RESEARCH PAPER

Prior Authorization and Canadian Public Utilization of Direct-Acting Oral Anticoagulants

Autorisation préalable et utilisation publique au Canada des anticoagulants oraux directs

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Prior Authorization and Canadian Public Utilization of Direct-Acting Oral Anticoagulants

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Abstract

Purpose: Provincial public drug formularies in Canada have different mechanisms for reimbursement of direct-acting oral anticoagulants (DOACs). We investigate how these differences influence DOAC utilization and expenditure across the country.

Methods: We conducted a population-based, cross-sectional study of all out-patient prescriptions for OACs dispensed to public beneficiaries between January 1, 2010, and June 30, 2015. We calculated quarterly rates of OAC use and expenditures stratified by OAC type and province.

Results: The greatest increase in quarterly rates of DOAC utilization occurred in provinces with more liberal mechanism of drug coverage: Ontario by 462%, Alberta by 425% and Quebec by 1,924%. This translated to increased expenditure on overall OAC by 270%, 204% and 390%, respectively. In contrast, provinces with more stringent mechanisms had low rates of DOAC utilization and expenditure.

Conclusions: DOAC utilization and expenditure is considerably different across Canada, associated with provincial difference in reimbursement mechanism.

Résumé

Objet : Les formulaires pharmaceutiques provinciaux au Canada prévoient divers mécanismes pour le remboursement des anticoagulants oraux directs (AOD). Nous avons étudié comment ces différences influent sur l'utilisation des AOD et sur les dépenses, dans l'ensemble du pays.

Méthode : Nous avons mené une étude transversale auprès de tous les patients externes auxquels étaient prescrit un anticoagulant oral entre le 1er janvier 2010 et le 30 juin 2015. Nous avons calculé les taux trimestriels d'utilisation d'anticoagulant oral et des dépenses, ventilés selon le type de coagulant et la province.

Résultats : La plus forte croissance des taux trimestrielles d'utilisation des AOD a eu lieu dans les provinces où le mécanisme de remboursement pour les médicaments est le plus libéral : Ontario, 462 %; Alberta, 425 %; et Québec, 1 924 %. À cela correspond également une hausse des dépenses pour l'ensemble des anticoagulants oraux, soit respectivement de 270 %, 204 % et 390 %. À l'opposé, les taux d'utilisation des AOD et les dépenses sont plus bas dans les provinces où les mécanismes de remboursement sont plus contraignants.

Conclusions : L'utilisation des AOD et les dépenses diffèrent sensiblement dans l'ensemble du Canada, en fonction des différences dans les mécanismes de remboursement des provinces.

Introduction

Direct-acting oral anticoagulants (DOACs) (rivaroxaban, dabigatran and apixaban) were introduced in Canada in 2008 for prophylaxis of venous thromboembolism after elective hip or knee replacement surgery (CADTH 2008). Prior to the introduction of DOACs, the only OAC was warfarin. Since DOAC introduction, there has been a cited shift in prescribing away from warfarin towards DOACs across Canada (Weitz et al. 2015). Compared to traditional anticoagulation management (i.e., warfarin, heparin), DOACs have been shown to be at least non-inferior for prevention of stroke or systemic embolism in patients with non-valvular atrial fibrillation (Connolly et al. 2009; Granger et al. 2011; Patel et al. 2011), as well as for treatment of deep vein thrombosis or pulmonary embolism (Agnelli et al. 2013; The EINSTEIN Investigators 2010; The EINSTEIN–PE Investigators 2012). They have also been shown to be superior for prophylaxis of deep vein thrombosis following hip or knee replacement surgeries (Eriksson et al. 2008; Lassen et al. 2010). In addition, they have fewer drug–drug or drug–food interactions and can be given in fixed doses without routine coagulation monitoring. DOACs have been mostly utilized by specialists in Canada under the influence of various practice guidelines (Camm et al. 2012; Verma et al. 2014; Weitz et al. 2015).

The cost-effectiveness of DOACs compared to warfarin has been found to be highly sensitive to patient characteristics, such as average time in therapeutic range (TTR), CHADS2 score and age (Coyle et al. 2013). CHADS2 score is commonly used to stratify ischemic stroke risk in patients with nonvalvular atrial fibrillation (Macle et al. 2014). It is cumulative based on six clinical features including congestive heart failure, hypertension, age ≥65 years, diabetes mellitus (1 point each), prior stroke or transient ischemic attack (2 points). DOACs have only been shown to be cost-effective compared to warfarin in certain atrial fibrillation populations based on international normalized ratio (INR) time in TTR below 64% (Connolly et al. 2009; Granger et al. 2011; Patel et al. 2011; Trusler 2015). Given the large price difference in the combined drug and lab monitoring costs (BC PharmaCare Special Authority 2013, 2016, 2017), reimbursement of DOACs is limited to patients meeting eligibility criteria. These criteria are fairly uniform across provinces. For example, among patients with non-valvular atrial fibrillation but without severe renal impairment, all provinces reimburse DOACs for patients who have tried warfarin for a minimum of two months but cannot reach the desired INR target, as well as for those with contraindications to warfarin and those with limited access to regular INR testing.

However, provincial public drug formularies differ considerably in the mechanism used to enforce these criteria (Table S1 in Appendix 1; available at: www.longwoods.com/content/25321). For instance, the special authority policy in British Columbia requires prescribers faxing or mailing a special authority request outlining each patient's eligibility for DOACs to provincial PharmaCare, which ultimately determines whether the patient meets the criteria for drug coverage (BC PharmaCare Special Authority 2013, 2016, 2017). Thus, patients cannot access DOACs until they receive approval from PharmaCare following

individual clinical review. In contrast, the Ontario Drug Benefit Program's Limited Use process requires only that prescribers confirm the indication and conditions for use by adding a specific "Reason for Use" code to the prescription (Ontario Drug Benefit Formulary/Comparative Drug Index 2016). These codes grant patients immediate access to DOACs without direct involvement of the provincial government.

Little is known about how these different approaches to DOAC accessibility influence utilization and expenditures related to these drugs. We explored how differential mechanism of DOAC coverage influenced the utilization and expenditure on DOACs on public drug formularies across Canada.

Methods

We conducted a population-based, cross-sectional study of all out-patient prescriptions for OACs dispensed to individuals covered by public drug programs in Canada between January 1, 2010, and June 30, 2015. The composition of provincial beneficiaries varies across Canada, as provincial governments independently provide public drug coverage for seniors, social assistance recipients and medically necessary hospital and physician services with varying eligibility and patient cost-sharing arrangements (Daw and Morgan 2012).

To interpret the results of public claims more accurately, we also separately conducted analysis of all privately funded new OAC (NOAC) prescriptions across Canada within the same time frame, including individuals covered by private insurance or by paying cash.

Data source for prescription claims

We obtained prescription data from IMS Geographic Prescription Monitor (GPM12), which contains data from a representative panel of approximately 65% of Canadian pharmacies. Total numbers of prescriptions and units dispensed, as well as associated costs, are projected monthly using geospatial methods based on the number of pharmacies in a given region, the size of the pharmacies and the distance between IMS-captured and uncaptured pharmacies. The projections are representative of provincial and national sales volumes. Data were available for Alberta, British Columbia, Manitoba, New Brunswick, Newfoundland, Nova Scotia, Ontario, Prince Edward Island, Quebec and Saskatchewan, and were stratified by type of OAC, payer type (public, private or NIHB) and province.

Data source for public beneficiaries

The National Prescription Drug Utilization Information System (NPDUIS), developed by the Canadian Institute for Health Information, and the Ontario Drug Benefit (ODB) database were used to obtain estimates of the number of individuals eligible for provincial drug coverage in Alberta, British Columbia, Saskatchewan, Manitoba, New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland & Labrador and Ontario between 2000 and 2014. Eligible individuals were defined as those dispensed at least one prescription for any drug in each calendar year. Because NPDUIS does not capture prescription

data for Quebec, we obtained estimates of eligible beneficiaries from aggregated data in the annual reports of each public drug program (Annual Management Report 2014). In all provinces, the number of individuals eligible for public drug coverage in 2015 was estimated based on linear extrapolation from previous years.

Data analysis

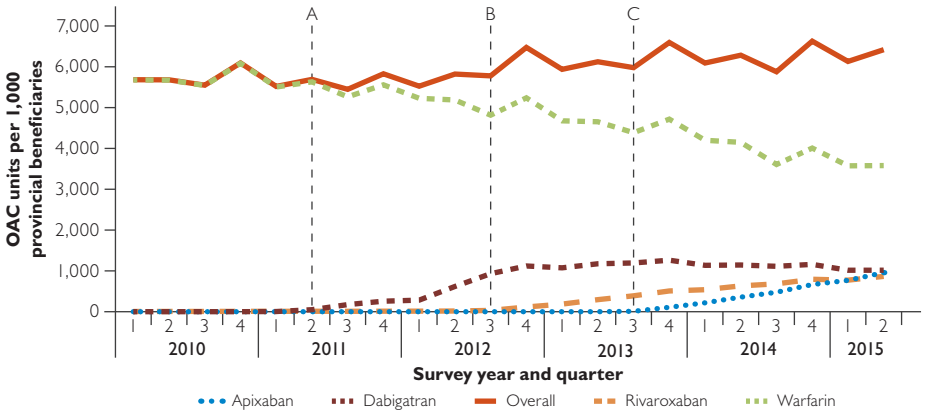
Rates of OAC use and expenditures were calculated quarterly for each province. For publicly funded prescriptions (i.e., public claims only), they were expressed as the number of units dispensed per 1,000 public beneficiaries and the total cost per 1,000 public beneficiaries. For privately funded prescriptions (i.e., private insurance claims or cash claims), the rates were expressed as the number of NOAC units dispensed per 1,000 provincial population. Quarterly estimates of provincial population were obtained from Stats Canada.

Results

Rates of publicly funded DOACs utilization at national level

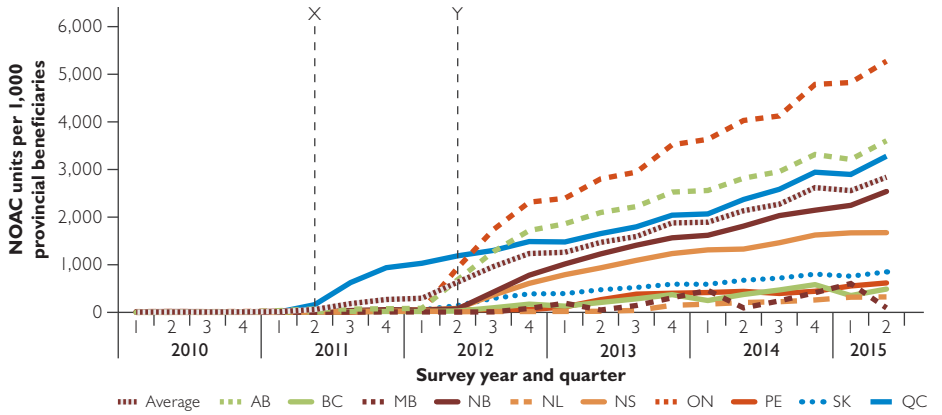
Over the 5-year study period, more than 1 billion OAC tablets or capsules were dispensed in Canada, and the overall quarterly rate of OAC dispensing remained relatively stable at approximately 6,000 units per 1,000 provincial beneficiaries (Figure 1). Nationally, the rate of publicly funded warfarin dispensing decreased by 36.9% from 5,677 to 3,580 units per 1,000 provincial beneficiaries over the study period, which aligned with the addition of each DOAC to public drug formularies in Canada (Weitz et al. 2015). By the second quarter of 2015, the rates of use of dabigatran, apixaban and rivaroxaban were similar (1,016, 957 and 865 units per 1,000 provincial beneficiaries, respectively; Figure 1).

FIGURE 1. Trends in publicly funded OAC dispensing in Canada (2010–2015)



OAC = oral anticoagulant. *Note:* A = First listing of dabigatran for stroke prevention in Quebec (April 2011). B = First listing of rivaroxaban for stroke prevention in Ontario (July 2012). C = First listing of apixaban for stroke prevention in Ontario (August 2013).

FIGURE 2. Trends in uptake of publicly funded NOACs by province (2010–2015)



NOAC = new oral anticoagulant. *Note:* X = Listing of dabigatran for stroke prevention in Quebec (April 2011). Y = Listing of dabigatran for stroke prevention in Ontario (April 2012), Alberta (May 2012), New Brunswick (June 2012) and Nova Scotia (June 2012).

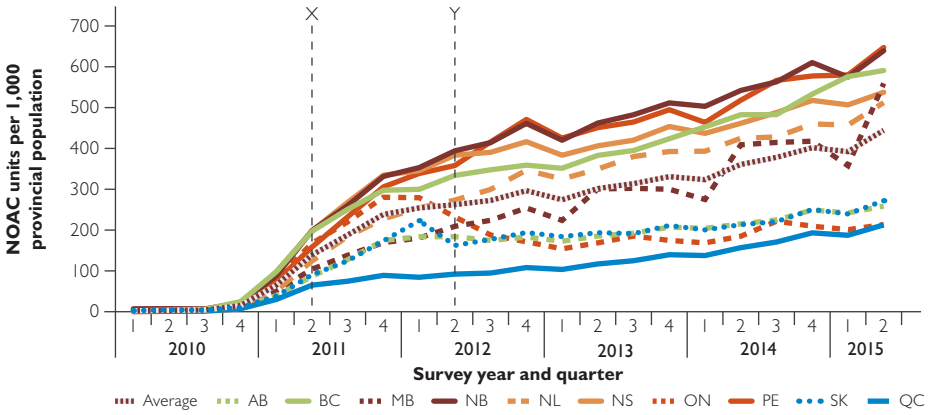
Interprovincial comparison of publicly funded DOACs utilization

While the overall rate of OAC dispensing has remained stable, the rate of warfarin dispensing has declined while the rate of DOAC dispensing has increased in each province (Figure 2 and Appendix 1). However, there is considerable interprovincial variation in DOAC uptake such that the provinces with more liberal mechanism of DOAC reimbursement criteria have much higher uptake of DOACs. These provinces include Ontario (5,275 units per 1,000 provincial beneficiaries), Alberta (3,604 units per 1,000 provincial beneficiaries) and Quebec (3,279 units per 1,000 provincial beneficiaries), where the rate of DOAC utilization was above the national average (2,839 units per 1,000 provincial beneficiaries). In all of the remaining provinces with more stringent mechanism, the rate of publicly funded DOAC use was low, ranging from 93 units (Manitoba) to 850 units (Saskatchewan) per 1,000 provincial beneficiaries in Q2 2015.

Interprovincial comparison of privately funded DOACs utilization

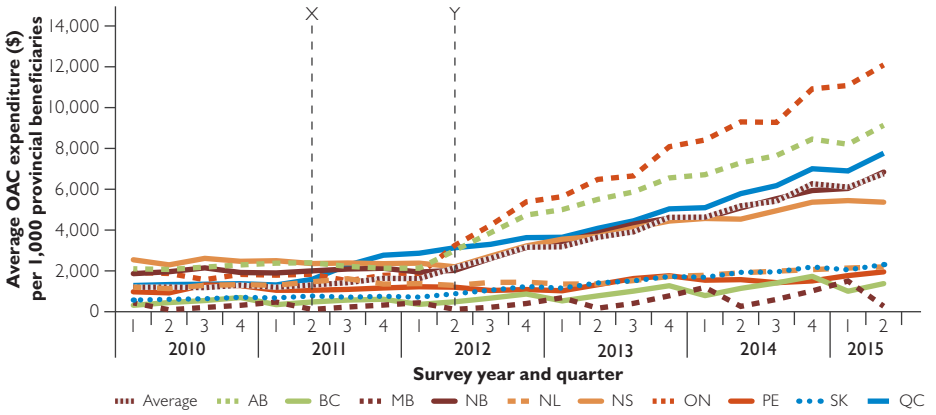
Privately funded DOACs uptake was in contrast to publicly funded DOACs uptake across Canada (Figure 3). Provinces with more liberal mechanism of public reimbursement had lower privately funded DOACs uptake. These provinces include Ontario (214 units per 1,000 provincial population), Alberta (259 units per 1,000 provincial population) and Quebec (212 units per 1,000 provincial population), where the rate of privately funded DOAC utilization was below the national average (444 units per 1,000 provincial population). In the remaining provinces with more stringent mechanism, the rate of privately funded DOAC use was higher, ranging from 272 units (Saskatchewan) to 647 units (Prince Edward Island) per 1,000 provincial population in Q2 2015.

FIGURE 3. Trends in uptake of privately funded NOACs by province (2010–2015)



NOAC = new oral anticoagulant. *Note:* X = Listing of dabigatran for stroke prevention in Quebec (April 2011). Y = Listing of dabigatran for stroke prevention in Ontario (April 2012), Alberta (May 2012), New Brunswick (June 2012) and Nova Scotia (June 2012).

FIGURE 4. Trends in average expenditure of publicly funded OAC by province (2010–2015)



OAC = oral anticoagulant. *Note:* X = Listing of dabigatran for stroke prevention in Quebec (April 2011). Y = Listing of dabigatran for stroke prevention in Ontario (April 2012), Alberta (May 2012), New Brunswick (June 2012) and Nova Scotia (June 2012).

Interprovincial comparison of publicly funded OACs expenditure

Rising DOAC utilization on public drug plans has translated to increasing provincial expenditure on OACs as a drug class such that the provinces with less stringent mechanism of DOAC reimbursement have considerably higher expenditure (Figure 4). Since provincial listing of DOACs for stroke prevention in April 2011 (Weitz et al. 2015), provincial expenditures on OACs increased ranging from 23% in Manitoba (from $218 to $267 per 1,000 provincial beneficiaries each quarter), where mechanism of DOAC reimbursement is more stringent, to 390% in Quebec (from $1,583 to $7,764 per 1,000 provincial beneficiaries each quarter), where mechanism is less stringent.

Furthermore, while DOACs account for 41% (86 million units of 209 million units) of all OACs dispensed across Canada, they account for 88% ($180 million of $204 million)

of OAC expenditure between July 2014 and June 2015 (Figure S3 in Appendix 1). This is particularly striking in Ontario and Quebec where DOAC reimbursement is less stringent, such that DOAC represented approximately 50% (47 million units of 97 million units and 25 million units of 53 million units, respectively) of OAC prescription volumes, but accounted for 90% ($97 million of $106 million and $53 million of $60 million, respectively) of OAC expenditures.

Discussion

In this population-based study spanning 5 years, we found varying patterns of DOAC utilization across Canada since their addition to provincial formularies in 2011, along with considerable interprovincial differences in public expenditures on OACs across Canada. Despite this, the overall population-adjusted rates of OAC utilization have been relatively stable across Canada during our study period, suggesting that these rising expenditures are not due to market expansion (Steinberg et al. 2013), but replacement of warfarin with DOACs.

Interprovincial differences in DOAC utilization were related to the differences in mechanism of provincial reimbursement. Publicly funded DOACs' uptake and associated expenditure were much higher in provinces with more liberal mechanism of reimbursement, such as Ontario, Alberta and Quebec, whereas privately funded DOACs' uptake remained much lower in these provinces. Specifically, Ontario and Quebec have the most liberal mechanism in Canada, where prescribers access DOACs for their patients by using special codes on the prescriptions allowing pharmacies to directly bill for DOACs. Consequently, DOACs make up almost half of all OAC volume in these provinces. Alberta has slightly more controlled DOAC access compared to Ontario and Quebec, involving screening of patients' past medication history by computer systems before reimbursing DOACs. Nevertheless, the ability for patients meeting the clinical criteria to immediately access DOACs following this review – as well as the fact that pharmacists can override the results of the computer screening – may have led to the high rate of DOAC uptake seen in this province. The five provinces with strict mechanism in which policies restrict access to DOACs until the completion of a clinical review for eligibility (British Columbia, Manitoba, Saskatchewan, Newfoundland & Labrador and Prince Edward Island) all had similarly low rates of DOAC uptake, suggesting that clinicians in provinces where prior authorization is not required may be interpreting eligibility criteria more broadly than intended.

Our results are consistent with published findings in other jurisdictions. In Denmark where public coverage of prescription costs is universally implemented (Vrangbæk 2008), utilization of warfarin was reduced by approximately 60% with increasing uptake of DOACs for stroke prevention from 2011 to 2013 after the introduction of DOACs to the market (Olesen et al. 2015). In the US, the proportion of ambulatory physician visits involving dabigatran prescriptions among OACs increased from 3.1% to 18.9% within a year following its FDA approval. This translated to an increase in dabigatran direct expenditure from $16 million

to $166 million, exceeding direct expenditure on warfarin ($144 million) on the US market (Kirley et al. 2012). In Canada, we found similar trends towards increasing uptake of publicly funded DOACs, and we were able to further demonstrate differential uptakes across Canadian provinces depending on the level of provincial enforcement for reimbursement criteria.

Several limitations of our study merit emphasis. First, we were unable to ascertain indications for anticoagulant therapy, and therefore could not address whether DOACs were being used according to clinical criteria in each province. Second, it is possible differences in the eligibility criteria and structure of benefits between provinces leads to differences in demographic and comorbidity status of individuals receiving publicly funded DOACs which could influence our findings. Because we did not have any individual-level information that allowed us to specifically analyze these differences, we were unable to determine the impact that these differences may have had on our findings. Third, our data were only available at the unit (i.e., tablet or capsule) level, and we could not conduct patient-level analyses to infer clinical appropriateness or clinical outcomes of DOAC use. Fourth, we cannot address drivers that potentially influence interprovincial difference in uptake of DOACs, such as interprovincial difference in promotion or sale activities or adoption by prescribers, especially in provinces with more liberal mechanism of reimbursement. Finally, we did not have any data for the Territories, so we could not provide any insight on DOAC utilization in those regions of Canada. However, these regions represent a small proportion (approximately 0.33%) of the total population of Canada (Statistics Canada 2015).

Conclusions

Since 2011, there have been increasingly divergent trends in DOAC utilization and related expenditures across Canada, likely reflecting interprovincial differences in mechanism of clinical criteria for these drugs. Future studies should examine characteristics and clinical outcomes of patients using DOACs in those provinces with liberal mechanism of reimbursement to determine the extent to which uptake aligns with intended clinical criteria for coverage (Xu et al. 2016). This is of importance to both policy makers and clinicians because these clinical criteria are generally designed to facilitate use of DOACs to populations in whom they have been shown to be both safe and cost-effective (Wells et al. 2012).

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