Exploring Patient Preferences with a Cross-sectional Discrete Choice Experiment: Insight into Once-daily Stroke Prevention Treatments in Atrial Fibrillation in Asia

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Background

- Atrial fibrillation is (AF) affects more than 16 million people in the Asia-Pacific region.[1]
- While AF increases the risk of stroke, direct oral anticoagulants (DOACs) can prevent stroke in patients with AF.
- DOACs include dabigatran, a direct thrombin inhibitor, and rivaroxaban, apixaban, and edoxaban, which are factor Xa inhibitors.
- Rivaroxaban is the most commonly prescribed DOAC globally; however, edoxaban is also frequently prescribed in the Asia-Pacific region including South Korea (31%) and Japan (28%).[2]
- DOACs have different treatment attributes, including different efficacy and safety profiles (e.g., risk of stroke, risk of bleeding), dosing frequency (e.g., twice daily vs. once daily), and treatment administration requirements (e.g., food intake).
- Because DOACs have different treatment attributes, it is important to understand preferences of patients and the benefit-risk trade-offs they are willing to make. Particularly important for DOACs is how patients view the trade-off between stroke risk and bleeding risk.
- While several studies have analyzed the preferences of patients with AF towards oral anticoagulant treatment,[3-5] this study is the first to our knowledge to assess patient preferences for DOACs in the Asia-Pacific region.

Objectives

- The objective of this study was to understand the willingness of patients with AF from China, Taiwan, or South Korea to make trade-offs between benefits, risks, and non-clinical characteristics of DOACs, such as intake frequency and intake with food.

Methods

Study design and eligibility

- A discrete choice experiment (DCE) was developed to elicit patient preferences for the attributes of DOACs. Design was informed by a targeted literature review on patient preferences for stroke prevention in AF, clinical data review, an attribute selection workshop, cognitive pilot interviews with 15 patients, and a quantitative pilot survey, conducted between January 2023 and March 2023.
- Patient-experienced outcomes such as fatal events, disabling events, and non-disabling events were found to be more relevant and understandable to patients than clinical endpoints, such as ischemic stroke or systemic embolism. Patient-experienced events were defined as attributes for the DCE.
- Eligible participants included residents of China, Taiwan, or South Korea who had a self-reported diagnosis of AF.

DCE

- Participants completed 12 DCE choice tasks between two hypothetical unlabeled treatments and one fixed non-treatment option.
- Each option was described by six attributes that would be meaningful to patients: risk of death, severe disability, mild or moderate disability, nondisabling events, intake with food, and intake frequency (**Figure 1**).
- Different attribute levels were combined using a D-efficient design.

Methods (Cont'd)

Data analysis

- DCE data were analyzed using mixed logit models, and marginal utilities and maximum acceptable risks of fatal events were calculated.
- A predicted choice probability (PCP) analysis was performed, where clinical data was weighted by preference to estimate the proportion of patients expected to choose an edoxaban-like profile (profile 1) or a rivaroxaban-like profile (profile 2).
- PCP treatment profiles were based on a meta-analysis of disabling and non-disabling events in DOAC trials[6] and fatality estimates[7]. Uncertainty in parameters was explored.

Figure 1. Example of a DCE Choice Task

	Treatment A	Treatment B	No Treatment
Disability Events over Next 3 Years	Severe Disabilities: 10 out of 100 (10%) Mild/Moderate Disabilities: 4 out of 100 (4%)	Severe Disabilities: 1 out of 100 (1%) Mild/Moderate Disabilities: 1 out of 100 (1%)	Severe Disabilities: 12 out of 100 (12%) Mild/Moderate Disabilities: 12 out of 100 (12%)
Non-disabling Events over Next 3 Years	30 out of 100 (30%)	50 out of 100 (50%)	41 out of 100 (41%)
Death over Next 3 Years	5 out of 100 (5%)	10 out of 100 (10%)	18 out of 100 (18%)
Intake with meal	Have to take the medicine with a meal	No requirement	
Frequency of dosing	Twice daily	Once daily	
Which option would you prefer?	☐	☐	☐

Results

Participant demographics (Table 1)

- A total of 307 patients completed the DCE in China (n=155), Taiwan (n=76) and South Korea (n=76) .
- The mean age was 48 years (range 19–72), and women (50%) and men (50%) were equally represented.
- Participants had been diagnosed with AF for 6 years on average.
- Most participants (64%) received their current anticoagulant treatment for more than 6 months and were receiving rivaroxaban (43%), warfarin (18%), apixaban (17%), dabigatran (7%), or edoxaban (5%).

Treatment attribute trade-offs

- Reduction in the risk of death was the most important attribute, followed by reduction in risk of disabilities and non-disabling events.
- Preferences for intake with food and intake frequency were heterogenous compared with clinical attributes.
- Participants with AF were willing to trade a lower risk of severe disability, minor or moderate disability, or non-disabling event for a slightly higher risk of death (**Figure 2**). For example, for every 1% decrease in the risk of severe disability, participants were willing to trade a 0.36% increase in the risk of death..

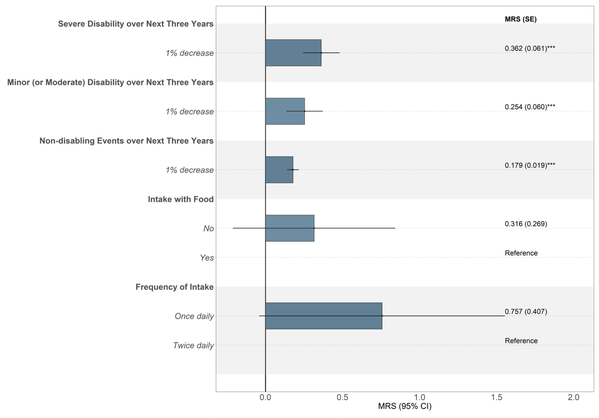
Results (Cont'd)

Table 1. Participant demographic and clinical characteristics

Characteristic	Overall (N=307)	China (N=155)	Taiwan (N=76)	South Korea (N=76)
Age (years)				
Mean (standard deviation)	48 (11.6)	50 (11.6)	42 (10.0)	48 (11.1)
Range (min, max)	19–72	19–72	20–61	24–70
Sex (male), n (%)	153 (50)	68 (44)	40 (53)	45 (59)
Employment status, n (%)				
Employed, full-time	227 (74)	90 (58)	71 (93)	66 (87)
Retired	63 (21)	58 (37)	2 (3)	3 (4)
Other*	17 (6)	7 (5)	3 (4)	7 (9)
Educational background, n (%)				
High school or less	93 (30)	56 (36)	15 (20)	22 (29)
College or higher	210 (68)	99 (64)	61 (80)	50 (66)
Other	4 (1)	0 (0)	0 (0)	4 (5)
Medical history, n (%)				
Cardiovascular disease	114 (37)	53 (34)	27 (36)	34 (45)
Diabetes	49 (16)	21 (14)	18 (24)	10 (13)
Bleeding (minor)	36 (12)	22 (14)	8 (11)	6 (8)
Stroke/transient ischemic attack/systemic embolism	33 (11)	17 (11)	10 (13)	6 (8)
Other vascular disease	29 (9)	5 (3)	18 (24)	6 (8)
Renal impairment	24 (8)	11 (7)	6 (8)	7 (9)
Liver impairment	22 (7)	11 (7)	5 (7)	6 (8)
Cancer	18 (6)	5 (3)	3 (4)	10 (13)
Bleeding (major)	16 (5)	8 (5)	1 (1)	7 (9)
Other thrombosis	16 (5)	7 (5)	3 (4)	6 (8)
No, none of these conditions	113 (37)	68 (44)	12 (16)	33 (43)
Self-Reported Overall Health, n (%)				
Excellent	45 (15)	14 (9)	19 (25)	12 (16)
Very good	50 (16)	14 (9)	23 (30)	13 (17)
Good	120 (39)	61 (39)	21 (28)	38 (50)
Fair	77 (25)	56 (36)	10 (13)	11 (14)
Poor	15 (5)	10 (6)	3 (4)	2 (3)

*Includes part-time employed, unemployed, student, homemaker/housewife, disabled, other

Figure 2. Maximum Acceptable Risk of Death over the Next Three Years



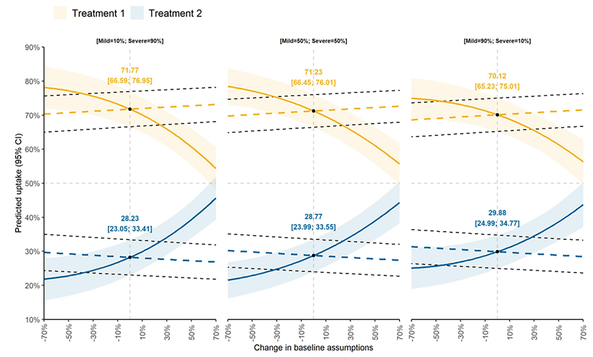
The minimal improvement in death reduction required by patients to accept 1% increase in poorer outcomes on other attributes is shown. Marginal rates of substitution were estimated to determine the willingness of a patient to swap one attribute change for another providing equal utility.

Abbreviations: CI, confidence interval; MRS, marginal rates of substitution; SE, standard error.

Treatment comparison

- Based on choice data, respondents generally preferred an edoxaban-like treatment profile over a rivaroxaban-like profile, over wide parametric ranges (**Figure 3**).
- The probability of the edoxaban-like profile being preferred decreased with higher non-disabling event incidence and increased with greater fatality incidence.
- The sensitivity analysis demonstrated that the explored variation in patient experience outcomes did not change the order of treatment preference.

Figure 3: PCP Sensitivity Analysis



Lines denote the probability of respondents preferring profile 1 (similar to that of edoxaban) over profile 2 (similar to that of rivaroxaban) for varying levels of mild and severe disabling events, non-disabling events, and fatal events. The shaded areas/areas within the dashed lines indicate 95% confidence intervals. Each line summarizes a change to baseline assumptions in non-disabling events (solid lines) and fatality rates (dashed lines), for different ratios of mild: severe disabling events, holding all else equal.

Abbreviation: CI = confidence interval; PCP, predicted choice probability

Conclusions

- This multi-country preference study shows that participants preferred treatment options that reduced the risk of death, disability, and non-disabling events.
- Participant choices were not influenced by treatment administration characteristics (i.e., intake with food and intake frequency); however, preference heterogeneity was observed.
- Among the efficacy-related outcomes, participants preferred a reduction in risk of death twice as much as reduction in risk of severe disability and three times as much as reduction in risk of mild or moderate disability.
- To guide shared decision-making, it is crucial to consider the distinct profiles of once-daily DOACs, ensuring the chosen option aligns with individual patient preferences.

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