

The budget impact of implementing atrial fibrillation-screening in European countries

Michaela Eklund ^{1*}, Lars Bernfort ¹, Kajsa Appelberg¹, Daniel Engler ^{2,3},
Renate B. Schnabel ^{2,3}, Carlos Martinez⁴, Christopher Wallenhorst⁴,
Giuseppe Boriani ⁵, Claire M. Buckley⁶, Søren Zöga Diederichsen⁷,
Jesper Hastrup Svendsen^{7,8}, Joan Montaner^{9,10,11}, Tatjana Potpara ^{12,13},
Lars-Åke Levin ¹, and Johan Lyth ¹

¹Unit of Healthcare Analysis, Department of Medical and Health Sciences, Linköping University, Linköping, Sweden; ²Department of Cardiology, University Heart & Vascular Center Hamburg, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; ³DZHK (German Center for Cardiovascular Research), Partner Site Hamburg/Kiel/Luebeck, Germany; ⁴Institute for Epidemiology, Statistics and Informatics GmbH, Frankfurt, Germany; ⁵Cardiology Division, Department of Biomedical, Metabolic and Neural Sciences, Italy University of Modena and Reggio Emilia, Policlinico di Modena, Modena, Italy; ⁶School of Public Health, University College Cork, Cork, Ireland; ⁷Department of Cardiology, Copenhagen University Hospital - Rigshospitalet, Inge Lehmanns Vej 7, 2100 Copenhagen, Denmark; ⁸Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Blegdamsvej 3B, 2200 Copenhagen, Denmark; ⁹Neurovascular Research Laboratory, Vall d'Hebron Institute of Research (VHIR) Universitat Autònoma de Barcelona, Barcelona, Spain; ¹⁰Institute de Biomedicine of Seville, IBI/S/Hospital Universitario Virgen del Rocío/CSIC/University of Seville; ¹¹Department of Neurology, Hospital Universitario Virgen Macarena, Seville, Spain; ¹²Medical Faculty, University of Belgrade, Belgrade, Serbia; and ¹³Cardiology Clinic, University Clinical Centre of Serbia, Belgrade, Serbia

KEYWORDS

Atrial fibrillation;
Budget impact analysis;
Screening;
ECG monitoring;
Anticoagulation;
Stroke prevention

A budget impact analysis estimates the short-term difference between the cost of the current treatment strategy and a new treatment strategy, in this case to implement population screening for atrial fibrillation (AF). The aim of this study is to estimate the financial impact of implementing population-based AF-screening of 75-year-olds compared with the current setting of no screening from a healthcare payer perspective in eight European countries. The net budget impact of AF-screening was estimated in country-specific settings for Denmark, Germany, Ireland, Italy, Netherlands, Serbia, Spain, and Sweden. Country-specific parameters were used to allow for variations in healthcare systems and to reflect the healthcare sector in the country of interest. Similar results can be seen in all countries AF-screening incurs savings of stroke-related costs since AF treatment reduces the number of strokes. However, the increased number of detected AF and higher drug acquisition will increase the drug costs as well as the costs of physician- and control visits. The net budget impact per invited varied from €10 in Ireland to €122 in the Netherlands. The results showed the increased costs of implementing AF-screening were mainly

*Corresponding author. Tel: +46 (0)13 28 89 68, Email: michaela.eklund@liu.se

driven by increased drug costs and screening costs. In conclusion, across Europe, though the initial cost of screening and more frequent use of oral anti-coagulants will increase the healthcare payers' costs, introducing population screening for AF will result in savings of stroke-related costs.

Introduction

The estimated prevalence of atrial fibrillation (AF) in 2016 was 7.7% in the population over 65 years old across Europe,¹ and the estimated lifetime risk for development of AF is over 24% by the age of 90 years². Incidence of AF is estimated to increase further in the future as the population ages³. In the European Union, it is estimated that the number of individuals with AF will more than double between 2010 and 2060. This increase is especially significant in the population 55 years or older.^{3,4} The increased prevalence of AF comes with a significant public health burden as AF is associated with significant morbidity and mortality.⁴ The risk of stroke is almost five-fold for a patient with AF, and 15-23% of all stroke-cases are attributed to AF.^{3,5} Asymptomatic AF seems to have similar risk for ischaemic stroke as symptomatic AF.⁶ Atrial fibrillation-related strokes are associated with worse outcomes in terms of severity, morbidity, and mortality compared to non-AF-related strokes.^{3,7,8} The increased severity of AF-related stroke also increases the costs of stroke by 50%.^{7,9} The total direct and indirect cost of stroke globally in 2017 was estimated at €835 billion.¹⁰

Oral anticoagulant (OAC) treatment may prevent 66% of AF-related ischaemic strokes.¹¹ However, uptake of OAC treatment is far from optimal even though European guidelines encourage the use of OAC treatment for AF, especially in patients at higher stroke risk, i.e. a higher CHA₂DS₂-VASc-score.⁹ Since untreated AF is associated with higher risk than treated AF, screening programmes could be used to identify undetected AF patients.⁹ Opportunistic screening by pulse palpation or ECG rhythm strip in patients aged 65 years or older is currently recommended in the ESC guidelines.⁹ However, opportunistic screening alone will likely fail to identify a significant proportion of people with AF not coming to medical attention. With systematic screening on the other hand, it may be possible to identify specific individuals at high risk of stroke and to reduce this risk through the use of anticoagulants.^{3,6}

A budget impact analysis (BIA) assesses the affordability of introducing a new healthcare intervention into a healthcare system.¹² Specifically, it estimates the expected annual change in total costs from the budget holders (payers) perspective. Budget holders and decision-makers commonly use BIA to determine whether an intervention is affordable and can be accommodated within the existing budget.¹² The BIA can also provide information on the financial implications of using an intervention in different patient populations, healthcare settings, and geographical regions. BIA is a valuable tool for healthcare decision-makers to assess the financial impact of introducing interventions into the healthcare system and to make informed decisions about

resource allocation.¹²⁻¹⁴ The BIA of AF-screening gives an understanding of the total financial burden of implementation. The incremental cost of implementing AF-screening, the net budget impact, compares the budget impact of screening with the current state of standard care. It presents any potential savings or extra spendings that the AF-screening induces and allows the budget holders to assess the overall budget impact.¹³

This study will estimate budget impact of AF-screening from a healthcare payer perspective in country-specific settings for Denmark, Germany, Ireland, Italy, Netherlands, Serbia, Spain, and Sweden. Country-specific parameters are used to allow for variations in healthcare systems, costs, population size, gender distribution, oral anti-coagulation treatment strategies, screening devices, and to meet the guidelines and needs of the healthcare sector in the country of interest. Previous BIAs regarding AF have studied the financial impact of different treatment strategies for detected AF. The motive has been that AF patients with moderate- and high risk for stroke should increase OAC use to decrease the clinical and economic burden of stroke. Generally, the results show cost savings as more effective treatment of AF results in fewer strokes.¹⁵⁻¹⁸

This study aims to estimate the financial impact of implementing systematic AF-screening of 75-year-olds compared with standard of care in eight European countries. A budget impact analysis is important since affordability is a critical factor for budget holders who need to make informed decisions on healthcare interventions and helps to quantify the potential budgetary effects of adopting new programs.

Methods

Budget impact model

This BIA is based on a cost-effectiveness (CE) model developed within the AFFECT-EU project (see [Figure 1](#)).¹⁹ The eligible population is individuals aged 65 and over, given their higher risk of AF. The model consisted of two parts: the first is a decision tree describing the screening procedure. The second part is a Markov model tracking long-term costs and effects, including treatment with OACs and the risk of clinical events. First, the number of screening-detected people is determined by age- and gender-specific prevalence of known and unknown AF as well as the sensitivity of the screening device. The second part of the model consists of the three states: (i) detected AF, (ii) non-detected AF, and (iii) no AF, followed by states describing the OAC treatment and the risk of stroke, bleeding, and mortality. The clinical events included in the model were ischaemic stroke (IS), haemorrhagic stroke, other intracranial bleeding, extracranial bleeding (EB), and systemic embolism (SE). Risk stratification for IS is based on CHA₂DS₂-VASc, but no risk stratification was made for other events.

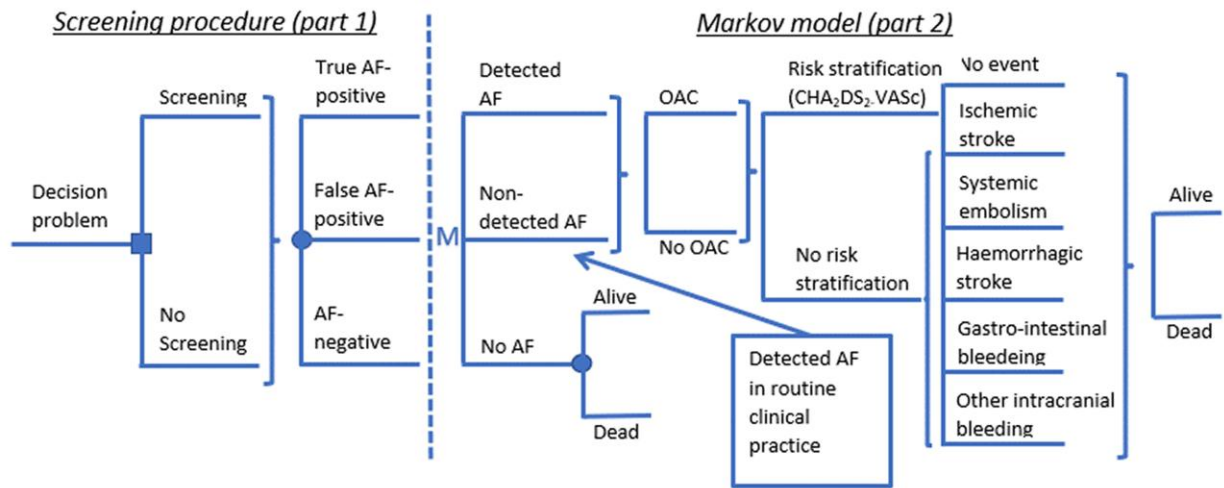


Figure 1 The AFFECT-EU cost-effectiveness model.

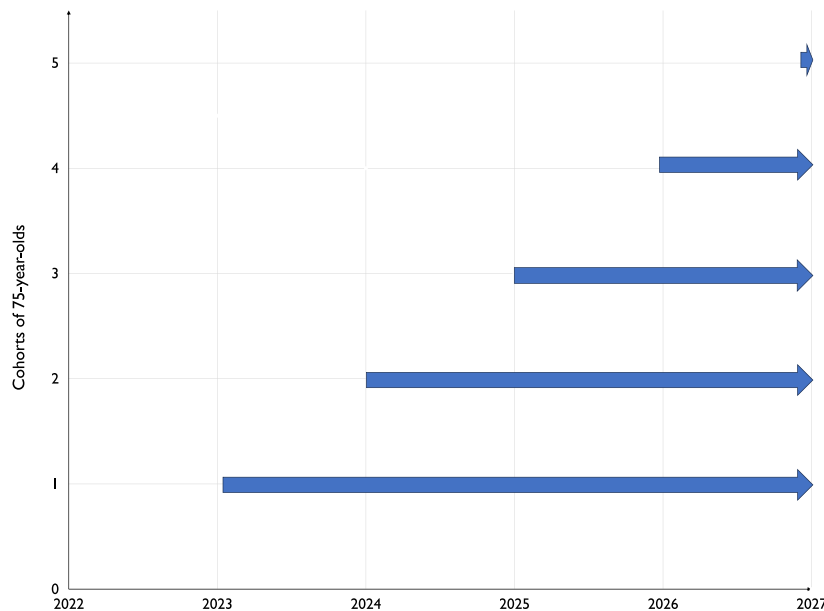


Figure 2 Description of open population where the 2023 cohort is followed up to 5 years, the 2024 cohort up to 4 years etc.

The BIA compares the financial impact of implementing AF-screening with the current strategy of no screening. The difference between these strategies is the net budget impact of implementing AF-screening, i.e. the potential added costs or cost savings of implementing AF-screening. The relevant costs are estimated and summed for the country-specific budget holder for both treatment strategies. The budget holders that are relevant in this study are the country-specific healthcare payer. Due to future external economic and political uncertainty budget holders typically have short-term budgets to adhere to. Hence, the BIA is performed with a 5-year time horizon.^{12,20} Because of the short-term budgets there are no discounting in the model.^{12-14,21}

The budget impact model is dynamic and considers various time-dependent factors such as patent expiration for direct oral anti-coagulants (DOACs), and age- and gender-dependent changes in the eligible population. The country-specific models

are developed with country-specific parameters and allowed for several adjustments to fit the local healthcare systems. The country-specific inputs were OAC treatment strategies, AF-prevalence, screening yield and preferred screening device, mortality, participant rate, population size, budget holder, and cost estimates. The BIA reflects real-world conditions where a new cohort of 75-year-olds is added to the model annually (open population, as per Figure 2) and presents the total cost of implementing of AF-screening over 5 years. The budget impact per invitee was estimated and presents the 5-year cost of inviting one 75-year-old in 2023 (closed population).

Country-specific budget holder

In Denmark, 98% of the population has chosen to belong to insurance coverage group 1. Since retirees (age > 66-68) rarely have any additional private insurance, we do not account for

Table 1 Input parameters

	Denmark	Germany	Ireland	Italy	Netherlands	Serbia	Spain	Sweden
Participant rate	51% ³⁹	62% ⁴⁰	51% ³⁹	51% ³⁹	51% ³⁹	51% ³⁹	51% ³⁹	51% ³⁹
Screening costs (€)	1.57 ⁴¹	2.50 ⁴¹	1.46 ⁴¹	1.39 ⁴¹	1.75 ⁴²	0.36 ⁴¹	1.22 ⁴¹	2.00 ⁴¹
Screening invitation cost per invitee	36 ^c	28 ^a	27 ⁴³	220 ^b	233 ⁴²	42 ⁴³	136 ⁴⁴	235 ⁴³
Choice of treatment, detected AF (%)	85.0% ^c	73.6% ^a	73.6% ^a	80.0% ^d	88.5% ⁴⁵	14.0% ⁴⁶	63.7% ⁴⁷	86.5% ⁴⁸
DOAC	10.0% ^c	19.4% ^a	19.4% ^a	15.0% ^d	8.1% ⁴⁵	74.0% ⁴⁶	36.3% ⁴⁷	6.5% ⁴⁸
VKA	5.0% ^c	7.0% ^a	7.0% ^a	5.0% ^d	3.4% ⁴⁵	12.0% ⁴⁶	0.0% ⁴⁷	7.0% ⁴⁸
No treatment	1.00 ⁴⁹	0.50 ^a	e	1.00 ^f	e	1.00 ^f	1.00 ^f	1.00 ^f
Costs associated with newly detected AF (€)	3.00 ⁴⁹	1.00 ^a	e	1.00 ^f	e	1.00 ^f	1.00 ^f	1.00 ^f
No. of cardiologist visits	265 ⁵⁰	112 ^a	e	125 ⁵¹	e	50 ⁵²	150 ⁵³	277 ⁵²
No. of PHC/GP visits	21 ⁵⁰	13 ^a	e	26 ⁵⁴	e	35 ⁵⁵	40 ⁵³	193 ⁵⁵
Unit cost cardiologist visit	328	118	225 ⁵⁶	151	388 ⁴²	85	190	470
Unit cost PHC visit								
Total cost								
DOAC (€)	879 ⁵⁷	1 038 ⁵⁸	792 ⁵⁹	506 ⁸	785 ⁶⁰	506 ⁶¹	1 059 ⁶²	631 ⁶¹
Annual drug cost	0	0	e	0.50 ^f	1.00 ⁴²	0.50 ^f	0.50 ^f	0.50 ^f
No. of cardiologist visits	1 ⁴⁹	1 ^a	e	1.25 ^f	0.50 ⁴²	1.25 ^f	1.25 ^f	1.25 ^f
No. of PHC/GP visits	e	e	e	125 ⁵¹	107 ⁴²	34 ⁵²	150 ⁵³	186 ⁵²
Unit cost cardiology visit	21 ⁵⁰	13 ⁶³	e	26 ⁵⁴	39 ⁶⁴	35 ⁵⁵	40 ⁵³	193 ⁵⁵
Unit cost PHC visit	21	13	231	95	127	60	125	334
Physician visits total								
VKA (€)	128 ⁶⁵	88 ⁵⁸	28 ⁵⁹	19 ⁶⁶	54 ⁶⁰	19 ⁶¹	21 ⁶⁷	63 ⁶¹
Annual drug cost	0	e	e	1.00 ^d	1.00 ⁴²	0.50 ^f	e	0.50 ^f
No. of cardiologist visits	0	e	e	1.00 ^d	0.50 ⁴²	0.50 ^f	e	0.50 ^f
No. of PHC visits	e	e	e	125 ⁵¹	107 ⁴²	34 ⁵²	e	186 ⁵²
Unit cost cardiology visit	e	e	e	26 ⁵⁴	39 ⁶⁴	35 ⁵⁵	e	193 ⁵⁵
Unit cost PHC visit	1 116 ⁴⁹	8	446 ⁴⁰	432	167 ⁴²	63	479 ⁶⁷	349
INR controls	1 116	329	446	568	293	97	479	538
Physician visits total								
Ischaemic stroke (annual) (€)								
Inpatient (≤1 year)	15 626 ⁶⁸	6 018 ⁴⁰	9 805 ⁶⁹	13 724 ⁷⁰	29 850 ⁴²	3 772 ⁷¹	6 563 ⁷²	20 862 ⁷¹
Outpatient (≤1 year)	486 ⁶⁸	4 014 ⁷³	2 657 ⁶⁹	—	2 994 ⁴²	727 ⁷¹	2 979 ⁷²	4 0234 ⁷¹
Other ⁿ (≤1 year)	—	8 331 ⁷³	3 917 ⁶⁹	—	10 069 ⁴²	3 445 ⁷¹	—	—
Out- and inpatient (>1 year)	1 272 ⁶⁸	4 331 ⁷³	4 584 ⁶⁹	10 618 ⁷⁴	—	3 772 ⁷¹	2 353 ⁷⁵	7 031 ⁷¹
Other ⁿ (>1 year)	—	948 ⁷³	15 364 ⁶⁹	—	6 628 ⁴²	727 ⁷¹	—	—
Haemorrhagic stroke (annual) (€)								
Inpatient (≤1 year)	18 075 ⁶⁸	13 182 ⁴⁰	9 609 ⁶⁹	22 084 ⁷⁰	27 218 ⁴²	5 878 ⁷¹	5 460 ⁷²	32 510 ⁷¹
Outpatient (≤1 year)	146 ⁶⁸	4 014 ⁷³	3 565 ⁶⁹	—	1 895 ⁴²	647 ⁷¹	2 424 ⁷²	3 576 ⁷¹
Other ⁿ (≤1 year)	—	8 331 ⁷³	3 811 ⁶⁹	—	10 069 ⁴²	3 352 ⁷¹	—	—
Out- and inpatient (>1 year)	1 287 ⁶⁸	4 331 ⁷³	4 928 ⁶⁹	10 618 ⁷⁴	—	1 203 ⁷¹	2 353 ⁷⁵	6 656 ⁷¹
Other ⁿ (>1 year)	—	948 ⁷³	17 368 ⁶⁹	—	6 628 ⁴²	7 161 ⁷¹	—	—

Continued

Table 1 Continued

	Denmark	Germany	Ireland	Italy	Netherlands	Serbia	Spain	Sweden
Other events (per event) (€)								
Systemic embolism	3 696 ⁴⁹	2 640 ⁷⁶	3 975 ⁶⁹	3 123 ⁷⁶	1 992 ⁴²	784 ⁷⁶	2 723 ⁷⁶	4 338 ⁷⁶
Other internal bleedings	4 597 ⁷⁶	3 446 ⁷⁶	2 669 ⁶⁹	4 075 ⁷⁶	4 614 ⁴²	1 024 ⁷⁶	3 553 ⁷⁶	5 661 ⁷⁶
Extracranial bleeding	3 877 ⁷⁶	2 906 ⁷⁶	2 669 ⁶⁹	3 437 ⁷⁶	10 823 ⁴²	863 ⁷⁶	2 997 ⁷⁶	4 775 ⁷⁶

^aR. Schnabel, personal communication. 22 February 2022.

^bG. Boriani, personal communication. 24 March 2022.

^cJ. H. Svendsen, personal communication. 30 March 2022.

^dG. Boriani, personal communication. 12 March 2022.

^eNot specified.

^fL. Friberg, personal communication. 17 May 2021.

^gG. Boriani, personal communication. 23 January 2023.

^hOther costs include rehabilitation and home care services.

any additional insurance.²² Group 1 covered patients are persons who do not pay out-of-pocket (OOP) for primary or specialist care. The budget holder of interest in Germany is the statutory health insurance (SHI), as 88% of the German population use the SHI and it is mandatory for everyone with an annual income below €60 750, including retirees (> 67 years).^{23,24} Ireland has a medical scheme that gives most patients 65 years and older free general practitioner (GP) services and prescription drugs. Since most Irish retirees are on the scheme, this is the budget holder of interest. According to the Irish BIA-guidelines one should take value added tax (VAT) paid by the budget holder into consideration in the BIA.^{13,25} But since there is no VAT on the costs considered in this model, VAT was excluded.²⁶ The national health service (NHS) covers all Italian healthcare costs^{27,28} and is hence the budget holder of interest. In the Netherlands, healthcare insurances cover all healthcare costs. There are some deductibles and insurance premiums, but those are assumed to be paid irrespective of the implementation of AF-screening or not.^{29,30} The Serbian healthcare system is mainly financed by the health insurance, Republic Foundation for Health Insurance (RFHI). There are some co-payments, but vulnerable groups and low-income individuals are exempt from this,³¹ hence RFHI is the budget holder of interest. In Spain, all retirees (age > 65) are enrolled in a healthcare insurance system. Thus, the budget holder in the model is the Spanish national health system (SNS).³² The Swedish healthcare system is mainly administered locally by regions and municipalities. The Ministry of Health and Social Affairs sets overall health policy, the regions finance and deliver healthcare services, and the municipalities are responsible for the care of the elderly and disabled.^{33,34} While both primary and specialist care are covered by the regional healthcare systems, there are co-payments for patients younger than 85.³³ However, for the eligible population aged 75 or older, we assumed that the maximum ceiling for OOP payments is reached regardless of whether screening is implemented or not. Hence, the regions are the budget holders of interest.

Inputs

Cost parameters in the model are adjusted for country-specific healthcare inflation to 2023 by Harmonised Indices of Consumer Prices by Classification of Individual Consumption by Purpose (Coicop)-divisions.^{35,36} Likewise, when needed, costs parameters are adjusted with healthcare Purchasing Power Parities³⁷ to fit the country of interest. The Danish and Swedish costs are recalculated to Euros by using the average August 2023 country-specific exchange rates.³⁸

All cost parameters are presented in [Table 1](#). To implement AF-screening, there is a cost for the invitation as well as the screening procedure. The latter is dependent on the cost of the screening device and the cost of interpreting the results. The devices used are a 12-lead ECG in Denmark, Germany, Ireland, and Serbia, handheld ECG in Netherlands, Spain and Sweden, and smartphones in Italy. In the Netherlands and Spain, there is an algorithm-based interpretation of the results while in the other countries there is a cardiologist interpretation. The sensitivity and specificity of the different screening devices can be found in [Supplementary material online, Table S1](#). For newly detected AF, costs associated with primary health care (PHC), and/or cardiologist visits are included.

Atrial fibrillation patients are usually treated with OACs, and no other treatment is considered in the model. The treatment for those with detected AF is either DOACs, vitamin K antagonists (VKAs), or no treatment at all. First line treatment was DOAC in all countries except for Serbia where VKA is the primary treatment. It is estimated that most patients receive the same dose of drug for lifetime. In all countries except Germany and

Sweden, all drug costs were covered by the healthcare payer. In Germany, the model considers that there is a co-payment for the patients for each prescribed drug covered by the SHI. The co-payment is 10% of the cost with a maximum of €10 and minimum of €5.²³ This implies that since DOAC was on average prescribed 3 times a year, with a cost above €100 per prescription we estimated an annual OOP payment of €30 per patient. Vitamin K antagonist on the other hand was prescribed on average 7 times a year to a cost below €50 which gives an annual OOP cost of €35 per patient. In Sweden, drugs covered by the national drug benefit scheme are subsidized by the state, resulting in a rebate for the patient, while not covered drugs results in full price for the patient. Thus, the state reimburses the regions for all drug costs covered by the national drug scheme the year following their occurrence.⁷⁷ Nevertheless, all drugs are assumed to be covered by the national drug benefit scheme. Regardless of the type of OAC treatment, there are costs for control visits, including both cardiology, PHC, and international normalized ratio (INR) controls. The latter only applies for VKA treatments, which demand more intensive monitoring.

Costs for stroke include in- and outpatient care as well as home care services and special housing. These costs differ from the first-year post-stroke to the following years. In Denmark and Sweden, the healthcare payer covers in- and outpatient care but home care services, rehabilitations, and special housing were paid by the municipality.^{22,33,34} Similarly, in Germany the statutory healthcare insurance covers in- and outpatient care and rehabilitation, while home care service and special housing is covered by the long-term care insurance in combination with some patient co-payments.^{24,27,28} Likewise, the SNS in Spain covers direct healthcare costs, but there are some OOP payments of non-healthcare costs for the patient, family, and social service.³²

Other event costs included in the model were SE, other internal bleedings, and EB. The cost for EB is assumed to be equal to gastrointestinal bleeding. All costs associated with other events are assumed to be paid by the healthcare systems. The CHA2DS2-VASc specific 3-months risks of ischaemic stroke for patients with DOAC, VKA, or no treatment as well as risk stratification for other events are described in [Supplementary material online, Table S2 and S3](#).

Due to patent expirations for DOACs, we performed sensitivity analyses where patents are expected to expire in 2026.⁷⁸ It is estimated that the proportion of patients treated with DOACs will increase, while the proportion receiving VKAs will decrease. This shift in proportions reflects the expected changes as DOACs become more widely available and affordable. Those proportions affect drug costs, physician visits associated with OAC treatment, cost of stroke, and other events. It also estimated that patent expiration of DOACs will decrease the annual cost of DOACs by 90%.

The age- and gender-divided population projections for the years 2023-2027 are retrieved from country-specific population databases (see [Supplementary material online, Table S4-S11](#)). Prevalent AF represent the number of individuals in the given age and gender group with known AF at the start of the year and incident AF present the number of individuals in the given age and gender group that get a non-screening-detected AF-diagnosis during the year. In the Netherlands, the projections are retrieved in 5-year age-groups (65-69, 70-74, 75-79, etc.), therefore a fixed population growth rate, as well as gender- and age-distribution is used to estimate the annual population. The same was done for Serbia where the population projections are in 5-year age-groups and 5-year intervals (2021, 2026, 2031).

The prevalence of known AF by sex and age is based on the average prevalence of seven published studies.^{3,79-84} Smoothing with linear interpolation was used to obtain 1-year intervals out of the original prevalence (5- or 10-year intervals). The

prevalence of unknown AF by sex and age were taken from a large meta-analysis investigating newly detected AFs found in various screening studies.⁸⁵ The number of screening-detected AFs was generated by multiplying the proportion of unknown AF with the number of screened individuals and with a device-specific sensitivity. To assess the impact of the screening yield, the number of patients with spontaneously found asymptomatic AF was subtracted from the cumulative number of patients with screening-detected AFs. The proportion of spontaneous detection of asymptomatic AF was estimated to 5% per year for patients with a screening-detected AF.⁸⁶ Detailed tables are found in [Supplementary material online, Table S12](#).

Results

Total budget impact of implementing population atrial fibrillation-screening

With the current standard of care, no population-based AF-screening, a large share of the costs was stroke-related costs. In most countries, costs for stroke had the largest budget impact in the no-screening analysis, while in Denmark it was the cost of drugs (see [Figure 3A and B](#) and [Table 2](#)). Since the cost of physician, specialist visits, and drug prescriptions generally increases with age, there was an increase in control visits as well as drug costs over time. The share of the other costs decreased over the studied time horizon. As there was an open population, the annual total costs increased as the number of detected AF increased. As the screening cost only applied to the new cohort of 75 years old entering the population each year the annual screening cost was approximately the same.

In Italy, the Netherlands, Serbia, Spain, and Sweden, the largest share of the budget impact of AF-screening was associated with screening costs followed by stroke costs (see [Figure 4](#)). In Denmark, Germany, and Ireland, the largest shares were from drug costs and stroke costs. Figures of the budget impact of AF-screening and no screening in total and per invited can be found in [Supplementary material online, Figures S1 and S2](#).

The net budget impact showed that implementation of AF-screening, increased savings of stroke-related costs in all countries since screening for AF decreased the number of strokes. It also increased the number of detected AF which in turn increased costs for physician visits for newly detected AF, drug costs, and OAC-treatment control visits. More detected AFs increased the use of OACs, which in turn increased the costs of bleedings. The increasing net budget impact was mainly driven by increased drug costs and screening costs.

Five-year budget impact of atrial fibrillation-screening per invitee

The per invitee budget impact of no screening for AF varied from €93 in Serbia to €364 in Germany ([Table 2](#)), and the budget impact of AF-screening per invitee varied from €114 in Serbia to €450 in the Netherlands ([Table 3](#)). Thus, the net budget impact per invited varied from €10 in Ireland to €122 in the Netherlands. These differences were mainly driven by the fact that Italy and the Netherlands had among the highest screening costs.

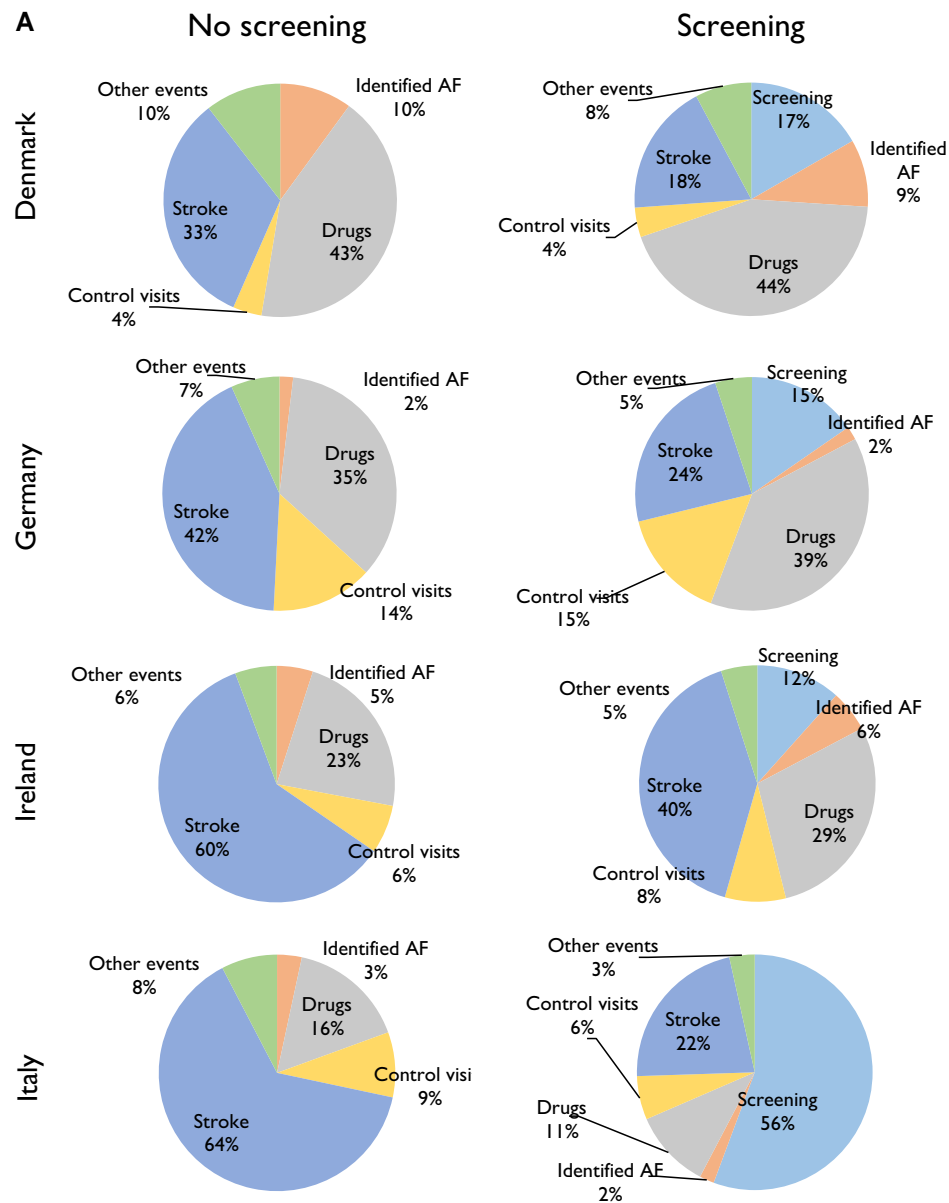


Figure 3 (A, B) Budget impact of no screening and screening divided into different cost types (%). Note: Identified AF = AF investigation and treatment initiation. Control visits = controls for OAC treatment. Other events include costs for systematic embolism and bleedings.

Sweden and Ireland had the largest savings in stroke costs of €31 per invitee. In both Germany and Sweden, there were other budget holders that pay for parts of the drug costs; hence, the healthcare payers had lower drug costs per invitee. Similarly in Denmark, Germany, Italy, Spain, and Sweden, there were other payers who received lower costs due to reduced number of strokes. Since Denmark, the Netherlands and Sweden had higher unit costs for physician visits, there were a larger increase of physician visit costs associated with AF investigation and treatment initiation in these countries.

There was an increase in the net budget impact per invitee (Figure 5) the first year following implementation of AF-screening, which then declined in the following years. This was due to the screening costs which only

occur the first year. The following years it show cost savings for all countries except for Germany to implement AF-screening. But in the longer run it seems to be a trend towards cost savings in all countries.

Sensitivity analyses

Sensitivity analyses were performed assuming that the patent for DOACs will expire in 2026 (Table 4). Due to the BIAs short time horizon, these changes had a marginal decreasing effect on the net budget impact of AF-screening for all countries.

Discussion

This is the first study that has estimated the added cost and/or cost savings of implementing an AF-screening

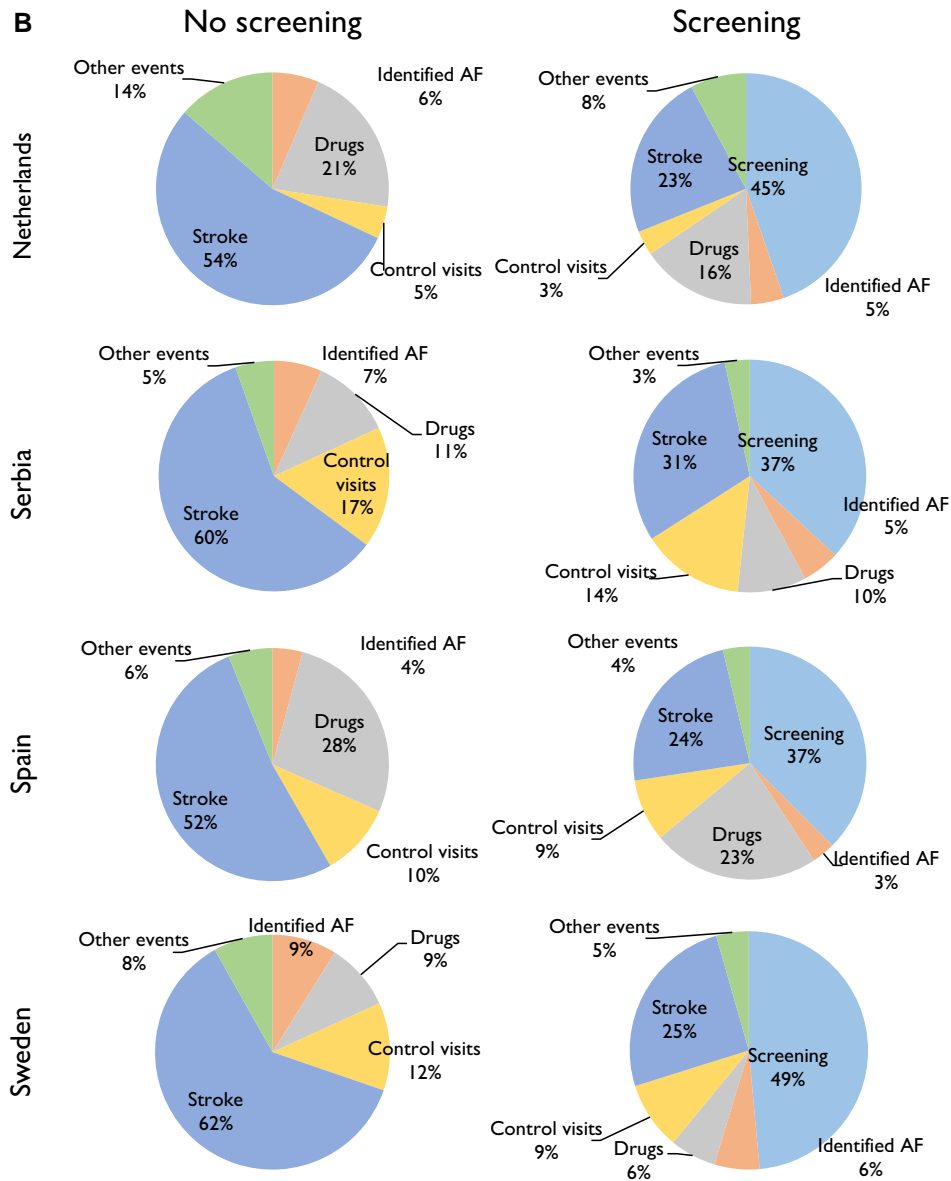


Figure 3 Continued

program for 75-year-olds in eight European countries (Denmark, Germany, Ireland, Italy, Netherlands, Serbia, Spain, and Sweden) from a healthcare payer perspective. Based on the results similar conclusions can be drawn in each country, AF-screening incurs savings of stroke-related costs since early detection of AF and subsequent preventative treatment reduces the number of AF-related strokes. However, the increased number of detected AF and higher drug acquisition will increase the drug costs as well as the costs of physician- and control visits. Increased use of OACs also increases the number of bleedings and bleeding-associated costs. The results showed that the increased costs of implementing AF-screening were mainly driven by increased drug and screening costs. However, the drug cost will decrease with introduction of generic DOACs, even if this

decrease is counterbalanced by the screening cost during the five years included in this BIA. By estimating the 5-year cost per invited in 2023, we showed that the cost per invitee is decreasing over time. The cost per invitee is decreasing annually towards cost saving in each country. The cost per invitee varies between countries, this is mainly explained by differences in cost of preferred screening devices.

The cost per quality adjusted life years measure is an important basis for priority setting, summarizing the cost and health effect over a lifelong perspective. It has previously been shown that implementation of population screening for AF is cost-effective in 75-year-olds.⁴³ Further opportunistic screening of AF in 65-year-olds and older is cost-effective.^{42,69,87} This means that AF-screening is money well spent and

Table 2 Cumulative budget impact of atrial fibrillation-screening 2023-2027 (in million Euros)

	Den	Ger	Ire	Ita	Net	Ser	Spa	Swe
<i>n</i> (millions of 75-year-olds 2023-2027)	0.29	4.02	0.19	3.19	0.74	0.31	2.13	0.50
Budget impact of no AF-screening								
AF investigation and treatment initiation	2.42	6.85	1.03	9.34	8.53	0.75	9.54	5.68
Drugs	10.24	127.09	4.75	44.47	27.70	1.27	62.23	5.90
Control visits OAC	0.96	51.22	1.37	24.64	5.91	1.90	23.14	7.71
Stroke	7.93	154.87	12.35	177.26	71.79	6.62	118.70	31.55
Other events	2.53	24.44	1.18	21.16	17.92	0.60	13.89	5.21
Total cost	24.07	364.46	20.68	276.88	131.85	11.15	227.51	124.18
Budget impact of AF-screening								
Screening	5.70	78.64	2.83	359.87	111.43	6.81	148.82	60.30
AF investigation and treatment initiation	3.19	9.58	1.38	13.00	11.49	0.96	12.82	7.60
Drugs	14.92	197.06	7.04	69.89	40.34	1.76	92.14	7.78
Control visits	1.40	79.05	2.03	38.73	8.61	2.63	34.26	11.45
Stroke	6.25	121.42	9.90	142.52	57.97	5.64	93.89	39.24
Other events	2.66	26.09	1.21	22.46	19.50	0.64	14.83	5.50
Total cost	34.11	511.83	24.39	646.46	249.34	18.45	396.76	63.74
Net budget impact of AF-screening								
Screening	5.69	78.64	2.83	359.87	111.43	6.81	148.82	60.30
AF investigation and treatment initiation	0.77	2.73	0.35	3.66	2.96	0.21	3.28	1.92
Drugs	4.67	69.98	2.28	25.42	12.65	0.49	29.91	1.88
Control visits	0.44	27.82	0.66	14.08	2.70	0.74	11.12	3.74
Stroke	-1.67	-33.45	-2.45	-34.74	-13.82	-0.99	-24.82	-7.69
Other events	0.14	1.65	0.04	1.29	1.57	0.04	0.94	0.29
Total cost	10.04	147.37	3.72	369.59	117.49	7.30	169.25	63.74

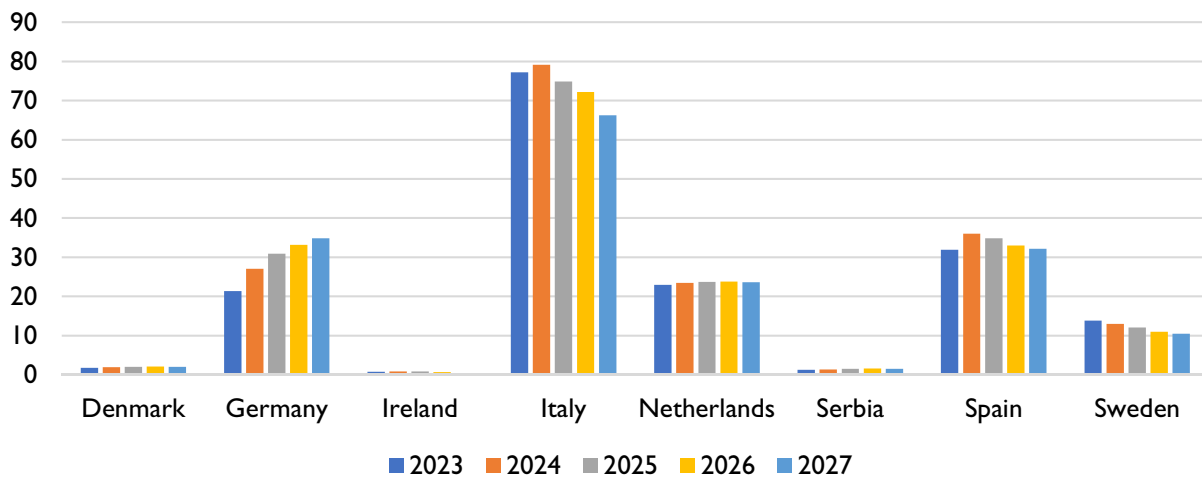


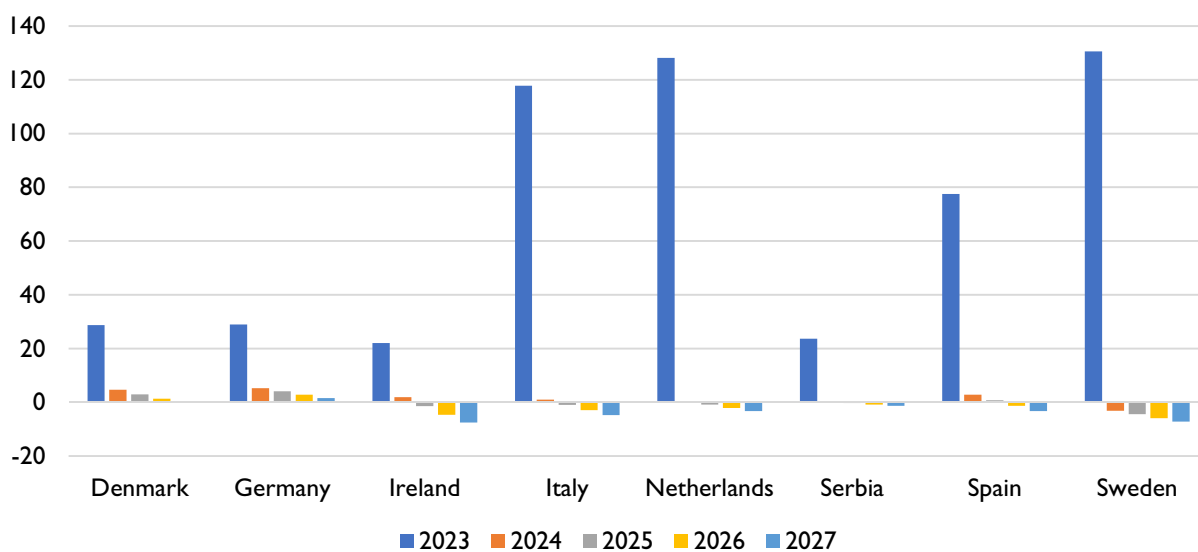
Figure 4 Annual net budget impact of atrial fibrillation-screening, total population (in million euros).

should be highly prioritized and implemented in healthcare systems. As an addition to these CE analyses, this BIA estimates the budget impact of AF-screening which can serve as the basis for affordability assessments. In this BIA, we show that there are relatively low added costs of implementing AF-screening in the studied countries. Even though systematic detected AF may not result in better prognosis than spontaneously detected AF, we have shown that systematic screening of 75-year-olds will incur important savings in stroke-related costs.

A BIA requires accurate and reliable data for costs and resource utilization both regarding the AF-screening and the current standard of care. The complexity of healthcare systems could make it challenging to collect such data. Therefore, estimates are collected from up-to-date, relevant sources and clinical trials. However, the availability and quality of valid estimates for input parameters differs between countries. Allowing for several budget holders for the same cost category catches some of the complexity in the country-specific healthcare systems. However, assumptions and estimates

Table 3 Five-year budget impact of atrial fibrillation-screening per invited (per 75-year-old) in 2023 (in Euros)

	Den	Ger	Ire	Ita	Net	Ser	Spa	Swe
Budget impact of no AF-screening								
AF investigation and treatment initiation	16	3	11	6	18	5	9	22
Drugs	83	80	62	35	74	11	71	22
Control visits	8	32	18	19	16	16	26	36
Stroke	69	93	172	132	177	57	136	175
Other events	18	13	13	14	43	5	14	22
Total cost	194	222	275	206	328	93	256	277
Budget impact of AF-screening								
Screening	20	20	15	113	120	22	70	121
AF investigation and treatment initiation	19	4	12	7	21	6	10	25
Drugs	108	108	81	48	96	13	92	26
Control visits	10	44	23	26	21	20	34	48
Stroke	55	75	140	108	146	49	111	144
Other events	19	14	14	15	46	5	15	23
Total cost	231	265	285	316	450	114	332	387
Net budget impact of AF-screening								
Screening	20	20	15	113	120	22	70	121
AF investigation and treatment initiation	3	1	2	1	3	1	1	4
Drugs	26	28	19	13	22	3	21	3
Control visits	2	11	6	7	5	4	8	12
Stroke	-14	-18	-31	-24	-30	-7	-25	-31
Other events	1	1	0	1	3	0	1	1
Total cost	34	43	10	110	122	22	77	110

**Figure 5** Annual net budget impact of atrial fibrillation-screening per invited in 2023 (in euros).

create uncertainties throughout the model. The BIA's short 5-year time horizon may not capture long-term effects, such as shifts in the prevalence of the condition treated or changes in healthcare resource utilization. The transferability of the budget impact results to other countries which were not object of this study is limited, due to differences in population sizes and structures, cost estimation methods, healthcare systems and

economic development levels. The results are also limited to 75-year-old participants and are not valid for a younger population. The total budget impact of AF-screening presents the total added cost of implementation in each country while the budget impact per invitee presents the added costs over 5 years for one invited 75-year-old in 2023. The latter is comparable between the studied countries.

Table 4 Budget impact of atrial fibrillation-screening, 2023-2027, direct oral anti-coagulant patent expiration (in million Euros)

	Den	Ger	Ire	Ita	Net	Ser	Spa	Swe
<i>n</i>	0.29	4.02	0.19	3.19	0.74	0.31	2.13	0.50
Budget impact of no AF-screening								
AF investigation and treatment initiation	2.42	6.85	1.03	9.34	8.53	0.75	9.54	5.68
Drugs	3.19	35.56	1.45	12.56	8.21	0.61	19.03	0.65
Control visits	0.98	42.87	1.45	22.13	5.86	1.64	21.15	7.97
Stroke	7.92	154.78	12.34	177.22	71.79	6.61	118.63	30.82
Other events	2.52	24.38	1.17	21.13	17.92	0.60	13.84	5.23
Total cost	17.03	264.44	17.44	242.38	112.31	10.20	182.19	93.62
Total cost 75-year-old ^a	144	170	239	182	282	87	212	116.95
Budget impact of AF-screening								
Screening	5.69	78.64	2.83	359.87	111.43	6.81	148.82	60.30
AF investigation and treatment initiation	3.19	9.58	1.39	13.00	11.49	0.96	12.61	7.60
Drugs	5.48	67.72	2.54	24.79	14.22	0.86	32.46	0.86
Control visits	1.41	66.21	2.11	34.96	8.53	2.22	30.50	11.84
Stroke	6.26	121.93	9.93	142.75	58.00	5.70	95.83	38.80
Other events	2.66	25.94	1.21	22.39	19.49	0.63	14.66	5.23
Total cost	24.69	370.03	19.99	597.75	223.15	17.18	334.89	143.90
Total cost per invitee ^a	173	203	243	288	397	108	281	58.34
Net budget impact of AF-screening								
Screening	5.69	78.64	2.83	359.87	111.43	6.81	148.82	60.30
AF investigation and treatment initiation	0.77	2.73	0.35	3.66	2.96	0.21	3.08	1.92
Drugs	2.29	32.16	1.09	12.23	6.00	0.25	13.44	0.21
Control visits	0.44	23.35	0.66	12.82	2.67	0.58	9.35	3.87
Stroke	-1.67	-32.85	-2.42	-34.47	-13.79	-0.91	-22.80	-7.98
Other events	0.13	1.56	0.03	1.26	1.57	0.03	0.82	0.30
Total cost	7.66	105.59	2.55	355.37	110.84	6.98	152.70	58.61
Total cost per invitee ^a	29	33	4	106	115	21	70	106

^aNot in millions.

Conclusion

In conclusion, across Europe, though the initial cost of screening and more frequent use of OACs will increase the healthcare payers' costs, introducing population screening for AF will result in savings of stroke costs.

Supplementary material

Supplementary material is available at *European Heart Journal Supplements* online.

Acknowledgements

We thank Christian Kronborg, Wim Lucassen, Maartje S. Jacobs, Aileen Callanan, and Breda Smyth for data and contributions to the model.

Funding

This work has received funding from the European Union's Horizon 2020 research and innovation programme under the grant agreement No 847770 (AFFECT-EU). Data from the LOOP Study was used and LOOP was supported by Innovation Fund Denmark [grant number 12-1352259], The Research Foundation for the Capital Region of Denmark, The Danish Heart Foundation [grant number 11-04-R83-A3363-22625], Aalborg University Talent Management Program, Arvid Nilssons Fond, Skibsreder

Per Henriksen, R og Hustrus Fond, the European Union's Horizon 2020 program [grant number 847770 to the AFFECT-EU consortium], Læge Sophus Carl Emil Friis og hustru Olga Doris Friis' Legat, and an unrestricted grant from Medtronic. R.B.S. has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme under the grant agreement No 648131, from the European Union's Horizon 2020 research and innovation programme under the grant agreement No 847770 (AFFECT-EU) and German Center for Cardiovascular Research (DZHK e.V.) (81Z1710103 and 81Z0710114); German Ministry of Research and Education (BMBF 01ZX1408A) and ERACoSysMed3 (031L0239). Wolfgang Seefried project funding German Heart Foundation. From the European Union's Horizon Europe research and innovation programme under the grant agreement No. 101095480 (HYPERMAKER).

Conflict of interest: M.E., J.L., L.B., and K.A. report no conflicts of interest. L.Å.L. has received lecture fees and advisory board fees from BMS/Pfizer, Bayer, Boehringer Ingelheim, and Zenico and own stocks in Astra Zeneca. J.H.S. reports to be a member of Medtronic and Vital Beats advisory boards and to have received speaker honoraria and research grants from Medtronic. R.B.S. has received lecture fees and advisory board fees from BMS/Pfizer and Bayer outside this work. D.E. reports no conflicts of interest. C.M. and C.W. are employees of the Institute for Epidemiology, Statistics and Informatics GmbH. The Institute for Epidemiology, Statistics and Informatics GmbH has

received grants from Astra Zeneca, Bayer, Bristol-Myers Squibb and CSL Behring outside the submitted work. S.Z.D. reports consultancy fees from VitalBeats, BMS/Pfizer, Cortrium, and Acesion Pharma, speaker grants from BMS/Pfizer and Bayer, and travel grants from Abbott and Boston Scientific. G.B. reports speaker's fees of small amount from Bayer, Boehringer Ingelheim, Boston, Daiichi Sankyo, Janssen, and Sanofi outside of the submitted work. C.M.B. reports no conflicts of interest.

Data availability

Data available on request.

References

- ESC Press Office. Atrial fibrillation set to affect more than 14 million over-65 s in the EU by 2060. 2019. <https://www.escardio.org/The-ESC/Press-Office/Press-releases/Atrial-fibrillation-set-to-affect-more-than-14-million-over-65s-in-the-EU-by-2060> (16 Oct 2023).
- Magnussen C, Niiranen TJ, Ojeda FM, Gianfagna F, Blankenberg S, Njolstad I et al. Sex differences and similarities in atrial fibrillation epidemiology, risk factors, and mortality in community cohorts: results from the BiomarcCaRE consortium (Biomarker for Cardiovascular Risk Assessment in Europe). *Circulation* 2017;136:1588-1597.
- Di Carlo A, Bellino L, Consoli D, Mori F, Zaninelli A, Baldereschi M et al. Prevalence of atrial fibrillation in the Italian elderly population and projections from 2020 to 2060 for Italy and the European Union: the FAI project. *EP Europace* 2019;21:1468-1475.
- Krijthe BP, Kunst A, Benjamin EJ, Lip GH, Franco OH, Hofman A et al. Projections on the number of individuals with atrial fibrillation in the European Union, from 2000 to 2060. *Eur Heart J* 2013;34:2746-2751.
- Wang L-JD, Leip TJ, Larson EP, Levy MG, Vasan D, S R et al. Lifetime risk for development of atrial fibrillation: the Framingham Heart Study. *Circulation* 2004;110:1042-1046.
- Wallenhorst C, Martinez C, Freedman B. Risk of ischemic stroke in asymptomatic atrial fibrillation incidentally detected in primary care compared with other clinical presentations. *Thromb Haemost* 2022;122:277-285.
- Ali AN, Howe J, Abdel-Hafiz A. Cost of acute stroke care for patients with atrial fibrillation compared with those in sinus rhythm. *Pharmacoeconomics* 2015;33:511-520.
- Vinding NE, Kristensen SL, Rorith R, Butt JH, Ostergaard L, Olesen JB et al. Ischemic stroke severity and mortality in patients with and without atrial fibrillation. *J Am Heart Assoc* 2022;11. doi: 10.1161/JAHA.121.022638.
- Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomstrom-Lundqvist C et al. 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): the task force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. *Eur Heart J* 2021;42:373-498.
- Wafa HA, Wolfe CDA, Emmett E, Roth GA, Johnson CO, Wang Y. Burden of stroke in Europe: thirty-year projections of incidence, prevalence, deaths, and disability-adjusted life years. *Stroke* 2020;51:2418-2427.
- Ruff CT, Giugliano RP, Braunwald E, Hoffman EB, Deenadayalu N, Ezekowitz MD et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. *Lancet* 2014;383:955-962.
- Mauskopf J, Earnshaw SR, Brogan A, Wolowacz S, Brodtkorb T-H. *Budget-Impact Analysis of Health Care Interventions*: Adis; 2017.
- Health Information and Quality Authority (HIQA). Guidelines for the Budget Impact Analysis of Health Technologies in Ireland. https://www.hiqa.ie/sites/default/files/2018-01/HIQA_BIA_Guidelines_2018_0.pdf (9 Sep 2022).
- National Institute for Health and Care Excellence (NICE). Assessing resource impact process manual: technology appraisals and highly specialised technologies. 2017. <https://www.nice.org.uk/Media/Default/About/what-we-do/Into-practice/assessing-resource-impact-process-manual-ta-hst.pdf> (20 Jan 2023).
- Uribe-Arango W, Reyes Sanchez JM, Castano Gamboa N. Budget impact analysis of anticoagulation clinics in patients with atrial fibrillation under chronic therapy with oral anticoagulants. *J Prim Care Community Health* 2021;12:21501327211000213.
- Hori M, Ikeda S, Okumura K, Matsuda S, Koretsune Y, Montouchet C et al. Clinical and economic impact of rivaroxaban on the burden of atrial fibrillation: the case study of Japan. *J Med Econ* 2016;19:889-899.
- Sussman M, Di Fusco M, Tao CY, Guo JD, Gillespie JA, Ferri M et al. The IMPact of untreated non-valvular atrial fibrillation on short-term clinical and economic outcomes in the US Medicare population: the IMPROVE-AF model. *J Med Econ* 2021;24:1070-1082.
- Orlowski A, Wilkins J, Ashton R, Slater R, Smith W, Belsey J. Budget impacts associated with improving diagnosis and treatment of atrial fibrillation in high-risk stroke patients. *J Comp Eff Res* 2020;9:253-262.
- Engler D, Heidbuchel H, Schnabel RB. Digital, risk-based screening for atrial fibrillation in the European community—the AFFECT-EU project funded by the European union. *Eur Heart J* 2021;42:2625-2627.
- Petrou P. Budget impact analysis: can we afford the added value? *J Med Econ* 2021;24:487-489.
- Institute for Quality and Efficiency in Health Care (IQWiG). General Methods. 2015;4.2. <https://www.iqwig.de/en/about-us/methods/methods-paper/> (22 Nov 2022).
- Vrangbæk K. International Health Care System Profiles - Denmark. International Health Care System Profiles. 2020. <https://www.commonwealthfund.org/international-health-policy-center/countries/denmark> (22 Nov 2022).
- Blümel M, Busse R. International health care system profiles - Germany, the commonwealth fund. International Health Care System Profiles 2020.
- Blümel M, Spranger A, Achstetter K, Maresso A, Litvinova Y, Busse R. European Observatory on Health Systems and Policies (ed.), *Germany: health system summary*. Europe: World Health Organization; 2022.
- European Observatory on Health Systems and Policies. *Ireland: Country Health Profile 2021*. Paris: State of Health in the EU, OECD Publishing; 2021.
- Value-Added Tax Consolidation Act (VATCA 2010), 46(1)(b) (2010). <https://www.irishstatutebook.ie/eli/2010/act/31/section/46/enacted/en/html> (10 Oct 2022).
- Giulio de Belvis A, Meregaglia M, Morsella A, Adduci A, Perilli A, Cascini F et al. Italy: health system review 2022. *Health Syst Transit* 2022;24:1-2364.
- Donatini A. International Health Care System Profiles - Italy. *The commonwealth fund, International Health Care System Profiles*. 2020. <https://www.commonwealthfund.org/international-health-policy-center/countries/italy> (10 Oct 2022)
- Tikkanen R, Osborn R, Mossialos E, Djordjevic AA, Wharton G. International Health Care System Profiles - Netherlands. *The commonwealth fund*. <https://www.commonwealthfund.org/international-health-policy-center/countries/netherlands> (20 Dec 2022)
- European Observatory on Health Systems and Policies. Netherlands: Country Health Profile 2021. State of Health in the EU. 2021.
- Bjegovic-Mikanovic V, Vasic M, Vukovic D, Jankovic J, Jovic-Vranes A, Santric-Milicevic M et al. Serbia: health system review 2019. *Health Syst Transit* 2020;21. <https://eurohealthobservatory.who.int/publications/i/serbia-health-system-review-2019> (10 Oct 2022).
- European Observatory on Health Systems and Policies. Spain: Country Health Profile 2021. State of Health in the EU. 2021.
- European Observatory on Health Systems and Policies. Sweden: Country Health Profile 2021. State of Health in the EU. 2021. ISSN: 9789264630383.
- Glenngård HA. International Health Care System Profiles - Sweden. The commonwealth fund, International Health Care System Profiles. 2020. <https://www.commonwealthfund.org/international-health-policy-center/countries/sweden> (11 Oct 2022).
- OECD. Consumer price indices (CPIs) - Complete database: HICPs and weights by COICOP by country. 2023. <https://stats.oecd.org/index.aspx?queryid=82187> (17 Sep 2023).
- Statistical Office of the Republic Serbia. Consumer price indices. 2023. <https://data.stat.gov.rs/Home/Result/03010601?languageCode=en-US> (12 Oct 2023).
- OECD. PPP Benchmark results. 2017. <https://stats.oecd.org/Index.aspx?DataSetCode=PPP2017> (09 Sep 2023).

38. Sveriges Riksbank. Crosskurs. <https://www.riksbank.se/en-gb/statistics/interest-rates-and-exchange-rates/search-cross-rates/>.
39. Svennberg E, Friberg L, Frykman V, Al-Khalili F, Engdahl J, Rosenqvist M. Clinical outcomes in systematic screening for atrial fibrillation (STROKESTOP): a multicentre, parallel group, unmasked, randomised controlled trial. *Lancet* 2021;**398**:1498-1506.
40. Schnabel RB, Wallenhorst C, Engler D, Blankenberg S, Pfeiffer N, Spruncker NA *et al*. Refined atrial fibrillation screening and cost-effectiveness in the German population. *Heart* 2021. doi:10.1136/heartjnl-2020-318882. (20 Feb 2023).
41. Levin LA, Husberg M, Sobocinski PD, Kull VF, Friberg L, Rosenqvist M *et al*. A cost-effectiveness analysis of screening for silent atrial fibrillation after ischaemic stroke. *Europace* 2015;**17**:207-214.
42. Jacobs MS, Kaasenbrood F, Postma MJ, van Hulst M, Tieleman RG. Cost-effectiveness of screening for atrial fibrillation in primary care with a handheld, single-lead electrocardiogram device in The Netherlands. *Europace* 2018;**20**:12-18.
43. Lyth J, Svennberg E, Bernfort L, Aronsson M, Frykman V, Al-Khalili F *et al*. Cost-effectiveness of population screening for atrial fibrillation: the STROKESTOP study. *Eur Heart J* 2023;**44**:196-204.
44. Welton NJ, McAleenan A, Thom HH, Davies P, Hollingworth W, Higgins JP *et al*. Screening strategies for atrial fibrillation: a systematic review and cost-effectiveness analysis. *Health Technol Assess* 2017;**21**:1-236.
45. Seelig J, Trinks-Roerdink E, Chu G, Pisters R, Theunissen L, Trines S *et al*. Determinants of label non-adherence to non-vitamin K oral anticoagulants in patients with newly diagnosed atrial fibrillation. *Eur Heart J Open* 2022;**2**. doi:10.1093/ehjopen/oeac022.
46. Potpara TS, Dan GA, Trendafilova E, Goda A, Kusljugic Z, Manola S *et al*. Stroke prevention in atrial fibrillation and 'real world' adherence to guidelines in the Balkan region: the BALKAN-AF survey. *Sci Rep* 2016;**6**:20432.
47. Atlas Nacional del Ictus. Stroke atlas 2019. <https://www.frenoalictus.org/proyectos-sociedad/atlas-del-ictus-1250> (12 Nov 2022).
48. Hjemdahl P, Braunschweig F, Holmström M, Johnsson H, von Euler M, Wallén H *et al*. Improved stroke prevention in atrial fibrillation: the Stockholm experience of the introduction of NOACs. *Lakartidningen* 2018;**115**.
49. Langkilde LK, Bergholdt Asmussen M, Overgaard M. Cost-effectiveness of dabigatran etexilate for stroke prevention in non-valvular atrial fibrillation. Applying RE-LY to clinical practice in Denmark. *J Med Econ* 2012;**15**:695-703.
50. Sundhedsdatastyrelsen. 05PR05 Kardiologisk undersøgelse. <https://sundhedsdatastyrelsen.dk/da> (21 Oct 2021).
51. SanitàPrivata. Quanto costa una visita cardiologica? 2020. <https://xn-sanitprivata-29a.it/> (20 Oct 2022).
52. Socialstyrelsen. NORD-DRG E800. <https://www.socialstyrelsen.se/en/> (21 Oct 2022).
53. Expatica. Going to the doctor in Spain: a guide for expats. 2022. <https://www.expatica.com/es/healthcare/healthcare-services/doctor-in-spain-576715/> (13 Oct 2022).
54. Omceoteramo. Tariffario minimo nazionale in euro. https://www.omceoteramo.it/uploads/model_1/normativa/tariffario.pdf (23 Nov 2022).
55. Sydöstra sjukvårdsregionen. Priser och ersättningar 2021. 2021. <https://sydostrasjukvardsregionen.se/samverkansnamnden/priser-och-ersattningar/> (10 Nov 2022).
56. Pat H. NCO-01-2022 Phase 2 of the Structured Chronic Disease Management Programme in 2022, 2022. <https://www.hse.ie/eng/about/who/gmscontracts/2019agreement/chronic-disease-management-programme/re-phase-2-of-the-structured-chronic-disease-management-programme-in-2022.html> (20 Nov 2022).
57. Danish medicines agency (Lægemiddelstyrelsen). Edoxaban 60 mg, pack=100. <https://laegemiddelstyrelsen.dk/en/> (21 Oct 2022).
58. Association of Statutory Health Insurance Physicians. Direct cost vka. 2021. <https://www.kbv.de/html/index.php> (20 Oct 2022).
59. HSE. PCRS Search Reimbursable Items. 2021. <https://www.hse.ie/eng/staff/pcrs/items/> (15 Nov 2022).
60. Medicijnkosten. 2022. <https://www.medicijnkosten.nl/> (02 Oct 2022).
61. FASS (Pharmaceutical Specialties in Sweden). Pharmaceutical prices in Sweden. <http://www.fass.se> (9 Sep 2021) dLa.
62. Oyagüez I, Suárez C, López-Sendón JL, González-Juanatey JR, De Andrés-Nogales F, Suárez J *et al*. Cost-effectiveness analysis of apixaban versus edoxaban in patients with atrial fibrillation for stroke prevention. *PharmacoEcon Open* 2020;**4**:485-497.
63. Einheitlicher Bewertungsmaßstab - EBM. schedule for 2022. 2022. <https://www.kbv.de/html/ebm.php> (20 Oct 2022).
64. Hakkaart-van Roijen L, Van der Linden N, Bouwman CAM, Kanters TA, Tan SS. Costing manual: Methodology of costing research and reference prices for economic evaluations in healthcare. *National Health Care Institute*. <https://www.zorginstituutnederland.nl/over-ons/publicaties/publicatie/2016/02/29/richtlijn-voor-het-uitvoeren-van-economische-evaluaties-in-de-gezondheidszorg> (21 Oct 2021)
65. Danish medicines agency (Lægemiddelstyrelsen). Warfarin 2*2.5 mg, pack=100. <https://laegemiddelstyrelsen.dk/en/> (21 Oct 2022).
66. Mennini F, Russo S, Marcellusi A. Budget impact analysis resulting from the use of dabigatran etexilate in preventing stroke in patients with non-valvular atrial fibrillation in Italy. *Farmecon Health Econ Ther Pathways* 2012;**13**:121-131.
67. González-Juanatey JR, Álvarez-Sabin J, Lobos JM, Martínez-Rubio A, Reverter JC, Oyagüez I *et al*. Cost-effectiveness of dabigatran for stroke prevention in non-valvular atrial fibrillation in Spain. *Revista Española de Cardiología (English Edition)* 2012;**65**:901-910.
68. Jakobsen M, Kolodziejczyk C, Fredslund EK, Poulsen PB, Dybro L, Johnsen SP. Societal costs of first-incident ischemic stroke in patients with atrial fibrillation—a Danish nationwide registry study. *Value Health* 2016;**19**:413-418.
69. Moran PS, Teljeur C, Harrington P, Smith SM, Smyth B, Harbison J *et al*. Cost-effectiveness of a national opportunistic screening program for atrial fibrillation in Ireland. *Value Health* 2016;**19**:985-995.
70. Fattore G, Torbica A, Susi A, Giovanni A, Benelli G, Gozzo M *et al*. The social and economic burden of stroke survivors in Italy: a prospective, incidence-based, multi-centre cost of illness study. *BMC Neurol* 2012;**12**:137.
71. Lekander I, Willers C, Von Euler M, Lilja M, Sunnerhagen KS, Pessah-Rasmussen H *et al*. Relationship between functional disability and costs one and two years post stroke. *PLoS One* 2017;**12**:e0174861.
72. Alvarez-Sabin J, Quintana M, Masjuan J, Oliva-Moreno J, Mar J, Gonzalez-Rojas N *et al*. Economic impact of patients admitted to stroke units in Spain. *Eur J Health Econ* 2017;**18**:449-458.
73. Kolominsky-Rabas PL, Heuschmann PU, Marschall D, Emmert M, Baltzer N, Neundörfer B *et al*. Lifetime cost of ischemic stroke in Germany: results and national projections from a population-based stroke registry. *Stroke* 2006;**37**:1179-1183.
74. Chiumente M, Gianino MM, Minniti D, Mattei TJ, Spass B, Kamal KM *et al*. Burden of stroke in Italy: an economic model highlights savings arising from reduced disability following thrombolysis. *Int J Stroke* 2015;**10**:849-855.
75. Lopez-Bastida J, Oliva Moreno J, Worbes Cerezo M, Perestelo Perez L, Serrano-Aguilar P, Montón-Álvarez F. Social and economic costs and health-related quality of life in stroke survivors in the Canary Islands, Spain. *BMC Health Serv Res* 2012;**12**:315.
76. Lanitis T, Kongnakorn T, Jacobson L, De Geer A. Cost-effectiveness of apixaban versus warfarin and aspirin in Sweden for stroke prevention in patients with atrial fibrillation. *Thromb Res* 2014;**134**:278-287.
77. 1177. Högkostnadsskydd och frikort i Östergötland 2023 [updated 2023-12-13]. <https://www.1177.se/Ostergotland/sa-fungerar-varden/kostnader-och-ersattningar/patientavgifter/> (10 Dec 2023).
78. Reuters. Bayer wins EU patent extension for best-selling xarelto drug. 2021. <https://www.reuters.com/business/healthcare-pharmaceuticals/bayer-wins-eu-patent-extension-best-selling-xarelto-drug-2021-10-29/> (16 Nov 2023).
79. Friberg L, Bergfeldt L. Atrial fibrillation prevalence revisited. *J Intern Med* 2013;**274**:461-468.
80. Johansson L, Norberg J, Jansson J-H, Bäckström S. Estimating the prevalence of atrial fibrillation in a general population using validated electronic health data. *Clin Epidemiol* 2013;**475**:475-481. <https://doi.org/10.2147/clip.s53420>. ISSN: 1179-1349.
81. Kjerpeseth LJ, Iglund J, Selmer R, Ellekjær H, Tveit A, Berge T *et al*. Prevalence and incidence rates of atrial fibrillation in Norway 2004-2014. *Heart* 2021;**107**:201-207.
82. Wilke T, Groth A, Mueller S, Pfannkuche M, Verheyen F, Linder R *et al*. Incidence and prevalence of atrial fibrillation: an analysis based on 8.3 million patients. *Europace* 2013;**15**:486-493.
83. Gómez-Doblas JJ, Muñoz J, Martín JJ, Rodríguez-Roca G, Lobos JM, Awamleh P *et al*. Prevalence of atrial fibrillation in Spain, OFRECE study results. *Rev Esp Cardiol (Engl Ed)* 2014;**67**:259-269.

84. Heeringa J, van der Kuip DA, Hofman A, Kors JA, van Herpen G, Stricker BH *et al.* Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. *Eur Heart J* 2006;**27**:949-953.
85. Lowres N, Olivier J, Chao T-F, Chen S-A, Chen Y, Diederichsen A *et al.* Estimated stroke risk, yield, and number needed to screen for atrial fibrillation detected through single time screening: a multicountry patient-level meta-analysis of 141,220 screened individuals. *PLoS Med* 2019;**16**:e1002903.
86. Aronsson M, Svennberg E, Rosenqvist M, Engdahl J, Al-Khalili F, Friberg L *et al.* Cost-effectiveness of mass screening for untreated atrial fibrillation using intermittent ECG recording. *Europace* 2015;**17**:1023-1029.
87. Sciera LK, Frost L, Dybro L, Poulsen PB. The cost-effectiveness of one-time opportunistic screening for atrial fibrillation in different age cohorts of inhabitants in Denmark aged 65 years and above. A Markov modelled analysis. *Eur Heart J Qual Care Clin Outcomes* 2020;**8**:177-1862.