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Physician and Patient Preferences for Nonvalvular Atrial Fibrillation Therapies

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ABSTRACT

Objectives: The objective of this study was to compare patient and physician preferences for different antithrombotic therapies used to treat nonvalvular atrial fibrillation (NVAF). **Methods:** Patients diagnosed with NVAF and physicians treating such patients completed 12 discrete choice questions comparing NVAF therapies that varied across five attributes: stroke risk, major bleeding risk, convenience (no regular blood testing/dietary restrictions), dosing frequency, and patients' out-of-pocket cost. We used a logistic regression to estimate the willingness-to-pay (WTP) value for each attribute. **Results:** The 200 physicians surveyed were willing to trade off $38 (95% confidence interval [CI] $22 to $54] in monthly out-of-pocket cost for a 1% (absolute) decrease in stroke risk, $14 (95% CI $8 to $21) for a 1% decrease in major bleeding risk, and $34 (95% CI $9 to $60) for more convenience. The WTP value among 201 patients surveyed was $30 (95% CI $18 to $42) for reduced stroke risk, $16 (95% CI $9 to $24) for reduced bleeding risk, and −$52 (95% CI −$96 to −6) for convenience. The WTP value for convenience among patients using warfarin was $9 (95% CI $1 to $18) for more convenience, whereas patients not currently on warfarin had a WTP value of −$90 (95% CI −$290 to −$79). Both physicians' and patients' WTP value for once-daily dosing was not significantly different from zero. On the basis of survey results, 85.0% of the physicians preferred novel oral anticoagulants (NOACs) to warfarin. NOACs (73.0%) were preferred among patients using warfarin, but warfarin (78.2%) was preferred among patients not currently using warfarin. Among NOACs, both patients and physicians preferred apixaban. **Conclusions:** Both physicians and patients currently using warfarin preferred NOACs to warfarin. Patients not currently using warfarin preferred warfarin over NOACs because of an apparent preference for regular blood testing/dietary restrictions.

Keywords: anticoagulants, atrial fibrillation, discrete choice experiment, preferences, willingness to pay.

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia observed in clinical practice [1], and its health and economic burden on society are significant. In 2010, approximately 5.2 million individuals in the United States had been diagnosed with AF as a result of increases in age-adjusted incidence and prevalence of risk factors such as obesity and hypertension as well as an overall aging population. AF prevalence in the United States is projected to grow to 12.1 million individuals by 2030 [2]. AF may lead to disabling symptoms and an increased chance of heart failure or mortality, and it is the leading risk factor for stroke [3,4]. In fact, AF is associated with an approximately fivefold increase in the risk of stroke and accounts for approximately 15% of all strokes nationally [5]. The direct treatment cost of AF in the United States is $29 billion (2015 USD) [6].

For patients with nonvalvular atrial fibrillation (NVAF)—which accounts for 95% of all AF diagnoses [3]—the American Heart Association/American College of Cardiology/Heart Rhythm Society guidelines recommend the use of oral anticoagulation treatments to reduce the risk of thromboembolic stroke among patients with CHA_2DS_2-VASc scores of 2 or more [7]. Vitamin K antagonists such as warfarin have long been the standard of care for NVAF [8], but in recent years the Food and Drug Administration has approved a number of novel oral anticoagulants (NOACs) to reduce the risk of stroke in patients with NVAF [9]. NOACs demonstrated a lower or similar stroke risk and a lower or similar risk of a major bleeding event relative to warfarin [10–13]. Although clinical guidelines recommend oral anticoagulation for patients with NVAF at increased risk of stroke, they do not specify any preferred treatments.

Each drug—dabigatran, rivaroxaban, apixaban, edoxaban, and warfarin—offers a different "bundle" of attributes to patients.

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From a clinical outcomes perspective, when compared with warfarin, dabigatran and apixaban have shown significant decreases in stroke risk, while apixaban and edoxaban have shown significantly lower risk of major bleeding [10–13]. The ancillary services required to administer each treatment also differ; patients on warfarin treatment require regular monitoring of their international normalized ratio (INR). Although home testing options are available [14], INR testing usually occurs at an anticoagulation clinic [15]. Different treatments also offer different dosing options (once vs. twice per day dosing) and may have dietary restrictions.

To better understand the relative importance of such clinical and nonclinical attributes of oral anticoagulants to patients and physicians, we surveyed both groups to measure the "patient-centered value" and the "physician-centered value" of each attribute [16]. Because the Institute of Medicine has selected "patient-centered" care as one of its quality improvement aims, it is necessary to assess differences in patient and physician preferences to ensure that oral anticoagulant treatment patterns also meet patient goals. Using a discrete choice experiment (DCE) framework, we identified patients' and physicians' preferred anticoagulant based on selected attributes, abstracting their choice from other market forces such as marketing effectiveness or first-mover advantages. We also investigated how patients' health and economic outcomes would change if prescribing patterns followed physician or patient preferences rather than current prescribing patterns. Although a number of previous studies have analyzed patient preferences for oral anticoagulant attributes [17–19], we believe this is the first study that directly compares patients' and physicians' preferences for oral anticoagulant attributes in the United States.

Methods

Survey Design

Our survey of patients and physicians relied on a DCE methodology to measure the value each group placed on different oral anticoagulant attributes. A DCE framework assumes that patients' and physicians' preferences for a treatment can be aggregated over their preferences for key attributes or features of that particular treatment. This framework allows one to estimate patients' and physicians' willingness to make tradeoffs between attributes and how changes in attributes change treatment choices. The DCE approach has been used to estimate the value of treatment attributes in a number of diseases such as arthritis [20], cancer [21], and type 2 diabetes [22].

This DCE presented patients and physicians with a series of questions, each with two treatment options. Each treatment option was described across five attributes: annual risk of a stroke, annual risk of a major bleeding event, dosing regimen (i.e., once or twice per day), convenience (whether regular blood testing and dietary modifications were required), and monthly patient out-of-pocket cost. These attributes were selected on the basis of six criteria: relevance of the attribute to patients' and physicians' choice of AF treatment, ease of quantifying the attribute within a DCE framework, overlap or correlation with other attributes, variation in the attribute across currently available treatments, and relevance to the research question of interest. We include cost as a relevant attribute to physicians because clinical treatment guidelines recommend that physicians should consider patient costs when choosing an antithrombotic treatment [23,24].

For each attribute selected, we calibrated the attribute levels presented to the patients and physicians in the survey on the basis of evidence from clinical trials or real-world data (Table 1). The monthly patient out-of-pocket cost was calibrated on the basis of publicly reported NOAC and warfarin co-payments from one large private health insurer and one large public health insurer [25,26]. The regular INR blood testing/dietary restriction and dosing frequency attribute levels were identified from the US Prescribing Information of each oral anticoagulant. The risk of stroke and major bleeding event attribute levels were calibrated from pivotal NOAC trials [27,28] to span the stroke and major bleeding risk for apixaban, dabigatran, edoxaban, rivaroxaban, and warfarin.

After the number of attributes and attribute levels were identified, yielding 108 unique attribute combinations ($3^3 \times 2^2$), we applied a fractional factorial design to determine the number of questions. Our fractional factorial design [29,30] included 12 questions comparing two hypothetical treatments in each question. The treatment attribute bundles in the 12 DCE questions were selected to maximize D-efficiency (a widely used metric to determine a survey's ability to efficiently estimate preferences) [31]. Following most DCE studies, we used a main effects

Table 1 – Attribute and attribute levels used in discrete choice experiment design.

Attribute	Levels	Attribute level	Source
Major bleeding risk (per year)	3	1.7%	
		2.7%	Pisters et al. [28]
		3.7%	LaHaye et al. [27]
Stroke risk (per year)	3	1.4%	
		3.1%	LaHaye et al. [27]
		4.7%	
Out-of-pocket cost (per month)	3	$5	US Department of Veterans Affairs [26]
		$25	Freeman et al. [46]
		$50	Intermountain Healthcare [25]
Convenience (regular blood testing and diet restrictions)	2	No regular blood testing and no diet restrictions	Warfarin FDA label
		Regular blood testing and diet restrictions required	
Dosing frequency (per day)	2	Once per day	Real-world antithrombotic therapies
		Twice per day	

FDA, Food and Drug Administration.