Trends in Prescribing Oral Anticoagulants in Canada, 2008–2014

Jeffrey I. Weitz, MD[1,2,3]; William Semchuk, MSc, PharmD[4]; Alexander G.G. Turpie, MD[2]; William D. Fisher, MD[5]; Cindy Kong, BRE[6]; Antonio Ciaccia, MSc[6]; and John A. Cairns, MD[7]

[1]Thrombosis and Atherosclerosis Research Institute, Hamilton, Ontario, Canada; [2]Department of Medicine, McMaster University, Hamilton, Ontario, Canada; [3]David Braley Research Institute, Hamilton, Ontario, Canada; [4]Regina Qu'Appelle Health Region, Regina, Saskatchewan, Canada; [5]McGill University Health Centre, Montreal, Quebec, Canada; [6]Bayer Inc, Mississauga, Ontario, Canada; and [7]Division of Cardiology, University of British Columbia, Vancouver, British Columbia, Canada

ABSTRACT

Purpose: The non–vitamin K antagonist oral anticoagulants (NOACs), dabigatran, rivaroxaban, and apixaban, provide several advantages over vitamin K antagonists, such as warfarin. Little is known about the trends of prescribing OACs in Canada. In this study we analyzed changes in prescription volumes for OAC drugs since the introduction of the NOACs in Canada overall, by province and by physician specialty.

Methods: Canadian prescription volumes for warfarin, dabigatran, rivaroxaban, and apixaban from January 2008 to June 2014 were obtained from the Canadian Compuscript Audit of IMS Health Canada Inc and were analyzed by physician specialty at the national and provincial levels. Total prescriptions by indication were calculated based on data from the Canadian Disease and Therapeutic Index for all OAC indications and for each commonly prescribed dose of dabigatran (75, 110, and 150 mg), rivaroxaban (10, 15, and 20 mg), and apixaban (2.5 and 5 mg).

Findings: The overall number of OAC prescriptions in Canada has increased annually since 2008. With the availability of the NOACs, the proportion of total OAC prescriptions attributable to warfarin has steadily decreased, from 99% in 2010 to 67% by June 2014, and the absolute number of warfarin prescriptions has been decreasing since February 2011. The greatest decline in proportionate warfarin prescriptions was in Ontario. In general, the increase of NOAC prescriptions coincided with the introduction of provinces' reimbursement of NOAC prescription costs. The proportion of total OAC prescriptions represented by the NOACs varied by specialty, with the greatest proportionate prescribing found among orthopedic surgeons, cardiologists, and neurologists.

Implications: Since their approval, the NOACs have represented a growing share of total OAC prescriptions in Canada. This trend is expected to continue because the NOACs are given preference over warfarin in guidelines on stroke prevention in patients with atrial fibrillation, because of growing physician experience, and due to the emergence of potential new indications. An understanding of the current prescribing patterns will help to encourage knowledge translation and possibly influence policy/reimbursement strategies. (*Clin Ther.* 2015;37:2506–2514) © 2015 The Authors. Published by Elsevier HS Journals, Inc.

Key words: NOAC, oral anticoagulants, prescribing trends.

INTRODUCTION

For decades, vitamin K antagonists, such as warfarin, were the only oral anticoagulant (OAC) agents indicated for the long-term prevention and treatment of arterial and venous thrombosis. Although warfarin is effective, its use is complicated by its numerous drug and food interactions, as well as the need for individualized patient dosing, requiring regular

Accepted for publication September 13, 2015.
http://dx.doi.org/10.1016/j.clinthera.2015.09.008
0149-2918/$ - see front matter

monitoring of coagulation to optimize efficacy and tolerability.[1,2] The non–vitamin K antagonist OACs (NOACs) are more convenient than is warfarin because they can be given in fixed doses without routine coagulation monitoring. In Canada, 3 NOACs are currently available: the oral thrombin inhibitor dabigatran etexilate, and the oral factor Xa inhibitors rivaroxaban and apixaban.

Although the NOACs were first approved in 2008 for the prevention of venous thromboembolism (VTE) after elective hip- or knee-replacement surgery, the most common use of the NOACs now is for stroke risk reduction in patients with atrial fibrillation (AF).[3] More recently, the NOACs were also approved for the treatment of deep vein thrombosis and pulmonary embolism.[4–6]

Little is known about the trends of prescribing OACs in Canada. This article provides the first look at OAC-prescribing trends in Canada, according to province and physician specialty, since the availability of the NOACs in 2008. Guidelines have embraced the use of NOACs, and in 2012, the Canadian Cardiovascular Society gave preference to NOACs over warfarin for stroke prevention in AF.[7] However, a major challenge for clinicians in following this recommendation is the lack of alignment with reimbursement systems in Canada.[8,9] An understanding of the uptake of NOACs may help to change policy/reimbursement strategies to reflect current guidelines and prescribing patterns.

MATERIALS AND METHODS

Data Sources

A detailed listing and description of the data sources are provided in the **Supplemental Material** in the online version at http://dx.doi.org/10.1016/j.clinthera.2015.09.008. Briefly, data on the numbers of prescriptions filled by retail pharmacies in Canada from January 2008 to June 2014, available from the Canadian CompuScript database, were obtained from IMS Health Canada Inc. These data provide the number of new, refill, and total prescription volumes for OACs, including formulation and strength, within each therapeutic class, at the national and provincial levels. The Physician Specialty Report, which can complement the Canadian Compuscript, shows new and total prescriptions dispensed according to physician specialty, specialty share by product and therapeutic class, and product market share by physician specialty. Data are available from Alberta, Saskatchewan, Ontario, Quebec, Nova Scotia, and New Brunswick; the other provinces and territories do not supply data to IMS Health Canada Inc. IMS Health Canada Inc captures all new and refill prescriptions (80% national prescription coverage) from a panel of over 5000 pharmacies, which are stratified by province, pharmacy type (retail chain, independent), and size. Prescription records are collected electronically and updated on a monthly basis. Sample data from the panel are extrapolated to estimate the prescriptions by all physicians in each province. The accuracy of these data is greater in provinces with greater pharmacy coverage. Extrapolated provincial totals were summed to provide a national estimate. *Total prescriptions* refers to all new and refill prescriptions dispensed from pharmacies. Data on each of the NOACs in all of the commonly used doses were obtained: dabigatran (75, 110, and 150 mg), rivaroxaban (10, 15, and 20 mg), and apixaban (2.5 and 5 mg). The total prescription share for each OAC was used for accounting for differences in NOAC dosing. For analysis of the per capita OAC-prescribing trends by province, the total number of pills was used for accounting for differences in prescription duration, thereby ensuring that provinces with shorter prescription durations (eg, Quebec) would not be overrepresented.

Data for determining the total prescriptions by indication were obtained from the Canadian Disease and Therapeutic Index (CDTI). The CDTI uses statistical information on the patterns and treatment of diseases encountered in office-based practices in Canada to help to understand disease trends and drug-prescribing patterns. Data on estimated drug use and estimated diagnostic visits are obtained at national and regional levels (5 regions: Maritimes, Quebec, Ontario, Prairies, and British Columbia) from physicians who fill out case records about their patients. The CDTI panel consists of 652 physicians in office-based medical practices covering 15 specialties. Each quarter, these physicians report on patients' visits during a 2-day period. Data from the CDTI do not include visits to non–primary care specialists or reflect patient self-medication. Although individual quarterly estimates of the national CDTI data have a high sampling error because of large sampling weights, quarterly and year-over-year

estimates are accurate compared with those of other drug expenditures and health care services utilization statistics.[10]

To assess factors that influence prescription changes, the numbers of NOAC prescriptions were also analyzed in relation to the timing of provincial reimbursement. In Canada (with the exception of Quebec), the decision to add a newly licensed nononcologic drug to provincial formulary listings is based on recommendations by the Canadian Agency for Drugs and Technologies in Health Common Drug Review (CDR).[11] The CDR not only evaluates the evidence supporting the efficacy and tolerability of a drug but also performs a pharmacoeconomic assessment. Based on the CDR findings, the Canadian Expert Drug Advisory Committee makes a final recommendation, which is used by the provinces to decide whether a new drug should be added to the provincial formulary. In Quebec, the Institut National d'Excellence en Santé et en Services Sociaux provides recommendations on whether to add new drugs to the formulary.[12]

Methodology for Estimating OAC Total Prescriptions by Indication

Factors by indication have been derived from the CDTI, based on the number of drug mentions by indication. The CDTI physician panel is instructed to record the diagnosis identified or treated during each patient visit. Information on diagnoses is coded by the IMS Health coders using the World Health Organization's *International Classification of Diseases, Ninth Revision*. Factors by indication are then applied to total prescriptions available from CompuScript to generate total prescriptions by indication.

RESULTS

Trends of OAC Prescribing by Orthopedic Surgeons in Canada

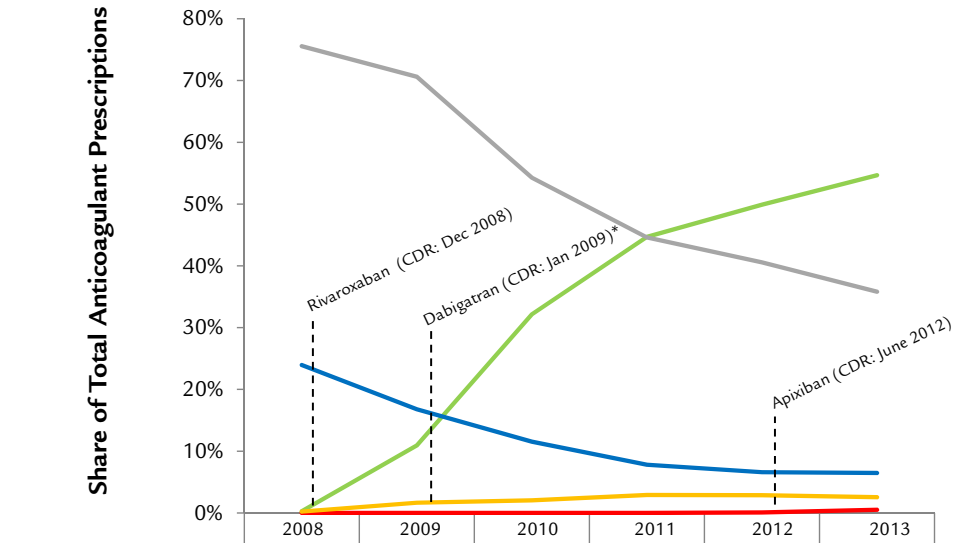
Health Canada first approved the use of dabigatran and rivaroxaban in 2008 and apixaban in 2011 for the prevention of VTE after elective hip- or knee-replacement surgery. Whereas rivaroxaban and apixaban received positive CDR recommendations in 2008 and 2012, respectively, dabigatran received a negative CDR recommendation in 2009.[10,13,14]

To determine the impact of the NOACs on VTE prevention after hip or knee arthroplasty, we reviewed trends of prescribing by orthopedic surgeons because they rarely prescribe OACs for other indications. Based on prescribing data in this specialty group, there has been a shift from warfarin and injectable anticoagulants to rivaroxaban (Figure 1). The largest increase in rivaroxaban prescribing occurred between 2009 and 2010, which corresponds to the timeframe when rivaroxaban was first listed on most provincial formularies (see Supplemental Table in the online version at http://dx.doi.org/10.1016/j.clinthera.2015.09.008). By 2013, rivaroxaban held a 55% share of the anticoagulant market in orthopedics, whereas dabigatran and apixaban together accounted for approximately 3%.

Overall OAC-Prescribing Trends in Canada

Apart from prescriptions generated by orthopedic surgeons, identifying the particular conditions for which OACs were prescribed is challenging because of their multiple approved indications and somewhat overlapping doses. Given the prevalences of AF and VTE and the number of arthroplasties per year, as well as current standards of care, we estimated that AF, VTE treatment, and thromboprophylaxis in orthopedic surgery account for 59%, 10%, and 1%, respectively, of all OAC prescriptions.[15] Although warfarin is used in the treatment of more conditions than are the NOACs, for this article we did not downward-adjust the warfarin-prescribing data to account for this when comparing prescription data between warfarin and the NOACs.

The total number of OAC prescriptions steadily increased, from ~4.8 to ~7 million from 2008 to 2013 (Figure 2A). Warfarin prescriptions increased until 2011, after which the number of warfarin prescriptions decreased and an increase in prescriptions for the NOACs was observed. The proportion of OAC prescriptions for warfarin fell from 99% in 2010 to 67% by June 2014 (Figure 2B). The decline in warfarin prescribing occurred during the same timeframe as the positive CDR recommendations for the use of dabigatran (2011), rivaroxaban (2012), and apixaban (2013) for stroke prevention in AF.[16–18] There was a significant increase in the prescribing of dabigatran before its positive recommendation from the CDR; dabigatran prescribing accelerated with its addition to provincial formularies (see Supplemental Table in the online version at http://dx.doi.org/10.1016/j.clinthera.2015.09.008). By contrast, the market



	2008	2009	2010	2011	2012	2013
apixaban	0%	0.00%	0.00%	0.00%	0.08%	0.50%
rivaroxaban	0%	10.94%	32.16%	44.69%	49.90%	54.68%
dabigatran etexilate	0%	1.65%	2.02%	2.91%	2.87%	2.54%
warfarin	24%	16.79%	11.53%	7.80%	6.59%	6.47%
injectable anticoagulant	76%	70.62%	54.28%	44.60%	40.57%	35.81%

Figure 1. Share of orthopedic surgeons' prescriptions of anticoagulant agents. Dates of Common Drug Review (CDR) recommendations for venous thromboembolism prevention after major orthopedic surgery are shown for each non–vitamin K oral anticoagulants. *Dabigatran received a negative CDR recommendation. Source: IMS Brogan Canadian Compuscript Physician Specialty Report.

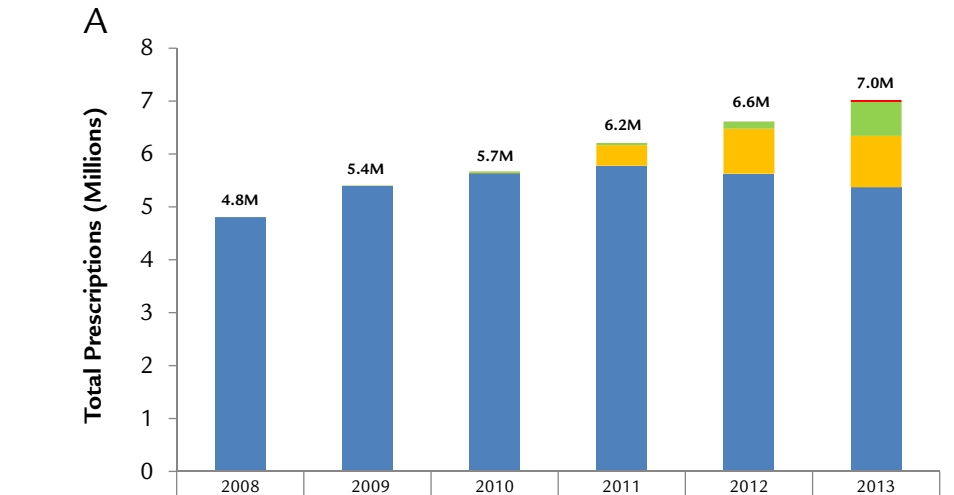
shares of rivaroxaban and apixaban increased only after they were added to provincial formularies.

OAC-Prescribing Trends, by Physician Subgroup

Since 2010, the proportionate prescribing of NOACs was highest among cardiologists and neurologists (see **Supplemental Figure 1A and 1D** in the online version at http://dx.doi.org/10.1016/j.clinthera.2015.09.008). By 2013, warfarin accounted for 45% and 51% of the total OAC prescriptions by cardiologists and neurologists, respectively (**Figure 3**). The proportionate share of dabigatran among the NOACs was surpassed in late 2013 by rivaroxaban, which gained 28% and 18% of the OAC market among cardiologists and neurologists, respectively, by June 2014 (see **Supplemental Figure 1A and 1D** in the online version at http://dx.doi.org/10.1016/j.clinthera.2015.09.008). Apixaban prescribing within these 2 specialties has steadily increased, gaining 18% of the market by cardiologists and neurologists, by the second quarter (Q2) of 2014 (see **Supplemental Figure 1A and 1D** in the online version at http://dx.doi.org/10.1016/j.clinthera.2015.09.008). By comparison, the increase in prescribing of the NOACs has been more gradual among internists, general practitioners, emergency department physicians, and hematologists, among whom warfarin retained 68% to 89% of the total OAC prescription share in 2013 (**Figure 3**). By Q2 2014, 57% of OAC prescriptions by internists were for warfarin (see **Supplemental Figure 1B** in the online version at http://dx.doi.org/10.1016/j.clinthera.2015.09.008), and warfarin represented 71% and 83% of OAC prescriptions from general practitioners and hematologists, respectively (see **Supplemental Figure 1C and 1E** in the online version at http://dx.doi.org/10.1016/j.clinthera.2015.09.008).

OAC-Prescribing Trends by Province

Across Canada, the greatest per capita usage of OACs was in New Brunswick, Nova Scotia, and Saskatchewan (**Figure 4**). Alberta and Manitoba had the lowest per capita OAC prescribing, whereas per



	2008	2009	2010	2011	2012	2013
apixaban	0	0	0	0	296	38,699
rivaroxaban	263	8,213	25,855	41,518	130,454	640,536
dabigatran etexilate	141	1,324	9,586	390,503	851,855	973,290
warfarin	4,804,647	5,396,701	5,634,072	5,776,816	5,626,882	5,368,792
Total OAC	4,805,051	5,406,238	5,669,513	6,208,837	6,609,487	7,021,317

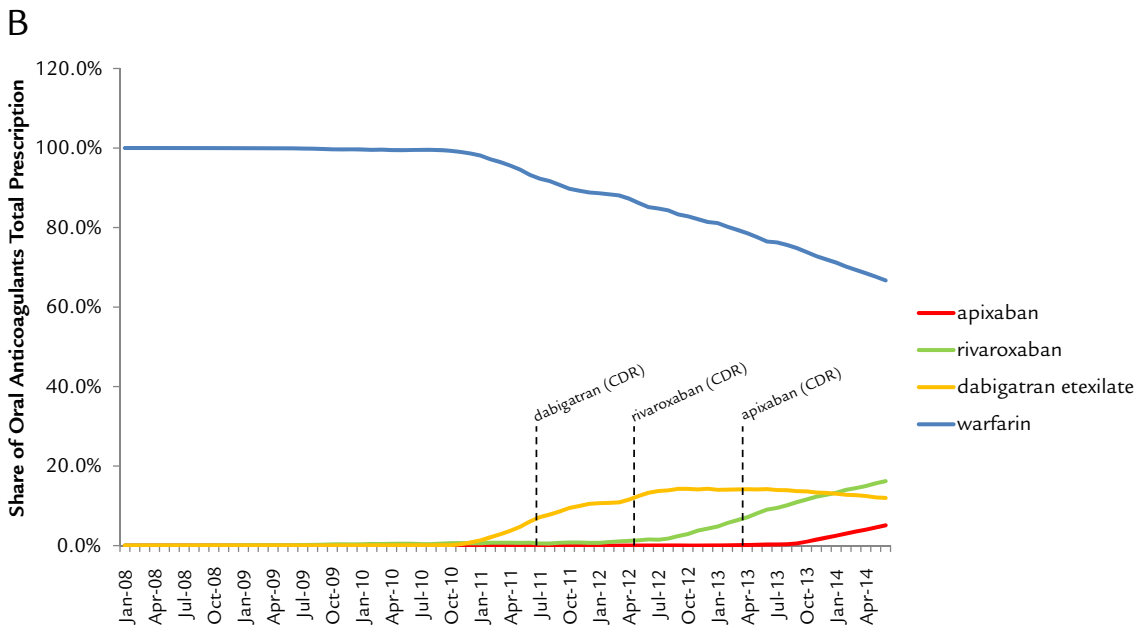
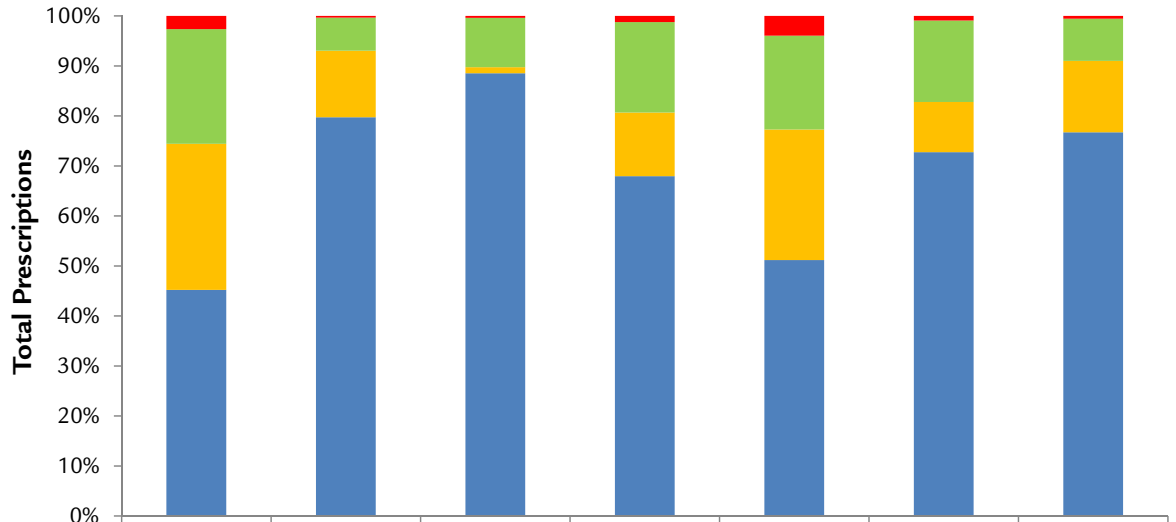


Figure 2. Total annual prescription volumes (A) and total monthly prescription shares (B) of oral anticoagulant (OAC) agents. Dates of Common Drug Review recommendations of each of the non–vitamin K antagonist OACs (NOACs) for stroke prevention in patients with atrial fibrillation are shown. Data on warfarin have not been adjusted to account for the fact that the approved indications for the NOACs represent only 70% of all OAC prescriptions. Source: IMS Brogan Canadian Compuscript.



	Cardiologists	GP/FM	Haematologists	Internists	Neurologists	Emergency Medicine	All Physicians
apixaban	11,722	17,362	381	3,486	583	63	33,597
rivaroxaban	102,202	348,811	9,885	51,635	2,774	1,128	516,435
dabigatran etexilate	130,250	700,419	1,212	36,270	3,857	695	872,703
warfarin	201,483	4,195,665	88,582	193,794	7,564	5,038	4,692,126
Total OAC	445,657	5,262,257	100,060	285,185	14,778	6,924	6,114,861

Figure 3. Total number of prescriptions for oral anticoagulants (OACs) prescribed by each physician specialty in 2013. Data on warfarin have not been adjusted to account for the fact that the approved indications for the non–vitamin K antagonist OACs (NOACs) represent only 70% of all OAC prescriptions. Source: IMS Brogan Canadian Compuscript Physician Specialty Report.

capita usage in British Columbia, Ontario, Quebec, Newfoundland, and Prince Edward Island was similar to the national average. For the provinces that were analyzed further (Ontario, Quebec, British Columbia, Alberta, Saskatchewan, Manitoba, New Brunswick, and Nova Scotia), dabigatran prescribing increased before provinces reimbursed the costs of stroke prevention in AF. The only exception to this finding was Quebec, where dabigatran prescriptions increased around the same time that reimbursement was approved (see **Supplemental Figure 2** in the online version at http://dx.doi.org/10.1016/j.clinthera.2015.09.008). This finding differs from the trends of increased prescribing of rivaroxaban and apixaban, the market growth of which increased only after reimbursement approval. The most rapid decline in warfarin use was in Ontario, where 57% of OAC prescriptions were for warfarin by the end of Q2 2014, compared with ~98% in Q4 2010 (see **Supplemental Figure 2A** in the online version at http://dx.doi.org/10.1016/j.clinthera.2015.09.008). By comparison, warfarin accounted for 68% to 76% of OAC prescriptions in British Columbia, Alberta, Saskatchewan, Manitoba, Quebec, New Brunswick, and Nova Scotia.

DISCUSSION

Our analysis of OAC-prescribing trends in Canada reveals an increase in overall OAC prescriptions since 2008, with an increase in the absolute number of warfarin prescriptions to 2011 followed by decreasing numbers since then. An analogous trend in OAC prescriptions has been reported among European countries, where, as in Canada, vitamin K antagonists still represent the majority of OAC prescriptions, despite the fact that several practice guidelines give

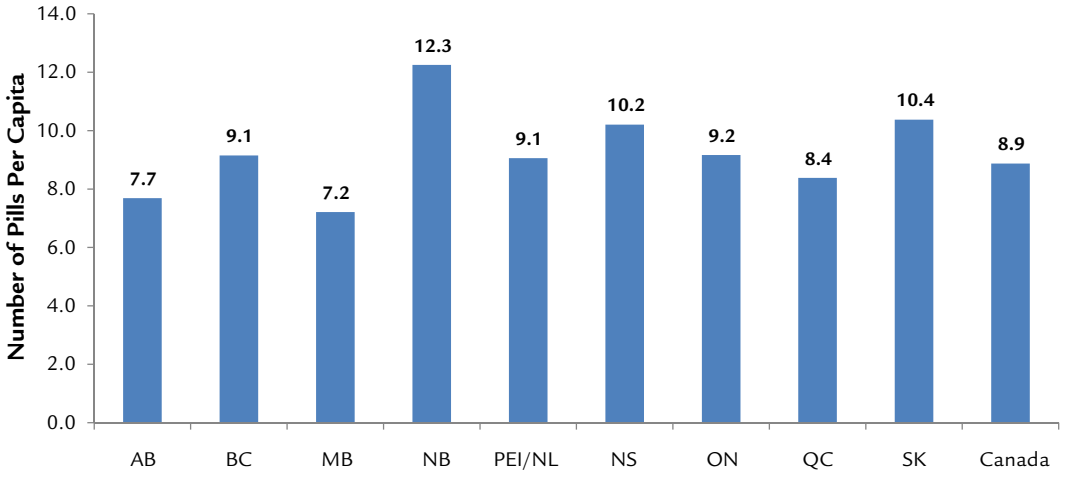


Figure 4. The number of oral anticoagulant (OAC) pills dispensed per capita for each Canadian province in 2013. Per capita OAC pills dispensed in each province were calculated by dividing the total OAC pills dispensed by the size of the population. Data do not include acenocoumarol, which has $<0.5\%$ market share; data on Canada do not include the Yukon and Northwest Territories. Source: IMS Brogan Canadian Compuscript and CANSIM, table 051-0001 (population as of July 1, 2013).

preference to the NOACs over warfarin for stroke prevention in the majority of patients with AF.[8,19–22]

There is considerable variation in the proportionate prescribing of warfarin and NOACs among physician subgroups. Based on the findings, the NOACs have been predominantly embraced by specialists, in particular, orthopedic surgeons, cardiologists, and neurologists. This finding is not surprising given that the most of the established indications for the NOACs are for thromboprophylaxis after hip or knee arthroplasty and stroke prevention in AF. Orthopedic surgeons rarely prescribe OACs for indications other than thromboprophylaxis, and cardiologists and stroke neurologists are the specialists most frequently involved in the treatment of patients with AF and patients with AF-related stroke, respectively. The increasing prescribing of NOACs is likely influenced by the Canadian Cardiovascular Society guidelines, which give preference to NOACs over warfarin in most patients with nonvalvular AF.[7,8,23] The growing prescribing of NOACs among physicians can also be attributed to the expanding number of indications for which the NOACs have been approved, in particular, the treatment of deep vein thrombosis and pulmonary embolism.

Of the NOACs, rivaroxaban acquired a substantial portion of the market share for anticoagulants for VTE prevention after major orthopedic surgery, because it was the first of the NOACs to be given a positive CDR recommendation.[13] Although apixaban was given a positive CDR recommendation for VTE prevention in orthopedics in 2012, it did not gain an appreciable market share, likely because most institutions already had incorporated rivaroxaban into their orthopedic care pathways and saw no advantage in introducing a second agent.

Multiple factors are likely involved in the differences in OAC-prescribing trends across the provinces. The choice between warfarin and a NOAC may be influenced by the availability of anticoagulation clinics and laboratories for international normalized ratio monitoring; in areas with limited access, NOACs may be preferred over warfarin because the use of NOACs does not require routine coagulation monitoring. The choice of therapy may also be affected by a patient's level of public or private insurance due to the higher cost of NOACs relative to warfarin.[24]

Although this analysis provides a robust assessment of OAC-prescribing trends in Canada, it had some limitations. First, OAC-prescribing data by physician specialty are available only from Alberta, Saskatchewan, Ontario, Quebec, Nova Scotia, and New

Brunswick; therefore, the results of the analysis of physician-specific trends cannot be accurately extrapolated across all provinces. Second, OAC prescriptions by physician subgroup were not stratified by indication; thus, changes in OAC-prescribing trends by each specialty could not be tracked according to their specific therapeutic use by each subgroup. Finally, this article does not provide information on prescriptions at the patient level, but rather looks at total prescriptions, preventing extrapolation to specific patient subgroups or disease trends.

Overall, the data show that NOACs represent a growing segment of the OAC market, with an overall decline in warfarin use and increased prescribing of the NOACs. An understanding of the increase in prescribing of the NOACs can aid in knowledge translation and promote the appropriate prescribing of these agents for current and new indications. Ongoing trials of the NOACs are exploring their tolerability and efficacy in novel clinical settings, including stroke prevention in patients with embolic stroke of undetermined source (dabigatran: RESPECT-ESUS [Dabigatran Etexilate for Secondary Stroke Prevention in Patients With Embolic Stroke of Undetermined Source], NCT02239120; rivaroxaban: NAVIGATE ESUS [Rivaroxaban Versus Aspirin in Secondary Prevention of Stroke and Prevention of Systemic Embolism in Patients With Recent Embolic Stroke of Undetermined Source], NCT02313909), stroke prevention in patients with AF undergoing cardioversion (edoxaban: ENSURE-AF [Edoxaban vs. Warfarin in Subjects Undergoing Cardioversion of Atrial Fibrillation], NCT02072434), and prevention of major adverse cardiovascular events in patients with coronary or peripheral artery disease (rivaroxaban: COMPASS [Rivaroxaban for the Prevention of Major Cardiovascular Events in Coronary or Peripheral Artery Disease], NCT01776424). With potential new indications, increasing awareness of the importance of stroke prevention in AF patients, and growing experience with NOACs, the trend for increased NOAC prescribing is expected to continue.

ACKNOWLEDGMENTS

The authors had complete editorial independence, have approved the final article and take full responsibility for the content of this publication. Ms Cindy Kong is an employee of Bayer Inc. and was involved in compiling, linking, and presenting the data from CompuScript and CDTI. Ms. Kong and Mr. Antonio Ciaccia, also an employee of Bayer Inc., were involved, along with the other authors, in interpreting the data and writing the manuscript for publication.

The statements, findings, conclusions, views, and opinions contained and expressed in this publication are based in part on data obtained under license from IMS Health Canada Inc concerning the following information services: CompuScript (including Physician Specialty Report 2008–2014) and CDTI. The statements, findings, conclusions, views, and opinions contained and expressed herein are not necessarily those of IMS Health Canada Inc or any of its affiliated or subsidiary entities.

The authors thank MEDUCOM Health Inc. for providing logistical support.

CONFLICTS OF INTEREST

Publication of this article was supported by Bayer Inc., who provided financial support to MEDUCOM Health for costs associated with logistics of manuscript preparation and submission.

Dr. Turpie has provided consultation to Bayer Inc and Daiichi Sankyo and has received speaker's honoraria from Bayer Inc, Janssen Inc, Boehringer Ingelheim Ltd, Bristol-Myers Squibb, and Pfizer. Ms. Kong and Mr. Ciaccia are employed by Bayer Inc, which markets rivaroxaban. Dr. Cairns has chaired or been a member of the Data and Safety Monitoring Boards of the following industry-sponsored trials: PALLAS (Sanofi-Aventis), SHIELD-2 (Forest Laboratories Inc), COMPASS (Bayer Inc) and ARTESIA (Bristol-Myers Squibb, Pfizer, Medtronic); has provided consultation to Boehringer Ingelheim Ltd, Bayer Inc, Pfizer, Bristol-Myers Squibb, Forest Laboratories Inc, and St. Jude Medical Inc; is a steering committee member of TOTAL (Medtronic, CIHR) and COMPLETE (AstraZeneca Inc, Boston Scientific, CIHR), and has received speaker's honoraria from Boehringer Ingelheim Ltd, Bayer Inc, Pfizer, and Bristol-Myers Squibb. The authors have indicated that they have no other conflicts of interest with regard to the content of this article.

SUPPLEMENTARY MATERIAL

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.clinthera.2015.09.008.

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Address correspondence to: Jeffrey Weitz, MD, David Braley Research Institute C5-121, 237 Barton Street East, Hamilton, ON L8L 2X2, Canada. E-mail: jeff.weitz@taari.ca

SUPPLEMENTARY MATERIALS

Supplementary Methods

There were three main data sources used for the publication:

i. IMS Brogan Canadian CompuScript Audit (of which the Physician Specialty Report is an extension of this audit)
ii. IMS Brogan Canadian Disease and Therapeutic Index (CDTI)
iii. CANSIM - Statistics Canada's key socioeconomic database

A) IMS Brogan Canadian CompuScript Audit is the main data source of all the prescription data.

The Canadian CompuScipt Audit provides data on prescriptions dispensed by retail pharmacies. The prescription data is reported at National and Provincial level. An extension of the CompuScript Audit is the Physician Specialty Report which provides the same data by physician specialties. Data is collected through a panel of over 5,600 retail pharmacies. The data is then projected to estimate prescriptions activity for retail pharmacies not on IMS Brogan panel. See below for type of pharmacies included/excluded and information collected:

Included:

i. Retail pharmacies (chain & independent)
ii. Mass-merchandisers with pharmacies
iii. Groceries with pharmacies
iv. Stores of all sizes
v. Pharmacies with Internet-free business (not included in sample, but are in the universe)

Excluded:

i. Hospital dispensaries

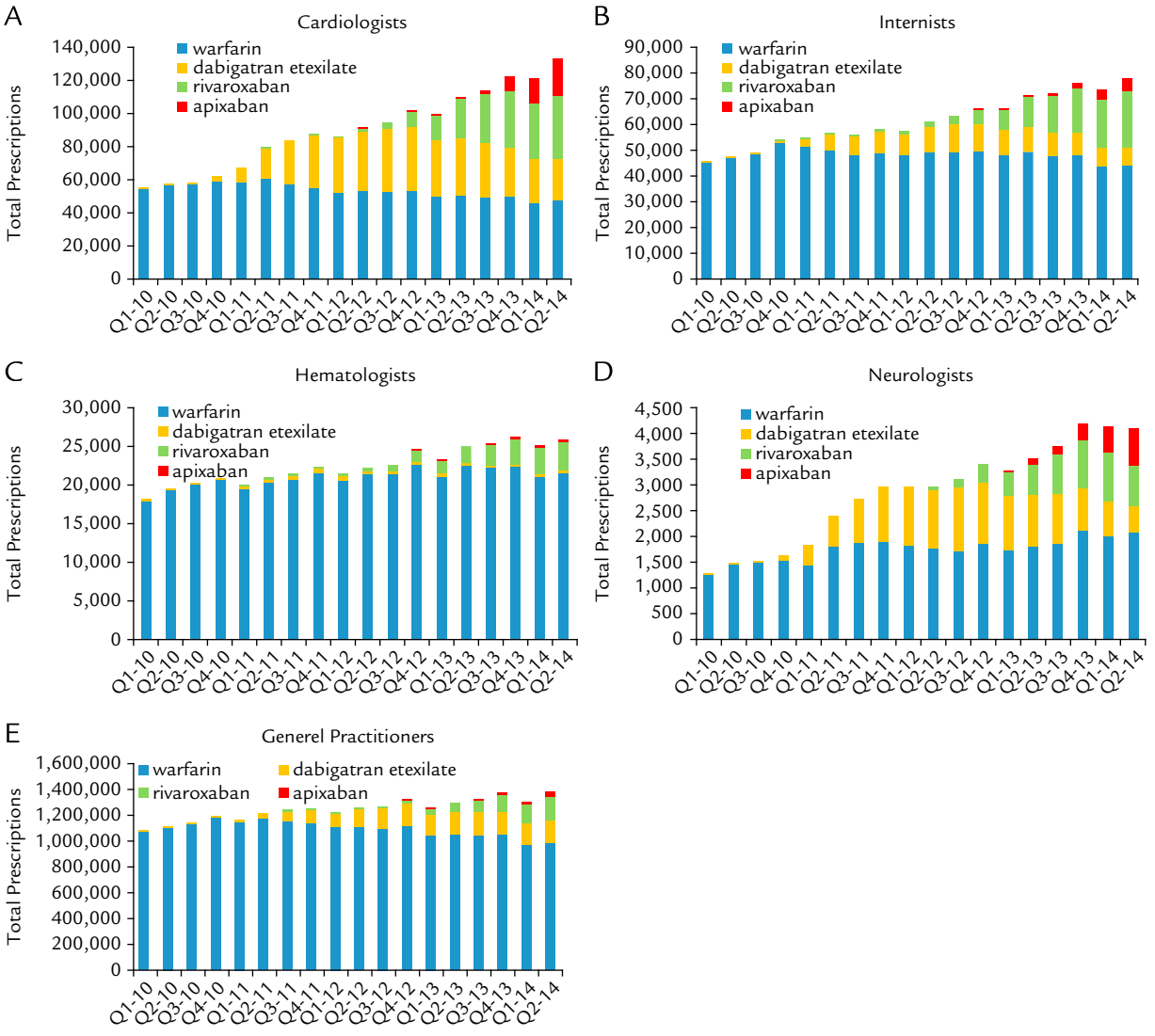
The following information is collected:

i. Product name
ii. Manufacturer name
iii. Product form/strength
iv. Prescription type: new or refill
v. Prescription size
vi. Prescription price (including the dispensing fee and mark up)
vii. Pharmacy ID
viii. MD license number (excluding British Columbia and Manitoba)

B) IMS Brogan Canadian Disease and Therapeutic Index (CDTI)

The Canadian Disease and Therapeutic Index (CDTI) is an IMS Brogan report that provides information on disease trends and treatments, including the therapeutic use of prescription medications by office-based physicians (approximately 650) stratified by region, and representing all major specialties. Each physician reports quarterly, over two consecutive days in which he/she has patient contact. Data from the CDTI does not include visits to non-primary specialties, such as anesthesiologists and pathologists, or reflect patient self-medication.

C) CANSIM is Statistics Canada's key socioeconomic database and includes data on Canadian population. Data is collected through census and various surveys conducted by Statistics Canada over the years.

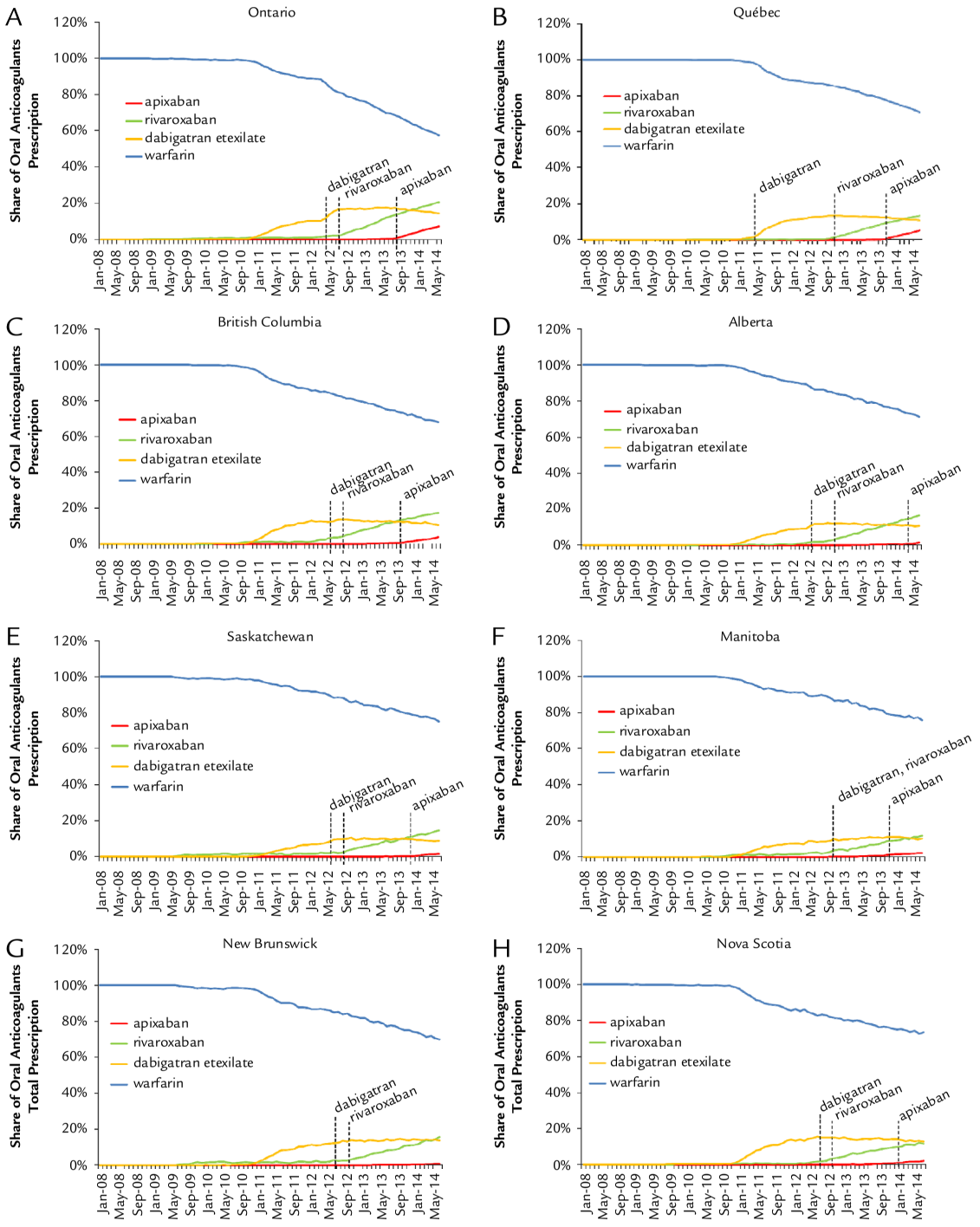


Supplementary Figure S1. Rate of OAC uptake by physician specialty: cardiologists (A), internists (B), hematologists (C), neurologists (d) and general practitioners (E). Warfarin data have not been adjusted to account for the fact that the approved indications for the NOACs only represent 70% of all OAC prescriptions. Source: IMS Health Canada Inc. (Brogan) Canadian Compuscript Physician Specialty Report.

Supplementary Table SI. Dates of provincial formulary listing for each of the NOACs for stroke prevention in AF and VTE prevention after major orthopaedic surgery.

	AF Stroke Prevention						VTE – Orthopaedics*			
	Dabigatran		Rivaroxaban		Apixaban		Rivaroxaban		Apixaban	
	Month	Year	Month	Year	Month	Year	Month	Year	Month	Year
Alberta	05	2012	10	2012	03	2014	04	2009	09	2012
British Columbia	05	2012	08	2012	09	2013	07	2010	12	2013
Manitoba	09	2012	09	2012	10	2013	08	2009	04	2014
New Brunswick	06	2012	09	2012	11	2014	06	2009	11	2014
Nova Scotia	06	2012	09	2012	12	2013	06	2009	05	2014
Ontario	04	2012	07	2012	08	2013	06	2009	08	2013
Québec	04	2011	10	2012	10	2013	06	2009	Not Listed	
Saskatchewan	05	2012	08	2012	11	2013	04	2009	04	2014

*Dabigatran is not reimbursed for VTE prevention after major orthopaedic surgery.



Supplementary Figure S2. Monthly OAC prescription share for each province (A to H). The date each NOAC was added to the provincial formulary for stroke prevention in AF is indicated. Data for PEI and NL not included. Warfarin data have not been adjusted to account for the fact that the approved indications for the NOACs only represent 70% of all OAC prescriptions. Source: IMS Health Canada Inc. (Brogan) Canadian Compuscript.