Health economic evaluation

Cost effectiveness of patient self-monitoring and patient self-testing in patients with warfarin treatment

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CONTENTS

BACKGROUND

Whilst warfarin has been shown to be effective, it has a narrow therapeutic index that necessitates frequent monitoring and dose adjustments (Hirsh et al. 2003). The aim of monitoring is to ensure that the International Normalized Ratio (INR) is maintained within the target therapeutic range (2.0 and 3.0), where warfarin treatment has been shown to offer an acceptable benefit/risk ratio (Fuster et al. 2006). TTR (time in therapeutic range) is calculated based on the proportion of time spent in the target INR range 2.0–3.0. In routine clinical practice the time individual patients spend in this target range varies considerably (Baglin and Rose 1998). Suboptimal anticoagulation (AC) is associated with poor outcomes either in terms of thrombotic events, hemorrhage or mortality (Jones et al 2005; Lehto et al 2017).

In 1992 the prevalence of anticoagulant (AC) treatment was 0.65% in a Finnish population study (Eskola et al. 1996). A more recent study from Finland states that the prevalence has more than doubled since, being 1.64 % in 2010 (Virjo et al. 2010). In Finland, it has been estimated that 8–16 % of the elderly use warfarin in 2010.

INR-levels are currently monitored in healthcare clinics. A study conducted in Oulu, Finland demonstrated that an average of 15.9 INR-tests per patient is taken per year (Leskelä et al 2013). It is estimated that in Helsinki alone approximately 10 000 patients are monitored by primary healthcare (Holvitie et al. 2014).

Patient self-monitoring means that patients self-monitor and self-adjust the dose of their oral anticoagulants. Patient self-testing means that patients measure their INR-value and report the results to healthcare professionals, who make treatment decisions based on these measurements (White et al. 1989).

COST-EFFECTIVENESS MODEL

A cost-effectiveness model was developed to provide an estimate of the cost-effectiveness of home monitoring systems compared to traditional monitoring of warfarin with atrial fibrillation patients in Finnish clinical setting. Home monitoring systems are divided to patient self-monitoring and patient self-testing. Direct and non-direct healthcare costs were included in the analysis with a life-time modelling timeframe (40 years). Cost-effectiveness was assessed on the basis of incremental cost-effectiveness ration (ICER) and the primary outcome was cost per life-year gained (€/LY).

A Markov model structure was selected to estimate the cost-effectiveness of the treatments. The model includes three model health states (treatment, post stroke and death). Transition between the states are driven by the probabilities of no event, bleeding, stroke or death as adapted from literature. The model structure is demonstrated in Figure 1.

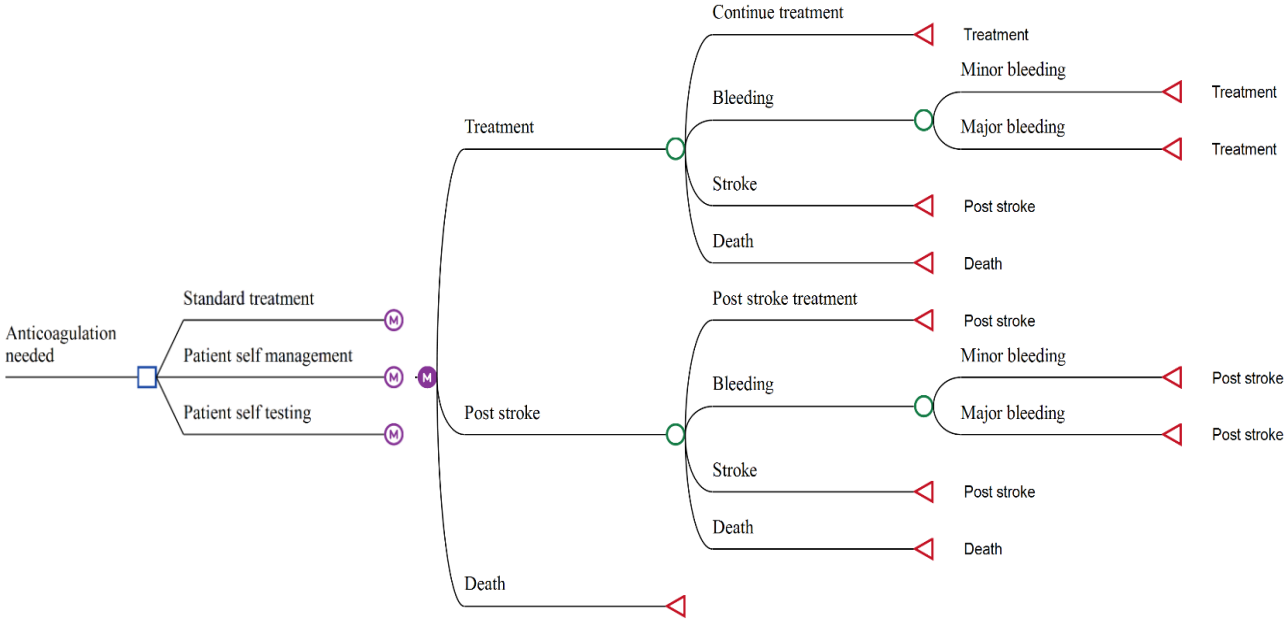

FIGURE 1. MODEL OVERVIEW

Atrial fibrillation (AF) is the main indication for warfarin use (Viitaniemi et al 1999). As the use of warfarin varies from indication to another the population was limited to AF patients.

The comparator included within the economic model is traditional INR-value measurement in healthcare units, which is modelled using the outcomes from a study by Leskelä et al. (2013). The publication analyses the warfarin treatment practices and outcomes in the city of Oulu, Finland.

The model includes two interventions, patient self-management and patient self-testing. The interventions differ by the resource use they require and consequently the costs. In many studies patient self-testing and self-management has been pooled together and compared with standard care (Heneghan et al. 2016; Heneghan et al. 2012; Ansell et al. 1995). In Heneghan et al. (2012) the effect of self-monitoring to TTR-values at 1 year was demonstrated to be 5,1% compared to standard care in AF patients (Heneghan et al. 2012). The improvement of TTR-values compared to standard treatment are therefore expected to be identical on patients self-testing and patient self-management.

The assessment is performed from the Finnish health care payer perspective with a life-time modelling timeframe of 40 years. Life time horizon was chosen to capture all relevant costs and health effects as the quality of warfarin treatment (TTR, %) has been associated with the risk of stroke, bleeding events and mortality in patients with AF (Lehto et al. 2017). All costs are expressed in Euros. A cycle length of 1 year was applied. Cost-effectiveness is assessed on the basis of incremental cost-effectiveness ratio (ICER) and the primary outcome measure is cost per life-year gained (€/LY).

Table 1 provides a summary of the decision problem the model addresses.

TABLE 1. SUMMARY OF THE POPULATION, INTERVENTION, COMPARATORS, OUTCOMES AND TIME HORIZON

Population	Patients on warfarin treatment on atrial fibrillation indication
Intervention	Patient self-management & patient self-testing of INR levels on warfarin treatment
Comparators	Traditional monitoring of INR levels on warfarin treatment in healthcare centres
Outcomes	Life years
Time Horizon	Lifetime (40 years)

COSTS

All unit costs are derived from published Finnish sources and presented in 2017 values.

Treatment cost was calculated based on published data, medicine costs in Finland and expert estimates on healthcare professional working hours in different care settings and phases. One nurse responsible for anticoagulation treatment in Hämeenlinna and Kokkola, Finland was interviewed. Average dose of warfarin was estimated at 5 mg per day (Puhakka 2011). Nurse and doctor cost were calculated from municipal salaries with the employer cost and index taken into concideration. Travel method was assumed to be evenly distributed between public transportation, private car and taxi (33,3%). Unit costs and appropriate sources are presented in appendix Table 6, Table 7 and Table 8. Treatment cost per patient is presented in Table 2. Yearly event costs are presented in Table 3

TABLE 2. YEARLY COST PER PATIENT

	SoC	PST	PSM
Medication	37,08 €	37,08 €	37,08 €
Healthcare professional	57,31 €	29,80 €	0,00 €
Laboratory	108,11 €	0,00 €	0,00 €
Remote monitoring leasing cost	0,00 €	480,00 €	480,00 €
Travel	92,22 €	0,00 €	0,00 €
Direct healthcare cost	202,50 €	546,88 €	517,08 €
Direct and non-direct healthcare cost	294,72 €	546,88 €	517,08 €

TABLE 3. YEARLY EVENT COSTS

	Direct	Direct non- healthcare	Source
Events (full year)			
Minor bleeding	228 €		9060, DRG 2016 (SHP2016 FULL)
Major bleeding	16 585 €	2 248 €	Linna et al 2017
Stroke	14 600 €	9 742 €	Linna et al 2017
Post stroke	9 425 €		Meretoja et al 2010

EFFECTS

Quality of current warfarin treatment in Finland measured by TTR (time in therapeutic range, %) was drawn from a study by Leskelä et al (2013). The effect of self-monitoring and self-testing was adopted from Heneghan et al (2012), in which a 5,1% improvement was demonstrated at 1 year compared to standard of care. The distribution of patients in each TTR (%) group and the difference between standard of care and new treatment options (patient self-monitoring, patient self-testing) are demonstrated in Figure 2. The outcomes were then used to calculate a weighted risk for bleeding, stroke, mortality and no-event for each 1-year cycle in each group groups (Table 4). The risk probabilities were adopted from a study evaluating the relationships between quality of warfarin therapy and the risks of these events in a Finnish AF patient population (Lehto et al 2017). Bleedings were divided into minor and major bleedings as in Bahit et al (2017).

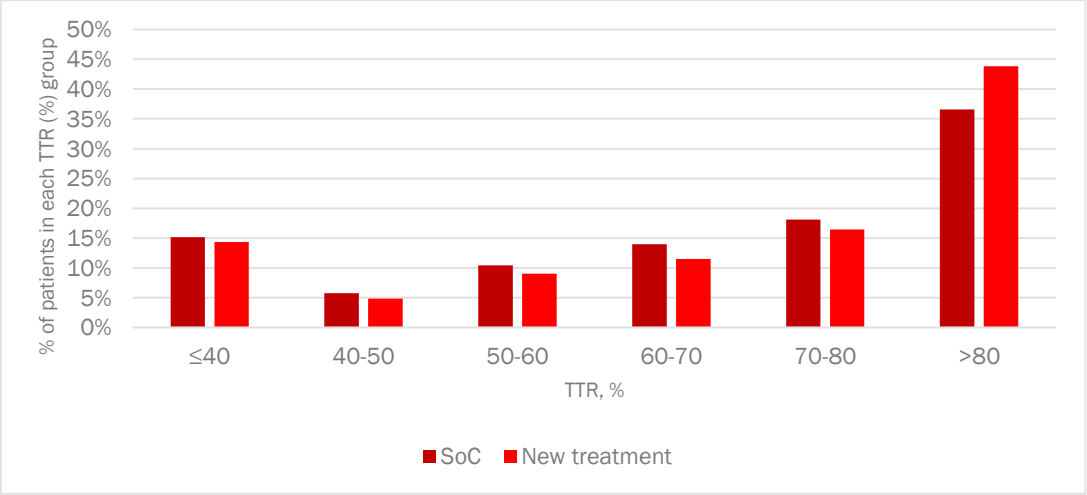

FIGURE 2. DISTRIBUTION OF PATIENTS BY TTR, %

TABLE 4. YEARLY EVENT RISK ON SOC AND PST/PSM

Event	SoC	PST/PSM
Bleeding	3,9 %	3,8 %
Minor	3,0 %	2,9 %
Major	0,9 %	0,9 %
Stroke	4,4 %	4,3 %
All-cause mortality	7,5 %	7,0 %
No event (calc)	84,2 %	84,9 %

RESULTS

The results of the cost effectiveness analysis show that PST and PSM are associated with increased survival and costs as presented in the Table 5. The incremental survival was 0,68 meassured as life years with additional costs of 6,047€ and 6,449€ for PSM and PST, respectively. The incremental cost effectiveness ratio (€/life year) is subsequently 8,915€/LY and 9,508€/LY for PSM and PST compared to current practices.

TABLE 5. RESULTS OF COST EFFECTIVENESS ANALYSIS

	Cost	Incr Cost	Eff	Incr Eff	Incr C/E
Standard treatment	61 743,57		12,283		
Patient self management	67 790,66	6 047,09	12,961	0,68	8 915
Patient self testing	68 192,62	6 449,04	12,961	0,68	9 508

PROBABILISTIC SENSITIVITY ANALYSIS

A probabilistic sensitivity analysis (PSA) was conducted to analyse the impact of parameter uncertainty and possibility of PST and PSM being cost-effective at a certain threshold. Normal distribution was utilized for all cost parameters and Beta distribution for all transition (event risk) parameters. The results of 10,000 iterations are presented in Figure 3 and Figure 4.

The results of the PSA demonstrated mean life years of 12,35, 13,03 and 13,04 for current treatment line, PSM and PST respectively. The mean costs accordingly were 62,202€, 68,244€ and 68,710€. The resulting mean ICER was 8,959€/LY for PSM and 9,531€/LY for PST compared to current treatment. Probabilistic results were consistent with the results from the deterministic base case analysis (ICER for PSM 8,915€/LY and PST 9,508€/LY).

All variables are tested within standard deviation of 10% of the mean estimate.

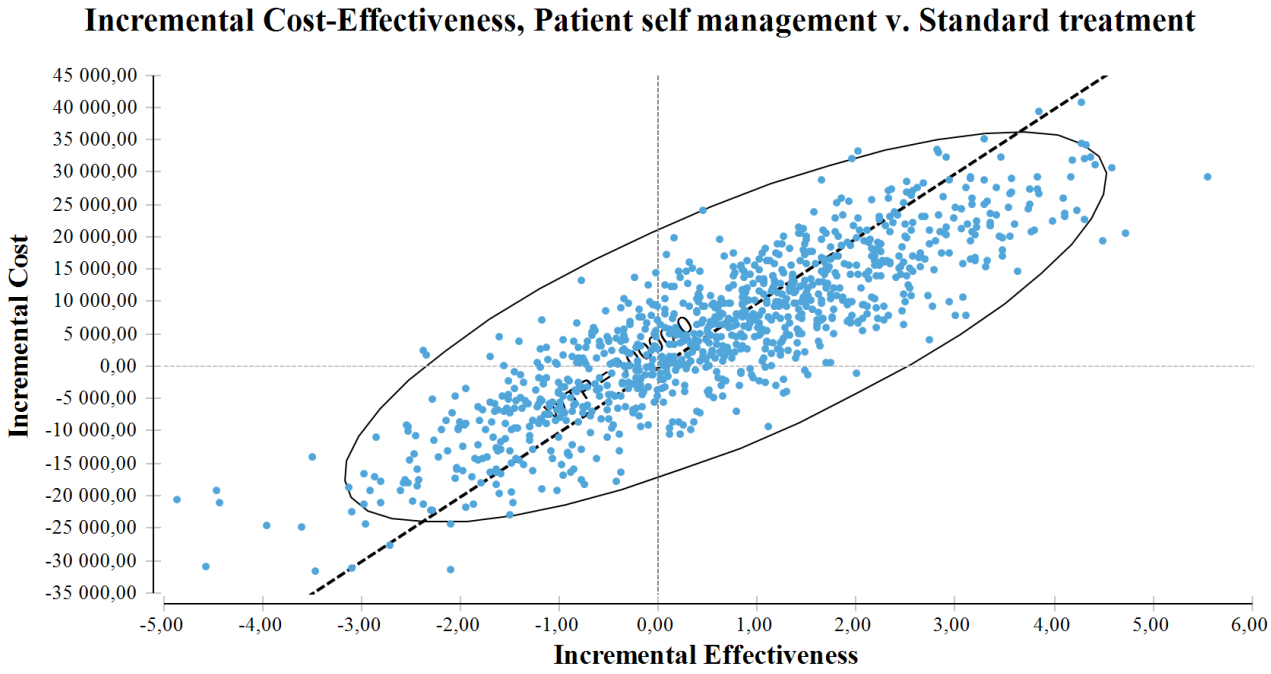

FIGURE 3. INCREMENTAL COST-EFFECTIVENESS, PATIENT SELF-MANAGEMENT VS STANDARD TREATMENT

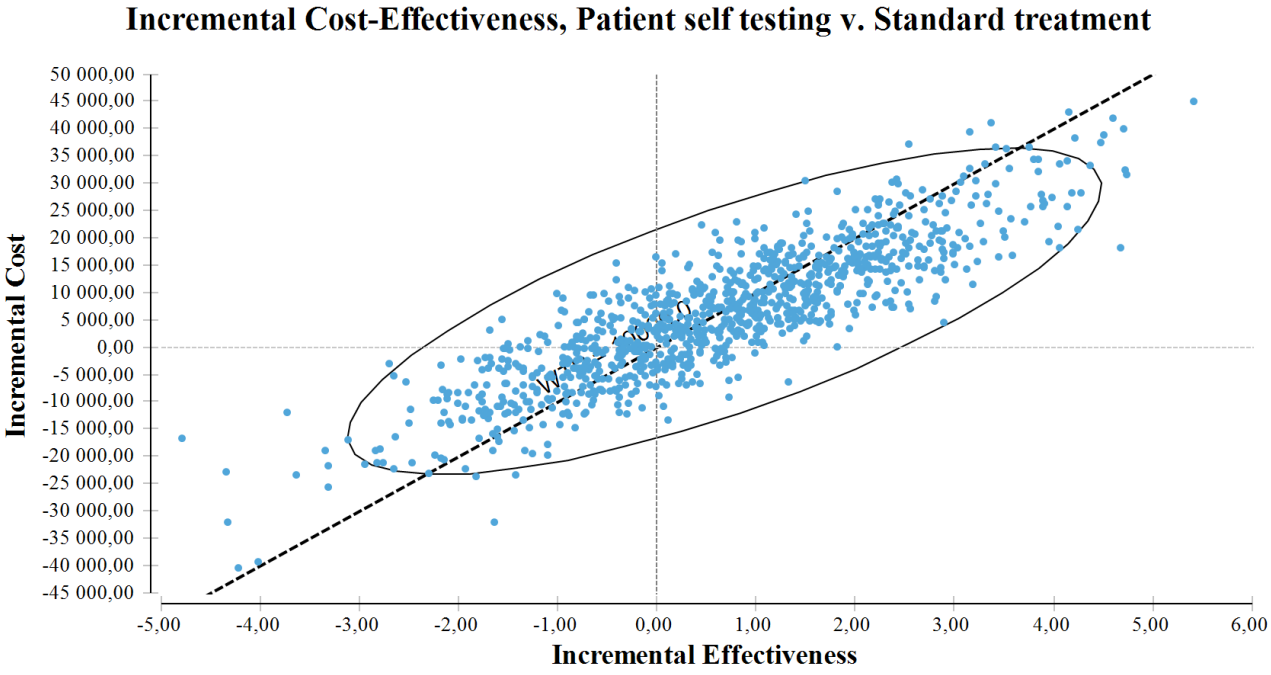

FIGURE 4. INCREMENTAL COST-EFFECTIVENESS, PATIENT SELF-TESTING VS STANDARD TREATMENT

CONCLUSIONS

This analysis estimated the cost-effectiveness of PST and PSM compared to current warfarin monitoring practices in patients with atrial fibrillation. The analysis was based on published Finnish data on quality of warfarin treatment, risks and costs with other publications utilised where Finnish data was not available. The model was conducted with a Markov model structure.

The results of the analysis suggest that monitoring warfarin treatment with self-testing (PST) and self-monitoring (PSM) can be regarded as cost-effective with a willingness-to-pay threshold of 8915€ and 9508€ per life year in comparison with current monitoring practices in patients with atrial fibrillation.

APPENDIX

TABLE 6. DRUG UNIT AND TITRATION RELATED COST.

Drug cost	#	Source
Cost per mg	0,02	Marevan 5mg 100pack
Warfarin cost per month €	3,09	
Titration related costs		
Nurse cost (€/min)	0,43	Kuntatalous 2017
Doc cost (€/min)	0,91	Kuntatalous 2017

TABLE 7. SOC, PST AND PSM TRETMENT-OPTION RELATED WORKING HOURS, NUMBER OF LABORATORY TESTS REQUIRED AND REMOTE MONITORING LEASING COST.

SoC		
Nurse min/visit	7,5	Assumption by expert nurse
Doc min/visit	1	Assumption by expert nurse
Number of tests / month	1,16	Aver. Holvitie et al 2014; Leskelä R-L et al. 2013
PST		
Nurse min/visit	5	Assumption by expert nurse
Doc min/visit	0	Assumption by expert nurse
Number of tests / month	1,16	Assumed same as SoC
PSM		
Nurse min/visit	0	Assumption
Doc min/visit	0	Assumption
Number of tests / month	1,155	Assumed same as SoC
Remote monitoring leasing cost/month €	40	
Laboratory related resource use		
INR cost / test €	3,8	EPSHP 2018
Lab cost / visit €	4	EPSHP 2018

TABLE 8. TRAVEL RELATED UNIT COSTS AND AVERAGE DISTANCE TO THE NEAREST PRIMARY HEALTHCARE UNIT IN FINLAND.

Travel		
Travel (km) - roundtrip	7,6	Tilastokeskus 2018
Bus €/one way ticket	2,2	HSL 2019
Taxi €/km	1	Taxi Helsinki 2019
Taxi starting cost	3,9	Taxi Helsinki 2019
Private car €/km	0,43	Veronmaksajien keskusliitto 2019

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