

Preferences for oral anticoagulant medications for managing atrial fibrillation

Dear Editor,

Stroke prevention in patients with atrial fibrillation (AF) using anticoagulants involves weighing the benefits of reduced ischemic stroke^{1,2} against the elevated risks of serious bleeding events.³ Warfarin and direct oral anticoagulants (DOACs) are the available oral anticoagulants for this indication. We developed a discrete choice experiment (DCE) survey⁴ to assess the preferences of older Singaporeans for oral anticoagulants for secondary stroke prevention in a hypothetical scenario of prior stroke and history of AF.

Participants aged 50 and above who might or might not be diagnosed with AF were recruited from outpatient neurology clinics at Singapore General Hospital after the ethics approval was obtained (CIRB: 2021/2454). Once informed consent was obtained, interviewers administered the web-enabled survey from January to May 2022. Participants were presented with 9 choice tasks and were asked to choose 1 option from 2 treatments and a “No treatment” option in each choice task. Each treatment was defined by 6 attributes: risk of stroke, risk of bleeding, availability of antidote in case of bleeding, frequency of blood monitoring, negative interactions with food/other drugs and monthly out-of-pocket cost. The attribute levels were selected based on values indicated in clinical trials^{1,2,5,6} and widely-used clinical guidelines.⁷ Participants were asked to assume that: (1) they were diagnosed with AF, and (2) the risk assessment by their doctor(s) indicated that they had a 7% risk of stroke and a 1% risk of major bleeding if they did not use oral anticoagulants for AF. An example choice task is shown in Supplementary Fig. S1.

The DCE required a minimum sample size of 125 based on the formula by Johnson and Orme.⁸ To analyse the data, we used a mixed logit model to allow for preference heterogeneity. Using the preference weights from the model, we calculated the relative attribute importance for each attribute out of 100%⁹ and calculated the probability of choosing different medications. We predicted the choice between warfarin and DOACs based on the different levels of cost and frequency of blood monitoring. NLOGIT 6.0 (Econometric Software, Plainview, NY, US) and Stata version 15.1 (StataCorp, College Station, Texas, US) software were used for data analyses.

We recruited 131 participants. The mean (standard deviation) age was 64.0 (9.0) years old. Most of the

sample were male (64%), married (73%) and Chinese (67%). Seventy-one percent of participants reported having pre-existing or chronic conditions, such as diabetes or cancer; 31% reported being diagnosed with stroke; and 33% reported a family history of stroke (Supplementary Table S1).

Participants preferred lower risk of stroke, lower risk of bleeding, availability of antidote for bleeding, few interactions with food and drugs and lower out-of-pocket cost. These findings are consistent with the findings from a systematic review on preferences for oral anticoagulation therapy.³ While participants generally preferred less frequent blood monitoring, they strongly disliked not having any blood monitoring and preferred to have blood tests every 3 months the most. There may be several reasons for our results. First, participants may not have realised that new DOAC medications do not require blood monitoring (as opposed to warfarin) and therefore expected some monitoring. They may also have perceived the lack of follow-ups as poor quality of care. Participants strongly disliked the “No treatment” option and those who reported having family who had stroke were less likely to choose the “No treatment” option.

The risk of stroke was the most important attribute (33%), followed by the monthly out-of-pocket cost (22%). Participants valued the risk of bleeding, availability of antidote and frequency of blood monitoring equally (approx. 12%). The least important attribute was the number of interactions with food/other drugs (8%) (Supplementary Fig. S2). Other studies¹⁰ also found that efficacy in stroke prevention was more important than bleeding risk.³

Table 1 shows the predicted choice of a new DOAC, warfarin and “No treatment” at different out-of-pocket costs and frequency of blood monitoring for the new DOAC. The cost of warfarin was assumed to be SGD10 per month in the predictions. When the cost of the new DOAC was SGD10 per month (same as warfarin), 33% would choose the new DOAC when blood monitoring was not required for the new DOAC and 58% would choose warfarin. When blood monitoring was required once every 3 months for the new DOAC, 51% would choose the new DOAC and 41% would choose warfarin. If the new DOAC costs SGD200, only 15% would choose the new DOAC when blood monitoring was not required, and 25% would choose it when blood monitoring was required once every 3 months. Overall,

Table 1. Predicted treatment choices (N=125).

Cost of new DOAC (SGD)	Frequency of blood test of new DOAC	New DOAC (%)	Warfarin (%)	No treatment (%)
200	None	15	76	9
100	None	21	70	9
50	None	27	64	9
10	None	33	58	9
200	Once/3 months	25	66	9
100	Once/3 months	36	55	9
50	Once/3 months	44	48	9
10	Once/3 months	51	41	8

DOAC: direct oral anticoagulants

New DOAC profile: risk of stroke: 3%, risk of bleeding: 2%, antidote for bleeding: no, interactions with food: few.

Warfarin profile: risk of stroke: 3%, risk of bleeding: 3%, antidote for bleeding: yes, interactions with food: many, frequency of blood monitoring: once every 3 months, out-of-pocket cost: SGD10.

No treatment profile: risk of stroke: 7%, risk of bleeding: 1%, out-of-pocket cost: SGD0.

fewer participants were predicted to prefer the new DOAC over warfarin if the cost of the new DOAC was higher than warfarin.

Predicted choice of “No treatment” remained stable at around 9% regardless of the out-of-pocket cost and blood monitoring frequency for the new DOAC. These findings emphasise the need for concerted efforts to explain the benefits associated with treatments, the treatment options, and provide clarification to alleviate concerns for patients to make decisions consistent with their preferences.

The main strength of our study was to systematically quantify how the predicted demand for different medications changed based on risks, blood monitoring frequency and out-of-pocket costs. To our knowledge, this is the only other study assessing patient preferences in Asia, following a previous study conducted in Japan. The main limitation of our study was that patients recruited were not necessarily diagnosed with AF. However, as these patients were recruited from the neurology departments, their concerns and therefore, preferences may be similar to those of newly-diagnosed AF patients who are at risk of stroke. Additionally, the preferences of the recruited patients were not subject to other influences, such as past consults, thus ensuring that the preferences and concerns may be akin to those of newly-diagnosed patients.

In summary, this study showed that the efficacy in stroke prevention and out-of-pocket cost were the top 2 attributes patients focused on when selecting medications for AF. A better explanation of each treatment's benefits

and risks can help patients to understand their options and potential consequences. Additionally, policymakers should consider lowering the out-of-pocket cost of these medications to promote medication use in efforts to reduce AF-related stroke. Incorporating patient preferences into treatment decisions will help them make informed decisions consistent with their preferences.

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¹ Department of Neurology, National Neuroscience Institute, Singapore
² Lien Centre for Palliative Care, Duke-NUS Medical School, Singapore
³ Signature Programme in Health Services and Systems Research, Duke-NUS Medical School, Singapore
⁴ Department of Population Health Services, Duke University, Durham, NC, US

Yu Zhi Pang ¹*MD*, Deidre Anne De Silva ¹*MBBS*,
Sean Ng ^{2,3}*BSc*, Vinh Anh Huynh ^{2,3}*BSocSci*,
Semra Ozdemir ^{2,3,4}*PhD*

Correspondence: Dr Semra Ozdemir, Lien Centre for Palliative Care,
Duke-NUS Medical School, 8 College Road, Level 4, Singapore 169857.
Email: semra.ozdemir@duke.edu