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Economic evaluation of oral anticoagulants for atrial fibrillation

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CoI

Conflict of interest: nothing to disclose

Objective

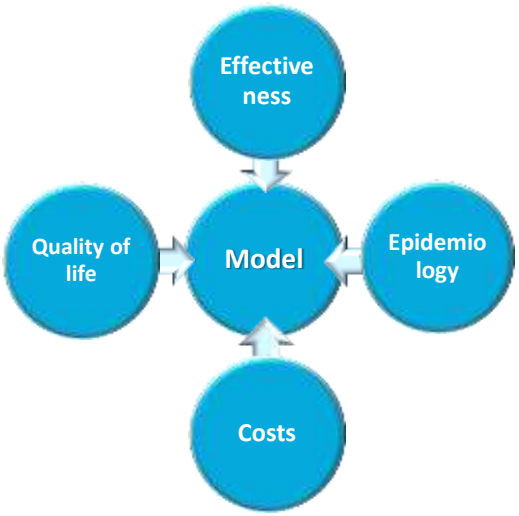
- To evaluate the relative cost effectiveness of warfarin, dabigatran, rivaroxaban and apixaban in a Norwegian setting.

Health economic evaluations

- Due to resource constraints, all new interventions that are effective cannot be introduced into the health care system.
- Hence, it is necessary to prioritize between these new interventions.
- Health economic evaluations can be a useful tool to illustrate the costs and health outcomes associated with different treatment options.

Models

- Models are an oversimplification of reality – which simulate outcomes and costs over time
- We perform model analyses to better investigate uncertainties both on costs and outcomes
- Needs assumptions and extrapolations from clinical data
- Timehorizon should be long enough to capture all relevant differences between intervention and compartor due to treatment

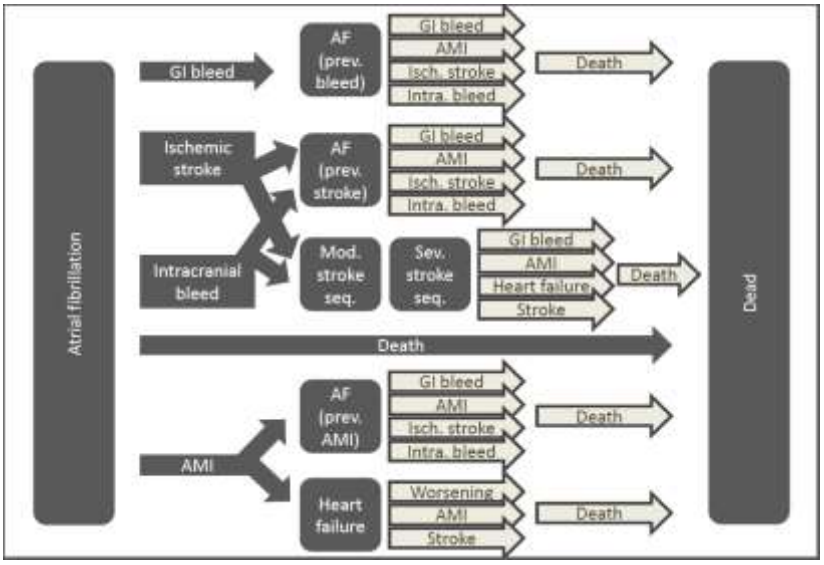


Models are an oversimplification of reality – which simulate outcomes and costs over time

Background

- Atrial fibrillation is a major risk factor for stroke, which again causes thousands of deaths and sequela.
- Atrial fibrillation patients at medium or high risk of stroke are recommended to use an oral anticoagulant to reduce the risk of stroke.
- The past few years, three new oral anticoagulants (NOACs), i.e. dabigatran, rivaroxaban and apixaban, have been introduced in competition with warfarin.

Model structure



Model input parameters

- Efficacy data were based on intention-to-treat analyses from the three major randomized clinical trials comparing each of the NOACs with warfarin.
- All QALY weights in the model are based on EQ-5D-3L (EuroQol 5 Dimensions 3 Levels), which is the most commonly used instrument for eliciting QALY values.

Input parameters continues

- Risks of events are incorporated into the model as one-year probabilities adjustable for different risk factors according to CHA_2DS_2-VASc and HAS-BLED.
- CHA_2DS_2-VASc and HAS-BLED are scoring algorithms that divide patients into risk groups according to how many of a predefined set of clinical risk factors they have.

Characterisation of the AF patiens

The medium risk group was defined to have no clinical risk factors apart from their age, hence a CHA_2DS_2-VASc of 2 and HAS-BLED of 1.

The high risk group was defined at CHA_2DS_2-VASc=4 and HAS-BLED=2, which is approximately the risk profile of an average atrial fibrillation patient in Scandinavia.

Risk of AMI, heart failure and death is based on Norwegian data for patients without AF multiplied by an increased risk due to AF.
These data are dependent upon age, but only given here for age 70.

Costs

- **Identify:** All important cost components
- **Quantify:** Unit of each cost component (number of doctor visits, amount of nurses time, other resource use, transport etc.)
- **Value:** Unity costs (salaries, price on equipment, etc)

Prices (€) of investigated drugs

Interventions	Pills per day	Dosage	Price	Pills per package	Price per pill	Price per day	Price per year
Apixaban	2	5 mg	288	168	1.71	3.42	1 250
Dabigatran	2	110 mg	101	60	1.68	3.36	1 228
Dabigatran	2	150 mg	101	60	1.68	3.36	1 228
Rivaroxaban	1	20 mg	292	100	2.92	2.92	1 066
Warfarin	2	2.5 mg	17	100	0.17	0.33	121

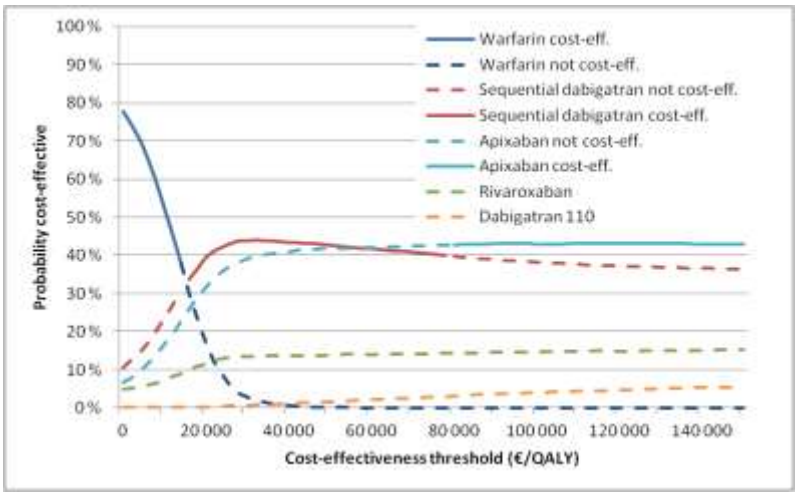
Expecte lifetime results for medium risk patients

Strategy	Lifetime costs (€)	Lifetime QALY*	Net health benefit**	Incremental analysis			Versus warfarin		
				Incremental costs (€)	Incremental effects (QALY)	ICER *** (€/QALY)	Incremental costs (€)	Incremental effects (QALY)	ICER (€/QALY)
Warfarin	47 498	5,706	5,103						
Sequential dabigatran	49 821	5,852	5,219	2 323	0,146	15 920	2 323	0,146	15 920
Apixaban	50 402	5,859	5,219	581	0,007	79 526	2 904	0,153	18 955
Rivaroxaban	50 611	5,810	5,167	790	-0,042	Dominated	3 113	0,104	29 990
Dabigatran 110 mg	54 104	5,806	5,119	4 283	-0,046	Dominated	6 606	0,100	66 121

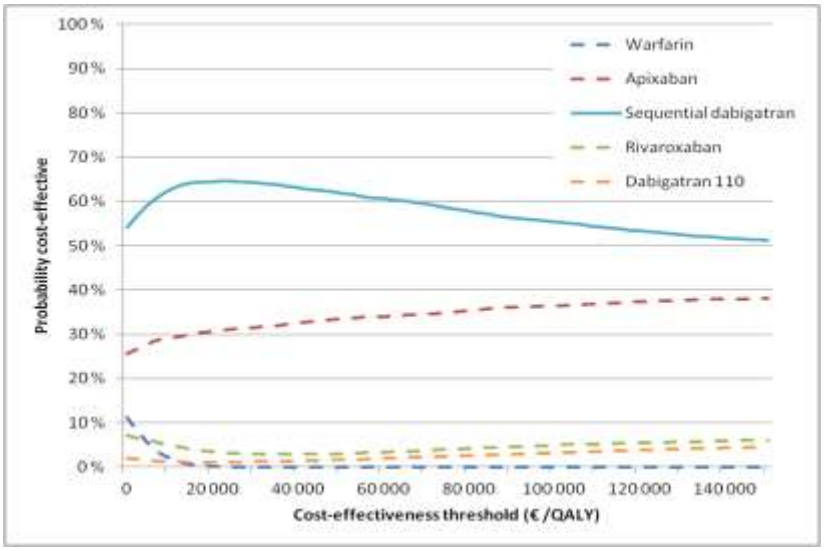
Expected lifetime results for high risk patients

Strategy	Lifetime costs (€)	Lifetime QALY*	Net health benefit**	Incremental analysis			Versus warfarin		
				Incremental costs (€)	Incremental effects (QALY)	ICER*** (€/QALY)	Incremental costs (€)	Incremental effects (QALY)	ICER (€/QALY)
Sequential dabigatran	66 508	4,955	4,110				-2 953	0,183	-16 102
Apixaban	68 657	4,947	4,075	2 149	-0,008	Dominated	-804	0,175	-4 585
Warfarin	69 461	4,771	3,889	2 953	-0,183	Dominated			
Rivaroxaban	71 849	4,888	3,975	7 402	-0,064	Dominated	2 388	0,117	20 492
Dabigatran 110 mg	73 909	4,891	3,952	2 149	-0,008	Dominated	4 448	0,119	37 250

Cost-effectiveness acceptability curve and frontier of medium risk atrial fibrillation patients



Cost-effectiveness acceptability curve and frontier of high risk atrial fibrillation patients



Conclusions

- There is considerable uncertainty regarding which of the oral anticoagulants is the most cost-effective alternative.
- However, apixaban and dabigatran (150mg up to age 80, 110mg after age 80) seems to be the most effective and cost-effective alternatives.
- Warfarin can only be a cost-effective alternative in Norway if the threshold for cost-effectiveness is much lower than assumed.

Key Points for Decision Makers

- The new oral anticoagulants are likely to yield additional health benefits in terms of quality adjusted life years (QALY) as compared to warfarin.
- Differences in health gains are however relatively small and prices are high.
- Sequential dabigatran (150mg up to age 80, thereafter 110mg as recommended by the European Medicines Agency) is the strategy most likely to be considered cost-effective, regardless of risk group.
- Assuming guidelines from the European Society of Cardiology and reducing dabigatran dosage at age 75 (instead of at age 80), apixaban becomes the most effective and cost-effective alternative.