Title - All manuscripts

When is it cost effective to use transthoracic echocardiography to aid the decision to prescribe oral anticoagulants in patients with newly diagnosed atrial fibrillation? An economic evaluation

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JM: Developed model; wrote first and subsequent drafts of manuscript;

MS: Created model; commented on all drafts of manuscript;

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Abstract

Background: Atrial fibrillation (AF) is common and increases stroke risk. Echocardiography is often performed as part of the cardiological evaluation of patients with AF to assist with stroke risk stratification (and hence, decisions on thromboprophylaxis with oral anticoagulants (OACs)). The cost effectiveness of such an approach is unknown.

Objective: To estimate the cost-effectiveness of using transthoracic echocardiography (TTE) in helping to make the decision whether to prescribe an OAC in newly diagnosed AF patients.

Design: Diagnostic economic modelling analysis.

Setting: England & Wales

Model: Diagnostic discrete event simulation model.

Comparisons: Decisions and consequences following from using TTE in combination with the $CHADS_2$ score (used for stroke risk stratification), compared with those when using $CHADS_2$ alone.

Treatments considered: Warfarin, dabigatran and rivaroxaban were all considered separately as OACs which may be prescribed as a result of the information provided by TTE.

Population: Newly diagnosed AF patients.

Main outcome measures: Quality adjusted life years gained, strokes averted, effects on cost and major bleeding events.

Results: For patients aged 50 years, using TTE does not appear clinically effective due to the problems of additional overtreatment. For patients aged 65 years, using TTE is more effective but more expensive, with incremental cost-effectiveness ratios which are below conventional willingness to pay thresholds when a newer OAC (rivaroxaban, dabigatran) is being considered, but not warfarin.

Conclusions: Using TTE to inform the decision whether to prescribe a newer OAC to newly diagnosed AF patients may be a clinically and cost-effective strategy.

Introduction

Background

Atrial fibrillation (AF) is a common arrhythmia affecting around 1-2% of the UK population and is a significant risk factor for stroke.[1] Managing AF effectively is therefore important for reducing mortality and morbidity risks that result from this condition. Oral anticoagulants (OACs) reduce the risk of stroke for AF patients, but can cause major bleeding. [2]

OACs also impose a cost burden, either directly due to drug acquisition costs in the case of newer OACs like dabigatran or rivaroxaban, or indirectly due to monitoring costs in the case of warfarin. In AF patients with an already low stroke risk, prescribing an OAC may not be clinically beneficial, as the average harm caused by additional major bleeding events can exceed the harm averted by preventing strokes. Because of this a range of risk prediction rules are used to identify the higher-risk patients who are likely to benefit from OACs.

A commonly used stroke risk prediction rule for assessing stroke risk is the $CHADS_2$ score, which is an acronym for: (C) congestive heart failure; (H) hypertension; (A) aged 75 years or older; (D) diabetes; prior stroke or transient ischemic attack (S_2) [3] The European Society of Cardiology 2010 guidelines for the management of atrial fibrillation, and subsequent 2012 focused update of these guidelines, emphasise identification of 'truly low risk' patients who do not need any form of antithrombotic therapy, and that even in low risk patients OACs should be considered in preference to aspirin monotherapy or aspirin-clopidogrel combination therapy. [3,4] This paper interprets this guidance as suggesting that patients should normally receive an OAC if their $CHADS_2$ score is not zero.

Transthoracic Echocardiography and the decision problem

This study considers whether additional diagnostic testing of newly diagnosed AF patients with $CHADS_2$ scores of zero could be a clinically and cost-effective strategy for appropriately managing their condition. The additional screening is with transthoracic echocardiography (TTE). A $CHADS_2$ score of zero means these patients would conventionally not be prescribed an OAC. However, TTE is

able to identify abnormalities of cardiac function and structure (ABN) which indicate that, despite the low $CHADS_2$ score, the patient has a high risk of stroke. [5,6] For these 'hidden' high-risk patients, prescribing an OAC is likely to be more beneficial than harmful, and so using TTE in this way improves their AF management. However, as no diagnostic is perfectly accurate, the use of TTE will produce some false positives, resulting in more patients with low stroke risk being prescribed OACs. Additionally, not all patients who are at higher stroke would be identified (false negatives), and so would remain untreated with OACs. For these reasons, not using TTE (the No TTE Strategy) could lead to better clinical outcomes for these AF patients than using TTE (the TTE Strategy).

If the TTE Strategy is clinically superior, however, it is then important to estimate whether it is also cost effective, meaning that the ratio of additional costs to additional clinical benefits of the TTE Strategy compared with No TTE strategy represents a good use of scarce resources. The National Institute for Health and Care Excellence (NICE) recommends that health benefits be defined in terms of quality-adjusted life years (QALYs), and conventionally applies thresholds ranging from £20,000 per QALY to £30,000 per QALY when deciding whether to recommend a health technology. [7] This modelling study uses this measure of health benefit and these thresholds.

Methods

The mathematical model developed estimated the consequences of using TTE to inform the decision whether to prescribe an OAC in a range of patient populations. Eight distinct cohorts were modelled, and separate scenarios were performed for each of three potential OACs: warfarin; dabigatran; and rivaroxaban. [8] A UK perspective is adopted, with costs incurred by the patient or wider society not considered. Costs were inflation-adjusted to 2012 UK values where necessary. Standard NICE discount rates for utilities and costs of 3.5% per annum are used. [9] A lifetime horizon is adopted, and in order to incorporate the effect of uncertainty on predicted outcomes, in order that the full consequences of mortality due to stroke or major bleeding events are compared. A probabilistic

model is used, meaning that where possible model parameter estimates are drawn from distributions rather than assumed to be fixed values.

Scenarios included

The recommended populations for treating with warfarin, rivaroxaban, and dabigatran are different in their clinical characteristics. Warfarin is recommended in patients with a $CHADS_2$ score of one or more; similarly the recent NICE recommendations for rivaroxaban are equivalent to stating that patients with a $CHADS_2$ score of one or more should receive it; and recent NICE recommendations for dabigatran are equivalent to stating that patients with a $CHADS_2$ score of one or more should receive it if they are also aged 65 years or more. [10,11] The purpose of this paper is not to identify the most appropriate OAC, which is a matter of clinician judgement, but to see if the use of TTE is clinically effective and cost-effective given the OAC under consideration. The scenarios in which a TTE may affect the OAC decision are described in Table 1 .

[Table 1 about here]

Model Overview

An overview of the model is presented in Figure 1. The model comprises a short-term diagnostic stage and a long-term patient outcome stage. In the short-term stage the clinical characteristics of a hypothetical patient are generated, including the presence of an ABN. Whether or not an ABN was identified and hence an OAC was prescribed is additionally determined. In the long-term simulation the patient's clinical outcomes are simulated. Over the patient lifetime the patient may experience a stroke or major bleeding event, both of which could cause death; patients may also die from another cause. Each of these events has associated cost and utility implications. By simulating the outcomes for a large number of hypothetical patients, the mean costs and mean QALYs for both the TTE Strategy and the No TTE strategy can be calculated. From these the incremental cost effectiveness ratio (ICER) of including TTE in the diagnostic package can be calculated.

[**Figure 1** about here]

In the No TTE Strategy, none of the patients with ABN would be treated with the OAC. In the comparator strategy, a percentage of these patients with ABN would receive the OAC due to TTE correctly identifying ABN, dependent on sensitivity of TTE. However, when specificity is less than perfect a proportion of patients without ABN would also receive treatment.

In the short-term diagnostic stage of the model the population are divided into true positives (TP), true negatives (TN), false positives (FP) and false negatives (FN). The relative size of each of the four groups is a function of the proportion of the population with ABN, referred to here as the true proportion high risk (TPHR), and the sensitivity and specificity of the diagnostic technology. These are defined as follows:

- Proportion of TPs = TPHR x sensitivity;
- Proportion of TNs = (1 –TPHR) x specificity;
- Proportion of FPs = (1 – TPHR) x (1 – specificity);
- Proportion of FNs = TPHR x (1 – sensitivity).

Within the context of the model, the No TTE strategy has a sensitivity of zero and a specificity of one, meaning for this strategy the population mix comprises TPHR false negatives and (1 - TPHR) true negatives.

Modelling long-term events

Prescribing an OAC reduces the risk of stroke, but increases risk of a potentially fatal major bleeding event. Three mutually exclusive outcomes could result from a stroke: death; a dependent state; and an independent state. Each outcome have different probabilities of occurrence, health related quality of life (HRQoL), and costs. Similarly, three mutually exclusive outcomes could result from a major bleeding event: death; an intracranial (IC) bleeding event; or a non-intracranial (NIC) bleeding event (assumed to be a gastrointestinal bleed). The severity of an IC bleed can vary substantially, and this variation of outcomes was itself simulated using data based on outcomes categorized by Glasgow Outcome Scale (GOS) score following traumatic brain injury. The full methodology used to produce these estimates is presented elsewhere. [12]

The model is dynamic and updated when events occur that affect an individual's stroke or major bleed risk. Examples of such events are: experiencing a stroke; withdrawal of an OAC following a major bleed; and reaching 75 years of age, which increases the $CHADS_2$ score by one point. It was assumed that if a patient experiences a stroke and is not already taking an OAC, they are prescribed OACs, provided they have not experienced a previous bleeding episode. If a patient suffers a severe intracranial haemorrhage (GOS category 2) as a result of taking OACs, their life expectancy was reduced to a maximum of 3.6 years with no QALY gain. [13] Additionally, the risk of a major bleeding event when taking dabigatran (150mg twice daily) was also assumed to change at the age of 75, as indicated by recent evidence comparing dabigatran with warfarin. [14]

Data sources used in model

A full list of the information used to populate the parameters in the model, including event risks, costs and utilities, is presented in **Error! Reference source not found.** in the appendix.

Estimating cost effectiveness

The adoption decision, defined as the strategy that is deemed most cost effective, is calculated from the mean values of the costs and the QALYs of each strategy. Scatterplots of estimates produced by the probabilistic sensitivity analysis (PSA) provide an indication of uncertainty surrounding the adoption decision. A point in the north-west quadrant indicates that the TTE Strategy is both more costly and less effective than the No TTE Strategy, and so ruled out by dominance. A point in the north-east quadrant indicates that the TTE Strategy is both more expensive and more clinically effective than the No TTE Strategy, and consideration is given to whether the ICER, the ratio of additional cost to additional benefit, is below a maximum acceptable incremental cost effectiveness ratio (MAICER). Scatterplots where the scatter covers more than one quadrant indicate some level of decision uncertainty, as different quadrants suggest different decisions. [15]

Deterministic sensitivity analyses

Sensitivity analyses were also undertaken on the joint uncertainty in the sensitivity and specificity of TTE in detecting ABN. The results for the joint uncertainty for three scenarios are presented in the main article. The remainder of these analyses are presented in the online appendix.

Results

Table 2 presents some summary statistics of simulated patient outcomes for the TTE Strategy and the No TTE Strategy, where the patient population is of 65 year old females with an initial $CHADS_2$ score of 0, and the OAC is assumed to be warfarin, rivaroxaban, or dabigatran. Figure 2 show the PSA scatterplots where the OAC is either warfarin (a), rivaroxaban (b), or dabigatran (c). Table 2 also shows the mean costs and mean QALYs of the No TTE Strategy and the TTE Strategy, and the ICER comparing these strategies. Results for other patient groups are included in the appendix.

[Table 2 about here]

[**Figure 2** about here]

Table 2 indicates that, irrespective of the OAC, using TTE in this way reduces the proportion of deaths caused by stroke, but increases the proportion of deaths caused by major bleed. On average, the scenarios not using TTE are estimated to result in a lower rate of dependent and independent strokes, and a higher rate of major bleeding events, including intracranial haemorrhages (ICHs). For all OAC scenarios, the number of life years is estimated to be slightly greater when a strategy incorporating TTE is used compared with the strategy without TTE, but these differences are relatively small (approximately 0.1 life years).

Figure 2 and Table 2 both suggest that the cost-effectiveness of the TTE strategy compared with the no TTE strategy depends on the OAC which would be prescribed. Where the OAC is warfarin (Table 3a), the ICER comparing the two strategies is almost £40 000 per QALY; where the OAC is rivaroxaban (Table 2b), the ICER reduces to around £23 000 per QALY, and where the OAC is dabigatran (Table 2c), the ICER reduces further to around £12 000 per QALY.

Deterministic sensitivity analyses

Table 3 shows how the estimated mean ICER depends on the sensitivity and specificity of the technology, assuming all other values are held at their mean levels, where the OAC is either a) warfarin, b) rivaroxaban, or c) dabigatran. If TTE had perfect sensitivity and specificity, then the additional cost per QALY is estimated to range from around £1,800/QALY for warfarin (a) to £1,100/QALY for dabigatran (c) [6]. However, due to the less than perfect specificity of TTE, estimated to be around 0.35, and the increased number of false positives predicted to be treated as a result of this, the ICERs increase to around £27,000-£59,000/QALY for warfarin (a), £18,000-£29,000 for rivaroxaban (b), and £10,000-£14,000 for dabigatran (c). As the ICER is a ratio, and the absolute differences in QALYs between strategies with and without TTE are small, the ICERs are shown to be highly sensitive to the values of sensitivity and specificity assumed for some scenarios.

Overview of results for other scenarios

The full results for the 10 scenarios considered are presented in the online appendix. A brief summary, indicating whether the results suggest TTE appears cost-effective at MAICERs of £20,000 /QALY or £30,000/QALY, is shown in Table 4. These results suggest that the addition of TTE to help make the decision whether to prescribe an OAC is more expensive and less effective than not using TTE in patients aged 50 years. In patients aged 65 years, the strategy using TTE appears cost-effective and conventional willingness-to-pay thresholds of between £20,000 and £30,000/QALY for dabigatran, and possibly for rivaroxaban. The cost-effectiveness of the strategy appears slightly more favourable for female than for male patients, but the choice of OAC and patient age appear to have much greater influence.

Discussion

In this study, we have shown that using TTE to inform the decision whether to prescribe a newer OAC to newly diagnosed AF patients may be a clinically and cost- effective strategy. Prior to producing this model, a systematic literature review was conducted to identify, summarise and appraise existing economic studies for evaluating the cost-effectiveness of TTE in patients with AF

and we identified no economic evaluations of the use of TTE in AF patients. Thus we believe this is the first such economic evaluation.

The model has a range of limitations and a number of assumptions have been made within the modelling. For example, only the $CHADS_2$ clinical risk prediction tool was used as the baseline strategy. An alternative to this tool is the CHA_2DS_2-VASc score, which is considered to be better at distinguishing low risk from very low risk patients, and is the only such tool recommended in the 2012 focused update of the ESC guidelines. [3,4,16,17] CHA_2DS_2-VASc was not used in these analyses as the recent NICE recommendations for the use of dabigatran and rivaroxaban both map onto specific $CHADS_2$ risk scores, but not specific CHA_2DS_2-VASc risk scores. [10,11] The dose of dabigatran was fixed at 150mg twice daily, rather than allowing some patients to receive a lower dose of 110mg twice daily. The stroke risk associated with patients with LA ABN was assumed not to change as a patient ages; ideally differential rates by age or by the number (and type) of abnormalities would be used but these data were not identified.

Within the study used to derive the sensitivity and specificity of TTE, transoesophageal echocardiography (TOE), was assumed to be a perfect gold standard, and so our model also made this assumption. [6] Using TOE as the gold standard, TTE was estimated to have a very high sensitivity but a specificity of only around 35 %. Within this model, this low specificity results in a considerable number of people effectively experiencing comparable risks of bleed without the increased benefits in terms of stroke risk reduction that is estimated in patients with a higher risk of stroke. If TTE were found to be superior to TOE at identifying certain types of ABN which expose patients to increased stroke risks, then the true benefits of TTE in improving patient management would be underestimated. The study used to derive sensitivity and specificity was relatively small, of fewer than 400 patients, and also formed the basis of our estimates of the TPHR. [6] This has made the assessment of the benefits of TTE uncertain. A further limitation is that the risk of death

unrelated to bleeding or stroke events was taken from lifetables and were not adjusted for the probability of bleeding or stroke mortality. [18]

A key uncertainty is whether there are incidental benefits that are accrued from a TTE other than identifying some forms of ABN. If these exist, and produce even small net QALY gains (> 0.0033) then TTE would be cost effective in all scenarios, assuming a cost of £66 per test. [19] As Table 3b indicates, the structural sensitivity analyses for this scenario indicate that even a diagnostic strategy with a joint sensitivity of one and specificity of zero (i.e. prescribing everyone with the OAC) may be cost effective compared with treating no-one. The implications of this result require further research.

Implications for Research

For some scenarios the cost effectiveness estimates generated by the model depend heavily on sensitivity and specificity estimates, as well as the true proportion of genuinely high risk (ABN that can be detected by TTE) patients in this sub-population of apparently 'low risk' patients. The model depends strongly on data reported in a single, relatively small study conducted outside of the UK, and so may misrepresent the true values of these parameters. Having a more robust source of evidence for these parameters, with direct relevance to England and Wales, is likely to significantly improve the accuracy of the mathematical models.

Additional research that would improve the validity of the model include identifying any incidental net benefits to the management of newly diagnosed AF patient that could result from routine screening with TTE following initial diagnosis.

Implications for clinical practice

If TTE were to be recommended for those patients with $CHADS_2$ scores of zero points, there will be an increase in the number of TTEs performed. This is unlikely to place a great burden on the majority of hospitals who are likely to have staff trained in the use of TTE machines. It is likely that additional

bed days are made available due to the reduction in stroke following appropriate management, although there is likely to be an increase in bleed related admissions.

Conclusion

This paper presented the results of mathematical models which simulated the effects of using TTE to help make the decision whether to prescribe an OAC in a range of patients with AF. It was estimated that when rivaroxaban or dabigatran is the OAC of choice then it appears cost-effective to use TTE in patients aged 65 years; when warfarin is the OAC of choice, then the addition of TTE does not appear cost-effective at standard willingness to pay thresholds of either £20,000 per QALY or £30,000/QALY. We suggest that if considering prescribing a newer OAC, it may be both clinically effective and cost effective to use TTE to help inform the decision in more elderly patients.

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$CHADS_2$ score	**Prescribe dabigatran**	**Prescribe warfarin**	**Prescribe rivaroxaban**
0	No	No	No
1	Yes (age 65 or over)	Yes (or aspirin)	Yes
2 or more	Yes	Yes	Yes
Cohorts simulated	**Scenarios considered for dabigatran**	**Scenarios considered for warfarin**	**Scenarios considered for rivaroxaban**
Males, age 50, $CHADS_2$ score of zero	No †	Yes	Yes
Females, age 50, $CHADS_2$ score of zero	No †	Yes	Yes
Males, age 65, $CHADS_2$ score of zero	Yes	Yes	Yes
Females, age 65, $CHADS_2$ score of zero	Yes	Yes	Yes
* Patient would automatically receive treatment. † OAC not permitted under NICE guidance			

Table 1 Simplified OAC indications by OAC, and patient cohorts run for each OAC

		Cause of Death (%)			*Average Number of Events*				*Cost-effectiveness*		
Strategy	**Life Years**	**Stroke**	**Bleed**	**Other**	**Dependent Strokes**	**Independent Strokes**	**ICH**	**NICH**	**Mean Cost (£)**	**Mean QALY**	**ICER**
Without TTE	17.132	9.0	0.9	90.2	0.087	0.192	0.007	0.052	1 974	9.94	39 569
With TTE	17.204	8.0	1.3	90.7	0.078	0.172	0.010	0.079	3 106	9.97	

a) Warfarin

		Cause of Death (%)			*Average Number of Events*				*Cost-effectiveness*		
Strategy	**Life Years**	**Stroke**	**Bleed**	**Other**	**Dependent Strokes**	**Independent Strokes**	**ICH**	**NICH**	**Mean cost (£)**	**Mean QALY**	**ICER**
Without TTE	19.460	10.5	1.1	88.4	0.103	0.223	0.009	0.066	1 955	9.95	22 751
With TTE	19.554	9.4	1.6	89.0	0.093	0.201	0.012	0.096	3 039	9.99	

b) Rivaroxaban

		Cause of Death (%)			*Average Number of Events*				*Cost-effectiveness*		
Strategy	**Life Years**	**Stroke**	**Bleed**	**Other**	**Dependent Strokes**	**Independent Strokes**	**ICH**	**NICH**	**Mean cost (£)**	**Mean QALY**	**ICER**
Without TTE	19.485	10.2	1.1	88.7	0.099	0.220	0.009	0.066	1 942	9.95	12 314
With TTE	19.598	9.0	1.6	89.4	0.089	0.195	0.012	0.097	2 946	10.01	

c) dabigatran

Table 2 Simulated outcomes for 65 year old females with newly diagnosed atrial fibrillation and an initial $CHADS_2$ score of 0, where the decision is to prescribe either a) warfarin; b) rivaroxaban; c) dabigatran. TTE: Transthoracic echocardiography; ICER: incremental cost effectiveness ratio (In £/QALY). QALY: Quality adjusted life year

Table 3 Illustration of the effect of different levels of sensitivity and specificity on ICER of TTE compared with no TTE in cohorts of female patients aged sixty five, and with an initial $CHADS_2$ score of zero, in making the decision whether to prescribe a) warfarin, b) rivaroxaban, or c) dabigatran. The four cells with sensitivity and specificity values closest to the empirical values are underlined. (Amounts in £1000 / QALY; >99; Over £99,000/QALY; D: Dominated; ∞: infinity)

a)		*Specificity*										
		0	**0.1**	**0.2**	**0.3**	**0.4**	**0.5**	**0.6**	**0.7**	**0.8**	**0.9**	**1**
Sensitivity	**0**	D	D	D	D	D	D	D	D	D	D	∞
	0.1	D	D	D	D	D	D	D	D	D	>99	8.1
	0.2	D	D	D	D	D	D	D	D	>99	24.4	4.6
	0.3	D	D	D	D	D	D	D	>99	39.9	12.9	3.4
	0.4	D	D	D	D	D	D	>99	54.7	21.0	9.0	2.8
	0.5	D	D	D	D	D	>99	68.9	28.8	14.4	7.0	2.5
	0.6	D	D	D	D	>99	82.4	36.5	19.8	11.1	5.8	2.3
	0.7	D	D	D	>99	95.4	44.1	25.1	15.2	9.1	5.0	2.1
	0.8	D	D	>99	>99	51.4	30.3	19.2	12.4	7.8	4.5	2.0
	0.9	D	>99	>99	58.6	35.4	23.2	15.7	10..6	6.9	4.1	1.9
	1	>99	>99	65.7	40.5	27.1	18.9	13.3	9.2	6.1	3.7	1.8

b)		*Specificity*										
		0	**0.1**	**0.2**	**0.3**	**0.4**	**0.5**	**0.6**	**0.7**	**0.8**	**0.9**	**1**
Sensitivity	**0**	D	D	D	D	D	D	D	D	D	D	∞
	0.1	D	D	D	D	D	D	D	D	D	77.0	7.3
	0.2	D	D	D	D	D	D	D	D	65.3	17.4	4.1
	0.3	D	D	D	D	D	D	>99	61.4	23.9	10.1	3.0
	0.4	D	D	D	D	D	>99	59.5	28.4	14.8	7.3	2.4
	0.5	D	D	D	D	>99	58.3	31.7	18.6	10.9	5.8	2.1
	0.6	D	D	>99	>99	57.5	34.2	21.8	14.0	8.7	4.8	1.9
	0.7	D	>99	>99	57.0	36.3	24.4	16.7	11.3	7.3	4.2	1.7
	0.8	>99	93.2	56.6	37.9	26.6	19.0	13.6	9.5	6.3	3.7	1.6
	0.9	87.0	56.2	39.3	28.5	21.1	15.6	11.5	8.2	5.6	3.4	1.5
	1	56.0	40.4	30.1	22.9	17.5	13.3	10.0	7.3	5.0	3.1	1.5

c)		*Specificity*										
		0	**0.1**	**0.2**	**0.3**	**0.4**	**0.5**	**0.6**	**0.7**	**0.8**	**0.9**	**1**
Sensitivity	**0**	D	D	D	D	D	D	D	D	D	D	∞
	0.1	D	D	D	D	D	D	D	D	>99	28.3	6.2
	0.2	D	D	D	D	D	>99	>99	46.8	23.8	11.2	3.3
	0.3	D	D	>99	>99	99.6	57.0	35.4	22.2	13.4	7.1	2.4
	0.4	>99	>99	97.7	63.5	43.6	30.6	21.5	14.7	9.5	5.3	1.9
	0.5	96.6	67.9	49.8	37.2	28.0	21.0	15.5	11.0	7.4	4.3	1.6
	0.6	54.5	42.5	33.5	26.4	20.7	16.1	12.2	8.9	6.1	3.6	1.4
	0.7	38.1	31.0	25.3	20.5	16.5	13.0	10.1	7.5	5.2	3.1	1.3
	0.8	29.3	24.5	20.4	16.8	13.7	11.0	8.6	6.4	4.5	2.8	1.2
	0.9	23.9	20.2	17.1	14.3	11.8	9.5	7.5	5.7	4.0	2.5	1.1
	1	20.1	17.3	14.7	12.4	10.3	8.4	6.7	5.1	3.6	2.3	1.1

Table 4 Qualitative summary of results of all 10 scenarios. ICERs presented to nearest £1,000/QALY. QALY: Quality Adjusted Lifeyear. ICER: Incremental Cost Effectiveness Ratio. NA: Not applicable. OAC: Oral anticoagulant. TTE: Transthoracic echocardiography. Simple Dominance: TTE strategy is more expensive and less effective than no TTE strategy.

Age	Gender	OAC	ICER of TTE compared with no TTE strategy	TTE optimal	
				At £20,000 / QALY	At £30,000 / QALY
50	male	warfarin	NA: Simple dominance	No	No
50	female	warfarin	NA: Simple dominance	No	No
65	male	warfarin	£67,000/QALY	No	No
65	female	warfarin	£40,000/QALY	No	No
50	male	rivaroxaban	NA: Simple dominance	No	No
50	female	rivaroxaban	NA: Simple dominance	No	No
65	male	rivaroxaban	£30,000/QALY	No	Borderline[1]
65	female	rivaroxaban	£23,000/QALY	No	Yes
65	male	dabigatran	£15,000/QALY	Yes	Yes
65	female	dabigatran	£12,000/QALY	Yes	Yes

[1] Precise ICER is £30,310/QALY, so the No TTE option is still optimal at £30,000/QALY.

Figure listings: