypertension, CVD, dyslipidemia, microalbuminuria, and smoking history), all medications prescribed to patients (i.e., lipid-lowering agents, ACEIs, ARBs, antiplatelets, and proton pump inhibitors [PPIs] as a reference control), provider/site characteristics (i.e., province of site and rurality of site) for each quarter of interest, and CPCSSN patient and provider data table (containing information on hierarchical relationship between patient, care provider, site, and network). Year of medical school (MD) graduation for providers was collected from the University of Toronto Practice-Based Research Network (UTOPIAN) network only owing to limited availability at other PBRNs.

All medications in CPCSSN database were coded using Anatomical Therapeutic Chemical codes; these codes were used to identify the relevant medications for this project (16). Long-term conditions were identified using CPCSSN-validated algorithms where available (i.e., diabetes and hypertension) (Supplementary Table 3). For the rest of the conditions, we used coded and free text diagnosis data from the CPCSSN health conditions table; this table populates data from the Cumulative Patient Profile (14). CVD was defined according to guideline and antiplatelet indications to include ICD-9 codes for coronary heart disease (410–414), cerebrovascular disease (430–438), and peripheral vascular disease (440–445) (17). Dyslipidemia was defined using appropriate medication history and coded and free text diagnosis data and included patients on lipid-lowering therapy or with LDL >2.0 mmol/L. Albuminuria was defined according to Diabetes Canada guidelines, whereby a urine albumin creatinine ratio <2 mg/mmol was categorized as normal, 2–20 mg/mmol as microalbuminuria, and >20 mg/mmol as macroalbuminuria (18). SES was measured in accordance with the Canadian Institute for Health Information method of deriving neighborhood-level deprivation indices on a quintile scale for each patient (19). Rurality was defined according to postal code whereby a second letter of "0" was considered rural and a second letter "1–9" considered urban (20). In accordance with recommendations of the World Health Organization and Health Canada, BMI was classified into categories of underweight (<18.5 kg/m^2), normal weight (18.5–24.99 kg/m^2), overweight (25–29.99 kg/m^2), obese class I (30–34.99 kg/m^2), obese class II (35–39.99 kg/m^2), and class III (≥40 kg/m^2) (21).

Analysis

This study used an interrupted time series (ITS) design. For the primary analysis, the proportion of eligible patients who had prescriptions for statins, ACEI/ARBs, or antiplatelets in each quarter was computed using a longitudinal data analysis (22). Quarterly intervals were chosen to introduce less fluctuation in the time series curve compared with a monthly approach (23). If patients had multiple visits within a quarter, the most recent record was used for all variables studied. A total of eight quarters before, one quarter during, and nine quarters after the intervention were analyzed. Patients were deemed to be prescribed a statin, ACEI/ARB, or antiplatelet agent if they had any prescription record in the four preceding quarters and one quarter after each quarter of interest (lag4, lead1) (Fig. 1). This approach was used to account for variation in refill protocols and prescription procedures among family physicians (i.e., some provide a prescription every 3 months and others provide multiple repeats) (24). Having four quarters before and one after each quarter of interest would provide a sufficient time frame to capture prescriptions given on a yearly basis. We also examined other approaches, including (lag0, lead0), (lag1, lead1), (lag2, lead2), (lag3, lead3), (lag4, lead4), and (lag4, lead1). We found that prescription rates for the latter three approaches were very similar, further justifying our selection of the (lag4, lead1) approach.

The launch of the Diabetes Canada guidelines and dissemination strategy in April 2013 was considered the intervention point (2013 quarter 2 [Q2]). A segmented regression model was used to assess baseline trend/slope, the level change immediately after intervention, and the trend/gradual change (25). We also measured the prescription rates of statin, ACEI/ARB, and antiplatelets using a cross-sectional study design, which deemed a patient to be using the medication if they had at least one prescription during the entire study period (2010 Q1–2015 Q4). This approach serves as a sensitivity analysis for the (lag4, lead1) approach and allowed us to test for subgroup differences in the proportion prescribed statin, ACEI/ARB, and antiplatelets.

Secondary analyses included the proportion of eligible patients attaining LDL (≤2.0 mmol/L) or BP (<130/80 mmHg) target. A carryover approach was implemented: each patient's most recent measurement was used in the following

quarters until a new measurement was recorded in the EMR. A segmented regression model was used to assess the baseline trend/slope, level change, and trend/gradual change for secondary outcomes (i.e., eligible patients attaining LDL or BP target).

Results were stratified by patient characteristics (age, sex, BMI, and SES), presence of risk factors/comorbidities (smoking, CVD, hypertension, dyslipidemia, and albuminuria), and provider characteristics (province of care and rurality). We assessed the statistical significance across patient, provider, and geographical characteristics for prescription rates for statins, ACEI/ARBs, and antiplatelet agents using χ^2 test (adjusted for multiple hypothesis testing). We used the method of false discovery rate to control for inflated type I error rates in multiple hypothesis testing procedures (26). PPI prescriptions were used as a reference to control for confounding factors. Using modified hypothesis testing, we look at the temporal difference in prescription rates of PPIs compared with those of all three vascular protective medications (e.g., statin 2011 Q2–2015 Q3 vs. PPI 2011 Q2–2015 Q3) and considered statistical significance at $P < 0.05$. The analyses were conducted using SAS, version 9.4 (27).

RESULTS

Primary Outcomes

The total number of patients enrolled in each dynamic cohort is outlined in Table 1. Quarterly cohort size ranged from 23,016 to 70,693 patients (Supplementary Table 4). Variation in population size was attributed to increasing recruitment of practices into the CPCSSN database over time. Results of the ITS analysis are presented in Table 2 and graphically in Fig. 2. There were no significant changes in the rate of statin, ACEI/ARB, antiplatelet, or PPI prescriptions prior to the release of the 2013 guidelines. After guideline publication, there was a significant change in slope for statins (−0.52% per quarter, SE 0.15, $P < 0.05$) and ACEI/ARBs (−0.38% per quarter, SE 0.13, $P < 0.05$) prescribed. A significant change in slope was also seen for PPI prescriptions (−0.18% per quarter, SE 0.05, $P < 0.05$). The change in slope was not significant for antiplatelets. The absolute difference in the rates of statin, ACEI/ARB, or antiplatelet prescriptions from the start (2011 Q2) to the end (2015 Q4) of the study period was significantly less than that of the PPI reference control ($P < 0.0001$).

Geographic Characteristics

Prescription rates in eligible patients were significantly higher in urban than rural practices for statins, ACEI/ARBs, and antiplatelets across the study period (Table 1). χ^2 test revealed significant differences in prescriptions rates between provinces for statins ($P < 0.001$), ACEI/ARBs ($P < 0.001$), and antiplatelets ($P < 0.001$). Statin and ACEI/ARB prescription rates were highest in the province of Quebec (74.2% for statins and 55.9% for ACEI/ARBs) and in the Maritimes provinces (64.8% for stains and 50.5% for ACEI/ARBs) and lowest in Alberta (45.1% for statins and 39.5% ACEI/ARBs) and British Columbia (35.2% for statins and 41.5% ACEI/ARBs).

Provider Characteristics

There were no significant differences between MD graduation groups for statin ($P = 0.152$) or ACEI/ARB ($P = 0.18$) prescriptions in the UTOPIAN population (Table 1). However, there were significant differences between MD graduation groups for antiplatelet prescriptions ($P < 0.001$). Antiplatelet prescription rates were 20.9% for MD graduation years of 1965–1979, 15.3% for 1980–1994, and 18.3% for ≥1995.

Patient Demographics and Risk Factors

Prescription rates according to patient characteristics are seen in Table 1. There were no significant sex-based differences in prescription rates for statins ($P = 0.99$), ACEI/ARBs ($P = 0.71$), or antiplatelet agents ($P = 0.15$). Patients with hypertension had significantly higher statin ($P < 0.001$), ACEI/ARB ($P < 0.001$), and antiplatelet ($P < 0.001$) prescription rates compared with patients without hypertension. Patients with CVD also had higher statin ($P < 0.001$) and ACEI/ARB ($P < 0.001$) prescription rates compared with patients without CVD. Patients without dyslipidemia had significantly lower rates of statin prescription ($P < 0.001$), ACEI/ARB prescriptions ($P < 0.001$), and antiplatelet prescriptions ($P < 0.001$) compared with those with dyslipidemia. Significant differences were detected for age groups, SES quintiles, smoking status, hypertension, dyslipidemia, and albuminuria for all three vascular protective medications ($P < 0.05$). Significant differences between BMI groups were seen with respect to ACEI/ARB prescriptions ($P < 0.001$).

Secondary Outcomes

LDL and BP Targets

Across the study period, LDL and BP targets were achieved by 47–57% and 61–66% of patients, respectively (Fig. 2*B* and *C*). The release of the 2013 guidelines did not significantly impact the proportion of patients achieving BP targets, as there were no significant changes in this proportion before, during, or after guideline release (Table 2). The release of the guidelines did not impact the proportion of patients achieving LDL targets, as there were no significant changes in this proportion during or after guideline release.

CONCLUSIONS

The results of this large study suggest that dissemination of the 2013 Diabetes Canada guidelines was not associated with any further improvements in physician prescribing behavior as measured by EMR prescription estimates for primary vascular protection in patients age ≥40 years with diabetes. While there was no change in prescriptions at the intervention point, a small but statistically significant decrease in slope after guideline publication was observed with statins and ACEI/ARBs, as well as the reference control. A negative change in slope (improved guideline adherence) was also observed with antiplatelets; however, this change was not significant. There were no significant changes with respect to LDL and BP targets at or after guideline intervention. Overall prescription rates were influenced by factors including rurality, province, and patient age and SES. While statistically significant changes were seen across patient/provider characteristics, these do not necessarily represent clinical significance given the large sample size.

Our time series analysis revealed a negative change in slope for statins, ACEI/ARBs, and PPIs. Owing to a lack of sufficient variation in the time series curves shown in Fig. 2*A*, we caution that this statistical inference can be affected by minuscule changes in prescription rates during any quarter pre– and post–guideline implementation (28).

Table 1—Patient, provider, and geographical characteristics for statin, ACEI/ARB, and antiplatelet prescriptions among patients with type 2 diabetes

	Statin medication			ACEI/ARB medication			Antiplatelet medication		
	N	%	*P*	*N*	%	*P*	*N*	%	*P*
Age (years)									
40–49	4,084	56.1	0.0006	—	—	—	814	13.4	0.001
50–59	9,766	58.6		3,023	39.8	<0.0001	2,125	15.3	
60–69	13,448	58.7		11,142	48.7		2,982	15.6	
70–79	10,769	58.3		8,910	48.2		2,377	15.4	
≥80	8,589	59.2		7,076	48.7		1,781	14.7	
BMI (kg/cm^2)									
<18.5	227	59.1	0.33	163	51.1	0.004	48	15.1	0.34
18.5–24.9	4,162	60.5		2,877	50.1		902	15.8	
25–29.9	9,455	60.4		6,431	49.3		1,947	14.8	
30–34.9	8,734	59.9		5,575	47.8		1,839	15.1	
35–39.9	4,857	59.3		2,915	47.5		987	14.4	
≥40	3,992	59.0		2,196	47.1		821	14.6	
Missing	15,229	55.5		9,994	45.6		3,535	15.5	
Sex									
Female	22,147	58.4	0.99	14,365	47.6	0.71	4,723	14.9	0.15
Male	24,505	58.4		15,786	47.4		5,355	15.3	
Missing	4	44.4					1	14.3	
SES quintiles									
1 (highest)	3,958	59.4	<0.0001	2,574	47.3	0.001	847	15.2	0.001
2	5,071	61.6		3,233	49.5		989	14.6	
3	4,577	61.1		2,919	48.4		948	15.1	
4	3,957	58.2		2,603	48.1		833	14.7	
5 (lowest)	4,134	56.0		2,595	45.7		778	12.7	
Missing	24,959	57.6		16,227	47.2		5,684	15.7	
Smoking status									
Current smoker	4,280	59.5	<0.0001	2,460	48.3	0.015	926	15.5	0.008
Nonsmoker	8,065	58.0		5,356	49.0		1,614	14.0	
Past smoker	9,798	63.4		6,500	50.5		1,956	15.1	
Missing	24,513	56.6		15,835	45.8		5,583	15.4	
Hypertension									
No	16,551	50.0	<0.0001	8,160	31.0	<0.0001	3,481	11.7	<0.0001
Yes	30,105	64.4		21,991	59.2		6,598	17.8	
Dyslipidemia									
No	8,461	41.3	<0.0001	6,485	39.3	<0.0001	2,240	13.2	<0.0001
Yes	38,195	64.3		23,666	50.3		7,839	15.8	
Albuminuria									
Microalbuminuria	11,190	69.5	<0.0001	7,623	60.0	<0.0001	2,645	20.5	<0.0001
Normal	13,861	63.2		8,438	48.7		2,898	15.4	
Macroalbuminuria	3,372	73.1		2,493	68.2		838	24.7	
Missing	18,233	49.0		11,597	38.9		3,698	11.7	
CVD									
No	36,395	54.6	<0.0001	23,456	44.2	<0.0001	10,079	15.1	N/A
Yes	10,261	77.8		6,695	64.1				
Rurality									
Rural	8,895	53.9	<0.0001	5,984	44.5	<0.0001	1,976	14.5	0.001
Urban	33,049	61.1		21,137	49.2		7,094	15.7	
Missing	4,712	50.9		3,030	42.9		1,009	12.8	
Province									
AB	5,804	45.1	<0.0001	4,022	39.5	<0.0001	1,076	9.9	<0.0001
BC	385	35.2		366	41.5		85	9.5	
MB	9,044	59.2		5,758	48.6		1,977	15.8	
MP	1,636	64.8		1,048	50.5		540	26.3	
NL	1,941	54.0		1,421	48.6		494	16.8	
NW	722	56.9		439	55.4		200	19.2	
ON	26,194	62.4		16,483	48.9		5,519	15.6	
QC	930	74.2		614	55.9		188	17.9	

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Table 1—Continued

	Statin medication			ACEI/ARB medication			Antiplatelet medication		
	N	%	*P*	*N*	%	*P*	*N*	%	*P*
MD graduation year									
1965–1979	1,871	70.6	0.15	1,241	57.0	0.18	472	20.9	<0.0001
1980–1994	5,769	67.8		3,764	54.9		1,094	15.3	
≥1995	5,872	69.2		3,688	56.1		1,323	18.3	
Non-UTOPIAN	33,144	55.0		21,458	44.8		7,190	14.4	
Total number of patients prescribed medication	46,656	58.4		30,151	47.5		10,079	15.1	
Total number of patients enrolled in dynamic cohort over study period	79,880	100		63,494	100		66,683	100	

AB, Alberta; BC, British Columbia, MB, Manitoba; MP, Maritime provinces; NL, Newfoundland and Labrador; NW, Northwest territories; N/A, not applicable; ON, Ontario; QC, Quebec.

This decrease was also seen with the PPI comparator, suggesting that external factors cannot be excluded. It is possible that there was no actual improvement in vascular protective medication prescribing after release of the 2013 guidelines. The CPCSSN population also involves a dynamic cohort, so a change in composition of patients, physicians, or sites included in the database in each quarter could also influence prescription rates. Entry to the dynamic cohort was random, and there would be no reason to suspect that patients with diabetes from practices joining CPCSSN later would be more likely to have lower prescribing rates. We also did not observe any remarkable shifts with respect to composition of site locations but did observe an increase in patients age 40–49 years from 5.89% to 9.15% across the study period. Patients in this age category had lower statin and ACEI/ARB prescription rates, and thus an increase in the proportion of these patients may have contributed to the measurable decrease seen in prescribing rates over time. It is also possible that an emerging focus on resource stewardship in medical education and practice influenced physicians to prescribe more cautiously, decreasing prescription rates over time (29).

Our prescription estimates are lower than those from 2003 to 2008 Diabetes Canada guideline evaluations (7,30). These studies used physician self-reported survey data subject to selection bias, as physicians willing to participate may be those who prescribe in accordance with guideline recommendations. A validation study is currently ongoing to compare our results with data from the Institute for Clinical and Evaluative Sciences (ICES), which encompasses publicly funded administrative health data for the Ontario population eligible for universal health coverage (31). Preliminary results from this study confirm no improvement in statin, ACEI, and ARB prescriptions at or after guideline intervention ($P > 0.05$). Statin prescription estimates were similar (62–65%) to those in the current study (52–56%), and increased rates may be attributed to the older population cohort included in ICES (age ≥65 years).

We observed better guideline adherence in urban areas and provinces, including Quebec, Ontario, and the Maritimes. It is possible that dissemination outreach strategies were less effective for removed locations including rural areas and provinces such as Northwest Territories, Alberta, and British Colombia. Increased distance from health care access leading to reduced frequency of physician visits may inhibit physicians in rural areas from adhering to guidelines (32). Physicians in rural areas report increased patient resistance to medical or preventative care as a barrier to guideline adherence (32). We also observed lower prescription rates among patients from lower SES brackets, which is consistent with low SES cohorts being less likely to receive guideline-recommended diabetes care (33).

National survey data from primary care providers across Canada highlight significant gaps in knowledge and

Table 2—ITS regression analysis of vascular protective medication prescribing rates

	Estimate	SE	*P*
Statin			
Intercept B_0	50.97	0.95	<0.0001
Preintervention trend B_1	0.33	0.10	0.0072
Level change	0.35	0.43	0.4280
Trend change	−0.52	0.15	0.0045
ACEI/ARB			
Intercept B_0	41.66	0.85	<0.0001
Preintervention trend B_1	0.14	0.09	0.1691
Level change	0.37	0.45	0.4218
Trend change	−0.38	0.13	0.0127
Antiplatelet			
Intercept B_0	9.75	0.44	<0.0001
Preintervention trend B_1	0.13	0.05	0.3918
Level change	−0.26	0.30	0.3918
Trend change	−0.06	0.06	0.3129
PPI			
Intercept B_0	18.92	0.36	<0.0001
Preintervention trend B_1	0.39	0.04	<0.0001
Level change	0.31	0.21	0.1586
Trend change	−0.18	0.05	0.0044

Preintervention trend, before guideline intervention; level change, at guideline intervention; trend change, difference in slope before/after guideline intervention.

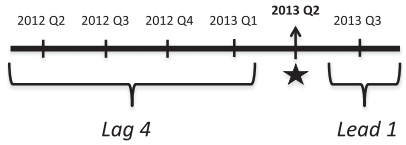

Figure 1—(Lag4, lead1) approach for sample quarter (2013 Q2). 2013 Q2 represents the quarter of interest. As illustrated, data from four lag quarters (2012 Q2–2013 Q1) and one lead quarter (2013 Q3) are included in the analysis for 2013 Q2.

behavior change constructs for vascular protection (9). While awareness of the 2013 Diabetes Canada vascular protective guidelines was 71% among survey respondents, only 22% had correct knowledge of guideline content for vascular protection upon questioning and only 21% reported adhering to guideline recommendations (9). It remains possible that despite ongoing dissemination efforts, prescription rates may have reached a ceiling in terms of any further improvements in uptake.

Limitations of this study should be acknowledged. First, the CPCSSN cohort involves a convenient sample of patients, providers, and practices, which limits the generalizability of findings. Second, results must be interpreted carefully, as prescription estimates may not correspond with actual medication usage. Third, the CPCSSN-validated case definition for diabetes differed from the 2013 Diabetes Canada guidelines definition. The CPCSSN definition includes both type 1 and type 2 diabetes, with an HbA_{1c} $\geq$7% or fasting glucose $\geq$7 mmol/L, while Diabetes Canada includes an HbA_{1c} $\geq$6.5% or fasting glucose $\geq$7 mmol/L. We suspect that CPCSSN was unable to capture some patients who would otherwise be considered to have diabetes by the Diabetes Canada guidelines, potentially overestimating the rates of statin and ACEI/ARB prescriptions, as usage of these medications is associated with higher HbA_{1c} levels (34,35). However, we suspect that this number would have been small, as patients can be captured by other diabetes criteria according to the CPCSSN case definition (14). Fourth, a lack of a validated case definition for CVD, microalbuminuria, and dyslipidemia in CPCSSN may reduce the specificity and sensitivity of multiple estimates. Finally, ITS analyses cannot infer cause-effect relationships, as external factors are not accounted for. An analysis of PPI prescriptions showed trends similar to those of the vascular protective prescriptions under investigation, suggesting that the potential for confounding effects cannot be excluded.

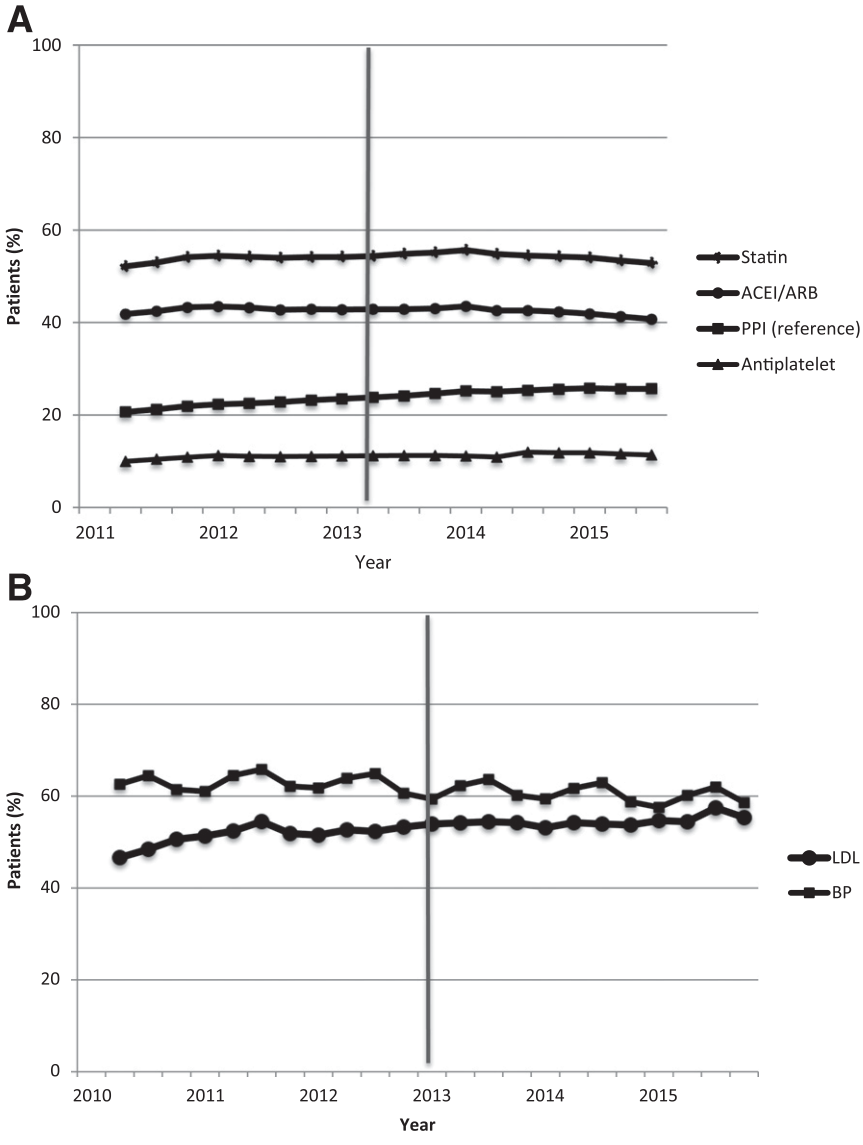

Figure 2—*A*: Proportion of eligible patients prescribed vascular protective medications in Canada, quarterly, from 2011 to 2015. Solid vertical line indicates the intervention point of guideline publication and dissemination (2013 Q2). *B*: Proportion of eligible patients achieving recommended LDL and BP targets in Canada, quarterly, from 2011 to 2015. Solid vertical line indicates the intervention point of guideline publication and dissemination (2013 Q2).

There are limitations unique to using practice-based EMRs, whereby accuracy and completeness can vary across different systems, providers, and sites, in turn affecting the validity of the study (36). It is possible that a full record of patient medications including those requiring manual input (nonprescription, specialist prescriptions) are not recorded in the EMR by all providers. Accordingly, data from nonprescription medications as a group are typically less accurate than prescription estimates (37). Antiplatelet agents carry significant bleeding risk, and we suspect that they would be more likely to be recorded in the EMR than other nonprescription medications with lower-risk profiles. There is also no reason to expect differences in the completeness of data pre– and post–guideline implementation.

Despite these limitations, this study captured trends in vascular protective medication prescriptions in a large sample of Canadian primary care patients

with diabetes. Previous studies have primarily used provincial data and are limited in their generalizability at a national level. Use of longitudinal data enabled assessment of trends over time and allowed for effective guideline evaluation at a population level. EMR data allowed for a more valid assessment of prescription rates, as self-reported data often overestimate medication adherence behavior (38). EMR data also allowed us to capture the rates of nonprescription medications including antiplatelet agents and data across greater age ranges (i.e., age <65 years), which are often unavailable with drug registry data.

We carried out statistical inference using an ITS design, which is considered a stronger research design than the traditional before-and-after longitudinal design and remains the recommended quasi-experiment design when a randomized control trial is not feasible at the community level (39,40). The total number of patients prescribed medications per quarter were aggregated into a single population-level proportion, and therefore results correspond with an intervention effect at the population level rather than the individual level. ITS has also been mainly used in conditions applicable to our study: a macro-level intervention (nationwide guideline dissemination strategy), a unidimensional outcome (prescription rates for vascular protective agents), and a large population (of primary care patients with diabetes) (25).

This study highlights a persistent gap in the management of vascular protection among patients with diabetes. Qualitative assessments are needed to assess the collective experience of physicians and elicit factors not captured in our quantitative design (i.e., registries which capture information about why a physician did not prescribe a guideline-recommended treatment). Further dissemination efforts should be targeted at groups with lower adherence rates including physicians from rural areas and those treating patients with lower SES. They may also involve EMR-based prompts to serve as reminders for providers. It is possible that a ceiling level of vascular protective medication uptake has been achieved; however, it is necessary to explore other reasons for guideline nonadherence and revise dissemination strategies accordingly before arriving at this conclusion.

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References

1. Tsiantou V, Karampli E, Zavras D, Athanasakis K, Pavi E, Kyriopoulos J. Is the rule of halves applicable in Diabetes Type 2? Evidence from Greece. Value Health 2014;17:A357
2. Kannel WB, McGee DL. Diabetes and cardiovascular disease. The Framingham study. JAMA 1979;241:2035–2038
3. Stone JA, Fitchett D, Grover S, Lewanczuk R, Lin P; Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Vascular protection in people with diabetes. Can J Diabetes 2013;37(Suppl. 1):S100–S104
4. Collins R, Armitage J, Parish S, Sleigh P, Peto R; Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5963 people with diabetes: a randomised placebo-controlled trial. Lancet 2003;361:2005–2016
5. Colhoun HM, Betteridge DJ, Durrington PN, et al.; CARDS Investigators. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. Lancet 2004; 364:685–696
6. Gerstein HC. Reduction of cardiovascular events and microvascular complications in diabetes with ACE inhibitor treatment: HOPE and MICRO-HOPE. Diabetes Metab Res Rev 2002;18 (Suppl. 3):S82–S85
7. Leiter LA, Berard L, Bowering CK, et al. Type 2 diabetes mellitus management in Canada: is it improving? Can J Diabetes 2013;37:82–89
8. Straus S, Tetroe J, Graham I. *Knowledge Translation in Health Care: Moving From Evidence to Practice*. Hoboken, NJ, Wiley, 2011, p. 336
9. Yu CH, Lillie E, Mascarenhas-Johnson A, Gall Casey C, Straus SE. Impact of the Canadian Diabetes Association guideline dissemination strategy on clinician knowledge and behaviour change outcomes. Diabetes Res Clin Pract 2018; 140:314–323
10. Farahani P, Johnson A, Whitehead M, Rohland S. Sex/gender-based pharmacology and statin utilization amongst elderly patients with diabetes. Clin Invest Med 2015;38:E371–E383
11. Shah BR, Booth GL, Lipscombe LL, Feig DS, Bhattacharyya OK, Bierman AS. Near equality in quality for medication utilization among older adults with diabetes with universal medication insurance in Ontario, Canada. J Eval Clin Pract 2014;20:176–183
12. McAlister FA, Campbell NRC, Duong-Hua M, Chen Z, Tu K. Antihypertensive medication prescribing in 27,822 elderly Canadians with diabetes over the past decade. Diabetes Care 2006;29:836–841
13. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol 2008;61:344–349
14. Williamson T, Green ME, Birtwhistle R, 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;12:367–372
15. Garies S, Birtwhistle R, Drummond N, Queenan J, Williamson T. Data Resource Profile: National electronic medical record data from the Canadian Primary Care Sentinel Surveillance Network (CPCSSN). Int J Epidemiol 2017;46: 1091–1092f
16. WHO Collaborating Centre for Drug Statistics Methodology. *Guidelines for ATC Classification and DDD Assignment 2018*. Oslo, Norway, WHO Collaborating Centre for Drug Statistics Methodology, 2017
17. Centers for Disease Control and Prevention, National Center for Health Statistics. International Classification of Diseases, Ninth Revision [Internet], 2011. Available from https://www.cdc.gov/nchs/icd/icd9cm.htm. Accessed 15 January 2017
18. McFarlane P, Gilbert RE, MacCallum L, Senior P; Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Chronic kidney disease in diabetes. Can J Diabetes 2013;37 (Suppl. 1):S129–S136
19. Canadian Institute for Health Information. Data and analysis methodology. In *Reducing Gaps in Health: A Focus on Socio-Economic Status in Urban Canada*. Ottawa, Canada, Canadian Population Health Initiative, 2008, p. 1–35
20. Postal Code OM Conversion File (PCCF), Reference Guide. 2016. Statistics Canada Catalogue no. 92-154-G. Available from https://www150.statcan.gc.ca/n1/pub/92-154-g/92-154-g2017001-eng.htm. Accessed 1 October 2017
21. World Health Organization. *Obesity: Preventing and Managing the Global Epidemic*. Geneva, World Health Organization, 1998

22. Selig JP, Preacher KJ, Little TD. Modeling time-dependent association in longitudinal data: a lag as moderator approach. Multivariate Behav Res 2012;47:697–716
23. Canadian Institute for Health Information. National prescription drug utilization information system database plan information document [Internet], 2012. Available from https://secure.cihi.ca/free_products/PlanInformation_1007_e1.pdf. Accessed 25 October 2017
24. Guirguis-Blake J, Keppel GA, Force RW, Cauffield J, Monger RM, Baldwin LM. Variation in refill protocols and procedures in a family medicine residency network. Fam Med 2012;44:564–568
25. Wagner AK, Soumerai SB, Zhang F, Ross-Degnan D. Segmented regression analysis of interrupted time series studies in medication use research. J Clin Pharm Ther 2002;27:299–309
26. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. J R Stat Soc Series B Stat Methodol 1995;57:289–300
27. SAS Institute. *SAS/STAT Software*, *Version 9.4*. SAS, Cary, NC, 2012
28. Anderson TW. *The Statistical Analysis of Time Series*. Vol. 19. Hoboken, NJ, John Wiley & Sons, Ltd., 2011
29. Levinson W, Huynh T. Engaging physicians and patients in conversations about unnecessary tests and procedures: Choosing Wisely Canada. CMAJ 2014;186:325–326
30. Braga M, Casanova A, Teoh H, et al.; Diabetes Registry to Improve Vascular Events (DRIVE) Investigators. Treatment gaps in the management of cardiovascular risk factors in patients with type 2 diabetes in Canada. Can J Cardiol 2010;26:297–302
31. Ishiguro L, Saskin R, Vermeulen MJ, Yates E, Gunraj N, Victor JC. Increasing access to health administrative data with ICES data & analytic services. Healthc Q 2016;19:7–9
32. Khoong E, Gibbert WS, Garbutt JM, Summer W, Brownson RC. Rural, suburban, and urban differences in factors that impact physician adherence to clinical preventive service guidelines elaine. J Rural Health 2016;150:137–143
33. Campbell DJT, Ronksley PE, Hemmelgarn BR, et al. Association of enrolment in primary care networks with diabetes care and outcomes among First Nations and low-income Albertans. Open Med 2012;6:e155–e165
34. Liew SM, Lee PY, Hanafi NS, et al. Statins use is associated with poorer glycaemic control in a cohort of hypertensive patients with diabetes and without diabetes. Diabetol Metab Syndr 2014;6:53
35. Huang X, Zhou Y, Xu B, et al. Glycated haemoglobin A1c is associated with low-grade albuminuria in Chinese adults. BMJ Open 2015;5:e007429
36. Jordan K, Porcheret M, Croft P. Quality of morbidity coding in general practice computerized medical records: a systematic review. Fam Pract 2004;21:396–412
37. Staroselsky M, Volk LA, Tsurikova R, et al. An effort to improve electronic health record medication list accuracy between visits: patients' and physicians' response. Int J Med Inform 2008;77:153–160
38. Stirratt MJ, Dunbar-Jacob J, Crane HM, et al. Self-report measures of medication adherence behavior: recommendations on optimal use. Transl Behav Med 2015;5:470–482
39. Soumerai SB, Starr D, Majumdar S. How do you know which health care effectiveness research you can trust? A guide to study design for the perplexed. Prev Chronic Dis 2015;12:E101
40. Biglan A, Ary D, Wagenaar AC. The value of interrupted time-series experiments for community intervention research. Prev Sci 2000;1:31–49