Cost-Effectiveness Analysis of Apixaban versus Edoxaban for Stroke Prevention in Non-Valvular Atrial Fibrillation Spanish Patients

de Andrés-Nogales F[1], Oyagüez I[1], Suárez C[2], López-Sendón JL[3], González-Juanatey JR[4], Suárez J[5], Polanco C[5]

[1] Pharmacoeconomics & Outcomes Research Iberia (PORIB), Madrid, Spain; [2] Internal Medicine Dpt. Hospital de La Princesa, Madrid (Spain); [3] Cardiology Dpt. Hospital Universitario La Paz, Madrid (Spain); [4] Cardiology Dpt. Complejo Hospitalario Universitario Santiago de Compostela, Santiago de Compostela (Spain); [5] Bristol-Myers Squibb, Madrid (Spain)

BACKGROUND

- Prevention of stroke in patients with non-valvular atrial fibrillation (NVAF) with non-vitamin K oral anticoagulant (NOAC) therapies is recommended in the latest guidelines of European Society of Cardiology[1].
- Prior researches showed that apixaban is a cost-effective option versus other NOACs dabigatran[2] and rivaroxaban[3].
- To date, no cost-effectiveness analyses versus edoxaban were retrieved in Spain.
- Edoxaban is the last NOAC introduced in the Spanish market.

OBJECTIVE

- 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 Spain.

METHODS

- The previously developed cost-effectiveness Markov model with 10 health states[2,3] was used to estimate the course of the disease in 6-week cycles, over the patients lifetime in a cohort of 1,000 patients. (Figure 1)

Figure 1. Markov economic model of stroke prevention in NVAF population
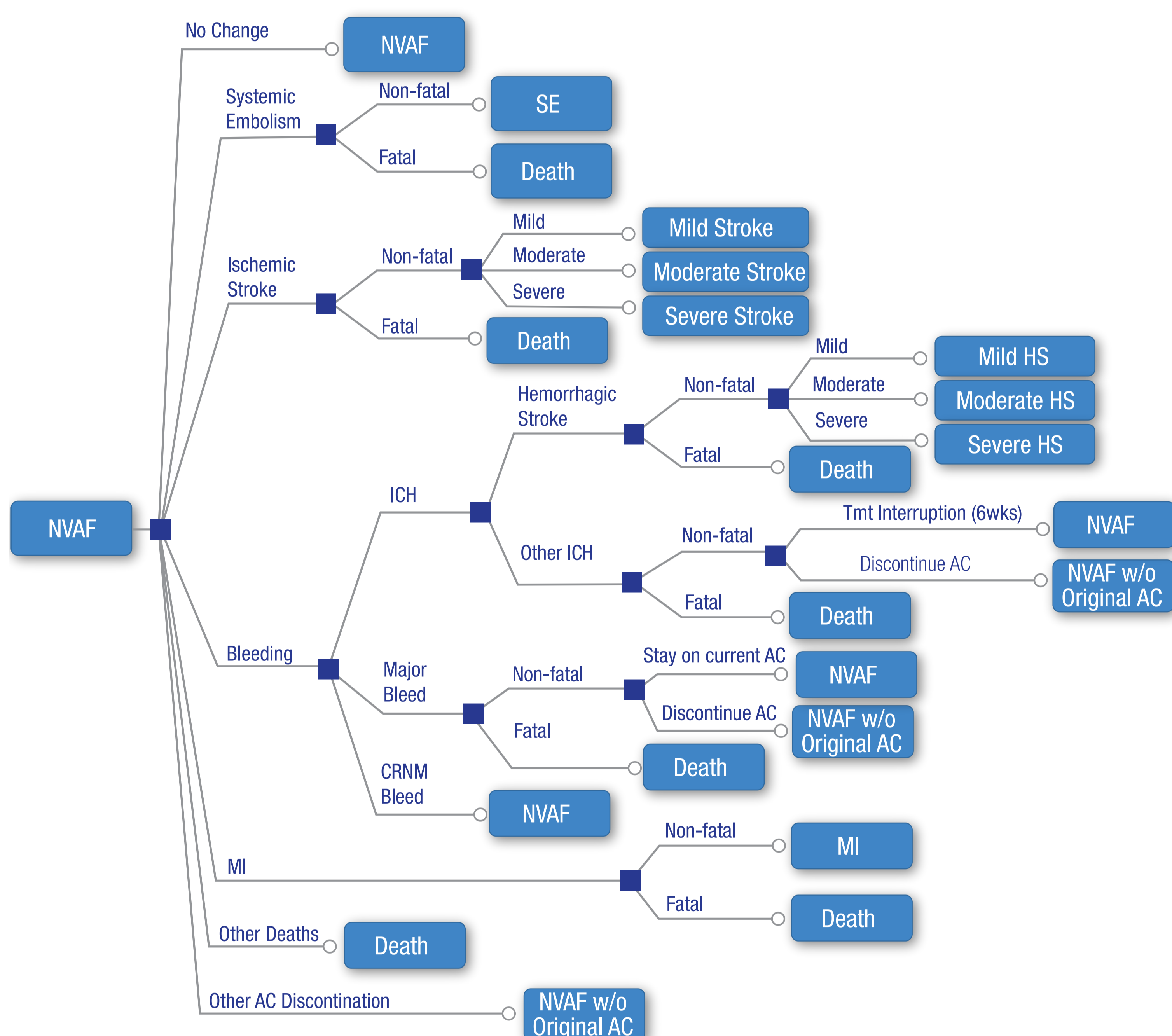
AC: anticoagulant; CRNM: clinically relevant non major; HS: Hemorrhagic stroke; ICH: Intracranial hemorrhage; MI: Myocardial infarction; NVAF: Non-valvular atrial fibrillation; SE: Systemic embolism; w/o: without

- 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 and mean CHADS₂ score (2.1)
- Consistently with previous studies[4], 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, randomised, double-blind warfarin-controlled trials:
  - ARISTOTLE trial[5] comparing apixaban versus warfarin
  - ENGAGE-AF trial[6] comparing edoxaban versus warfarin
- Estimated Hazard ratios for edoxaban versus apixaban were applied to event rates on apixaban arm of ARISTOTLE trial[5].
- Following clinical practice in Spain, acetylsalicylic 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 were derived from a subgroup of patients with prior vitamin K antagonists exposure from the AVERROES trial[7].
- The utilities assigned to each health states were derived from scores of EQ-5D questionnaire obtained in a sample of NVAF patients in UK[8].
- As detailed in previous studies[2-4], temporal decrements of utilities were also applied for complications[8].
- The analysis was performed from the Spanish National Health System (NHS) and societal perspective[9].
- Total cost (€, 2018) estimation considered:
  - Drug acquisition costs, which were calculated considering retail price including VAT (4%)[10] with national mandatory deductions (-7.5%) applied, and according to SmPC authorized dosages: €2.80 daily for apixaban and €2.69 daily for edoxaban.
  - Cost of acute and long-term complications were obtained from several Spanish published sources[2,3].
    - Cost of complications' acute-management represented the average cost of Diagnostic related groups (DRG) official prices, established by the Autonomous Regions.
    - Cost of complications' maintenance-management, estimated as a monthly cost, was obtained from several Spanish published sources.
  - Cost of yearly renal monitoring[11] and monthly-cost of expected dyspepsy (1.67%)[5] related to any of the anticoagulant treatments.
  - Cost of NVAF clinical follow-up (a routine visit every 3 months).
  - Non-medical costs for both acute and maintenance complications- management are referred to informal costs and were obtained from Spanish literature[12].
- Annual discount rate (3%) was applied for both, costs and health outcomes[13].
- Sensitivity analyses (SA) were 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. (Table 1)
- Consequently apixaban would yield 0.056 incremental life-years gained and 0.042 additional qualy-adjusted-life years (QALYs) per patient. (Table 1)
- Total incremental lifetime cost for apixaban compared to edoxaban would be €403 (2.2%) per patient for NHS perspective and €352 (1.0%) per patient for societal perspective.
- Cost per QALY gained with apixaban versus edoxaban resulted €9,606 for NHS perspective and €7,805 for societal perspective. (Table 1)

Table 1. Base case results for a lifetime horizon

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
Outcomes (per patient)	**Apixaban**	**Edoxaban**	**Difference apixaban vs edoxaban**
Life years gained	9.767	9.711	0.056
QALYs	6.924	6.882	0.042
Costs (per patient) (€)	**Apixaban**	**Edoxaban**	**Difference apixaban vs edoxaban**
Total costs (NHS perspective)	€18,887.19	€18,484.14	€403.05
Total costs (societal perspective)	€32,296,89	€31,971.43	€325.46
Incremental cost-effectiveness ratio (€/life year gained)		**Apixaban vs edoxaban**	
NHS perspective		€7,281	
Societal perspective		€5,879	
Incremental cost-utility ratio (€/QALY gained)		**Apixaban vs edoxaban**	
NHS perspective		€9,606	
Societal perspective		€7,805	

CRNM: Clinically relevant non-major; HS: Hemorrhagic stroke; ICH: Intracranial haemorrhage; MI: Myocardial infarction; QALYs: Quality-adjusted life years; SE: Systemic embolism

Figure 2 . Probabilistic Sensitivity Analyses results

NHS perspective

Societal perspective
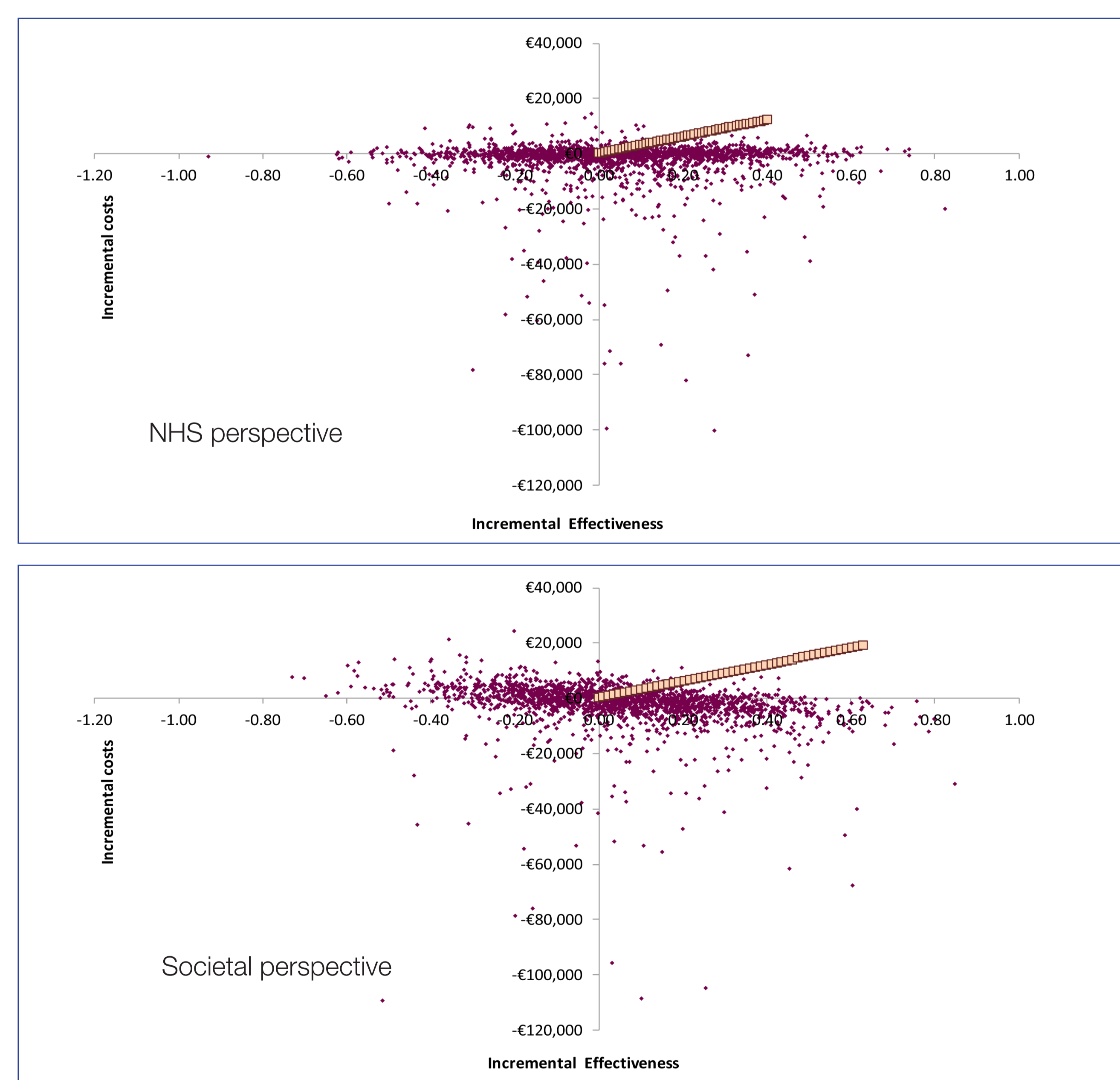
- In probabilistic SA, 70% and 63% of the 2,000 MonteCarlo iterations performed were under an hypothetical willingness-to pay threshold of €30,000 per QALY for NHS and societal perspective, respectively. (Figure 2)

CONCLUSION

- In Spain, in a 1,000 NVAF patients cohort, apixaban would avoid 42 events compared to edoxaban.
- The incremental cost for apixaban versus edoxaban is around €400 per patient during its lifetime.
- Based on the model outcomes, apixaban could be considered a cost-effective alternative vs edoxaban for stroke prevention in NVAF population, in Spain.

REFERENCES

1 Camm AJ, et al. Eur Heart J. 2012;33(21):2719-47.
2 Betegon L, et al. Eur J Clin Pharm. 2014;16:0.
3 Canal C, et al. Pharmacoecon Span Res Artic. 2015;12:93-103.
4 Lip GYH, et al. Clin Ther. 2015;37:2476-88.
5 Granger CB, et al. N Engl J Med. 2011;365:981-92.
6 Giugliano RP, et al. N Engl J Med. 2013;369:2093-104.
7 Connolly SJ, et al. N Engl J Med. 2011;364:806-17

8 Sullivan P, et al. Med Decis Making. 2011;31:800-4.
9 Sanders GD, et al. JAMA. 2016;316:1093-103.
10 BOT Plus. www.portalfarma.com
11 eSalud. Oblikue consulting. www.oblikue.com
12 Beguiristain JM, et al. Rev Neurol. 2005;40:406-11.
13 Lopez-Bastida J, et al. Eur J Health Econ. 2010;11:513-20.