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Cost-Effectiveness of New Oral Anticoagulants Compared with Warfarin in Preventing Stroke and Other Cardiovascular Events in Patients with Atrial Fibrillation

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A B S T R A C T

Objectives: The primary objective was to assess the cost-effectiveness of new oral anticoagulants compared with warfarin in patients with nonvalvular atrial fibrillation. Secondary objectives related to assessing the cost-effectiveness of new oral anticoagulants stratified by center-specific time in therapeutic range, age, and $CHADS_2$ score. **Methods:** Cost-effectiveness was assessed by the incremental cost per quality-adjusted life-year (QALY) gained. Analysis used a Markov cohort model that followed patients from initiation of pharmacotherapy to death. Transition probabilities were obtained from a concurrent network meta-analysis. Utility values and costs were obtained from published data. Numerous deterministic sensitivity analyses and probabilistic analysis were conducted. **Results:** The incremental cost per QALY gained for dabigatran 150 mg versus warfarin was $20,797. Apixaban produced equal QALYs at a higher cost. Dabigatran 110 mg and rivaroxaban were dominated by dabigatran 150 mg and apixaban. Results were sensitive to the drug costs of apixaban, the time horizon adopted, and the consequences from major and minor bleeds with dabigatran. Results varied by a center's average time in therapeutic range, a patient's $CHADS_2$ score, and patient age, with either dabigatran 150 mg or apixaban being optimal. **Conclusions:** Results were highly sensitive to patient characteristics. Rivaroxaban and dabigatran 110 mg were unlikely to be cost-effective. For different characteristics, apixaban or dabigatran 150 mg were optimal. Thus, the choice between these two options may come down to the price of apixaban and further evidence on the impact of major and minor bleeds with dabigatran.

Keywords: anticoagulants, atrial fibrillation, cardiovascular, cost-effectiveness, warfarin.

Introduction

Approximately 250,000 Canadians are affected by atrial fibrillation (AF) [1]. Patients with AF have a substantially increased risk of death and have higher annual rates of mortality [1,2]. AF and stroke are more common among the elderly [3,4].

Preventing events such as stroke is an important part of managing patients with AF. Antithrombotic strategies for patients with AF include anticoagulant drugs, vitamin K antagonists , such as warfarin, and antiplatelet agents, such as aspirin. Vitamin K antagonists reduce the risk of stroke in patients with AF but are associated with some drawbacks, including a need for laboratory monitoring, an increased risk of bleeding complications, and several food and drug interactions [5,6]. Recently, a number of new oral anticoagulants (NOACs) have been approved, including dabigatran, a direct thrombin inhibitor, and the direct factor Xa inhibitors, rivaroxaban and apixaban.

While dabigatran, apixaban, and rivaroxaban have been demonstrated to be effective in preventing stroke/systemic embolism in patients with AF, the comparative cost-effectiveness of these NOACs is not clear. Currently, treatment with warfarin including regular international normalized ratio monitoring costs less than $300 per annum. The new anticoagulants examined in this study cost more than $1100 per annum. Thus, the cost-effectiveness of these agents will depend on the balance between the increased benefits in terms of stroke prevention, the effect on bleeding rates, and the increased drug costs [7–11]. This analysis is the first systematic, independent analysis of the cost-effectiveness of all three NOACs in comparison to warfarin in patients with nonvalvular AF.

This study involved incorporating data from a concurrent systematic review into an economic model of NOAC use in Canada [12]. The primary objective was to assess the cost-effectiveness of NOACs compared with warfarin—with additional

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stratified analysis based on center-specific time in therapeutic range (TTR), age, and $CHADS_2$ score.

Methods

Study Objective

In addition to the primary objective stated above, secondary objectives relate to assessing the cost-effectiveness of NOACs stratified by center-specific TTR, age, and $CHADS_2$ score.

Type of Economic Evaluation

Analysis was a cost-utility analysis with cost-effectiveness assessed by the incremental cost per quality-adjusted life-year (QALY) gained [13]. Sensitivity analysis was conducted by using the incremental cost per life-year gained. Analysis adopts a third-party payer perspective relating to a provincial ministry of health.

Target Population

The target population for the economic analysis was Canadians with nonvalvular AF requiring anticoagulation. For the base-case analysis, a typical patient profile from the RE-LY randomized controlled trial (RCT) was adopted: an average age of 72 years with no previous stroke or myocardial infarction (MI) [14]. Sensitivity analysis was conducted by adopting alternate patient profiles including data from the ARISTOTLE and ROCKET-AF trials [15,16].

Treatments

Treatments compared were warfarin, dabigatran 150 mg twice daily and 110 mg twice daily, rivaroxaban, and apixaban. Because of concerns about the use of dabigatran 150 mg in elderly patients, a sensitivity analysis was conducted including an additional comparator: switching patients from the dabigatran 150 mg twice-daily dose to the 110 mg twice-daily dose from age 80 years onwards.

Model Structure

The analysis was conducted by developing a Markov cohort model. The cohort was followed from initiation of pharmacotherapy to death while simulating the incidence of events associated with the patient population. At each time point, a proportion of the cohort can be in one of many health states that relate to the potential events common in this patient group, the treatment currently being received, and history with respect to transient ischemic attack (TIA)/stroke (major or minor) and MI. Specific events modeled were TIA, stroke (fatal, major or minor), bleeding (fatal, intracranial hemorrhage [ICH], major non-ICH, and minor), MI, pulmonary embolism (PE: fatal or nonfatal), and death without an event. The probability that such events occur is influenced by a number of factors including treatment and patient characteristics (Fig. 1). Patients who experience a stroke, major bleed, or ICH on treatment were assumed to continue with aspirin treatment alone, although a sensitivity analysis was conducted that assumed that patients would remain on therapy. The relative efficacy of the newer anticoagulants versus warfarin is assumed to continue for the duration of the patients' lifetime while they continue on therapy.

Time Horizon

Base-case analysis adopted a lifetime horizon (maximum of 40 years posttreatment initiation), with sensitivity analysis adopting horizons of 20 years, 10 years, and 2 years (average duration of

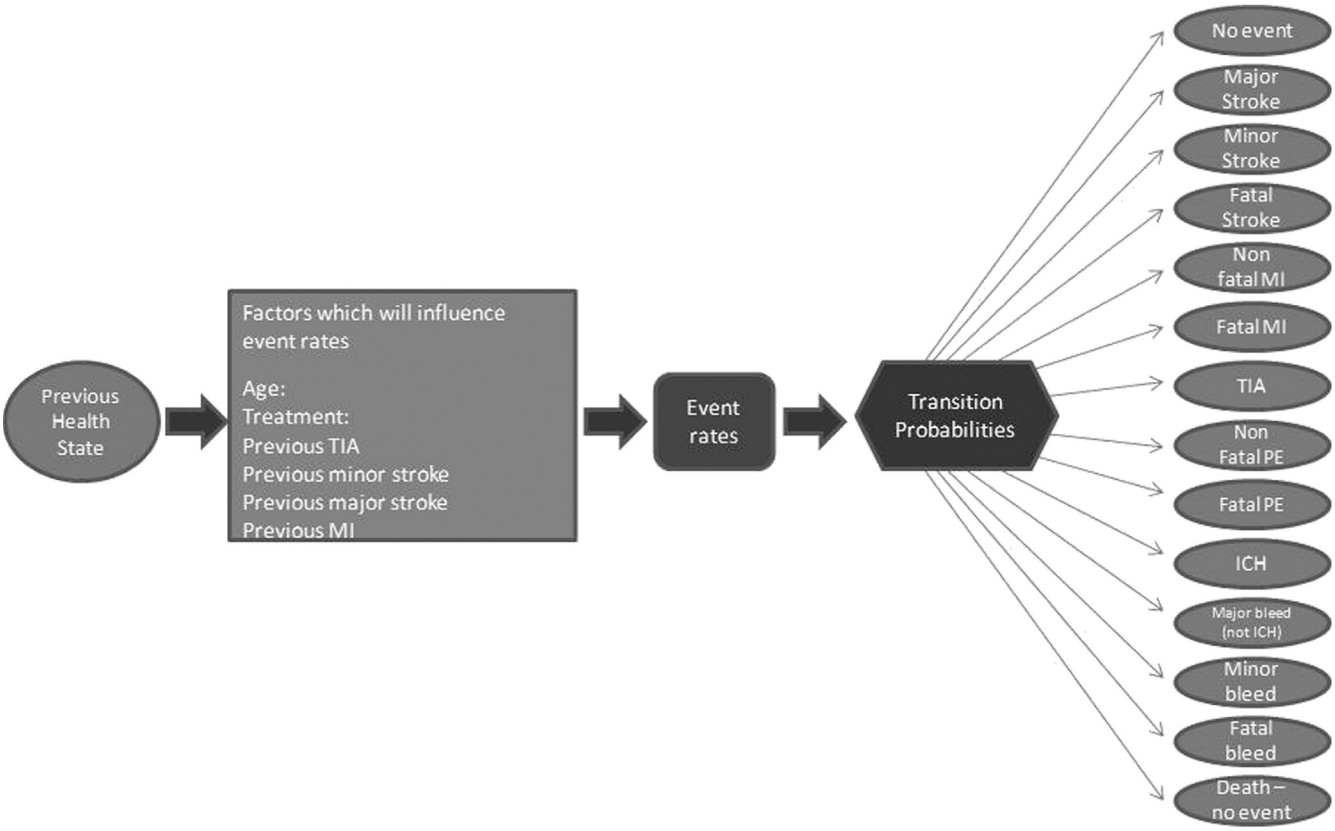

Fig. 1 – Schematic of Markov Model.