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CLINICAL RESEARCH
Arrhythmias

Cost-effectiveness of population screening for atrial fibrillation: the STROKESTOP study

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See the editorial comment for this article 'Screening for atrial fibrillation to prevent stroke: increasing enthusiasm but outcomes still lag', by E.S. Spatz and J. Herrin, https://doi.org/10.1093/eurheartj/ehac696.

Abstract

Aims Previous studies on the cost-effectiveness of screening for atrial fibrillation (AF) are based on assumptions of long-term clinical effects. The STROKESTOP study, which randomised 27 975 persons aged 75/76 years into a screening invitation group and a control group, has a median follow-up time of 6.9 years. The aim of this study was to estimate the cost-effectiveness of population-based screening for AF using clinical outcomes.

Methods and results The analysis is based on a Markov cohort model. The prevalence of AF, the use of oral anticoagulation, clinical event data, and all-cause mortality were taken from the STROKESTOP study. The cost for clinical events, age-specific utilities, utility decrement due to stroke, and stroke death was taken from the literature. Uncertainty in the model was considered in a probabilistic sensitivity analysis. Per 1000 individuals invited to the screening, there were 77 gained life years and 65 gained quality-adjusted life years. The incremental cost was €1.77 million lower in the screening invitation group. Gained quality-adjusted life years to a lower cost means that the screening strategy was dominant. The result from 10 000 Monte Carlo simulations showed that the AF screening strategy was cost-effective in 99.2% and cost-saving in 92.7% of the simulations. In the base-case scenario, screening of 1000 individuals resulted in 10.6 [95% confidence interval (CI): −22.5 to 1.4] fewer strokes (8.4 ischaemic and 2.2 haemorrhagic strokes), 1.0 (95% CI: −1.9 to 4.1) more cases of systemic embolism, and 2.9 (95% CI: −18.2 to 13.1) fewer bleedings associated with hospitalization.

Conclusion Based on the STROKESTOP study, this analysis shows that a broad AF screening strategy in an elderly population is cost-effective. Efforts should be made to increase screening participation.

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Structured Graphical Abstract

Key Question

Is population-based screening for atrial fibrillation in an elderly population cost-effective?

Key Finding

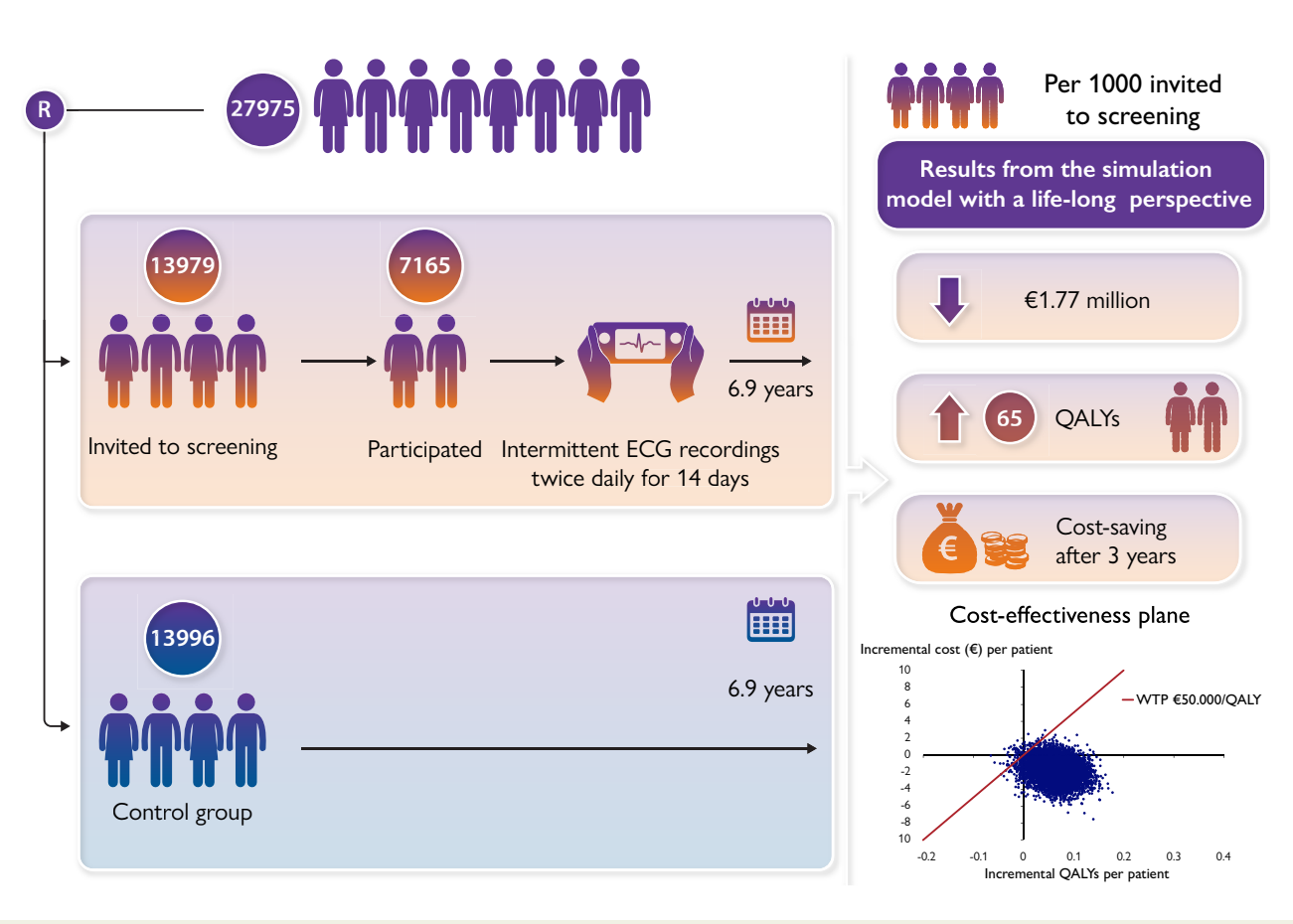
Per 1000 individuals invited to screening:

- 65 QALYs were gained
- €1.77 million lower cost

After three years the screening intervention was cost-saving.

Take Home Message

Screening for atrial fibrillation in an elderly population gains quality adjusted life years, reduces costs and is cost-effective.



QALY, quality-adjusted life year.

Keywords Atrial fibrillation • Screening • Stroke prevention • Cost-effectiveness • Markov modelling

Introduction

Atrial fibrillation (AF) is associated with increased mortality and morbidity. Notably the risk of ischaemic stroke is increased up to five times.[1] As AF is commonly asymptomatic, it can remain undetected. In ~10% of stroke patients, AF is only diagnosed after the stroke event.[2]

Treatment with oral anticoagulants (OACs) in patients with AF lowers the risk of ischaemic stroke by almost two-thirds, reduces all-cause mortality by 25%, but increases the risk of bleeding.[3] However, the introduction of direct oral anticoagulants (DOACs) has significantly decreased the risk of haemorrhagic stroke and major bleeding compared with warfarin.[4] Screening for AF has been recommended in recent

European guidelines on the presumption that early discovery of AF will enable OAC and prevent future strokes.[5] Previous studies on the cost-effectiveness of AF screening are based on assumptions of long-term clinical effects, which cause uncertainty for decision-makers.[6–14] The STROKESTOP study randomized 27 975 persons aged 75/76 years living in two regions of Sweden into a screening invitation group and a control group and has a median follow-up time of 6.9 years. The primary results of the STROKESTOP study showed a significant reduction in the primary endpoint in favour of the screening group.[15] The long-term follow-up from this first randomised population screening trial for AF provides new data for a cost-effectiveness analysis. The aim of this study was to estimate the cost-effectiveness of population-based screening for AF in 75/76-year-old individuals.

Methods

Analytic approach

The cost-effectiveness analysis was based on data from the STROKESTOP study and was a pre-specified secondary outcome of the trial. These data were extrapolated to a life-time perspective using a half-year cycle length decision analytic Markov model. Such a model consists of multiple health states individuals can be in and move between based on specific transition probabilities. In the model, we analysed 1000 hypothetical individuals who were invited to screening and 1000 individuals who were not invited to screening based on the patient characteristics in the STROKESTOP study. The screening group was run separately for participants and non-participants in the Markov model because the risk of thrombo-embolic events, bleeding, and death differed between groups.[15] The results from the two groups were merged, mirroring the group randomized to screening invitation. *Figure 1* shows the Markov model and health states. Both deterministic and probabilistic sensitivity analyses were performed to study the uncertainty of parameters and assumptions. The 95% confidence intervals were calculated from the probabilistic sensitivity analysis using the percentile method. Most of the data were taken from within the trial, but some data were retrieved from published literature and registers (*Table 1*).

The STROKESTOP study

The aim of the STROKESTOP study was to assess if systematic screening for AF could reduce mortality and morbidity compared with no screening. In short, all 75/76-year-old individuals from two regions in Sweden (Stockholm and Halland, $n = 28\,768$) were randomized either to be invited to screening or to be part of the control group. Of the 13 979 randomized to be invited to screening for AF, 7165 (51.3%) participated and were equipped with a hand-held ECG recorder (Zenicor-EKG; Zenicor Medical Systems AB, Stockholm, Sweden). The participants were instructed to perform 30 s recordings twice daily for 2 weeks, and AF was defined as any AF with at least one 30 s recording with an irregular rhythm without *p* waves or a minimum of two similar episodes lasting 10–29 s during the 2 weeks of intermittent recording. The group invited to screening and the control group were followed for a minimum of 5.5 years with regard to the primary outcome, which was a combined endpoint of ischaemic or haemorrhagic stroke, systemic embolism, bleeding leading to hospitalization, and all-cause death on intention-to-treat analysis. The National Patient Register, the Prescription Register, and the Cause of Death Register were used for follow-up on endpoints. The results are described elsewhere in detail, but to summarize there were fewer primary endpoint events occurring in the intervention group [4456 (31.9%) of 13 979; 5.45 events per 100 years (95% CI 5.52–5.61)] compared with the control group [4616 (33.0%) of 13 996; 5.68 events per 100 years (5.52–5.85); hazard ratio 0.96 (95% confidence interval 0.92–1.00); $P = 0045$].[15, 21, 22] The number needed to invite to the screening in order to avoid one event was 91. There were no significant differences between the group invited to screening and the control group in the pre-specified secondary endpoints in the intention-to-treat analysis with regard to ischaemic stroke, haemorrhagic stroke, hospitalization from major bleeding, death or dementia, analysed separately, whereas in the as-treated analysis, a significant reduction of ischaemic stroke was seen in the participants compared with the control group. The median follow-up time for data used in the report of the endpoints was 6.9 years,[15] and these data are regarded as within-trial data in this health-economic study. Clinical trial registration NCT01593553.

Risk of events

The risks for moving into different health states were taken from the STROKESTOP study, and the definition of the events, ischaemic stroke, haemorrhagic stroke, and systemic embolism was in accordance with the STROKESTOP study.[15] However, hospitalization for major bleeding was divided into four health states: (i) other intracranial bleeding (ICD-10 code I61 was excluded), (ii) gastrointestinal bleeding, (iii) urogenital bleeding, and (iv) other bleeding. To obtain the half-year probability for these states, we fitted curves using exponential and Weibull distribution. We then compared the Akaike information criteria of the two curves, and if these values differed <2%, we preferred the exponentially distributed curve. See *Table 1* for probabilities for each group in the model.

Prevalence of atrial fibrillation and oral anticoagulant use

The prevalence of AF by age was estimated in the same way as for events. However, previous studies have shown that the prevalence of AF continues to increase up to 80–85 years of age.[23] The prevalence at higher ages is less reliable; therefore, for ages 85 and older in the model, we apply the same prevalence as for 85-year-old individuals. The percentage of individuals taking OAC was obtained every half-year for each group up until 7 years of follow-up, after which we assumed that the percentage remained constant.

Death probabilities

Age-specific mortality rates were taken from Swedish life tables for the year 2019. As this was a random sample of the entire population in two regions of Sweden, these rates were used as death risks in the control group. To obtain the death risk for participants and non-participants, we used STROKESTOP data on non-stroke-related deaths. We then applied an exponential distribution with the control group as a reference and obtained risk ratios (RRs) for each group. These RRs were then multiplied with the age-specific mortality rates to get the death risks for these groups. After the follow-up period of 7 years, we conservatively assumed that the risk of dying was the same in all groups. Because stroke is associated with a substantially increased risk of dying, we decided to depart from overall mortality rates and instead applied stroke-specific death rates for the first year following a stroke. These probabilities were separate for ischaemic and haemorrhagic strokes and were taken from a Swedish study using population-based data.[16]

Resource usage and unit costs

Table 1 lists all the unit costs used in the model. Resources used in the screening procedure included invitations to screening, device costs, staff costs, materials, equipment, and additional examinations due to difficulties in diagnosing AF. The screening unit cost was estimated by the Karolinska Trial Alliance in 2016. For the unit cost of investigation associated with a new AF diagnosis, we assumed that all individuals had an echocardiogram, an initial cardiology visit, followed by a primary care physician visit. After the screening procedure, resource usage related to thrombo-embolic events, bleedings, and OAC treatment was included in the model. A societal perspective was used, but no production loss was included as only a very low proportion of individuals were expected to be employed due to their high age (≥75 years). We assumed that all individuals used DOAC, and the direct drug cost was obtained from Pharmaceutical Specialties in Sweden. Additional to the direct drug cost, individuals using DOAC were estimated on average to make 0.5 cardiologist visits and 1.25 primary care physician

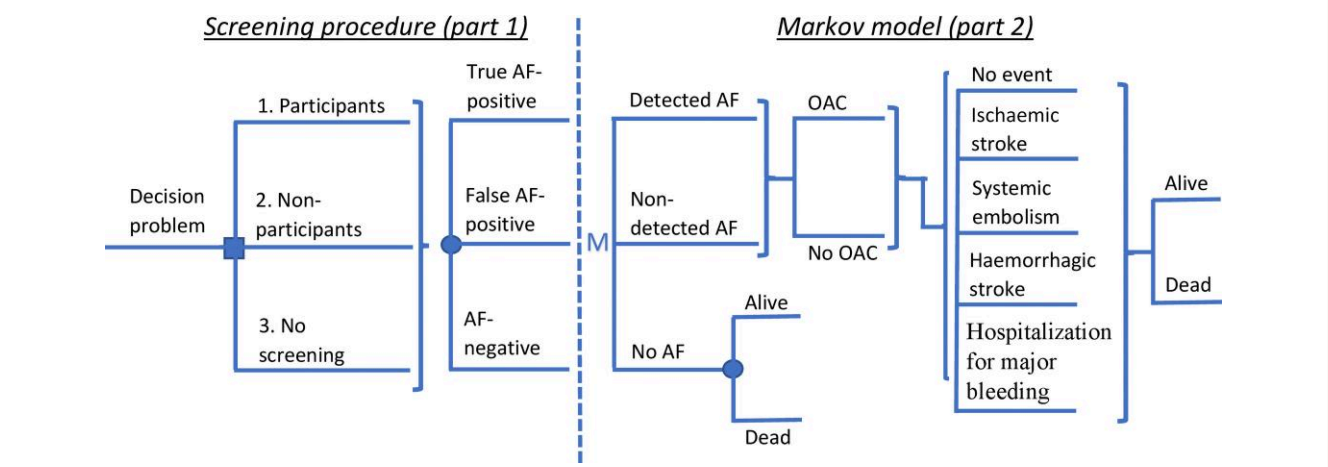


Figure 1 Basic description of the structure in the decision analytic Markov model. The decision problem and screening procedure is described in Part 1 of the model, while Part 2 is based on the risk of thrombo-embolic events and bleedings. Part 2 was repeated every half-year up to 7 years (within trial) and then data were extrapolated to the rest of the life of the hypothetical individuals. Hospitalization for major bleeding is divided into the following health states: (i) other intracranial bleeding (ICD 10 code I61 was excluded), (ii) gastrointestinal bleeding, (iii) urogenital bleeding, and (iv) other bleeding. AF, atrial fibrillation; OAC, oral anticoagulant; M, Markov model.

visits annually. The unit cost of a primary care physician was obtained from the Southeast Healthcare region of Sweden. Unit costs for thrombo-embolic events and bleeding were obtained from the published literature. We could not find a unit cost for urogenital bleeding, but we assume that it is the same as for other bleeding. A 3% discount rate was used for both costs and effects. All unit costs were adjusted to the year 2021 using the price index with quality-adjusted salaries for regions (LPIK), and converted to euros using the exchange rate on 21 April 2021 (1€ = 10.2 SEK).

Utility weights

The quality-adjusted life year (QALY) weights used in the model were attributed to the participants' age based on the utility in the overall population of Sweden.[19] The study by Burstrom *et al.*[19] does not present QALY weights for persons older than 88 years, but we assumed equal QALY weights beyond the age of 88 years. Both ischaemic and haemorrhagic strokes are associated with reduced quality of life, and we thus applied QALY decrements for stroke patients as presented by Luengo-Fernandez *et al.*[20] Quality-adjusted life year decrements were divided by time after stroke and were separate for ischaemic and haemorrhagic strokes according to data from this study. *Table 1* presents the quality of life and utility decrements used in the model.

Participation rate

In addition to the main analyses, we modelled what could be expected to happen to the cost-effectiveness of screening if we, hypothetically, could increase the participation rate. We tested this by using two different rates of participation: 65 and 80%. This analysis shows the number of resources that could be saved by an increased participant rate and thus how much could potentially be spent on different campaigns. In this analysis, we created a new group in the model consisting of a random sample from the non-participation group. The size of the new group was estimated by 1000 × (new participant rate – original participant rate). We assumed that these individuals have the same mortality as individuals in the non-participation group, except for the proportion of patients having AF. Patients in the new group with AF were assumed to have the same mortality as those in the control group, and the risk for thrombo-embolic events and bleeding was assumed to follow the risk in the participant group.

Results

Base-case scenario

In the base-case scenario, screening of 1000 individuals resulted in 10.6 [95% confidence interval (CI): −22.5 to 1.4] fewer strokes (8.4 ischaemic and 2.2 haemorrhagic strokes), 1.0 (95% CI: −1.9 to 4.1) more cases of systemic embolism, and 2.9 (95% CI: −18.2 to 13.1) fewer bleedings associated with hospitalization (*Table 2*). Overall, there were 7.8% fewer strokes in the group invited to the screening compared to the control group (*Table 2*). Per 1000 individuals invited to screening, there were 77 gained life years and 65 gained QALYs. The incremental cost per gained QALY was −€27 156 and in total, the cost was €1.77 million lower in the screening invitation group. Gained QALYs to a lower cost means that the screening strategy was dominant. The screening strategy became cost-saving after 3 years (*Figure 2*). The total cost for stroke and systemic embolism was €1.91 million lower in the screening intervention group. The total cost for bleedings associated with hospitalization was €0.01 million lower and the screening that identified individuals with new AF and OAC use was €0.15 million higher in the screening intervention group.

Probabilistic sensitivity analysis

Figure 3 shows the incremental cost-effectiveness plane from 10 000 Monte Carlo estimates of incremental costs per patient and benefits per patient invited to AF screening with no screening. The result from the probabilistic sensitivity analysis showed that the AF screening strategy was cost-effective—if the willingness to pay is set to €50 000/QALY—in 99.2% of the simulations. Atrial fibrillation screening was dominant in 92.7% of the simulations. The screening strategy remained dominant even if the bleeding was excluded from the model.

Deterministic sensitivity analyses

Table 3 presents the deterministic sensitivity analyses. Limiting the time horizon to the within-trial period of 7 years still showed that the screening strategy was dominant vs. non-screening. The sensitivity analyses also

Table 1 **Markov model inputs: event probabilities, utilities, and costs.**

Model input parameters				
6-month probabilities for events*	**Participants**	**Non-participants**	**Controls**	**Source**
Ischaemic stroke	0.00367	0.00500	0.00464	Strokestop
Haemorrhagic stroke	0.00060	0.00094	0.00085	Strokestop
Systemic embolism	0.00025	0.00043	0.00029	Strokestop
Other intracranial bleeding	0.00133	0.00165	0.00139	Strokestop
Gastrointestinal bleeding	0.00182	0.00331	0.00273	Strokestop
Urogenital bleeding	0.00171	0.00199	0.00191	Strokestop
Other bleeding	0.00246	0.00337	0.00284	Strokestop
Atrial fibrillation				
Baseline prevalence (at year 0)	*13.9% (10.2 +3.7)*	*14.1%*	*12.8%*	Strokestop
Prevalence change of atrial fibrillation (used up to 85 year, then prevalence is assumed to be constant)				
6-month change*	0.00647	0.00682	0.00610	Strokestop
AF-patients on OAC treatment (within-trial data up to 7 years, then OAC use is assumed to be the same as year 7)				
Value year 0 and 7	75%, 87%	74%, 86%	73%, 89%	Strokestop
***Risk ratios (RR) (non-stroke related death)** *				
RR vs controls	0.577	1.404	1.000 (Ref)	Strokestop
Death	**0-6 months**	**6-12 months**	**>12 months**	**Source**
Death after Ischaemic stroke	0.188	0.063	Same as normal population	[16]
Death after Haemorrhagic stroke	0.377	0.067	Same as normal population	[16]
Costs				
Screening related cost and cost for new AF				
Screening cost	€ 235	Zenicor		Budget Strokestop 2 Karolinska Trial Alliance (KTA) 2016
AF	€ 512	One cardiology visit and 1 visit at primary health care centre		Nord-DRG E83O and local price list
OAC (per 6-months)	€ 574	Direct drug cost+cost for controls (0.25 cardiology visits and 1.25 visits at primary care centre every year)		Nord-DRG E80O and local price list
Stroke	**0-6 months**	**6-12 months**	**>12 months (per year)**	**Source**
Ischaemic stroke	€ 18,521	€ 20,488	€ 18,529	[17]
Haemorrhagic stroke	€ 28,861	€ 19,633	€ 20,536	[17]
Systemic embolism and bleeding	**One-time cost**			**Source**
Systemic embolism	€ 4,476			[18]
Other intracranial bleeding	€ 5,841			[18]
Gastrointestinal bleeding	€ 4,926			[18]
Urogenital bleeding	€ 1,873			Assumption, same as other bleeding
Other bleeding	€ 1,873			[18]
General quality of life	**76-79 years**	**80-88 years**	**89+ years**	**Source**
General age-specific weights	0.794	0.733	0.733	[19]

Continued

Table 1 *Continued*

Model input parameters				
6-month probabilities for events*	**Participants**	**Non-participants**	**Controls**	**Source**
QALY-decrement due to stroke	**0-6 months**	**6-12 months and 12-24 months**	**24-60 months and >60 months**	**Source**
Ischaemic stroke	0.190	0.150 and 0.150	0.190 and 0.190	[20]
Haemorrhagic stroke	0.270	0.200 and 0.180	0.040 and 0.070	[20]

**The lambda value was obtained from an exponential distribution*

Table 2 Total number of events per 1,000 individuals and cost-effectiveness of intervention compared with controls based on a lifetime horizon

Total number of events	Participants (n=513)	Non-participants (n=487)	Total intervention (n=1000)	Controls (n=1000)	Incremental
Ischaemic stroke	50.5	56.1	106.6	115.0	-8.4
Haemorrhagic stroke	8.2	10.6	18.8	21.0	-2.2
Systemic embolism	3.4	4.8	8.2	7.2	1.0
Other intracranial bleeding*	18.3	18.5	36.9	34.4	2.5
Gastrointestinal bleeding*	25.1	37.1	62.2	67.5	-5.3
Urogenital bleeding*	23.4	22.4	45.8	47.3	-1.4
Other bleeding*	33.8	37.9	71.7	70.3	1.4
Cost-effectiveness					
Life years	5,527	4,569	10,097	10,020	77
QALYs	4,118	3,401	7,520	7,454	65
Life-time costs	€ 12,224,240	€ 13,125,292	€ 25,349,532	€ 27,117,618	-€ 1,768,086
Cost per gained life year					-€ 23,011
Cost per gained QALY					***-€ 27,156***

**Bleedings associated with hospitalisation*

showed that even if the cost associated with screening, and the cost associated with newly diagnosed AF, and annual AF cost are increased five times, the screening strategy was still dominant vs. non-screening.

Increasing the participation rate

The result from the participation rate simulation showed that if the participation rate was increased to 65%, 2.6 more QALYs per 1000 individuals would be gained at an additional cost of €0.06 million. If willingness to pay is set to €50 000/QALY, we could spend a total of €0.07 million per 1000 individuals on screening activities with the aim of increasing the participation rate. Simulating a participation rate of 80%, 5.4 more QALYs per 1 000 individuals were gained at an additional cost of €0.2 million.

Discussion

This is the first health-economic study using actual long-term clinical follow-up data from a randomized trial in screening for AF. Using within-trial data with a median follow-up time of 6.9 years extrapolated to a Markov model with a life-time perspective, the main results showed that screening for AF was associated with both lower costs and gained QALYs (*Structured Graphical Abstract*). The screening strategy was thus dominant vs. non-screening and cost-saving, after 3 years. This was mainly explained by a low cost for screening and OAC treatment, in addition to fewer cases of stroke in the screening invitation group.

This study is based on the Swedish cost structure and cost levels. Since healthcare systems and cost levels vary for different countries, the results could therefore not be directly applied in other healthcare systems.

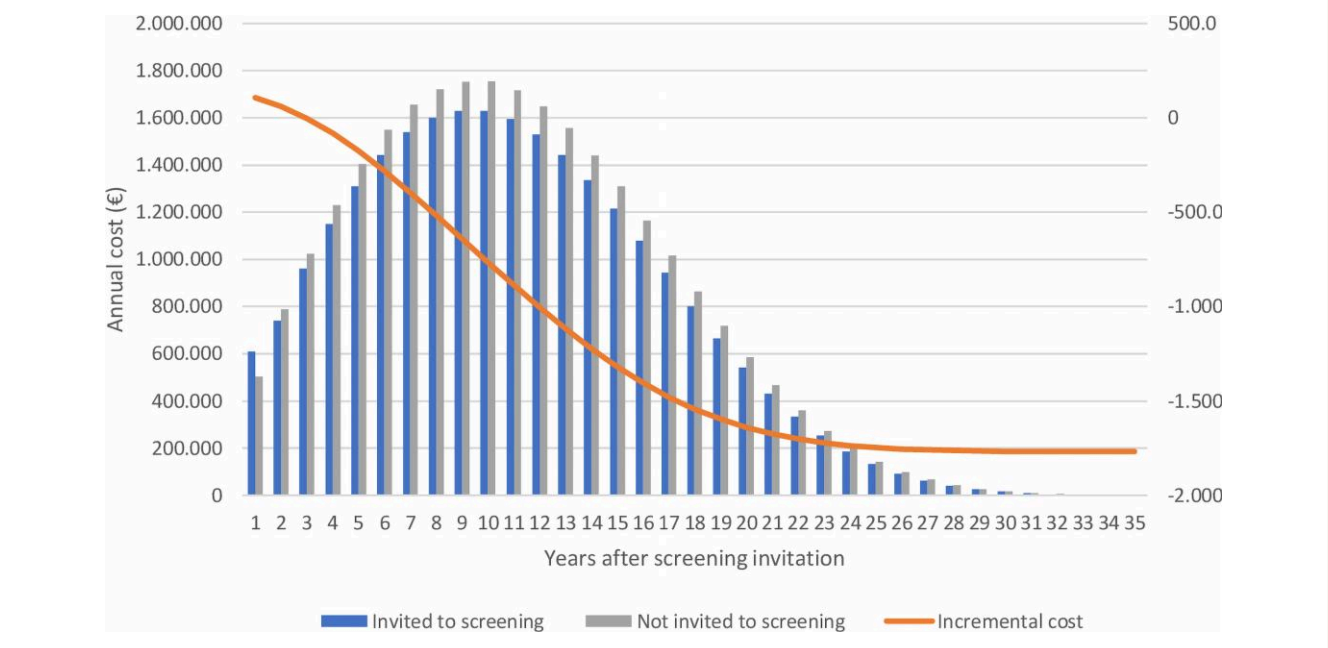


Figure 2 Annual cost (€) for 1000 individuals invited to screening compared with 1000 individuals not invited to screening (left *y*-axis) and incremental cost (€) (right *y*-axis) per 1000 individuals. *X*-axis displays elapsed time from screening invitation in years. Break-even (the incremental cost ≤ 0) occurs 3 years after screening invitation, which means that the screening strategy then becomes cost-saving.

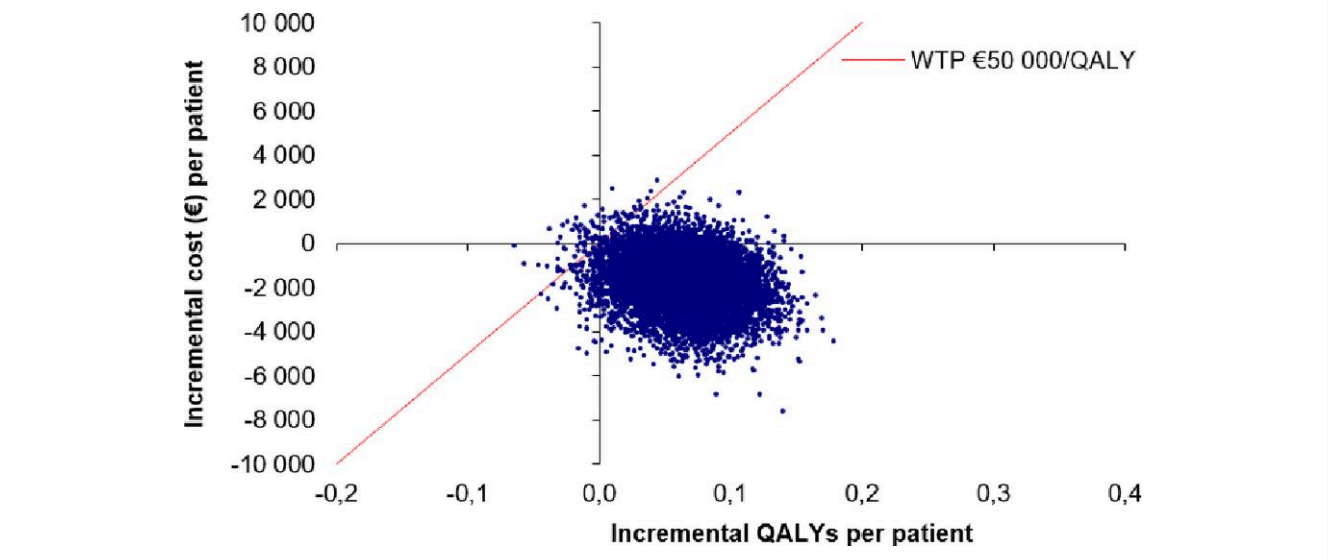


Figure 3 Incremental cost-effectiveness plane showing 10 000 Monte Carlo estimates of incremental costs per patient and benefits per patient of atrial fibrillation screening compared with no screening. Atrial fibrillation screening was found to be cost-effective if willingness to pay is set to €50 000 in 99.2% of the simulations. Atrial fibrillation screening resulted in gained QALYs in 98.4% and saved costs in 94.0% of the simulations. Atrial fibrillation screening was dominant in 92.7% of the simulations.

To the best of our knowledge, nine other cost-effectiveness analyses of screening for AF exist, and the majority of them show cost-effectiveness for AF screening. However, these studies are all based on assumptions, and different screening strategies (population-based/opportunistic), screening devices, and age inclusion criteria are used.[6–14] In prior studies, the incremental cost-effectiveness ratio varied between dominant to €23 004/QALY for screening directed at individuals 65 years or older.[7, 10, 11, 13] For screening directed at 75-year-old individuals, the incremental cost-effectiveness ratio varied between dominant and €39 485/QALY.[6, 8, 12, 14] A previous Swedish health-economic study partly based on early STROKESTOP data showed a cost-effectiveness of €4313 per QALY.[6] Compared with our previous study, we can

Table 3 One-way sensitivity analyses of cost-effectiveness for 1,000 individuals invited to screening compared with 1,000 individuals not invited to screening (€)

	Cost per QALY gained (€)
Base case	Dominant
Time horizon	
7 years (within trial)	Dominant
15 years	Dominant
Discounting rate	
0%	Dominant
10%	Dominant
Cost of ischaemic stroke	
50% lower	Dominant
200% higher	Dominant
Cost of haemorrhagic stroke	
50% lower	Dominant
200% higher	Dominant
Risk ratio death (non-participants vs controls)	
20% lower	Dominant
20% higher	€ 31,168
Risk ratio death (participants vs controls)	
20% lower	Dominant
20% higher	€ 181,460
Diminishing risk ratio for death after within-trial period	
Risk ratio equals 1 after 5 years	Dominant
Risk ratio equals 1 after 10 years	Dominant
Screening and AF related costs	
500% higher	Dominant

now show that the cost-effectiveness has improved compared with previous estimates. Using within-trial data, fewer assumptions were made as estimates of event risks were improved. Further improved unit cost estimates for long-term societal costs of ischaemic and haemorrhagic stroke were included, which showed an increase in stroke-related costs.[6]

The major strength of this study is that our health-economic model is based on actual long-term study data with relatively few assumptions. For example, no assumptions about the rate of spontaneous AF detection and stroke risk differences between normally detected AF and screening-detected AF had to be made. Some assumptions have been necessary to make because STROKESTOP did not include actual cost data and quality-of-life estimates related to events. All our assumptions have been conservative, and we have applied average event risks, costs, and QALYs. For example, we used a conservative cost estimate for AF-related strokes and counted that as similar to a non-AF-related stroke, although outcomes are more severe overall for AF-related strokes. A limitation in the study was that functional disability as estimated by the modified Rankin's scale (mRS) was not available for stroke patients in the STROKESTOP study, and mRS-specific cost estimates presented by Lekander *et al.*[17] could not be used. Stroke cost is highly dependent on the level of mRS, and the use of mRS-specific cost estimates would likely have provided better cost estimations and more accurate uncertainty estimates in the model.[17] For patients with AF who sustained an ischaemic stroke event despite adequate OAC therapy, it was counted as a regular stroke event. This might overestimate stroke severity as anticoagulation with vitamin K antagonists, resulting in a PT/INR above 2.0, reduces the severity of stroke;[24] however with regard to DOAC, evidence on the severity of stroke is sparse.[25–28]

A weakness in the STROKESTOP study was that it did not show statistical significance for ischaemic stroke ($P = 0.08$), haemorrhagic stroke ($P = 0.27$), or hospitalization for major bleeding ($P = 0.65$). Notably, the composite endpoint of ischaemic or haemorrhagic stroke, systemic embolism, hospitalization for bleeding, or death from any cause showed statistical significance ($P = 0.045$). In this health-economic analysis, all relevant parameters were used irrespective of statistical significance in the STROKESTOP study. The model takes all input parameters into account and estimates expected costs and QALYs, which is the relevant approach for policy-making.[29] The uncertainty in each parameter is included in the probabilistic sensitivity analysis, which is recommended as the preferred method in health-economic evaluations.[30, 31] If a parameter estimate is highly uncertain, for instance, the probability of haemorrhagic stroke, this parameter will have little impact on the results.

The participation rate in this population-based screening study was just over 50%. This is lower than in some population-based prevalence studies that showed participation rates between 60 and 82%.[32–34] In our analysis, we compared the groups invited to screening (consisting of the group participating and the group choosing not to participate) with the control group that was not invited.

In the model, there were more cases of another intracranial bleeding but fewer cases of gastrointestinal bleeding in the screening group compared with the control group. Overall, there were fewer bleeding events in the screening group. This is counterintuitive, as OAC therapy increases bleeding risks. However, as the point estimate for bleeding is uncertain, the model accounts for this, and thus, the impact of bleeding is minimal in our model with an incremental cost for bleeding of $10 000 in favour of screening. The probabilistic sensitivity analysis, which includes the uncertainty of the bleeding parameters, shows that excluding bleeding from the model does not affect the probability that the screening strategy was dominant.

The benefits and risks of OAC therapy in screening-detected AF and in patients with a low burden of AF have been the topic of debate. In the STROKESTOP study, OAC therapy was initiated in participants with newly detected AF based on the assumption that these patients would be similar to asymptomatic patients with incidentally detected AF. Asymptomatic patients have been shown to have similar risks of AF-related morbidity and mortality as symptomatic patients,[35] with similar benefits of OAC therapy.[36] In contrast with studies of more prolonged monitoring, the STROKESTOP study used a very brief duration of monitoring, and one can assume that AF detected during this brief timespan likely reflects a high AF burden. Indeed, over time, many participants in the STROKESTOP study progressed to permanent AF.[37]

The low participation rate is a concern because the individuals not participating had increased mortality and the highest event rates of

stroke and bleeding. Therefore, great efforts should be made to reach non-participants. This is, of course, costly; however, our simulations indicate that money could be saved by increasing the participation rate and preventing ischaemic strokes through early initiation of stroke-protective OAC treatment. In the STROKESTOP II study, a 2% increase in the participation rate in Stockholm was achieved by decentralized screening, and more attendees with low sociodemographic factors participated.[38] A comparison of the two included regions in the STROKESTOP study showed a much higher participation rate in the smaller, rural region of Halland (61.2%) than in the capital region of Stockholm (47.6%).[39] If population-based AF screening were to be implemented, reducing the geographic distance to the screening centre could possibly increase the participation rate. Existing implemented screening programmes for aortic aneurysm, breast cancer, and cervical cancer, although aimed at considerably younger age groups, show participation rates of around 80%.[40–42]

The implication of this study is that population-based AF screening for 75/76-year-old individuals is cost-effective at a probability of 99.2% and cost-saving at a probability of 92.7% and should therefore be implemented. Further research should be focused on finding the optimal screening strategy, including increasing participation, age at the start of screening, and the number of screening occasions.

Based on the STROKESTOP study, this analysis shows that a broad AF screening strategy in an elderly population is cost-effective. Efforts should be made to increase screening participation.

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Data availability

The data underlying this article cannot be shared publicly due to for the privacy of individuals that participated in the study. The data will be shared on reasonable request to the corresponding author.

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