

**Prescribing Pattern of Novel Oral Anticoagulants following
Regulatory Approval for Atrial Fibrillation in Ontario, Canada**

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44 this article are those of the authors. No endorsement by the
45 Institute for Clinical Evaluative Sciences or IMS Brogan is
46 intended or should be inferred.
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3 The approval of novel oral anticoagulants (NOACs) for
4 atrial fibrillation (AF) began in October 2010 with dabigatran
5 and rivaroxaban in January 2012. Their recommendation as first-
6 line therapy by the Canadian Cardiovascular Society (CCS)
7 guidelines represent an expansion of the clinical armamentarium
8 for anticoagulation and stroke prophylaxis.¹⁻³ However, patients
9 in “real-world” clinical practice often differ from participants
10 of clinical trials used to inform the development of these
11 guidelines.^{4,5} With respect to NOACs, age is of particular
12 interest as a variable given the higher bleeding risk and
13 impaired renal function in older patients,^{6,7} combined with lack
14 of antidote for NOACs.⁸

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Prescription trends of oral anticoagulants in Canada since the arrival of NOACs have not been evaluated. In this study, we sought to determine these patterns , including changes in prescription rate by various age groups.

Methods

We obtained dispensed medication data for Ontario residents aged 20 and above who filled prescriptions for an oral anticoagulant (warfarin, dabigatran, rivaroxaban) between October 2010 and September 2012. Aggregate monthly prescription volumes of each medication were obtained from IMS Brogan

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3 (Canadian CompuScript Audit), which collects prescription
4 records from Canadian retail pharmacies regardless of payer type.
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8 To investigate changes in prescribing patterns by age
9 groups, we calculated monthly prescriptions per 100,000
10 population in each of five age categories: 20-39, 40-59, 60-64,
11 65-84 and over 85. Furthermore, percentage of prescriptions
12 filled by those aged 65 years and older was calculated and
13 compared to similar data reported from the Randomized Evaluation
14 of Long-Term Anticoagulation Therapy (RE-LY) study.⁷ Population
15 data were based on estimates from the Ontario Ministry of
16 Finance.⁹
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31 **Results**

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33 Over the 24-month period, monthly prescriptions of NOACs
34 increased more than 20-fold, from 16 to 336 prescriptions per
35 100,000 individuals. This increase was led by dabigatran, which
36 rose from 3 to 274 prescriptions per 100,000 individuals (**Figure**
37
38 **1**). By September 2012, dabigatran and rivaroxaban represented
39 17.2 and 3.9% of all oral anticoagulant prescriptions in Ontario
40 to adults aged 20 and above respectively. Monthly prescriptions
41 of warfarin over the study period have decreased from 149,730 to
42 129,130 (linear regression accounting for autoregression:
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p=0.007 for trend).

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3 Dabigatran prescription rates within age groups were
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5 highest amongst individuals aged 85 and above, followed by those
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7 between 65 and 84 years of age (**Figure 2**). Since April 2012, the
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9 proportion of dabigatran prescriptions filled by patients aged
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11 65 and over has exceeded the percentage of participants of the
12
13 same age group enrolled in dabigatran arms of the RE-LY trial
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15 (87.3% vs. 83.2%, $p < 0.0001$ by Chi-square).
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21 **Interpretation**

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23 We have found a rapid uptake of dabigatran in Ontario since
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25 its approval for AF, with onset preceding its coverage by the
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27 Ontario Public Drug Programs in April 2012. The rate of warfarin
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29 prescription declined with the rise in NOAC prescription. We
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31 also observed that dabigatran was heavily prescribed to
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33 individuals aged 85 and above, a group in which RE-LY data
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35 suggest a more favorable bleeding risk profile with warfarin
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37 compared to dabigatran.^{6,7}
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43 The incorporation of new data from clinical studies into
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45 practice guidelines helps promote a uniform standard of care
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47 across Canada that is rooted in current best-evidence.
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49 Concomitant with the initial publication of CCS guidelines in
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51 January 2011 that recommended preference of dabigatran over
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53 warfarin and its subsequent update in April 2012,^{3,10} dabigatran
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3 has been actively integrated into the care of AF patients.
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5 However, our findings suggest that the uptake of dabigatran has
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7 been most accelerated in the highest age category. While AF
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9 incidence increases with age, the rapid rise in dabigatran
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11 utilization amongst a group of patients whose age markedly
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13 exceeds that of an average RE-LY study participant raises
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15 questions about the effectiveness and safety of the “real-world”
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17 application of this new knowledge.
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22 Our study has several limitations. Our analysis was based
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24 on prescription volume rather than patient volume. This creates
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26 potential bias in cases where differential prescribing frequency
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28 exists between medications. However, analysis restricted to new
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30 prescriptions yielded similar trends (data not shown). While
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32 prescription volumes cannot be stratified by indications and
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34 therefore include NOAC use in orthopedic surgery, its
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36 contribution to the overall prescription pattern is likely very
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38 limited: dabigatran and rivaroxaban have been approved for this
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40 indication since 2008, but prescriptions remained low until
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42 their approval for AF.
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48 Within 2 years of their approval, NOACs have become rapidly
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50 integrated into the care of AF patients in Canada. While patient
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52 outcomes and healthcare utilization cannot be directly inferred
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54 from prescription trends, the growth in NOAC uptake in the
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3 elderly, a high-risk population, emphasize the urgent need to
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5 evaluate these outcomes.
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31 **Figure Titles**
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36 **Figure 1.** Monthly prescription rates for warfarin, dabigatran
37 and rivaroxaban in Ontario among adults aged 20 and above,
38 adjusted by population.
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43 **Figure 2.** Age-stratified monthly prescription volumes for
44 dabigatran in Ontario among adults aged 20 and above, adjusted
45 by population.
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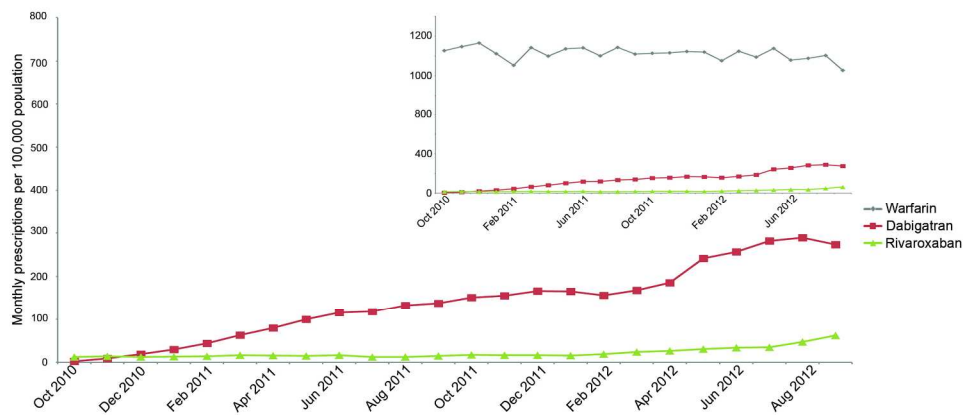
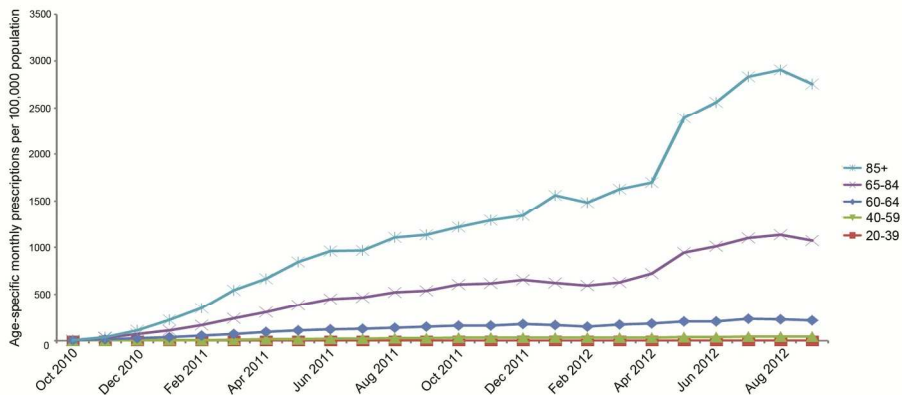


Figure 1. Monthly prescription rates for warfarin, dabigatran and rivaroxaban in Ontario among adults aged 20 and above, adjusted by population.
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