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Impact of cost on use of non-vitamin K antagonists in atrial fibrillation patients in Ontario, Canada

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Abstract
Canadian guidelines recommend non vitamin K antagonists (NOACs) in preference to vitamin K antagonists (VKAs) for stroke prevention in patients with atrial fibrillation (AF), but NOACs are more expensive than VKAs. Canada has a universal healthcare system that covers the cost of NOACs for select patient groups. Ability to pay for NOACs may influence their use. We reviewed medical charts of Hamilton General Hospital outpatients under the age of 65 with a new diagnosis of AF who were referred for initiation of OAC therapy. We contacted these patients by phone and asked them to complete a questionnaire regarding their OAC choice, economic factors that may have influenced this choice (income, insurance) and the financial burden of OAC therapy. We included 110 patients, mean age 56 years, and 26.4% females. NOAC users had a higher median neighborhood income than VKA users ($p=0.0144$, $n=110$). 73 patients responded to the questionnaire. NOAC users reported higher annual household income ($p=0.0038$, $n=73$). Patients with private insurance were more likely to use NOACs than those without insurance ($p=0.0496$, $n=73$). The cost of NOACs and ability to pay is a determinant of their use Ontario patients under the age of 65. This two tiered provision of care appears to contradict the values of Canada's universal healthcare system.

Keywords Non vitamin K antagonists (NOACs) · Vitamin K antagonists (VKAs) · Cost · Atrial fibrillation

Highlights

- Canadian guidelines recommend NOACs in preference to VKAs for stroke prevention in AF, but NOACs cost more
- Canada has a universal healthcare system that covers the cost of NOACs in persons over the age of 65 and in select groups under the age of 65.
- Ability to pay for NOACs influences their use in patients in Ontario
- This two tiered provision of healthcare contradicts the values of Canada's universal healthcare system

Introduction

Atrial fibrillation (AF) increases the risk of stroke fivefold [1]. Oral anticoagulants (OACs) reduce the risk of stroke in by at least two-thirds [2], but some Canadians with AF remain untreated [3, 4]. Underuse of OACs is an important preventable cause of stroke.

The introduction over the past decade of a new class of non-vitamin K antagonist oral anticoagulants (NOACs) has expanded treatment options for patients with AF. Canadian guidelines recommend NOACs in preference to warfarin because of their superior safety and greater ease of use [5].

Canada has a universal healthcare system, but public funding for drugs is restricted to patients over the age of 65 and social security recipients. Many people under the age of

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65 have no drug coverage. High out-of-pocket (OOP) costs of prescription drugs has previously been identified as an access barrier for some Canadians [6]. The importance of cost as a determinant of NOAC use for stroke prevention in patients with AF is not known.

We undertook a single center observational study in order to explore whether cost is a determinant of the decision to prescribe NOACs in patients with AF.

Methods

We studied patients with a diagnosis of AF who were attending Cardiology or Thrombosis outpatient clinics at the Hamilton General Hospital (HGH) for initiation of oral anticoagulation (OAC). The study was approved by the Hamilton Integrated Research Ethics Board (HiREB) (Project 1808).

Patients were eligible for inclusion if they were under the age of 65 and were previously untreated with long term OAC. Patients were excluded if they had a contraindication to warfarin or NOACs.

A single reviewer (SM) reviewed charts of patients attending cardiology or thrombosis outpatient clinics between 1st January 2014 and 1st June 2016 to identify potentially eligible patients. These patients were contacted by telephone, and after obtaining informed consent, a questionnaire was administered to evaluate the extent to which cost of NOAC influenced their use in participating patients.

Ability to pay was assessed by income and insurance coverage as reported by patients. Median neighbourhood income was calculated using postal code (Environics Analytics 2015 database). Patients who classified the financial burden of OAC therapy as "nil", "slight", "somewhat", "significant" or "unmanageable". Cost related non-adherence (CRN) to prescription medications was addressed by asking patients whether or not they had ever left a prescription unfilled due to cost, delayed filling a prescription due to cost, or taken less of a medication due to cost.

Baseline characteristics and ability to pay of patients treated with vitamin K antagonists (VKAs) was compared with those treated with NOACs. Continuous variables were assessed used a Student's *t* test, and categorical variables were assessed using a Fisher's exact test. The Cochran Armitage trend test was performed to assess the presence or absence of a linear trend for ordinal variables.

Results

110 eligible participants were identified through chart review. 80 (71%) were successfully contacted, and 7 further participants were excluded. 73 questionnaires were completed (Fig. 1). Baseline characteristics of the included patients are summarized in Table 1.

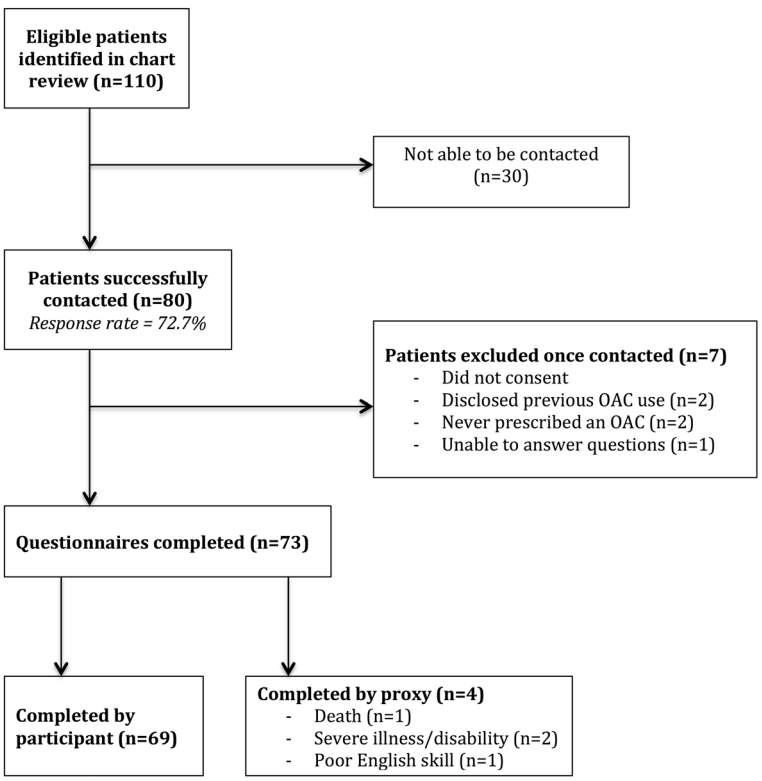

Fig. 1 Study composition. *OAC* oral anticoagulants

The mean age of patients was 56 and 26.4% were female. There was no significant age or sex difference between patients prescribed VKAs and those prescribed NOACs.

Compared with those prescribed a VKA, patients prescribed NOACs were more likely to have a $CHADS_2$ score of 0 (32 vs. 0%, p = 0.0037). Of the 28 patients with $CHADS_2 = 0$ prescribed NOACS, 17 underwent ablation.

The median neighbourhood income was higher in patients prescribed a NOAC compared with those prescribed a VKA ($101,506 vs. $84,119, p = 0.0144).

Ability to pay for NOACs

Increasing annual household income was associated with increasing use of NOAC (p for trend = 0.0038, Fig. 2).

Participants with private health insurance were more likely to receive a NOAC compared to those with no private insurance (p = 0.0496, Fig. 3).

We also found that unemployment was strongly associated with VKA use (p = 0.0010), and married participants were more likely to use NOACS (p = 0.0439). We found no relationship between highest level of education and prescription of NOAC compared with a VKA.

Table 1 Baseline characteristics

	Total (n = 110)	VKA (n = 29)	NOAC (n = 81)	p-value
Age mean (standard deviation)	56.45 (6.94)	56.90 (7.90)	56.30 (6.61)	0.6912
Sex (female), N (%)	29 (26.36)	9 (31.03)	20 (24.69)	0.6238
$CHADS_2$ score, N (%)				
0	30 (27.27)	2 (6.90)	28 (34.57)	0.0034
1	45 (40.91)	9 (31.03)	36 (44.44)	0.2722
2+	35 (31.82)	18 (62.07)	17 (20.99)	0.0001
Median neighbourhood income ($CAD)		84,119	101,506	0.0144

CAD Canadian dollar, *NOAC* non-vitamin K antagonists, *VKA* vitamin K antagonist

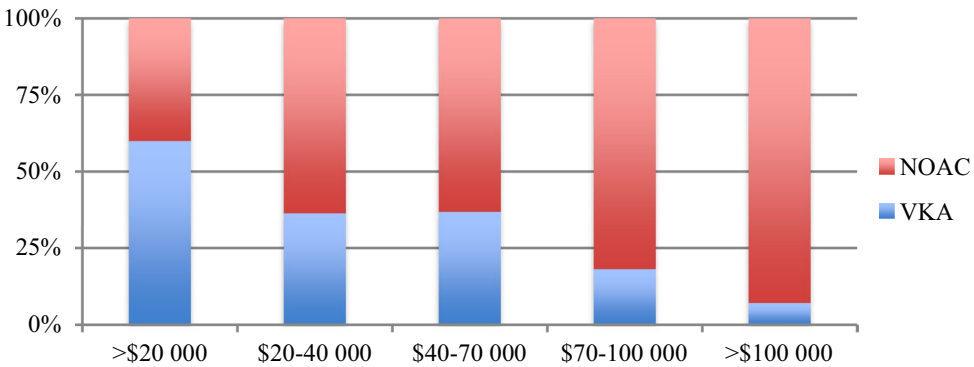

Fig. 2 Annual household income. This graph shows the proportional distribution of NOAC versus VKA study participants in the income brackets shown. *NOAC* non-vitamin K antagonists, *VKA* vitamin K antagonist

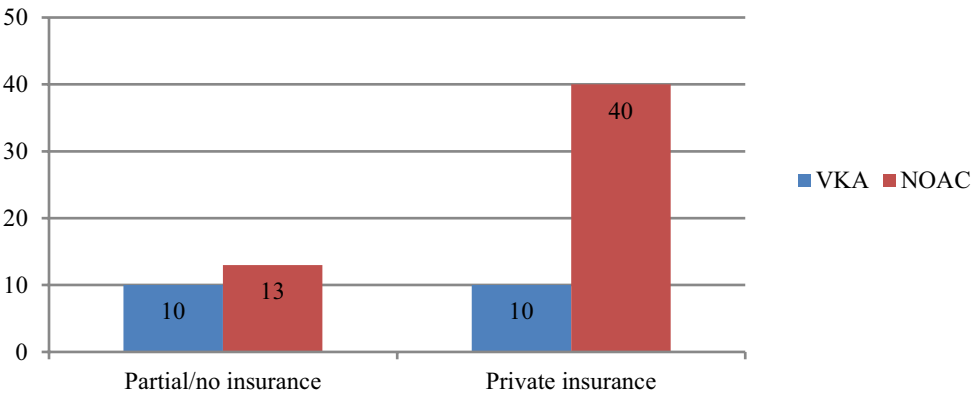

Fig. 3 Insurance coverage. This graph shows the number of VKA and NOAC participants with partial/no health insurance versus private health insurance. *NOAC* non-vitamin K antagonists, *VKA* vitamin K antagonist

Cost of OAC and financial burden

Two-thirds of patients (65.8%) reported that OACs did not pose a financial burden, irrespective of which OAC they were prescribed (Fig. 4).

After deducting costs covered by insurance, 77.5% of NOAC users paid less than $20/month for their medication, compared to 58.8% of VKA patients. 41% of VKA users paid full price for their medications ($25/month), compared with 15% of NOAC users.

VKA users were more likely than NOAC users to report that cost influenced their adherence to oral anticoagulant treatment (13 vs. 40%, p = 0.0207, Table 2). Thus, compared with NOAC users, VKA users were more likely to avoid medication use due to the cost. VKA users were also more likely than NOAC users to ask for/receive free samples from a health provider (55 vs. 20.75%, p = 0.0088). A higher proportion of VKA users reported that they spent less on basic needs in order to buy medicine, however this did not reach statistical significance (30 vs. 11.32%, p = 0.0772).

Table 2 CRN results

	VKA N = 20 (%)	NOAC N = 53 (%)	p-value
Left a prescription unfilled	2 (10.00)	4 (7.55)	0.6628
Delayed filling a prescription	5 (25.00)	5 (9.43)	0.1245
Filled some but not all prescriptions	4 (20.00)	5 (9.43)	0.2462
Taken a medication less frequently	5 (25.00)	3 (5.66)	0.0313
Taken a medication in smaller doses	4 (20.00)	1 (1.89)	0.0181

CRN cost related non adherence, *NOAC* non-vitamin K antagonists, *VKA* vitamin K antagonist

Discussion

We found that cost was an important determinant of access to NOACs in a cohort of cardiology and thrombosis outpatients with AF under the age of 65 in Ontario. Thus, patients who were prescribed NOACs had higher income, more comprehensive insurance coverage, and lower unemployment than those prescribed VKAs. Compared to patients prescribed NOACs, patients prescribed VKAs were more likely to report non-adherence to prescribed medications due to cost.

Our finding that patients with a lower income were more likely to be prescribed VKAs than NOACs is consistent with an Ontario study by Sholzberg et al. who found that people in a higher income quintile were more likely to switch to warfarin from NOACs than those of a lower income quintile [7]. Sholzberg et al. included 34,797 AF patients treated with a VKA before NOACs were included on the provincial formulary. Those in the highest income quintile (who are more likely to have insurance) were 50% more likely to switch to NOACs than those in the lowest quintile. This finding is likely to be associated with both greater ability to afford expensive prescriptions, and higher likelihood of having prescription drug coverage in the higher income group.

Our finding that private insurance was associated with NOAC use is consistent with previous North American research. Lauffenberger conducted a review of over 70,000 American patients treated with an oral anticoagulant and reported that prescription drug coverage was strongly associated with choice of oral anticoagulant; more comprehensive insurance coverage increased the likelihood of being prescribed a NOAC [8]. Although many private insurance plans require copayments for dispensing fees or a portion of drug costs, privately insured patients in our cohort were unlikely to have out of pocket costs exceeding $20/month. By reducing or eliminating the cost of medications, insurance can improve access irrespective of socioeconomic status. A previous Ontario study showed that lower income seniors used less NOACs than higher income seniors before they became subsidized through

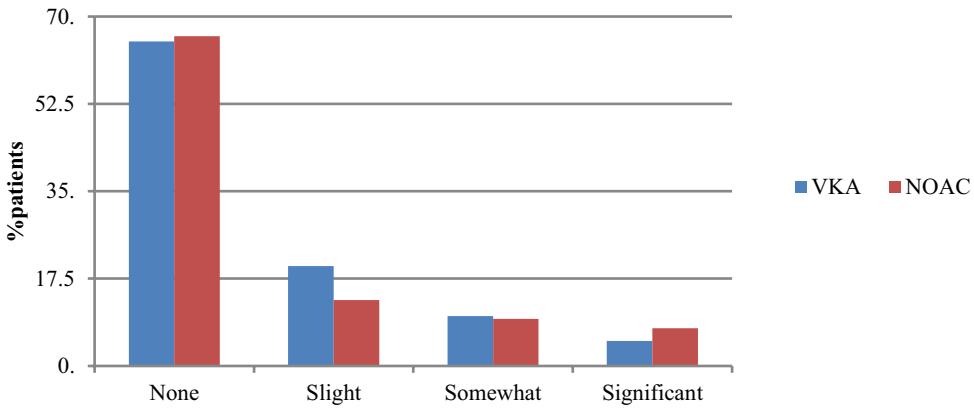

Fig. 4 Financial burden of oral anticoagulants. This graph shows the percentage of VKA and NOAC participants reporting that oral anticoagulants are "no financial burden", "a slight financial burden", "somewhat of a financial burden" or a "significant financial burden". *NOAC* non-vitamin K antagonists, *VKA* vitamin K antagonist

provincial insurance for those over 65. When they became subsidized, income quintile no longer predicted access [7].

Compared to patients covered by private insurance, those with prescription drug coverage from either the federal or provincial government were more likely to use VKAs. Public insurance in Ontario requires patients to have a contraindication to warfarin or to have failed a 3-month trial of warfarin to be eligible for subsidized NOACs [9].

Our finding that uninsured patients are less likely to use NOACs provides further support for our hypothesis that cost of NOACs is a barrier to their use. Furthermore, irrespective of whether patients were prescribed a VKA or NOAC, there was no difference in perceived financial burden. This suggests that only patients with ability to pay for NOACs were prescribed them.

Cost related non-adherence is defined as medication underuse due to OOP drug costs and includes unfilled prescriptions, delayed prescriptions, smaller and fewer doses than prescribed [10–12]. In our study, VKA users were more likely to report cost related non-adherence. Our results are consistent with those of Zheng et al. who found that 9 of 60 Ontario patients (15%) presenting to a general internal medicine rapid assessment clinic reported some form of cost related non-adherence in the past year [6]. Cost related non-adherence was strongly associated with lower income and less insurance coverage.

Our study has several potential limitations. First, we restricted our study to AF patients under the age of 65 attending a single centre in Ontario. Our results may not be generalizable to Ontario patients older than 65.

Second, patients in our study were more likely to be prescribed VKAs if they had a $CHADS_2$ score > 2. The explanation for this is unclear but may be affected by their need to take multiple medications to treat co-morbid conditions (e.g., hypertension, diabetes), which increases costs. Third, some aspects of the questionnaire were subject to recall bias. We addressed the potential for both recording and recall bias by also recording median neighborhood income (directly from the postcode), which is a validated measure used to estimate household income in population based studies [13, 14]. Finally, the response rate was 72.7%, and we cannot exclude the possibility that results were systematically different in those who did not respond.

In summary, our results indicate that ability to pay for NOACs influences their use in Ontario patients. This finding appears to contradict the values of Canada's universal healthcare system.

Compliance with ethical standards

Conflict of interest PK is the recipient of an educational grant from the Haematology Society of Australia and New Zealand. JE is the recipient of a mid-career award from the Heart and Stroke Foundation and holds the Jack Hirsh/Population Health Research Institute Chair in Thrombosis and Atherosclerosis, and has received honoraria from AstraZeneca, Bayer, Boehringer-Ingelheim, Bristol-Myer-Squibb, Daiichi-Sankyo, Eli-Lilly, Glaxo Smith-Kline, Janssen and Sanofi-Aventis. JE has received grants and/or in-kind support from Astra-Zeneca, Bayer, Boehringer-Ingelheim, Bristol-Myer-Squibb, Glaxo-Smith-Kline, Pfizer, Janssen and Sanofi Aventis. The rest of the authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

Research involving human and animal participants This article does not contain any studies with animals performed by any of the authors.

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