

Informing the Design of a Discrete Choice Experiment for Evaluating Warfarin Pharmacogenetic Testing Among Mandarin-speaking Chinese Warfarin Patients in Singapore: A Mixed Methods Analysis

Dear Editor,

Specific genetic variants have a substantial effect on warfarin dose response but warfarin pharmacogenetic testing (WPGT) is still not routine clinical practice. Apart from clinical validity, economics, social, ethical and legal implications are also important aspects in the implementation of WPGT. Several studies have revealed high interest in pharmacogenetic testing (PGT) but also concerns over privacy, confidentiality and cost.^{1,2} However, these studies were all conducted in non-Asian populations, whom may have different perceptions and attitudes towards PGT from Asians due to cultural differences. On the economic front, the cost-effectiveness of WPGT is inconclusive³ and no cost-benefit analyses, where willingness-to-pay (WTP) is used to value health benefits in monetary terms,⁴ have been done. The discrete choice experiment (DCE) methodology is an increasingly popular method not just for generating health preferences in healthcare decision-making, but also to elicit WTP.⁵ In a DCE, individuals are asked to state their preferences between alternative choice sets with each choice set defined by a number of attributes, which may include cost and efficacy in the context of WPGT. To the best of our knowledge, there has been no preference study for WPGT in any population internationally.

Although the DCE is relatively intuitive, this methodology is unfamiliar to the Asian population, especially in the field of healthcare. We hereby report the results of a developmental study aimed specifically to (i) determine the effectiveness of WPGT educational materials, (ii) identify concerns about WPGT, (iii) identify the most relevant efficacy attribute(s) for the DCE, and (iv) determine participants' ability to understand and complete the DCE.

Mandarin-speaking Chinese warfarin patients of age \geq 21 years were recruited from the anticoagulation clinics at the National University Hospital between April to May 2011 using convenience sampling. Patients with signs of cognitive function problems, as perceived by the interviewer, were excluded. Individual voice-recorded, face-to-face interviews were conducted in Mandarin, using a semi-structured interview protocol with the aid of show cards. The interview was divided into several sections: (i) education on WPGT and post-education evaluation, (ii) selection of 1 to 2 (from 5 shortlisted) efficacy attributes important to WPGT, (iii) a trial DCE (using attributes 3 and 4 (Table 1), and cost), and (iv) post-DCE evaluation.

The ability to understand WPGT after education was assessed based on the patients' ability to explain it in their

Table 1. Combinations of Efficacy Attributes Chosen by Patients, n (%)

Most important attribute*	Second most important attribute*						Total
	1	2	3	4	5	NIL	
1	-	1 (2.3)	0	0	0	2 (4.7)	3 (7.0)
2	1 (2.3)	-	1 (2.3)	0	1 (2.3)	1 (2.3)	4 (9.3)
3	2 (4.7)	3 (7.0)	-	1 (2.3)	4 (9.3)	6 (14.0)	16 (37.2)
4	4 (9.3)	4 (9.3)	1 (2.3)	-	1 (2.3)	1 (2.3)	11 (25.6)
5	0	1 (2.3)	1 (2.3)	5 (11.6)	-	2 (4.7)	9 (20.9)
Total	7 (16.3)	9 (20.9)	3 (7.0)	6 (14.0)	6 (14.0)	12 (27.9)	43 (100)

Patients were asked to choose up to 2 attributes that they found most important. The numbers choosing the various combinations of attributes are tabulated.

*Attribute 1: Chance of having accurate starting dose; Attribute 2: Time to stable dose; Attribute 3: No. of INR (International Normalized Ratio) tests until stabilisation; Attribute 4: Risk of serious ADR (Adverse Drug Reaction) in first 3 months; Attribute 5: Risk of hospitalisation due to serious ADR in first 6 months.

own words, state at least 1 potential benefit and interviewer rating patients at least 4 points (out of 5) with regard to their understanding. The ability to understand and complete the DCE was assessed based on the post-DCE evaluation (whether any problems were encountered, ability to verbalise thought process or make comments that indicate their understanding) and the ability to complete all choice sets offered. The DCE was designed in an iterative manner, with the trial DCE introduced only after the 5th patient and administered to 44 patients with 5 using 5 choice sets and 39 using 7 choice sets.

Of 174 patients approached, 43 were ineligible, 81 refused and 50 agreed to participate, giving a response rate of 38.2%. Of those who refused participation, 47 (58%) were males. One patient was dropped due to perceived poor cognitive function, resulting in a final sample size of 49.

Overall, 65% of them were deemed able to understand the WPGT. Those who could understand WPGT were younger (mean age: 52.1 vs 64.8 years, t -test $P = 0.0029$) and more educated ($\chi^2 P = 0.007$). Those who did not know their time to stable dose also tended not to understand WPGT, compared to those who were able to state a duration ($\chi^2 P = 0.002$). Overall, 30 patients (68.2%) were able to understand the DCE, and most could handle all the choice sets presented. A large majority (93.3%) of those who could understand WPGT also understood the DCE.

Of 43 patients who completed the section on choice of efficacy attributes, number of International Normalized Ratio (INR) tests until stabilisation and risk of serious adverse drug reactions (ADR) in the first 3 months were most commonly chosen (Table 1). Three patients (6.3%) had some concerns about WPGT prior to being told the possible risks. One was concerned about what was actually tested (e.g. unintended tests) and another stated anxiety as a concern. The third patient was opposed to genetic testing but could not verbalise her exact concerns. After being shown the possible risks of WPGT, 7 patients (14.6%), including the 3 who expressed prior concerns, said they would be concerned about at least one of the risks. The most commonly cited concerns were the possibility of other disease risks being revealed from the WPGT results, and being labeled, thus affecting self-perception and causing anxiety.

This semi-qualitative study focused on targeted aspects of WPGT and DCE methodology in preparation for a larger survey. The relationship between understanding of WPGT with age and educational status, coupled with the fact that few patients offered any constructive criticisms about the show cards suggest that it was their inherent characteristics rather than inadequacy of the show cards or explanation that affected their ability to understand it. There are several limitations in this study. Firstly, sampling was non-random so generalisability of the results may be limited. Secondly,

there may be some non-response bias. Males were over-represented but since gender was not associated with any of the outcomes, this is unlikely to have biased the results. Thirdly, understanding of the DCE was based on the interviewer's perception, which may be subjective. However, interviewer bias is likely to be minimal given that explicit criteria were used and the same interviewer conducted all the interviews. Lastly, in this exercise, we assumed that patients' view alone is sufficient in the choice of DCE attributes, which is not necessarily so.

Conclusion

In conclusion, the educational materials on WPGT were effective and the DCE is feasible when accompanied with good explanation. Patients are concerned over potential WPGT risks, highlighting the need to communicate these risks clearly. Finally, the 2 most relevant efficacy attributes that should be used in the DCE were number of INR tests until stabilisation and risk of serious ADR in the first 3 months.

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