

Cost-effectiveness analysis of apixaban compared to other DOACs for prevention of stroke in Austrian atrial fibrillation patients

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Objectives

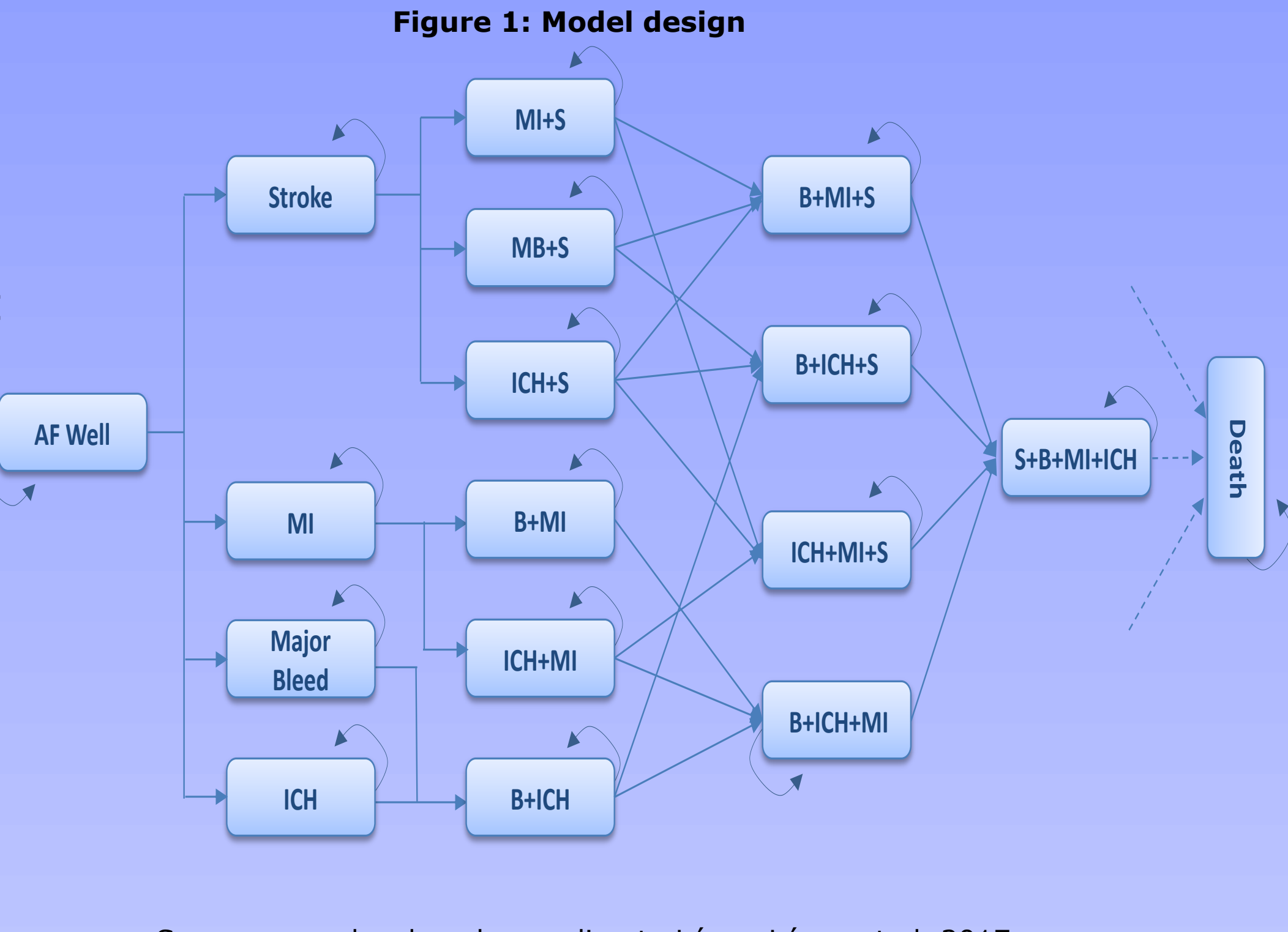
Several direct oral anticoagulants (DOACs) have been approved by the European Medicines Agency since 2008. Unlike warfarin these drugs do not require regular blood monitoring. These medications directly inhibit the blood’s ability to form blood clots. DOACs prevent strokes at least as good as warfarin (some studies have even shown better efficacy) in patients with atrial fibrillation. The aim of the present cost-effectiveness analysis is to analyze apixaban compared to other DOACs and vitamin K antagonists (warfarin) in Austria.

Methods

A Cost-Utility-Model was developed to simulate lifetime costs and quality-adjusted life-years (QALYs) of DOACs and warfarin. Markov-modeling techniques based on a published model by José A López-López (2017) conducted a meta-analysis of 23 randomized trials with 94,656 atrial fibrillation patients (median age, 70) focusing on the effects of 3 direct factor Xa inhibitors and 1 direct factor II inhibitor was incorporated. Each year a patient has a probability of suffering a clinically relevant or major (extracranial) bleed, an intracranial hemorrhage (ICH), an ischemic stroke or a myocardial infarction (MI), remaining healthy, or deceasing. Sensitivity-analysis accounted for uncertainty. Direct-costs (2018€) were derived from published sources from the payer’s perspective. QALYs, life-years (LYs) and costs were discounted (5% p.a.).

Model description

- A Markov model was developed (Figure 1).
- The model assumes the lifetime perspective.
- The model was carried out from the health care perspective.
- The model includes the health states "AF Well", "4 events" (ischemic strokes, heart attacks, intracranial haemorrhages, clinically relevant extracranial heavy bleeding) as well as the "combination of events" and "death".



Source: own developed according to López-López et al. 2017

Comparators (therapeutic alternatives)

- Apixaban 5mg
- Dabigatran 150mg
- Rivaroxaban 20mg
- Dabigatran 110mg
- Edoxaban 60mg
- Warfarin (VKA) 3mg

Clinical Data

Since the therapeutic alternatives were not analyzed in a study, it was necessary to perform an indirect comparison based on a network meta-analysis (NMA). The NMA includes 23 randomized trials involving a total of 94,656 patients (see López-López et al. 2017).

Resource Use and Costs

- Costs of oral anticoagulants (based on reimbursement price)
- Event costs: The costs of ischemic stroke and heart attack (first year and subsequent years) were determined by means of a systematic review, which provided information on resource use. Event costs include: inpatient, rehabilitation, outpatient and drug costs.
- Cost of major bleeding and intracranial haemorrhage has been estimated on the basis of the publication by Belisari et al. (2016), who documented the burden of surgery as a result of oral anticoagulation. Regarding these two events, only costs in the first year are taken into account. For dabigatran, the presence of idarucizumab was considered.

Outcomes

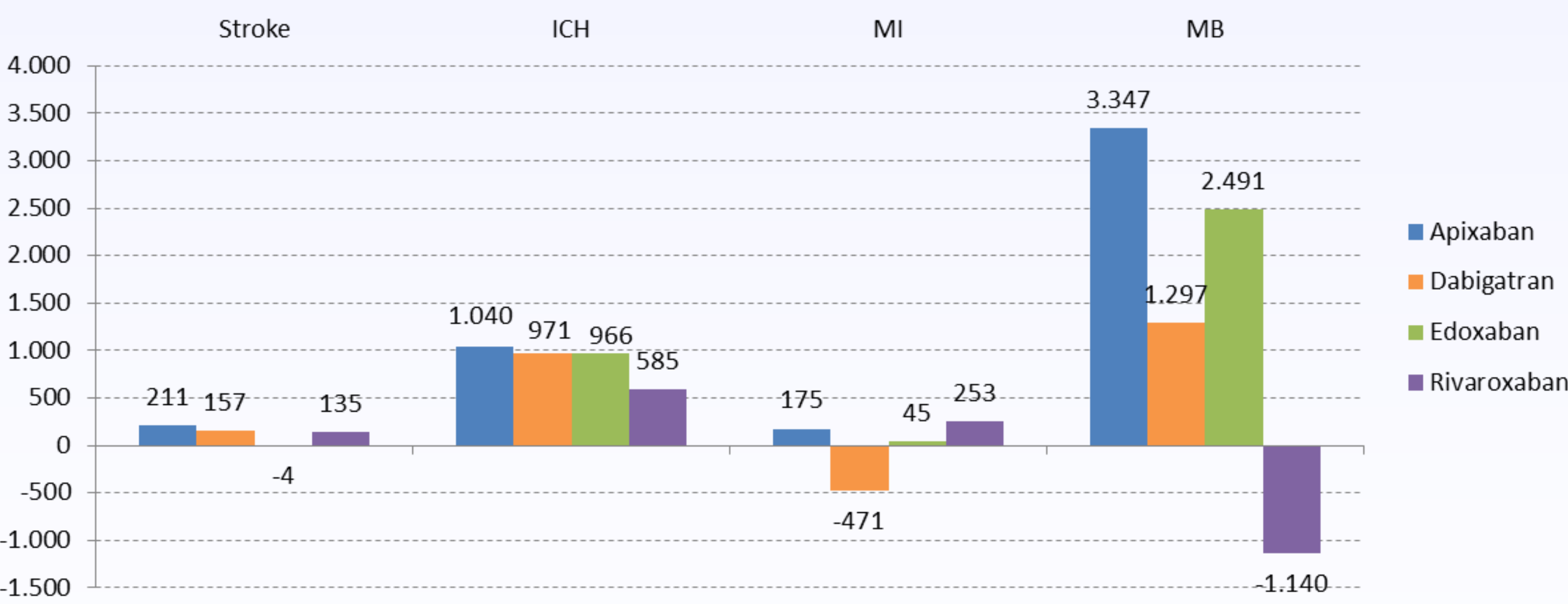
The following outcomes are QALYs (quality-adjusted life-years), life-years (LYs) and saved events.

Results

Preventable Events

Figure 2 depicts the potentially preventable events per year when all atrial fibrillation patients (n=179,000) are treated with a given DOAC instead of VKA.

Figure 2: Overview of the preventable events per comparator vs. VKA

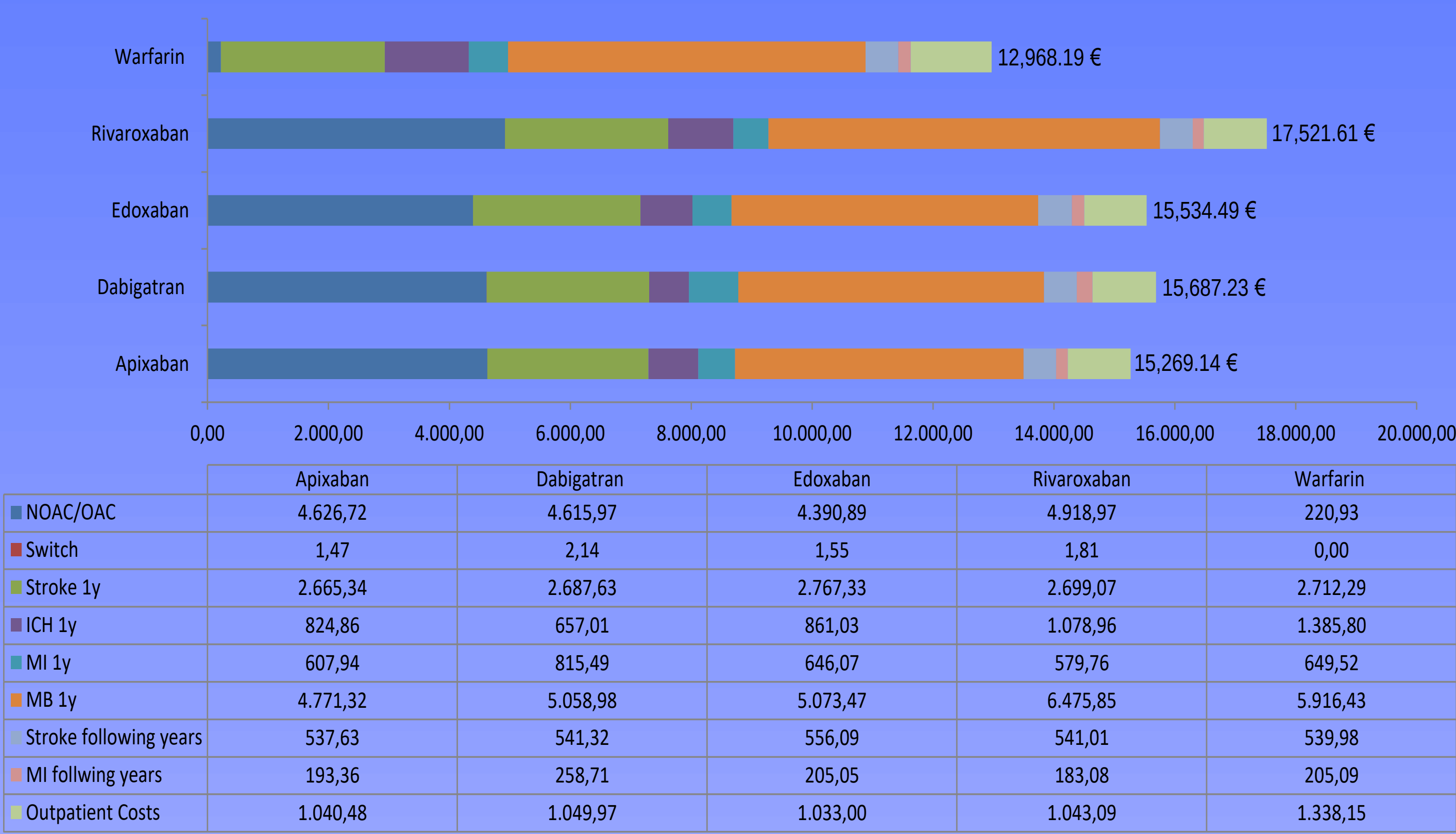


Source: own calculations according to López-López et al. 2017 Dabigatran 110mg and 150mg weighted results

Costs

In the base-case, warfarin had the lowest cost of 12,968 € (SD, 666 €) followed by apixaban 5mg (15,269 € ± 743 €), edoxaban 60mg (15,534 € ± 778 €), dabigatran 110/150mg (15,687 € ± 780 €), and rivaroxaban 20mg (17,522 € ± 868 €). Warfarin (VKA) causes the lowest cost (Figure 3).

Figure 3: Overview of cost components and total costs per comparator



Source: own calculations according to López-López et al. 2017

Dabigatran 110mg and 150mg weighted results

Cost-effectiveness results

Apixaban dominates dabigatran, edoxaban, rivaroxaban and is cost-effective against warfarin. Assuming a willingness-to-pay of about 28,000 € for each year of perfect health (one QALY). Apixaban had the highest quality-adjusted life-years estimate at 5.45 (SD, 0.06) (Table 1).

Table 1: Cost-effectiveness results

Strategy	Apixaban	Dabigatran	Edoxaban	Rivaroxaban	Warfarin
Total costs (€) per patient	15,269.14	15,687.23	15,534.49	17,521.61	12,968.19
Difference (€)		-418.09	-265.35	-2,252.47	2,300.95
QALYs	5.452	5.430	5.401	5.450	5.271
Difference		0.022	0.051	0.002	0.181
ICER/QALY (€)		DOMINANT	DOMINANT	DOMINANT	12,743.07
LYs	7.04	7.01	6.97	7.04	6.81
Difference		0.03	0.06	0.0	0.23
ICER/LY (€)		DOMINANT	DOMINANT	DOMINANT	10,070.55

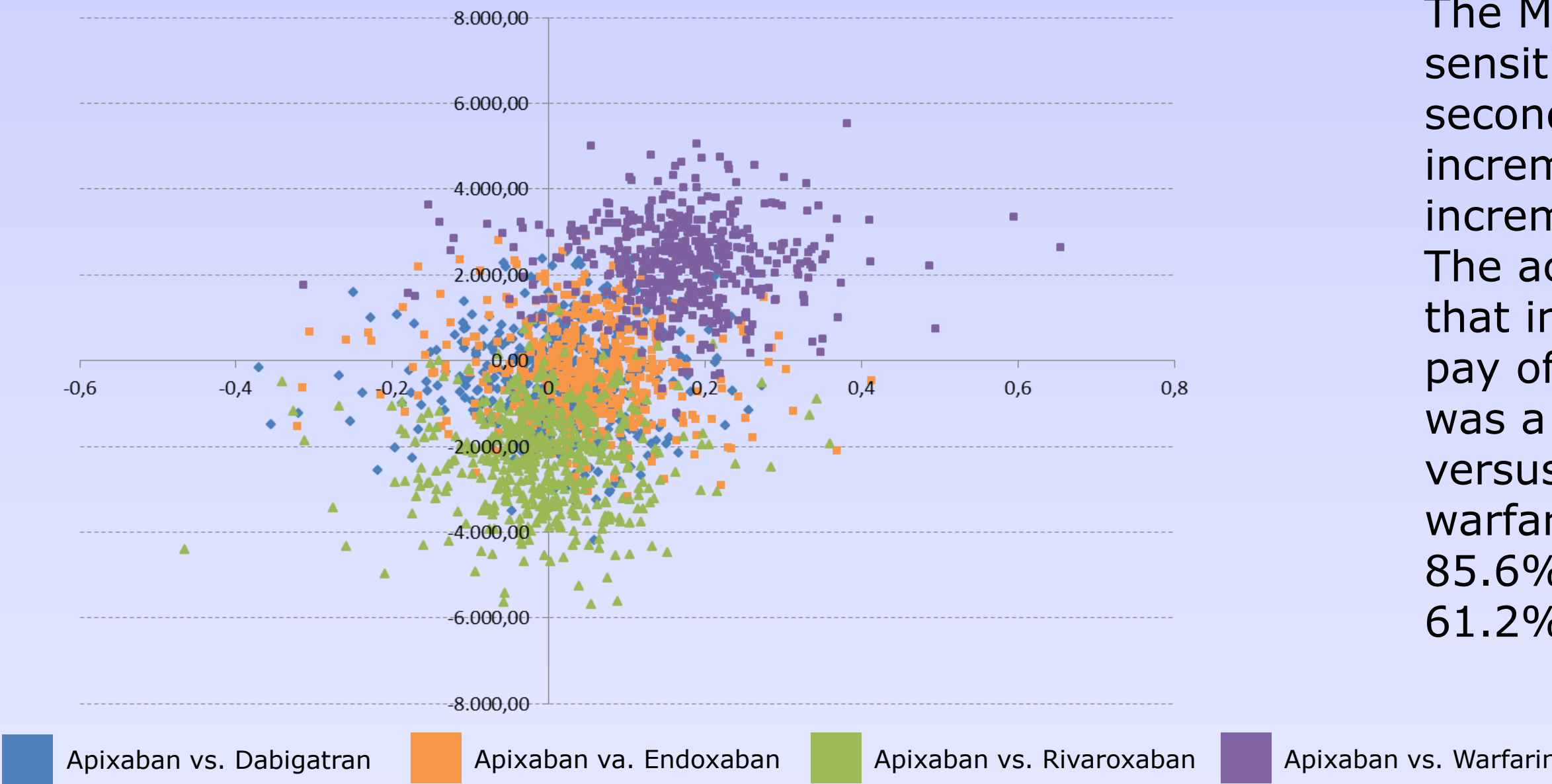
Source: own calculations

Dabigatran 110mg and 150mg weighted results

Sensitivity Analysis

Probabilistic and deterministic sensitivity analysis were carried out to examine the robustness of the model.

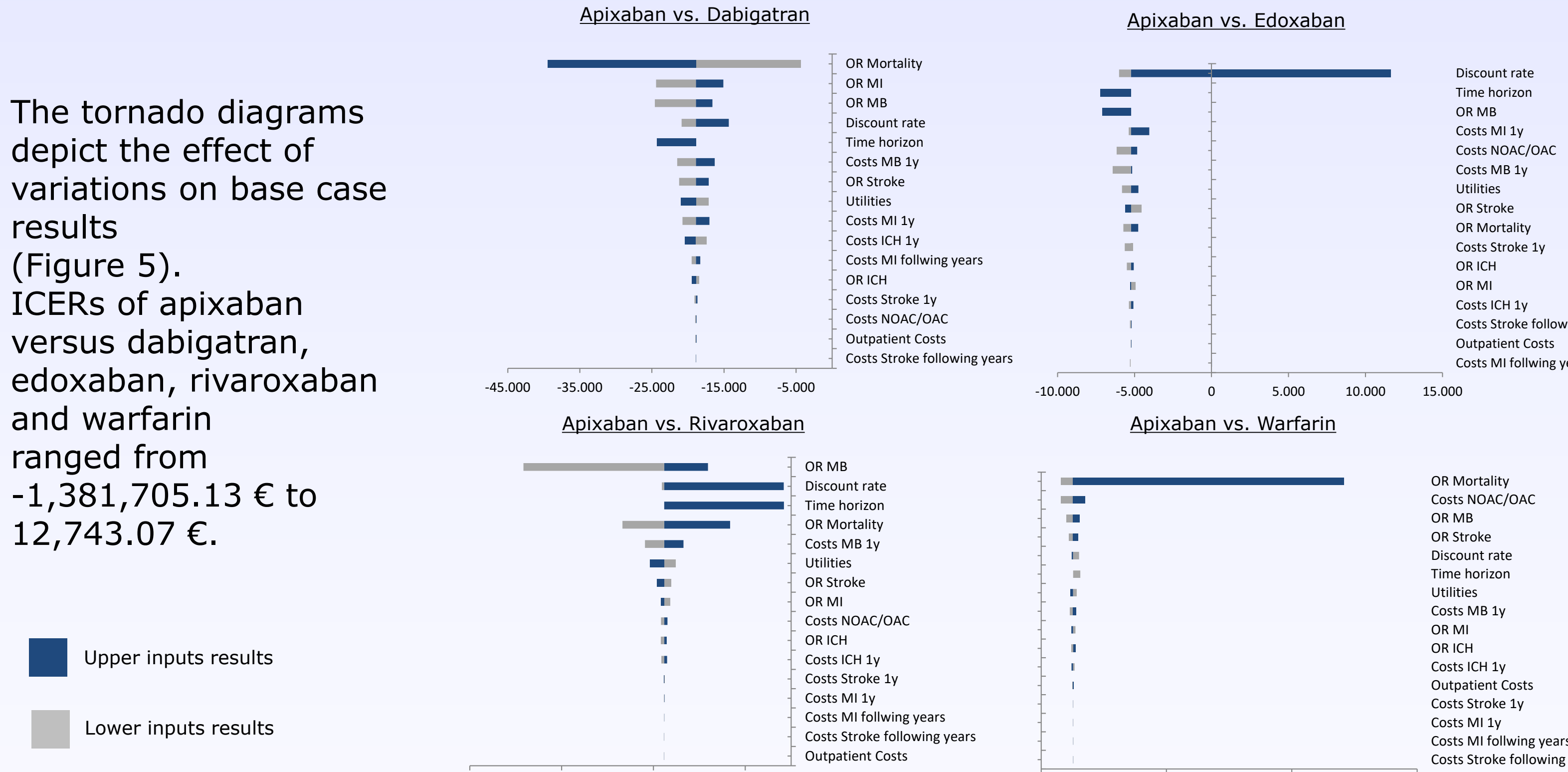
Figure 4: Scatterplot, Apixaban vs. Comparator



Source: own calculations

The Monte-Carlo probabilistic sensitivity analysis results of 500 second-order simulations plotting incremental cost versus incremental effects (Figure 4). The acceptability-curve revealed that in case of a willingness-to-pay of about 28,000 € apixaban was a cost-effective strategy versus edoxaban, dabigatran, warfarin and rivaroxaban in 85.6%, 79.0%, 76.4% and 61.2% of the simulations.

Figure 5: Tornado diagrams



Source: own calculations

Conclusion

In patients with atrial fibrillation and an increased risk of stroke, prophylaxis with apixaban was highly cost-effective from the perspective of the Austrian health care system.

References

López-López JA, Sterne JAC, Thom HHZ, Higgins JPT, Hingorani AD, Okoli GN, Davies PA, Bodalia PN, Bryden PA, Welton NJ, Hollingworth W, Caldwell DM, Savović J, Dias S, Salisbury C, Eaton D, Stephens-Boal A, Sofat R. Oral anticoagulants for prevention of stroke in atrial fibrillation: systematic review, network meta-analysis, and cost effectiveness analysis. *BMJ*. 2017 Nov 28;359:j5058. doi: 10.1136/bmj.j5058.

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Additional literature with the author