# Abstract

**Background:** Atrial fibrillation (AF)is common and increases stroke risk. Echocardiography is commonly performed as part of the cardiological evaluation of patients with AF expecially 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 modeling analysis.

**Setting:** United Kingdom.

**Model:** Diagnostic discrete event simulation model.

**Comparisons:** Decisions and consequences following from using TTE in combination with CHADS2, a standard clinical decision tool, were compared with those when using CHADS2 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. Cohorts were simulated where the CHADS2 scores alone would not lead to a decision to prescribe OACs. Both males and females were considered, assumed to be aged either 50 or 65 years of age, and with different existing risk profiles.

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

**Results:** At conventional willingness-to-pay thresholds of £20,000/QALY or £30,000/QALY, using TTE rather than no TTE appears to be the optimal strategy when the patients have a CHADS2 score of one rather than zero points when used to make the decision whether to prescribe warfarin; or in patients aged 65 rather than 50 years when used to make the decision to prescribe dabigatran or rivaroxaban.

**Conclusions:** It appears that, irrespective of the OAC, scenarios exist where the use of TTE is both clinically effective and cost-effective.

# 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] Effective management of AF and the associated stroke risk is important for reducing mortality and morbidity risks that result from this arrhhythmia. Oral anticoagulants (OACs) reduce the risk of stroke, but could potentially cause major bleeding. [2]

As well as exposing patients to a risk of major bleeding events, OACs impose a cost burden, either directly due to drug acquisition costs in the case of newer OAC drugs like dabigatran or rivaroxaban, or indirectly due to monitoring costs in the case of warfarin. It should be noted that even where an intervention is clinically effective it does not necessarily follow that it is also cost effective. If the risk of stroke in the patient is low, then the increased health risks associated with OACs may outweigh the benefits, and so a range of diagnostic tools are used to identify higher-risk patients, including clinical prediction rules using patient history and characteristics.

A commonly used risk prediction rule for assessing stroke risk is the CHADS2 score, which is an acronym for (C) congestive heart failure, (H) hypertension, (A) aged 75 years or older or (D) diabetes; and prior stroke, transient ischemic attack (S2) [3] In the 2010 European guidelines, if the CHADS­2 score is one point or over, the OAC should be prescribed. In patients with a CHADS2 score of zero, additional risk factors such as being between over 65 years old, being female, and vascular diseases should be considered as part of the CHA2DS2-VASc score. [3] The latter score is the only recommend stroke score in the 2012 focused update of the ESC guidelines. [4]

## Transthoracic Echocardiography and the decision problem

The present study assesses whether performing an additional, slightly more expensive diagnostic test in the population of interest would lead to better clinical outcomes on average (clinical effectiveness). The populations to be modelled are patients with newly diagnosed AF. Based on clinical history, they will either have an initial CHADS2 risk score of zero or one point, since those with CHADS2 scores greater are likely to be treated without requiring further diagnostic testing. If additional testing is clinically effective, it is also important to evaluate whether it is cost effective at standard NICE decision-making thresholds. The additional diagnostic test of interest is transthoracic echocardiography (TTE), a non-invasive procedure that allows imaging of the heart and blood flow. Importantly, it can detect some forms of left atrial abnormality (LA ABN), which has been shown to lead to an increased stroke risk. [5,6] As some types of LA ABN can be detected by TTE, but not by CHADS2, TTE can be used to identify patients with a higher risk of stroke who otherwise may not receive OACs. In this study a discrete event simulation (DES) model was developed to simulate the long-term implications of performing TTEs in the population of interest when deciding whether to prescribe OACs. Patients whose CHADS2 scores are below the threshold at which the OAC would be prescribed are additionally assessed using TTE. If TTE indicates a LA ABN exists then they are also prescribed OACs. As a result of this, more people will be prescribed OACs when TTE is included in the diagnostic package than when it is not. The use of TTE will increase expenditure, however, potential cost savings could arise as a result of preventing strokes and the costs to the NHS that result from them.

# 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. These are listed in Table 1. The health economic outcome of interest is the quality adjusted life year (QALY). A UK perspective is adopted, with costs incurred by the patient or wider society not considered. Standard NICE discount rates for utilities and costs of 3.5% per annum are used. [7] A lifetime horizon is adopted, and in order to incorporate the effect of uncertainty on predicted outcomes, 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

Warfarin, rivaroxaban, and dabigatran are each recommended in patients with different clinical characteristics. Warfarin is recommended in patients with a CHADS2 score of one or more; the recent NICE recommendations for rivaroxaban are equivalent to stating that patients with a CHADS2 score of one or more should receive it; and recent NICE recommendations for dabigatran are equivalent to stating that patients with a CHADS2 score of one or more should receive it if they are also aged 65 years or more[8,9]. The scenarios in which a TTE may affect the OAC decision are described in Table 1.

## 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 patient are generated, and whether or not an LAABN was identified and hence an OAC was prescribed is 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 are assumed could lead to death, or they may die from another cause. Each of these events has associated cost and utility implications. By simulating the outcomes for a large number of patients, the average associated costs and utilities following alternative diagnostic strategies (with and without the use of TTE) were estimated, allowing estimation of the mean costs and mean QALYs for both strategies, and from these the incremental cost effectiveness ratio (ICER) of including TTE in the diagnostic package.

In the baseline strategies, none of the patients with LA ABN were treated with the OAC even though their high stroke risk means that the benefits would on average outweigh the risks. In the comparator strategy, a percentage of these patients with LA ABN would receive the OAC due to TTE correctly identifying LA ABN, dependent on sensitivity of TTE. However, when specificity is less than perfect a proportion of patients without LA ABN would also receive it.

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

* Proportion of true positives = TPHR x sensitivity;
* Proportion of true negatives = (1 –TPHR) x specificity;
* Proportion of false positives = (1 – TPHR) x (1 – specificity);
* Proportion of false negatives = TPHR x (1 – sensitivity).

Within the context of the model, the baseline strategy (no TTE) can be considered a diagnostic strategy with a sensitivity of zero and a specificity of one, so the baseline population mix comprises TPHR false negatives and the remainder (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 has different utilities, probabilities 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. [10]

The model is updated when events occur that affect an individual’s stroke or 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 CHADS2 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 (Glasgow Outcome Scale category 2) as a result of taking OACs, their life expectancy was reduced to a maximum of 3.6 years with no QALY gain. [11] 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. [12]

## 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 Table 2.

## Estimating cost effectiveness

The scatterplots of estimates produced by the PSA provide an indication of the clinical and cost-effectiveness of the TTE option compared with the no TTE option. If the majority of the scatter are in the north west quadrant of these graphs, then this indicates that the TTE option is both more costly and less effective than the no TTE option, and this is said to be ruled out by simple dominance. Scatter in the north east quadrant indicates that, compared with no TTE, TTE is both more expensive but also more clinically effective; in these cases, it is important to identify whether the ratio of incremental costs to incremental benefits – the incremental cost-effectiveness ratio (ICER) - is below a given threshold value, defined as maximum acceptable incremental cost effectiveness ratios (MAICERS). Treatment options are usually described as ‘cost effective’ if their ICER is below the MAICER, and not cost effective otherwise. The probabilities that the addition of TTE is cost-effective at was calculated for MAICERs ranging from £0/QALY to £50,000/QALY. This information was used to create cost-effectiveness acceptability frontiers (CEAFs) for each of the scenarios. CEAFs show the probability of the adoption decision being cost-effective. [13]

## Deterministic sensitivity analyses

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

# Results

Due to the large number of scenarios run, for brevity only the results for two scenarios are discussed in detail, although the results for the other scenarios are also provided and the implications briefly summarised. These two scenarios are of fifty year old males with initial CHADS2 scores of zero, and where the clinical decision to make is whether to prescribe either a) warfarin, or b) rivaroxaban, as the OAC.

Table 3 compares the simulated patient experience when TTE is added to the decision making process either for fifty year old males with an initial CHADS2 score of zero, where the clinical decision is to prescribe either a) warfarin or b) rivaroxaban. For both cohorts the effect of using TTE to inform the decision is to increase the number of life years, decrease the proportion of patients dying of strokes, but increase the proportion dying of major bleeding events. While the proportion of patients suffering strokes is decreased in the TTE arms compared with the No TTE arms, the proportion experiencing either intracranial haemorrhages (ICH) or nonintracranial haemorrhages (NICH) is increased.

For the cohort of fifty year old males with a CHADS2 score of zero, Table 4 presents the following: a) a scatterplot of one thousand probabilistic sensitivity analysis runs; b) the cost effectiveness acceptability frontier (CEAF); c) the mean cost and mean QALY associated with each option, and the ICER, with jackknifed 95% confidence interval, associated with these mean values. [14] Table 5 presents the equivalent information for the cohort with an initial CHADS2 score of one point.

For the cohort with an initial CHADS2 score of zero points (Table 4), the scatterplot shows that (a) that the majority of the estimates are in the north west quadrant, indicating that the TTE strategy is dominated by (is both more expensive and less effective than) the No TTE strategy and the mean ICER is negative. These results suggest that TTE can harm patients falsely diagnosed with LA ABN due to higher bleed risks with little reduction in absolute stroke risk. The CEAF indicates that the no TTE strategy is the adoption strategy at all MAICER levels between £0 and £50,000/QALY. The estimated probability of TTE being cost effective is only 7.8% at a MAICER of £20,000/QALY, and 9.6% at a MAICER of £30,000/QALY.

## Deterministic sensitivity analyses

Table 7 shows how the mean ICER estimated depends on sensitivity and specificity of the technology, assuming all other values are held at their mean levels. These results indicate that the most favourable ICER of TTE in this context could be around £3,600/QALY in the cohort with a CHADS2 score of zero (a), and £3,300/QALY in the cohort with an initial CHADS2 score of one (b). This is seen by considering the bottom right cells, where both sensitivity and specificity are 1, i.e. a perfect test. In the CHADS2 of one point cohort, TTE remains a cost-effective strategy compared with No TTE, almost irrespective of the sensitivity and specificity of the test. For the cohort with a CHADS2 score of zero, TTE only appears cost effective, assuming a MAICER of £20,000/QALY, where both sensitivity and specificity are very high, near the bottom right hand corner of the table.

## Overview of results for other scenarios

The results for all 14 scenarios considered are presented in the online appendix. A brief summary, indicating whether the results suggest TTE appears the optimal strategy at MAICERs of £20,000 /QALY or £30,000/QALY, is shown in Table 8. These results suggest that using TTE to make the decision whether to prescribe warfarin may be cost-effective in all patients with a CHADS2 score of one point. It also suggests that it may be cost effective to use TTE to help make the decision whether to prescribe dabigatran in older patients (aged 65 years), and it may be borderline cost effective, if assuming a MAICER of £30,000/QALY, to use TTE to make the decision whether to prescribe rivaroxaban in older patients (age 65 years). Gender has a slight effect on these results, but the choice of OAC, initial CHADS2 risk score, and patient age appear to have much greater influence.

# Discussion

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. This review identified no economic evaluations of the use of TTE in AF patients, so it is believed that this is the first.

The model has a range of limitations and a number of assumptions have been made within the modelling. For example, only the CHADS2 clinical risk prediction tool was used as the baseline strategy. An alternative to this tool is CHA2DS2-VASc, which is considered to be better at distinguishing low risk from very low risk patients. [15,16] CHA2DS2-VASc was not used in these analyses as CHADS2 is the more established instrument, and the recent NICE recommendations for the use of dabigatran and rivaroxaban both map onto specific CHADS2 risk scores, but not specific CHA2DS2-VASc risk scores. [8,9] The dose of dabigatran was set 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 is 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 corresponds to an increased proportion of ‘false positives’ being included in the patient population mix, and so TTE results in a considerable number of people effectively experiencing increased risks of bleed without the increased benefits in terms of stroke risk reduction estimated in patients with a higher risk of stroke. If TTE were found to be superior to TOE at identifying certain types of LA 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. [17]

A key uncertainty is whether there are other benefits that are accrued from a TTE other than identifying LA 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. As Table 7b 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 (LA ABN positive) 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 is likely to significantly improve the accuracy and validity of the mathematical models. The extent to which these cost-effectiveness estimated relates to healthcare in the UK depends on how similar the populations and healthcare systems are, which could be a matter for further research.

Additional research that would improve the validity of the model include identifying any additional 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

Should TTE be recommended for those patients with CHADS2 scores of zero or one point, 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 found that using TTE appears cost effective when the OAC of choice is warfarin and the patient population has a CHADS2 risks score of one point, but not zero points. It also found that when rivaroxaban or dabigatran is the OACs of choice then it appears cost-effective to use TTE in patients aged 65 years. These results suggest that, irrespective of the OAC, it may be both clinically effective and cost effective to use TTE to help inform the decision in all but the patients with the lowest estimated stroke risk.

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Figure 1 Graphical representation of the mathematical model

|  |  |  |  |
| --- | --- | --- | --- |
| **CHADS2 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, CHADS2 score of zero | No † | Yes | Yes |
| Females, age 50, CHADS2 score of zero | No † | Yes | Yes |
| Males, age 65, CHADS2 score of zero | Yes | Yes | Yes |
| Females, age 65, CHADS2 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

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Category** | **Description** | **References** |
| **Risks/Probabilities** | Death from other causes | Nonparametric | UK Lifetables. [17] |
| Sensitivity and Specificity of TTE in detecting LA ABN | Jointly estimated from Dirichlet distribution  (FN, TP, TN, FP) =  (5, 87, 83, 159) | Table 2 of Providencia et al 2012 [6] |
| Proportion of patients with LA ABN | Beta(2.5, 22.5) for CHADS2  Beta(0.5, 11.5) for CHA2DS2-VASc  (Both with prior of 0.5 added to both cell counts.) | Table 2 of Providencia et al 2012 [6] |
| Annual stroke risk by CHADS2 score | Simulated from Lognormal distribution | Friberg 2012[18] |
| Annual stroke risk in those with LA ABN | Simulated from Lognormal distribution | Connolly et al 2009 [19] |
| Relative risk (RR) of stroke in patients receiving dabigatran | Indirect comparison simulation approach | Lip et al 2006 for RR of warfarin compared with placebo [20]  Eikelboom et al 2011 for RR of dabigatran compared with warfarin[12] |
| Annual major bleeding risk for patients receiving dabigatran | Stratified by age. Credible interval calculated using simulation approach | Eikelboom et al 2011 [12] |
| Outcome following stroke | Simulation & mapping based approach | Method described in report using results published in Rivero-Arias et al 2010 [21] |
| Outcome following a major bleeding event | Previous estimates | Simpson et al 2010 [22] |
| **Utilities** | Baseline utilities by age and gender | Regression based approach | Ara et al 2010 [23] |
| Utility multiplier following stroke, utility multiplier following major non-fatal intracranial bleed | Simulation & mapping based approach | Method described in report results published in  Rivero-Arias et al 2010 [21] |
| **Costs** | Annual cost of dabigatran | £920.43 | NICE FAD, 2011 [24] |
| Annual cost of rivaroxaban | £767 | London New Drugs Group [25] |
| Annual cost of warfarin | £252 to £259 including monitoring costs | BNF [26] |
| Cost of TTE | £66 | NHS Reference Costs [27] |
| Cost of death due to stroke | £7,019 (95% CrI £6,975 to £7,064) | Sandercock et al 2002 [28] |
| Costs in stroke survivors | Various. Differing according to dependent and independent states. Subdivided into ongoing and continuing costs | NHS Reference Costs [27]  NHS Stroke Strategy Impact Assessment [29]  Unit Costs of Health and Social Care 2010 [30] |
| Costs of fatal bleed | Assumed identical to costs of death due to stroke | |
| Costs of nonfatal bleed | Various  Depends on whether bleed is gastrointestinal or intracranial. If intracranial, depends on severity of resulting disability | NHS Reference Costs [27] |

Table 2 Parameters used in model

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Strategy |  | Cause of Death (%) | | | Average Number of Events | | | |
| Life Years | Stroke | Bleed | Other | Dependent Strokes | Independent Strokes | ICH | NICH |
| warfarin | No initial treatment | 28.840 | 11.7 | 1.3 | 87.1 | 0.120 | 0.242 | 0.010 | 0.075 |
| TTE with those diagnosed with LA ABN treated | 28.928 | 10.8 | 1.8 | 87.4 | 0.111 | 0.223 | 0.014 | 0.112 |
| rivaraxoaban | No initial treatment | 28.861 | 11.5 | 1.3 | 87.2 | 0.117 | 0.239 | 0.010 | 0.075 |
| TTE with those diagnosed with LA ABN treated | 28.963 | 10.5 | 1.8 | 87.6 | 0.108 | 0.219 | 0.014 | 0.113 |
| TTE = Transthoracic Echocardiography; LA ABN = Left Atrial Abnormality; ICH = Intracranial haemorrhage; NICH = Non- intracranial haemorrhage | | | | | | | | | |

Table 3 Simulated patient experience: fifty year old males with a CHADS2 score of zero, where the OAC prescribed is either a) warfarin, or b) rivaroxaban

Table 4 Cost effectiveness information for the scenario where TTE is used to inform the decision whether to prescribe Warfarin to fifty year old males with an initial CHADS2 score of zero (Dashed lines in the cost-effectiveness acceptability frontier indicate that the No TTE strategy is optimal, and solid lines indicate that the TTE strategy is optimal)

|  |  |
| --- | --- |
| X:\EchoAF\R\Figures\W_50_0_M__PSA.jpeg | X:\EchoAF\R\Figures\W_50_0_M__CEAF.jpeg |
| a ) Scatterplot of difference in costs (£) against differences in QALYs | b) Cost-effectiveness Acceptability Frontier |
| |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | |  | **Mean Cost** | **Mean QALY** |  |  | **Mean** | **Jackknifed 95% Credible Intervals** | | | | | | | *No TTE* | £ 2,459 | 13.60 |  | ***ICER (£/QALY)*** | -£ 26,489 | -£ 26,552 | to | | -£ 26,408 | |  | | *TTE* | £ 4,712 | 13.51 |  | *Interpretation:* | *Dominated* | | |  | |  |  | | |
| c) Mean costs, QALYs and ICERs | |

Table 5 Cost effectiveness information for the scenario where TTE is used to inform the decision whether to prescribe Warfarin to fifty year old males with an initial CHADS2 score of one (Dashed lines in the cost-effectiveness acceptability frontier indicate that the No TTE strategy is optimal, and solid lines indicate that the TTE strategy is optimal)

|  |  |
| --- | --- |
| X:\Echo AF\EchoAF\R\Figures\W_50_1_M__PSA.jpeg | X:\Echo AF\EchoAF\R\Figures\W_50_1_M__CEAF.jpeg |
| a ) Scatterplot of difference in costs (£) against differences in QALYs | b) Cost-effectiveness Acceptability Frontier |
| |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | |  | **Mean Cost** | **Mean QALY** |  |  | **Mean** | **Jackknifed 95% Credible Intervals** | | | | | | *No TTE* | £ 7,334 | 12.00 |  | ***ICER (£/QALY)*** | £ 6,274 | £ 7,296 | to | £ 6,278 | |  | | *TTE* | £ 10,343 | 12.48 |  | *Interpretation:* | *Neither dominated nor dominating. Appears cost effective at £20,000/QALY* | | | |  |  | | |
| c) Mean costs, QALYs and ICERs | |

Table 7 Illustration of the effect of different levels of sensitivity and specificity on ICER of TTE compared with no TTE in cohorts of male patients aged fifty in making the decision whether to prescribe warfarin. 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)

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| ***CHADS2*** | | *Sensitivity* | | | | | | | | | | |
| ***of zero*** | | **0** | **0.1** | **0.2** | **0.3** | **0.4** | **0.5** | **0.6** | **0.7** | **0.8** | **0.9** | **1** |
| *Specificity* | **0** | D | D | D | D | D | D | D | D | D | D | ∞ |
| **0.1** | D | D | D | D | D | D | D | D | D | D | 8.4 |
| **0.2** | D | D | D | D | D | D | D | D | D | D | 5.7 |
| **0.3** | D | D | D | D | D | D | D | D | D | 70.7 | 4.9 |
| **0.4** | D | D | D | D | D | D | D | D | D | 26.2 | 4.4 |
| **0.5** | D | D | D | D | D | D | D | D | >99 | 17.1 | 4.2 |
| **0.6** | D | D | D | D | D | D | D | D | 65.6 | 13.1 | 4.0 |
| **0.7** | D | D | D | D | D | D | D | D | 35.0 | 10.9 | 3.8 |
| **0.8** | D | D | D | D | D | D | D | >99 | 24.5 | 9.5 | 3.8 |
| **0.9** | D | D | D | D | D | D | D | 63.9 | 19.2 | 8.5 | 3.7 |
| **1** | D | D | D | D | D | D | >99 | 40.2 | 16.0 | 7.8 | 3.6 |

Table 8 Qualitative summary of results of all 10 scenarios

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Age | Gender | OAC | Incremental cost effectiveness ratio (TTE) of TTE compared with no TTE | 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 |  | No | No |
| 65 | female | warfarin |  | No | No |
| 50 | male | rivaroxaban | NA: Simple dominance | No | No |
| 50 | female | rivaroxaban | NA: Simple dominance | No | No |
| 65 | male | rivaroxaban |  | No | No [[1]](#footnote-1) |
| 65 | female | rivaroxaban |  | No | Yes |
| 65 | male | dabigatran |  | Yes | Yes |
| 65 | female | dabigatran |  | Yes | Yes |

# Appendix

## Sensitivity and Specificity tables

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| |  |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | ***W\_50*** | | *Sensitivity* | | | | | | | | | | | | ***0\_M*** | | **0** | **0.1** | **0.2** | **0.3** | **0.4** | **0.5** | **0.6** | **0.7** | **0.8** | **0.9** | **1** | | *Specificity* | **0** | D | D | D | D | D | D | D | D | D | D | ∞ | | **0.1** | D | D | D | D | D | D | D | D | D | D | 8.4 | | **0.2** | D | D | D | D | D | D | D | D | D | D | 5.7 | | **0.3** | D | D | D | D | D | D | D | D | D | 70.7 | 4.9 | | **0.4** | D | D | D | D | D | D | D | D | D | 26.2 | 4.4 | | **0.5** | D | D | D | D | D | D | D | D | >99 | 17.1 | 4.2 | | **0.6** | D | D | D | D | D | D | D | D | 65.6 | 13.1 | 4.0 | | **0.7** | D | D | D | D | D | D | D | D | 35.0 | 10.9 | 3.8 | | **0.8** | D | D | D | D | D | D | D | >99 | 24.5 | 9.5 | 3.8 | | **0.9** | D | D | D | D | D | D | D | 63.9 | 19.2 | 8.5 | 3.7 | | **1** | D | D | D | D | D | D | >99 | 40.2 | 16.0 | 7.8 | 3.6 | |
| 1. W\_50\_0\_M |
| |  |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | ***W\_50*** | | *Sensitivity* | | | | | | | | | | | | ***0\_F*** | | **0** | **0.1** | **0.2** | **0.3** | **0.4** | **0.5** | **0.6** | **0.7** | **0.8** | **0.9** | **1** | | *Specificity* | **0** | D | D | D | D | D | D | D | D | D | D | ∞ | | **0.1** | D | D | D | D | D | D | D | D | D | D | 8.4 | | **0.2** | D | D | D | D | D | D | D | D | D | D | 5.9 | | **0.3** | D | D | D | D | D | D | D | D | D | 56.8 | 5.0 | | **0.4** | D | D | D | D | D | D | D | D | D | 25.2 | 4.6 | | **0.5** | D | D | D | D | D | D | D | D | >99 | 17.1 | 4.4 | | **0.6** | D | D | D | D | D | D | D | D | 53.2 | 13.4 | 4.2 | | **0.7** | D | D | D | D | D | D | D | >99 | 32.3 | 11.2 | 4.1 | | **0.8** | D | D | D | D | D | D | D | 97.4 | 23.7 | 9.9 | 4.0 | | **0.9** | D | D | D | D | D | D | D | 52.0 | 19.1 | 8.9 | 3.9 | | **1** | D | D | D | D | D | D | >99 | 36.2 | 16.2 | 8.2 | 3.9 | |
| 1. W\_50\_0\_F |
| |  |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | ***W\_65*** | | *Sensitivity* | | | | | | | | | | | | ***0\_M*** | | **0** | **0.1** | **0.2** | **0.3** | **0.4** | **0.5** | **0.6** | **0.7** | **0.8** | **0.9** | **1** | | *Specificity* | **0** | D | D | D | D | D | D | D | D | D | D | ∞ | | **0.1** | D | D | D | D | D | D | D | D | D | D | 8.9 | | **0.2** | D | D | D | D | D | D | D | D | D | 29.8 | 4.9 | | **0.3** | D | D | D | D | D | D | D | D | 62.8 | 13.9 | 3.6 | | **0.4** | D | D | D | D | D | D | D | >99 | 25.0 | 9.3 | 2.9 | | **0.5** | D | D | D | D | D | D | >99 | 38.8 | 15.9 | 7.1 | 2.5 | | **0.6** | D | D | D | D | D | >99 | 56.6 | 23.4 | 11.8 | 5.8 | 2.3 | | **0.7** | D | D | D | D | D | 80.4 | 32.1 | 16.9 | 9.4 | 5.0 | 2.1 | | **0.8** | D | D | D | D | >99 | 42.3 | 22.6 | 13.3 | 7.9 | 4.4 | 1.9 | | **0.9** | D | D | D | >99 | 54.5 | 28.9 | 17.5 | 11.0 | 6.9 | 4.0 | 1.8 | | **1** | D | D | >99 | 69.3 | 36.1 | 22.1 | 14.4 | 9.5 | 6.1 | 3.6 | 1.7 |  1. W\_65\_0\_M |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| |  |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | ***W\_65*** | | Sensitivity | | | | | | | | | | | | ***0\_F*** | | **0** | **0.1** | **0.2** | **0.3** | **0.4** | **0.5** | **0.6** | **0.7** | **0.8** | **0.9** | **1** | | *Specificity* | **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 | 39.8 | 12.9 | 3.4 | | **0.4** | D | D | D | D | D | D | >99 | 54.5 | 20.9 | 9.0 | 2.8 | | **0.5** | D | D | D | D | D | >99 | 68.6 | 28.8 | 14.4 | 7.0 | 2.5 | | **0.6** | D | D | D | D | >99 | 82.0 | 36.5 | 19.8 | 11.1 | 5.8 | 2.3 | | **0.7** | D | D | D | >99 | 94.7 | 44.0 | 25.1 | 15.2 | 9.1 | 5.0 | 2.1 | | **0.8** | D | D | >99 | >99 | 51.3 | 30.3 | 19.2 | 12.4 | 7.8 | 4.5 | 2.0 | | **0.9** | D | >99 | >99 | 58.4 | 35.4 | 23.2 | 15.7 | 10.6 | 6.9 | 4.1 | 1.9 | | **1** | >99 | >99 | 65.4 | 40.4 | 27.1 | 18.9 | 13.3 | 9.2 | 6.1 | 3.7 | 1.8 | |
| 1. W\_65\_0\_F |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| |  |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | ***R\_50*** | | *Sensitivity* | | | | | | | | | | | | ***0\_M*** | | **0** | **0.1** | **0.2** | **0.3** | **0.4** | **0.5** | **0.6** | **0.7** | **0.8** | **0.9** | **1** | | *Specificity* | **0** | D | D | D | D | D | D | D | D | D | D | ∞ | | **0.1** | D | D | D | D | D | D | D | D | D | D | 7.5 | | **0.2** | D | D | D | D | D | D | D | D | D | D | 5.1 | | **0.3** | D | D | D | D | D | D | D | D | D | 38.2 | 4.3 | | **0.4** | D | D | D | D | D | D | D | D | D | 19.0 | 3.9 | | **0.5** | D | D | D | D | D | D | D | D | 82.0 | 13.3 | 3.6 | | **0.6** | D | D | D | D | D | D | D | D | 35.4 | 10.5 | 3.5 | | **0.7** | D | D | D | D | D | D | D | >99 | 23.2 | 8.9 | 3.3 | | **0.8** | D | D | D | D | D | D | D | 54.8 | 17.7 | 7.8 | 3.2 | | **0.9** | D | D | D | D | D | D | >99 | 34.4 | 14.5 | 7.1 | 3.2 | | **1** | D | D | D | D | D | D | 78.5 | 25.5 | 12.4 | 6.5 | 3.1 | |
| 1. R\_50\_0\_M |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| |  |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | ***R\_50*** | | *Sensitivity* | | | | | | | | | | | | ***0\_F*** | | **0** | **0.1** | **0.2** | **0.3** | **0.4** | **0.5** | **0.6** | **0.7** | **0.8** | **0.9** | **1** | | *Specificity* | **0** | D | D | D | D | D | D | D | D | D | D | ∞ | | **0.1** | D | D | D | D | D | D | D | D | D | D | 7.5 | | **0.2** | D | D | D | D | D | D | D | D | D | D | 5.2 | | **0.3** | D | D | D | D | D | D | D | D | D | 35.2 | 4.4 | | **0.4** | D | D | D | D | D | D | D | D | D | 19.1 | 4.0 | | **0.5** | D | D | D | D | D | D | D | D | 63.0 | 13.7 | 3.8 | | **0.6** | D | D | D | D | D | D | D | D | 32.9 | 11.0 | 3.7 | | **0.7** | D | D | D | D | D | D | D | 90.7 | 22.9 | 9.4 | 3.6 | | **0.8** | D | D | D | D | D | D | D | 46.8 | 17.9 | 8.3 | 3.5 | | **0.9** | D | D | D | D | D | D | >99 | 32.2 | 14.9 | 7.5 | 3.4 | | **1** | D | D | D | D | D | D | 60.7 | 24.8 | 12.9 | 6.9 | 3.4 | |
| 1. R\_50\_0\_F |
| |  |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | ***R\_65*** | | *Sensitivity* | | | | | | | | | | | | ***0\_M*** | | **0** | **0.1** | **0.2** | **0.3** | **0.4** | **0.5** | **0.6** | **0.7** | **0.8** | **0.9** | **1** | | *Specificity* | **0** | D | D | D | D | D | D | D | D | D | D | ∞ | | **0.1** | D | D | D | D | D | D | D | D | D | >99 | 8.0 | | **0.2** | D | D | D | D | D | D | D | D | >99 | 20.4 | 4.4 | | **0.3** | D | D | D | D | D | D | D | >99 | 31.5 | 10.8 | 3.1 | | **0.4** | D | D | D | D | D | D | >99 | 41.5 | 16.9 | 7.5 | 2.5 | | **0.5** | D | D | D | D | D | >99 | 50.7 | 22.7 | 11.7 | 5.8 | 2.2 | | **0.6** | D | D | D | D | >99 | 59.1 | 28.2 | 15.7 | 9.0 | 4.8 | 1.9 | | **0.7** | D | D | D | >99 | 66.7 | 33.4 | 19.6 | 12.1 | 7.4 | 4.1 | 1.7 | | **0.8** | D | D | >99 | 73.8 | 38.4 | 23.4 | 15.2 | 9.9 | 6.3 | 3.6 | 1.6 | | **0.9** | D | >99 | 80.3 | 43.2 | 27.1 | 18.1 | 12.4 | 8.4 | 5.5 | 3.3 | 1.5 | | **1** | >99 | 86.3 | 47.7 | 30.6 | 21.0 | 14.8 | 10.5 | 7.3 | 4.9 | 3.0 | 1.4 | |
| 1. R\_65\_0\_M |
| |  |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | ***R\_65*** | | *Sensitivity* | | | | | | | | | | | | ***0\_F*** | | **0** | **0.1** | **0.2** | **0.3** | **0.4** | **0.5** | **0.6** | **0.7** | **0.8** | **0.9** | **1** | | *Specificity* | **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 | |
| 1. R\_65\_0\_F |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| |  |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | ***D\_65*** | | *Sensitivity* | | | | | | | | | | | | ***0\_M*** | | **0** | **0.1** | **0.2** | **0.3** | **0.4** | **0.5** | **0.6** | **0.7** | **0.8** | **0.9** | **1** | | *Specificity* | **0** | D | D | D | D | D | D | D | D | D | D | ∞ | | **0.1** | D | D | D | D | D | D | D | D | D | 44.1 | 6.8 | | **0.2** | D | D | D | D | D | D | D | >99 | 36.0 | 12.8 | 3.6 | | **0.3** | D | D | D | D | D | >99 | 84.7 | 33.4 | 16.2 | 7.6 | 2.5 | | **0.4** | D | D | D | D | >99 | 62.0 | 32.0 | 18.3 | 10.5 | 5.5 | 1.9 | | **0.5** | D | D | >99 | >99 | 52.3 | 31.2 | 19.8 | 12.7 | 7.9 | 4.3 | 1.6 | | **0.6** | >99 | >99 | 79.3 | 46.9 | 30.7 | 20.9 | 14.4 | 9.8 | 6.3 | 3.6 | 1.4 | | **0.7** | >99 | 66.5 | 43.5 | 30.3 | 21.8 | 15.8 | 11.4 | 8.0 | 5.3 | 3.1 | 1.2 | | **0.8** | 58.8 | 41.1 | 30.0 | 22.4 | 16.9 | 12.7 | 9.4 | 6.7 | 4.5 | 2.7 | 1.1 | | **0.9** | 39.3 | 29.8 | 22.9 | 17.8 | 13.8 | 10.6 | 8.0 | 5.8 | 4.0 | 2.4 | 1.0 | | **1** | 29.6 | 23.4 | 18.6 | 14.8 | 11.7 | 9.2 | 7.0 | 5.2 | 3.6 | 2.2 | 1.0 | |
| 1. D\_65\_0\_M |
| |  |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | ***D\_65*** | | *Sensitivity* | | | | | | | | | | | | ***0\_F*** | | **0** | **0.1** | **0.2** | **0.3** | **0.4** | **0.5** | **0.6** | **0.7** | **0.8** | **0.9** | **1** | | *Specificity* | **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 | |
| 1. D\_65\_0\_F |

# Fifty year old males, initial CHADS2 score of 0, treated with Warfarin

## Results

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Cause of Death (%) | | | Average Number of Events | | | |
| Strategy | Life Years | Stroke | Bleed | Other | Dependent Strokes | Independent Strokes | ICH | NICH |
| No initial treatment | 28.840 | 11.7 | 1.3 | 87.1 | 0.120 | 0.242 | 0.010 | 0.075 |
| TTE with those diagnosed with LA ABN treated | 28.928 | 10.8 | 1.8 | 87.4 | 0.111 | 0.223 | 0.014 | 0.112 |
| TTE = Transthoracic Echocardiography; LA ABN = Left Atrial Abnormality; ICH = Intracranial haemorrhage; NICH = Non- intracranial haemorrhage | | | | | | | | |

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| --- | --- |
| X:\EchoAF\R\Figures\W_50_0_M__PSA.jpeg | X:\EchoAF\R\Figures\W_50_0_M__CEAF.jpeg |
| a ) Scatterplot of difference in costs (£) against differences in QALYs | b) Cost-effectiveness Acceptability Frontier |
| |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | ***W\_50\_0\_M*** | **Mean Cost** | **Mean QALY** |  |  | **Mean** | **Jackknifed 95% Credible Intervals** | | | | | | | *No TTE* | £ 2,459 | 13.60 |  | ***ICER (£/QALY)*** | -£ 26,489 | -£ 26,552 | to | | -£ 26,408 | |  | | *TTE* | £ 4,712 | 13.51 |  | *Interpretation:* | *Dominated* | | |  | |  |  | | |
| c) Mean costs, QALYs and ICERs | |

# Fifty year old females with initial CHADS2 score of 0, treated with Warfarin

## Results

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Cause of Death (%) | | | Average Number of Events | | | |
| Strategy | Life Years | Stroke | Bleed | Other | Dependent Strokes | Independent Strokes | ICH | NICH |
| No initial treatment | 31.633 | 13.5 | 1.6 | 84.9 | 0.139 | 0.278 | 0.012 | 0.091 |
| TTE with those diagnosed with LA ABN treated | 31.734 | 12.6 | 2.1 | 85.2 | 0.130 | 0.259 | 0.017 | 0.130 |
| TTE = Transthoracic Echocardiography; LA ABN = Left Atrial Abnormality; ICH = Intracranial haemorrhage; NICH = Non- intracranial haemorrhage | | | | | | | | |

|  |  |
| --- | --- |
| X:\EchoAF\R\Figures\W_50_0_F__PSA.jpeg | X:\EchoAF\R\Figures\W_50_0_F__CEAF.jpeg |
| a ) Scatterplot of difference in costs (£) against differences in QALYs | b) Cost-effectiveness Acceptability Frontier |
| |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | ***W\_50\_0\_F*** | **Mean Cost** | **Mean QALY** |  |  | **Mean** | **Jackknifed 95% Credible Intervals** | | | | | | | *No TTE* | £ 2,815 | 14.27 |  | ***ICER (£/QALY)*** | -£ 34,078 | -£ 34,175 | to | | -£ 33,952 | |  | | *TTE* | £ 5,405 | 14.19 |  | *Interpretation:* | *Dominated* | | |  | |  |  | | |
| c) Mean costs, QALYs and ICERs | |

# Sixty five year old males with initial CHADS2 score of 0, treated with Warfarin

## Results

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Cause of Death (%) | | | Average Number of Events | | | |
| Strategy | Life Years | Stroke | Bleed | Other | Dependent Strokes | Independent Strokes | ICH | NICH |
| No initial treatment | 17.131 | 9.0 | 0.9 | 90.2 | 0.087 | 0.192 | 0.007 | 0.052 |
| TTE with those diagnosed with LA ABN treated | 17.204 | 8.0 | 1.3 | 90.7 | 0.078 | 0.172 | 0.010 | 0.079 |
| TTE = Transthoracic Echocardiography; LA ABN = Left Atrial Abnormality; ICH = Intracranial haemorrhage; NICH = Non- intracranial haemorrhage | | | | | | | | |

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| --- | --- |
| X:\EchoAF\R\Figures\W_65_0_M__PSA.jpeg | X:\EchoAF\R\Figures\W_65_0_M__CEAF.jpeg |
| a ) Scatterplot of difference in costs (£) against differences in QALYs | b) Cost-effectiveness Acceptability Frontier |
| |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | ***W\_65\_0\_M*** | **Mean Cost** | **Mean QALY** |  |  | **Mean** | **Jackknifed 95% Credible Intervals** | | | | | | *No TTE* | £ 1,527 | 9.12 |  | ***ICER (£/QALY)*** | £ 66,793 | £ 66,217 | to | £ 67,599 | |  | | *TTE* | £ 2,467 | 9.13 |  | *Interpretation:* | *Neither dominated nor dominating* | | | |  |  | | |
| c) Mean costs, QALYs and ICERs | |

# Sixty five year old females with initial CHADS2 score of 0, treated with Warfarin

## Results

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Cause of Death (%) | | | Average Number of Events | | | |
| Strategy | Life Years | Stroke | Bleed | Other | Dependent Strokes | Independent Strokes | ICH | NICH |
| No initial treatment | 19.447 | 10.6 | 1.1 | 88.3 | 0.105 | 0.225 | 0.009 | 0.065 |
| TTE with those diagnosed with LA ABN treated | 19.531 | 9.6 | 1.6 | 88.8 | 0.096 | 0.205 | 0.012 | 0.095 |
| TTE = Transthoracic Echocardiography; LA ABN = Left Atrial Abnormality; ICH = Intracranial haemorrhage; NICH = Non- intracranial haemorrhage | | | | | | | | |

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| --- | --- |
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| a ) Scatterplot of difference in costs (£) against differences in QALYs | b) Cost-effectiveness Acceptability Frontier |
| |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | ***W\_65\_0\_F*** | **Mean Cost** | **Mean QALY** |  |  | **Mean** | **Jackknifed 95% Credible Intervals** | | | | | | *No TTE* | £ 1,974 | 9.94 |  | ***ICER (£/QALY)*** | £ 39,485 | £ 39,291 | to | £ 39,754 | |  | | *TTE* | £ 3,106 | 9.97 |  | *Interpretation:* | *Neither dominated nor dominating* | | | |  |  | | |
| c) Mean costs, QALYs and ICERs | |

# Fifty year old males with initial CHADS2 score of 0, treated with Rivaroxaban

## Results

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Cause of Death (%) | | | Average Number of Events | | | |
| Strategy | Life Years | Stroke | Bleed | Other | Dependent Strokes | Independent Strokes | ICH | NICH |
| No initial treatment | 28.861 | 11.5 | 1.3 | 87.2 | 0.117 | 0.239 | 0.010 | 0.075 |
| TTE with those diagnosed with LA ABN treated | 28.963 | 10.5 | 1.8 | 87.6 | 0.108 | 0.219 | 0.014 | 0.113 |
| TTE = Transthoracic Echocardiography; LA ABN = Left Atrial Abnormality; ICH = Intracranial haemorrhage; NICH = Non- intracranial haemorrhage | | | | | | | | |

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| --- | --- |
| X:\EchoAF\R\Figures\R_50_0_M__PSA.jpeg | X:\EchoAF\R\Figures\R_50_0_M__CEAF.jpeg |
| a ) Scatterplot of difference in costs (£) against differences in QALYs | b) Cost-effectiveness Acceptability Frontier |
| |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | ***R\_50\_0\_M*** | **Mean Cost** | **Mean QALY** |  |  | **Mean** | **Jackknifed 95% Credible Intervals** | | | | | | | *No TTE* | £ 2,449 | 13.61 |  | ***ICER (£/QALY)*** | -£ 34,060 | -£ 34,170 | to | | -£ 33,910 | |  | | *TTE* | £ 4,614 | 13.54 |  | *Interpretation:* | *Dominated* | | |  | |  |  | | |
| c) Mean costs, QALYs and ICERs | |

# Fifty year old females with initial CHADS2 score of 0, treated with rivaroxaban

## Results

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Cause of Death (%) | | | Average Number of Events | | | |
| Strategy | Life Years | Stroke | Bleed | Other | Dependent Strokes | Independent Strokes | ICH | NICH |
| No initial treatment | 31.657 | 13.3 | 1.6 | 85.1 | 0.136 | 0.275 | 0.012 | 0.091 |
| TTE with those diagnosed with LA ABN treated | 31.772 | 12.4 | 2.1 | 85.5 | 0.127 | 0.255 | 0.017 | 0.130 |
| TTE = Transthoracic Echocardiography; LA ABN = Left Atrial Abnormality; ICH = Intracranial haemorrhage; NICH = Non- intracranial haemorrhage | | | | | | | | |

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| --- | --- |
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| a ) Scatterplot of difference in costs (£) against differences in QALYs | b) Cost-effectiveness Acceptability Frontier |
| |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | ***R\_50\_0\_F*** | **Mean Cost** | **Mean QALY** |  |  | **Mean** | **Jackknifed 95% Credible Intervals** | | | | | | | *No TTE* | £ 2,779 | 14.27 |  | ***ICER (£/QALY)*** | -£ 47,535 | -£ 47,773 | to | | -£ 47,271 | |  | | *TTE* | £ 5,315 | 14.22 |  | *Interpretation:* | *Dominated* | | |  | |  |  | | |
| c) Mean costs, QALYs and ICERs | |

# Sixty five year old males with initial CHADS2 score of 0, treated with rivaroxaban

## Results

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Cause of Death (%) | | | Average Number of Events | | | |
| Strategy | Life Years | Stroke | Bleed | Other | Dependent Strokes | Independent Strokes | ICH | NICH |
| No initial treatment | 17.141 | 8.8 | 0.9 | 90.3 | 0.085 | 0.190 | 0.007 | 0.052 |
| TTE with those diagnosed with LA ABN treated | 17.221 | 7.8 | 1.3 | 90.9 | 0.076 | 0.169 | 0.010 | 0.080 |
| TTE = Transthoracic Echocardiography; LA ABN = Left Atrial Abnormality; ICH = Intracranial haemorrhage; NICH = Non- intracranial haemorrhage | | | | | | | | |

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| --- | --- |
| X:\EchoAF\R\Figures\R_65_0_M__PSA.jpeg | X:\EchoAF\R\Figures\R_65_0_M__CEAF.jpeg |
| a ) Scatterplot of difference in costs (£) against differences in QALYs | b) Cost-effectiveness Acceptability Frontier |
| |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | ***R\_65\_0\_M*** | **Mean Cost** | **Mean QALY** |  |  | **Mean** | **Jackknifed 95% Credible Intervals** | | | | | | *No TTE* | £ 1,510 | 9.12 |  | ***ICER (£/QALY)*** | £ 30,310 | £ 30,179 | to | £ 30,487 | |  | | *TTE* | £ 2,393 | 9.15 |  | *Interpretation:* | *Neither dominated nor dominating* | | | |  |  | | |
| c) Mean costs, QALYs and ICERs | |

# Sixty five year old females with initial CHADS2 score of 0, treated with rivaroxaban

## Results

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Cause of Death (%) | | | Average Number of Events | | | |
| Strategy | Life Years | Stroke | Bleed | Other | Dependent Strokes | Independent Strokes | ICH | NICH |
| No initial treatment | 19.460 | 10.5 | 1.1 | 88.4 | 0.103 | 0.223 | 0.009 | 0.066 |
| TTE with those diagnosed with LA ABN treated | 19.554 | 9.4 | 1.6 | 89.0 | 0.093 | 0.201 | 0.012 | 0.096 |
| TTE = Transthoracic Echocardiography; LA ABN = Left Atrial Abnormality; ICH = Intracranial haemorrhage; NICH = Non- intracranial haemorrhage | | | | | | | | |

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| --- | --- |
| X:\EchoAF\R\Figures\R_65_0_F__PSA.jpeg | X:\EchoAF\R\Figures\R_65_0_F__CEAF.jpeg |
| a ) Scatterplot of difference in costs (£) against differences in QALYs | b) Cost-effectiveness Acceptability Frontier |
| |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | ***R\_65\_0\_F*** | **Mean Cost** | **Mean QALY** |  |  | **Mean** | **Jackknifed 95% Credible Intervals** | | | | | | *No TTE* | £ 1,955 | 9.95 |  | ***ICER (£/QALY)*** | £ 22,751 | £ 22,681 | to | £ 22,844 | |  | | *TTE* | £ 3,039 | 9.99 |  | *Interpretation:* | *Neither dominated nor dominating* | | | |  | | | |
| c) Mean costs, QALYs and ICERs | |

# Sixty five year old males with initial CHADS2 score of 0, treated with dabigatran

## Results

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Cause of Death (%) | | | Average Number of Events | | | |
| Strategy | Life Years | Stroke | Bleed | Other | Dependent Strokes | Independent Strokes | ICH | NICH |
| No initial treatment | 17.158 | 8.6 | 0.9 | 90.5 | 0.081 | 0.188 | 0.007 | 0.053 |
| TTE with those diagnosed with LA ABN treated | 17.251 | 7.5 | 1.3 | 91.2 | 0.072 | 0.163 | 0.010 | 0.081 |
| TTE = Transthoracic Echocardiography; LA ABN = Left Atrial Abnormality; ICH = Intracranial haemorrhage; NICH = Non- intracranial haemorrhage | | | | | | | | |

|  |  |
| --- | --- |
| X:\EchoAF\R\Figures\D_65_0_M__PSA.jpeg | X:\EchoAF\R\Figures\D_65_0_M__CEAF.jpeg |
| a ) Scatterplot of difference in costs (£) against differences in QALYs | b) Cost-effectiveness Acceptability Frontier |
| |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | ***D\_65\_0\_M*** | **Mean Cost** | **Mean QALY** |  |  | **Mean** | **Jackknifed 95% Credible Intervals** | | | | | | *No TTE* | £ 1,489 | 9.13 |  | ***ICER (£/QALY)*** | £ 14,728 | £ 14,693 | to | £ 14,782 | |  | | *TTE* | £ 2,321 | 9.18 |  | *Interpretation:* | *Neither dominated nor dominating* | | | |  | | | |
| c) Mean costs, QALYs and ICERs | |

# Sixty five year old females with initial CHADS2 score of 0, treated with Dabigatran

## Results

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Cause of Death (%) | | | Average Number of Events | | | |
| Strategy | Life Years | Stroke | Bleed | Other | Dependent Strokes | Independent Strokes | ICH | NICH |
| No initial treatment | 19.485 | 10.2 | 1.1 | 88.7 | 0.099 | 0.220 | 0.009 | 0.066 |
| TTE with those diagnosed with LA ABN treated | 19.598 | 9.0 | 1.6 | 89.4 | 0.089 | 0.195 | 0.012 | 0.097 |
| TTE = Transthoracic Echocardiography; LA ABN = Left Atrial Abnormality; ICH = Intracranial haemorrhage; NICH = Non- intracranial haemorrhage | | | | | | | | |

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|  |  |
| --- | --- |
| X:\EchoAF\R\Figures\D_65_0_F__PSA.jpeg | X:\EchoAF\R\Figures\D_65_0_F__CEAF.jpeg |
| a ) Scatterplot of difference in costs (£) against differences in QALYs | b) Cost-effectiveness Acceptability Frontier |
| |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | ***D\_65\_0\_F*** | **Mean Cost** | **Mean QALY** |  |  | **Mean** | **Jackknifed 95% Credible Intervals** | | | | | | *No TTE* | £ 1,942 | 9.95 |  | ***ICER (£/QALY)*** | £ 12,314 | £ 12,290 | to | £ 12,348 | |  | | *TTE* | £ 2,946 | 10.01 |  | *Interpretation:* | *Neither dominated nor dominating* | | | |  |  | | |
| c) Mean costs, QALYs and ICERs | |

1. The optimal strategy switches from no TTE to TTE at a MAICER of £30,400/QALY. [↑](#footnote-ref-1)