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COST-EFFECTIVENESS ANALYSIS OF APIXABAN VERSUS EDOXABAN FOR STROKE PREVENTION IN NON-VALVULAR ATRIAL FIBRILLATION PORTUGUESE PATIENTS

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BACKGROUND

- **Non-valvular atrial fibrillation (NVAF)** is the most frequent cause of cardiac arrhythmia and the main responsible for stroke and thromboembolic events.
- The last guidelines of European Society of Cardiology[1] recommended **anticoagulation therapy** as a preventive measure of the associated complications.
- Considering the different options available, there is a need of evidence about the **efficiency** of the anticoagulant treatment in these patients.
  - **Apixaban have previously demonstrated to be a cost-effective option** compared to other NOAC: dabigatran[2] and rivaroxaban[3].
  - **Edoxaban** have been approved for stroke prevention in NVAF patients.

OBJECTIVE

- The objective of this study is to assess the **cost-effectiveness** of **apixaban 5 mg b.i.d** (twice a day) compared to **edoxaban (60 mg daily)** for stroke prevention in patients with NVAF in Portugal.

METHODS

- **Patient population**: characteristics of the 1,000 NVAF patients included in the hypothetical cohort assessed were obtained from **ARISTOTLE apixaban trial**[4]:
  - average age (70 years)
  - 35.5% of females
  - mean $CHADS_2$ score (2.1)

- The **efficacy** of therapies, represented in **clinical event rates per 100 patients-year**, and the safety data were derived from a **Bucher indirect treatment comparison** method of two phase III randomized, double-blind warfarin-controlled trials:
  - **ARISTOTLE** trial[4] comparing apixaban versus warfarin
  - **ENGAGE-AF** trial[5] comparing edoxaban versus warfarin

METHODS

A Markov model with **10 health states**[2,3] (clinical events derived from NVAF risk of embolism and anticoagulation) was used to estimate the course of the disease in **6-week cycles**, over the **patients lifetime**.

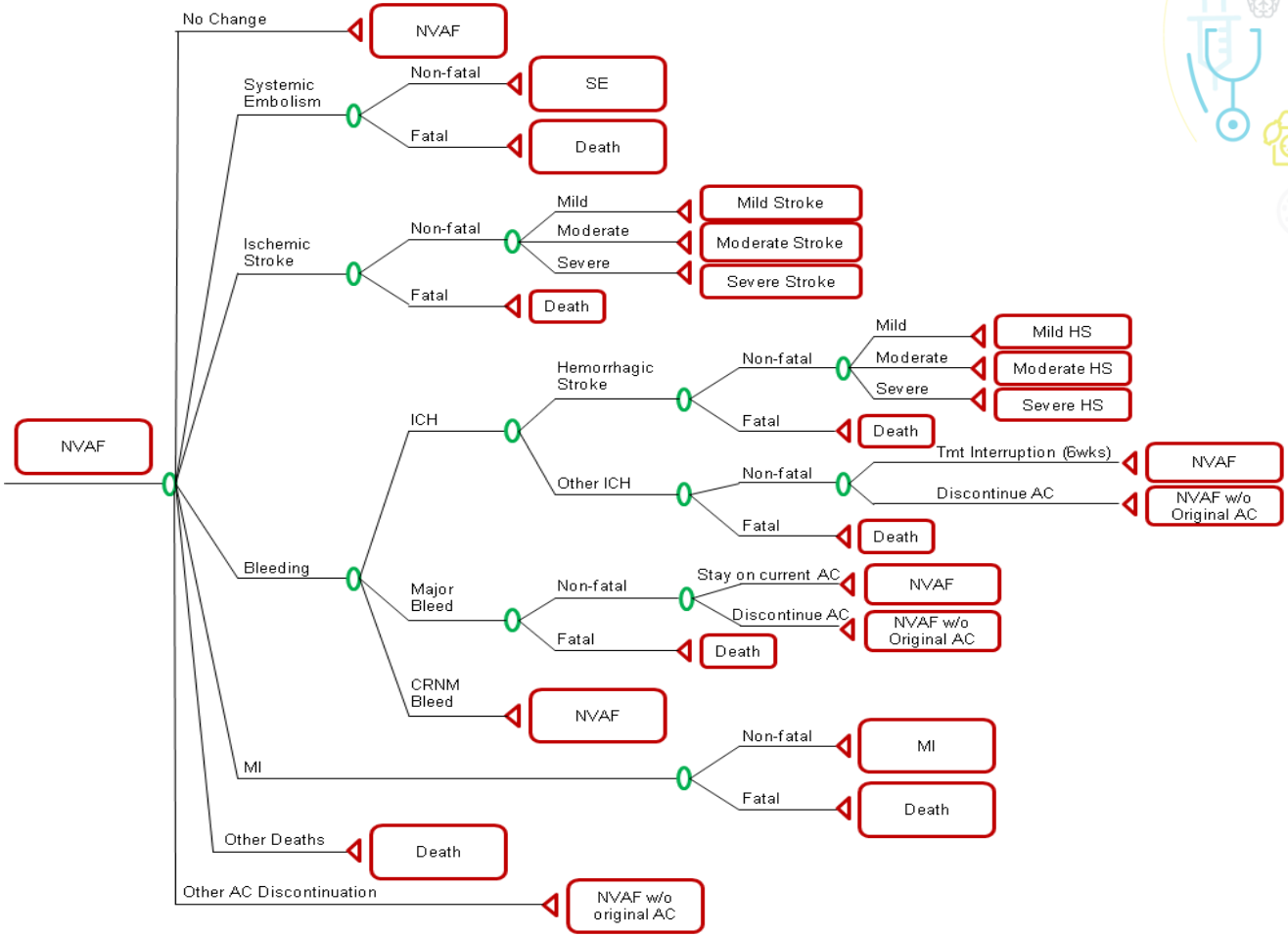

Figure 1. Markov economic model of stroke prevention in NVAF population

AC: anticoagulant;
CRNM: clinically relevant non major;
HS: Hemorrhagic stroke;
ICH: Intracranial hemorrhage;
MI: Myocardial infarction;
NVAF: Non-valvular atrial fibrillation;
SE: Systemic embolism; w/o: without

METHODS

- The estimated **Hazard Ratios (HR) for edoxaban versus apixaban** were applied to event rates of ARISTOTLE trial[4].

- **Acetyl salicylic acid (ASA) administration** was considered as 2nd line for those patients who stopped or withdrew the 1st line therapy with any of the two main drugs assessed.
  - Event rates for ASA derived from a subgroup of patients with prior vitamin K antagonists exposure from the AVERROES trial[6].

- The **utilities** assigned to each health states were derived from scores of **EQ-5D** questionnaire obtained in a sample of NVAF patients in UK[7].

- Temporal **decrements of utilities** were also applied for **complications**.

METHODS

- The analysis was performed from the **National Health System (NHS) perspective**.
- The **total cost (€, 2019)** estimation considered:
  - **Drug acquisition costs**, which were calculated considering retail price including VAT and reimbursement rate 69% applied, and according to SmPC authorized dosages: 10mg/daily for apixaban and 60mg/ daily for edoxaban.
  - Cost of **acute and long-term complications** were obtained from several national databases[8].
  - Cost of yearly **renal monitoring** [9] and monthly-cost of expected **dyspepsy** (1.67%)[4] related to any of the anticoagulant treatments.
  - Cost of **NVAF clinical follow-up** (a routine visit every 3 months)
  - **Non-medical costs** for both for acute and maintenance are referred to informal care cost and were obtained from Portuguese literature.
- **Annual discount rate (5%)**[9] was applied for both, costs and health outcomes.
- **A sensitivity analysis (SA)** was performed to assess the robustness of the model results.

RESULTS

- In a 1,000 NVAF patients cohort, during their lifetime, **apixaban would avoid numerous complications** in comparison to edoxaban.

Number of events in total population	Apixaban	Edoxaban	Difference apixaban vs edoxaban
Ischemic stroke	**248**	**253**	**-5**
Hemorrhagic stroke	**28**	**28**	**0**
Systemic Embolism	**26**	**26**	**0**
Other ICH	**13**	**14**	**-1**
Other major bleeds	**176**	**182**	**-6**
CRNM bleeds	**308**	**337**	**-29**
Myocardial infarction	**91**	**93**	**-2**
Other cardiovascular hospitalization	**1,270**	**1,267**	**3**
Deaths due to stroke, HS, MI, SE	**334**	**336**	**-2**

Table 1a. Clinical events (base case results)

CRNM: Clinically relevant non-major; HS: Hemorrhagic stroke; ICH: Intracranial haemorrhage; MI: Myocardial infarction; SE: Systemic embolism.

RESULTS

Outcomes (per patient)	Apixaban	Edoxaban	Difference apixaban vs edoxaban
Life years gained	8.601	8.555	0.045
QALYs	6.105	6.071	0.034
Costs (per patient) (€)	**Apixaban**	**Edoxaban**	**Difference apixaban vs edoxaban**
Total costs (payer perspective)	€9,555.68	€9,533.40	€25.28
Cost-effectiveness results			
Incremental cost-effectiveness ratio (ICER) (€/LYG)			**€557,36**
Incremental cost-utility ratio (ICUR) (€/QALY gained)			**€739,64**

Table 1b. Incremental costs and outcomes (base case results)

LYG: Life years gained; QALYs: Quality-adjusted life years

RESULTS

- From a NHS perspective, apixaban would yield per each patient:
  - **0.045** life-years gained (LYG)
  - **0.034** additional quality-adjusted-life year (QALY).

- The total **incremental cost** for apixaban compared to edoxaban would be **€25.28** per patient.

- The **incremental cost-utility ratio (ICUR)** of apixaban versus edoxaban resulted in **€739.64 per QALY gained**.

RESULTS

In **probabilistic SA**, **77%** and **79%** of iterations were under an hypothetical willingness-to pay threshold of €20.000/QALY and €30.000/QALY, respectively for NHS perspective.

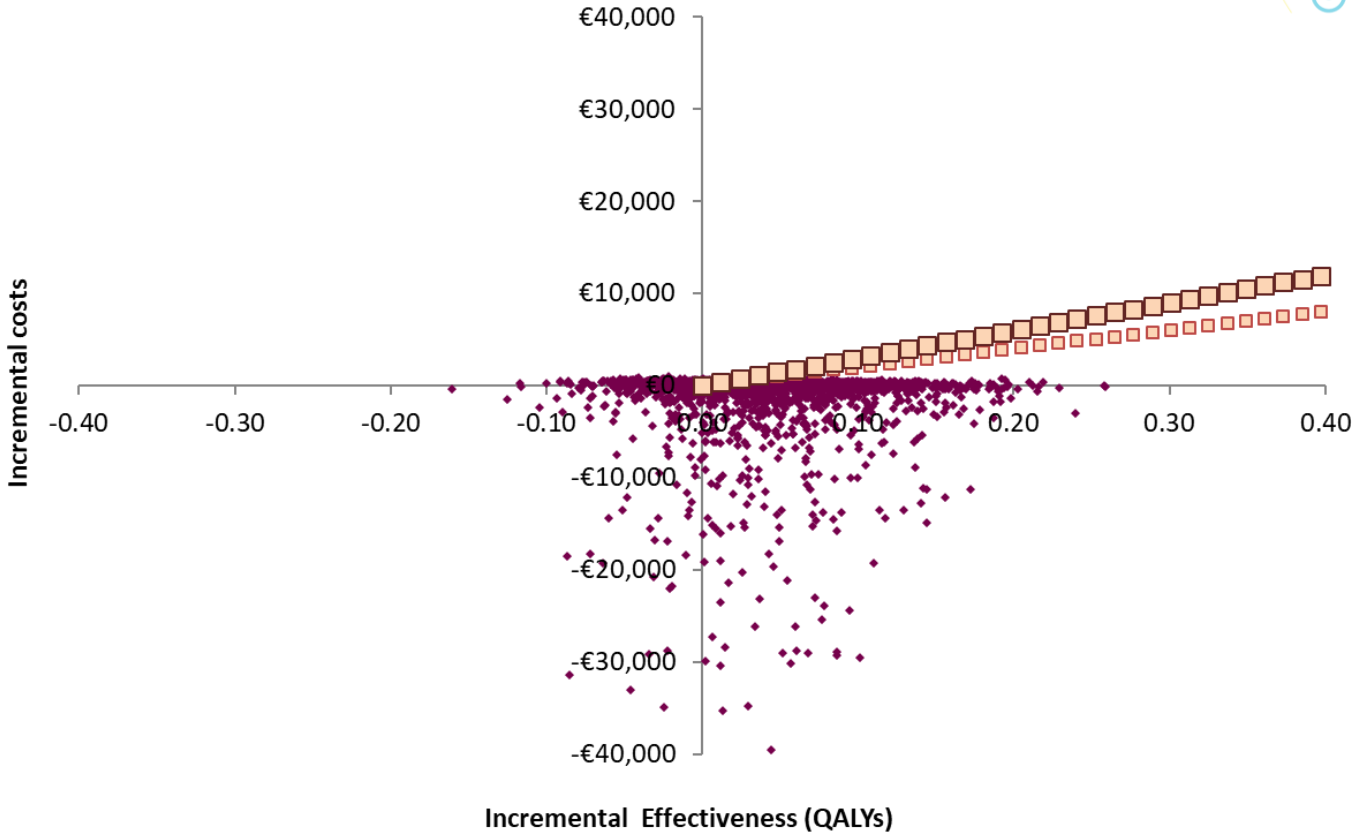

Figure 2 . Probabilistic SA results

CONCLUSION

- According to the shown model outcomes, apixaban could be considered a cost-effective alternative for stroke prevention in NVAF patients in Portugal, when compared with edoxaban.

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