Cost-Effectiveness and Screening Performance of ECG Handheld Machine in a Population Screening Programme: the Belgian Heart Rhythm Week Screening Programme

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ABSTRACT

Aims: Overall, 40% of patients with atrial fibrillation (AF) are asymptomatic. The usefulness and cost-effectiveness of AF screening programmes are debated. We evaluated if an AF screening programme with a handheld ECG machine in a population-wide cohort has a high screening yield and is cost-effective.

Methods: We used a Markov-model based modelling analysis on 1000 hypothetical individuals that matched the Belgian Heart Rhythm Week Screening Programme. Subgroup analyses of subjects ≥65 and ≥75 years old were performed. Screening was performed with one-lead ECG handheld machine Omron® HeartScan HCG-801. **Results:** In both overall population and subgroups, the use of the screening procedure diagnosed a consistently higher number of diagnosed AF than not screening. In the base-case scenario, the screening procedure resulted in 106.6 more AF patient-years, resulting in 3 fewer strokes, 10 more life-years and 5 more QALYs. The number needed-to-screen (NNS) to avoid 1 stroke was 361. In subjects ≥65, we found 80.8 more AF patient-years resulting in 3 fewer strokes, 4 more life-years and 5 more QALYs. The NNS to avoid 1 stroke was 354. Similar results were obtained in subjects ≥75 years, with a NNS to avoid one stroke of 371. In the overall population, the incremental cost-effectiveness ratio for any gained QALY showed that the screening procedure was cost-effective in all groups.

Conclusions: In a population-wide screening cohort, the use of a handheld ECG machine to identify subjects with newly diagnosed AF was cost-effective in the general population, as well in subjects \geq 65 and \geq 75 years old.

Keywords: atrial fibrillation; screening; outcomes; cost-effectiveness analysis.

INTRODUCTION

Atrial fibrillation (AF) is the most incident and prevalent heart rhythm condition¹. Despite this, AF patients are very frequently asymptomatic, thus exposing patients to an increased risk for stroke and major adverse events^{2,3}, with around a quarter of patients diagnosed with AF only after the first stroke occurrence⁴.

In the 2016 European Society of Cardiology (ESC) guidelines, screening procedures for AF early detection are recommended opportunistically for subjects \geq 65 years (Class I, Level of Evidence B)¹. Systematic screening is only suggested, with a low evidence grade (Class IIb, Level of Evidence B), in very elderly patients (\geq 75 years) or those at high risk of stroke¹.

The debate about whether to use opportunistic or systematic screening approaches remains controversial. Opportunistic screening is more cost-effective than systematic ones⁵. A large systematic review reported that opportunistic and systematic screening programmes reported a similar number of new AF diagnosis⁶. Several studies using population-wide or systematic screening programmes, using handheld ECG machines or new technologies-base systems, have reported that these programmes are feasible to identify a significant number of new AF cases^{7–10}, as well as being also cost-effective in reducing major adverse events, particularly reducing stroke and its related healthcare costs^{9–11}.

The aim of this paper was to perform a cost-effectiveness analysis (CEA) and a screening performance analysis using a population-wide screening model designed after the Belgian Heart Rhythm Week (BHRW) screening programme.

METHODS

Analytic Approach

Modelling analysis about the use of a population-wide screening programme was based on a Markov model [Figure 1] for decision making processes about AF detection, clinical management and life-long follow-up. This model has been built taking into account the different health states in which the simulated individual can be and move between.

The statistical definition of the model is that of a discrete-time discrete-state stochastic process with first-order Markov property. This implies that conditionally on the current health status for the specific simulated individual, the future status of the same individual is independent of previous events. Using a simulation model, we analyzed 1000 hypothetical individuals who matched the population of the BHRW screening programme⁷. Simulations have been performed for the overall population of adults, as well as for subgroups of subjects \geq 65 years and \geq 75 years old. The model design was computed to account for a screening procedure undertaken yearly for 40 consecutive years and simulated the natural dynamics of the cohort considered.

The simulation of the natural disease progression and the effect of the screening procedure required data including prevalence, incidence, the risk of events, morbidity, and mortality. The data, extracted from a Belgian setting, were obtained from the BHRW screening programme study⁷ and additionally supplemented with data coming from the available scientific literature. Main parameters used to build the

model are reported in Table 1. The simulation has been replicated 10,000 times and results are based on average simulated quantities of interest. Sensitivity analyses were performed both by assessing the variability of quantities over the simulation replicas, and therefore obtaining acceptability curves; and by repeating the study after varying input parameters in a grid of reasonable values (not shown).

Study Setting and Use of Handheld ECG

Study design and main results of the BHRW screening programme have been reported^{7,12}. Briefly, the BHRW screening programme is a Belgian national campaign on awareness about AF, designed along with an untargeted voluntary screening programme organized by the Belgian Hearth Rhythm Association (BeHRA) held 1 week a year. Adult subjects have been invited, through press conferences and a massive communicational campaign from the main national Belgian media, to attend the screening procedure and a clinical questionnaire filled independently and anonymously by each subject. From 2010 to 2014 a total of 82,569 Belgian citizens were screened⁷.

ECG tracings were collected through a handheld 1-lead ECG machine (Omron, HeartScan HCG-801) with a 30-s long recording. Use of this hand-held machine has been previously validated as highly accurate to detect the presence of AF, compared to a standard 12-leads ECG¹³. All the procedures were nurse-led.

AF Prevalence and Distribution of Thromboembolic Risk

According to previously published results, the overall prevalence of AF detected in the BHRW screening programme was 1.4%⁷ and after the exclusion of patients with

a previously reported history of AF, a final prevalence of unknown AF was 1.1%. Stratifying patients per age subgroups, in patients older than 65 years unknown AF was found in 2.0% of patients, while those subjects ≥75 years had a final prevalence of 3.1% for detected unknown AF. Prevalence of newly detected AF based on occasional pulse check was evaluated according to previously published data¹⁴.

In the general cohort of subjects enrolled in BHRW programmed median [IQR] CHA₂DS₂-VASc was 2 [1-3], with 15.5% of subjects with CHA₂DS₂-VASc 0, 33.5% with CHA₂DS₂-VASc 1 and 51% with CHA₂DS₂-VASc \geq 2. Meanwhile, 86.0% of subjects \geq 65 years had a CHA₂DS₂-VASc \geq 2.

Risk of Adverse Events and Thromboembolic Risk Treatment

The primary aim of a screening programme for AF is ultimately to reduce the occurrence of thromboembolic events, namely ischemic stroke. AF is an independent risk factor for stroke occurrence, increasing up to 5-fold the risk of stroke¹⁵. Concomitant presence of other risk factors, *i.e.* age, hypertension, congestive heart failure, diabetes mellitus, etc., increases this risk exponentially¹⁵. Nowadays, thromboembolic risk is routinely evaluated at baseline and is pivotal in the clinical decision-making process of prescribing oral anticoagulation (OAC) therapy¹. Thromboembolic risk stratification is made using a clinical scoring system, the CHA₂DS₂-VASc score¹⁶, largely evaluated and validated in several AF cohorts¹⁵.

Thromboembolic risk in AF patients untreated with OAC, to compute the model presented, was considered as progressively increasing according to CHA₂DS₂-VASc score, as previously reported in ESC 2010 Guidelines¹⁷. To simplify the model,

patients were considered eligible for OAC prescription for a CHA₂DS₂-VASc score ≥2. Death risk for patients without AF were based on epidemiological data about general Belgian population and changes in mortality risk due to AF presence, as well as relative risk reduction in death rates have been considered according available literature^{18–20}.

Recently released ESC guidelines for treatment of AF patients recommended for thromboembolic risk reduction, the use of non-vitamin K antagonist oral anticoagulants (NOACs) over vitamin K antagonist (VKA), namely warfarin¹. Considering that no indication exists to preferentially use one NOAC over the others¹ and according to the class-effect in reduction of both thromboembolic and bleeding risk that NOACs presented²⁰, to keep the model simple and strictly focused on the efficacy of the screening procedure, the model was computed considering that when a patient was diagnosed with a new onset AF a generic NOAC was prescribed, considering the overall ability in reduction of both thromboembolic and bleeding risk demonstrated by all NOACs²⁰.

Resources and Costs

Handheld ECG machines cost $500 \in$ and could be reused over 5 years (annual cost $100 \in$). We considered 2.5 mean devices for each centre, for a total of 90 centres throughout Belgium, as reported in the main BHRW paper⁷. As stated above, all screening procedures were nurse-led, with an estimated time of 5 min/test and an overall cost of $34.28 \in$ per hour for each nurse.

Costs about OAC treatment and associated monitoring, as well as all costs related to the occurrence of any stroke or major bleeding, were taken from a Belgian-specific setting according to previously published data about modelling analysis in AF in Belgium²¹. Main costs considered in the model are reported in Table 1.

Utility Weights

To calculate the quality-adjusted life year (QALY), baseline estimates were based on a Belgian setting. Discounts in QALYs according AF diagnosis and adverse events occurrence were calculated from specific utility weights according previously published data for CEA modelling analysis in the Belgian population²¹.

RESULTS

Base Case Scenario

After running the Markov model 10,000 times to generate 1000 simulated subjects each time, average results about subjects diagnosed with new AF have been reported in Figure 2. We found that the number of patients diagnosed with AF is consistently and steadily higher when the population screening procedure is applied, in the overall population, in patients ≥65 years old and in patient ≥75 years old. In the base-case scenario (Table 2), screening of 1000 subjects from the overall population resulted in 106.6 more patients with detected AF. Consequently, 3 fewer strokes were obtained with 10 more life years and 5 more QALYs. The number needed-toscreen (NNS) to avoid 1 stroke was 361 patients screened.

In patients ≥65 years old use of screening procedure identified 80.8 more patients with new AF diagnosis, resulting in 3 fewer strokes, 4 more life years and 5 more

QALYs. The NNS to avoid 1 stroke was 354. Furthermore, in patients ≥75 years old the screening procedure resulted in 71.1 more patients diagnosed with AF, resulting in 3 fewer strokes, 13 more life years and 11 more QALYs. The NNS to avoid one stroke was 371 screenings performed.

According to Table 2, in the overall population, the incremental cost-effectiveness ratio (ICER) for any gained life year was $11,787.8 \in$, while the ICER for any gained QALY was $24,344.5 \in$. Furthermore, in patients ≥ 65 years old and ≥ 75 years old the ICER for any gained life year was $19,377.6 \in$ and $17,692.6 \in$, respectively and the ICER for any gained QALY was $5,875.6 \in$ and $6,707.6 \in$, respectively.

Sensitivity Analyses

In order to study the uncertainty and variability of all variables considered, a probabilistic analysis was performed. The results are reported as acceptability curves [Figure 3]. The probabilistic analysis shows that if the willingness to pay for a QALY is higher than 4000 €, screening is probably cost-effective for the general population, subjects ≥65 years and subjects ≥75 years.

DISCUSSION

Our modelling cost-effectiveness analysis, in a sample of 1000 hypothetical individual, shows that a population screening programme based on a handheld ECG machine is effective in identifying a consistently higher number of subjects affected with unknown AF, in general population and in both subjects older \geq 65 years and \geq 75 years. Identification of an increased number of patients with AF, if properly treated with OAC, ultimately lead to a reduction in the number of strokes occurred

over subjects' lifetime. Finally, the implementation of such a screening programme results in a clear cost-effective gaining in quality of life in subjects older \geq 65 years and \geq 75 years, while provided a limited advantage when considered among the general population, with ICER for gained QALY just barely below 25,000 \in .

In the last years, research regarding use of screening strategies to identify patients with asymptomatic AF has developed, building up an increasing amount of evidence^{22,23}. Two recently published expert consensus from international experts and scientific societies strongly support and recommend performing AF screening in all subjects ≥65 years, even though it is not suggested as systematic and compulsory strategy, but rather than in an opportunistic way^{22,23}. This approach matches that suggested by International AF guidelines¹ as well as by consensus guidance stemming from primary care environment²⁴. Furthermore, use of a systematic AF screening is suggested to be considered for subjects \geq 75 years²², even though guidelines underline how the evidence supporting this type of recommendation is scarce (class of recommendation IIb, level of evidence B)¹. In this context, our data support the use of a population screening in both subjects ≥65 years and ≥75 years old, providing evidence that such programme will result in a significant increase of AF diagnosis and reduction of events, still remaining costeffective. Regarding this aspect, we would comment on the evidence that while a lower NNS was found for subjects ≥65 years old, compared to the general population, in the subjects \geq 75 years old we found, contrary on what was expected, a slightly higher NNS compared to those ≥65 years old. We can postulate that since the risk of AF progressively increases with age, being greater in subjects ≥75 years old, the likelihood that AF is diagnosed incidentally would be higher than in younger

ones then an increased NNS is needed to avoid the occurrence of a single stroke. Another possible explanation could be related to the small proportion of subjects ≥75 years considered compared to the other age strata, that could have partially influenced this aspect.

Recently the US Preventive Services Task Force (USPSTF) released a recommendation regarding the use of ECG screening for AF in older (\geq 65 years) adults²⁵. After a systematic revision of current literature²⁶, which concluded that there is not enough evidence to establish the balance between benefits and harms of ECG screening²⁶, USPSTF did not make any recommendation regarding the use of ECG screening, claiming the need for further evidence²⁵. The summary of evidence and the subsequent statement are limited by the fact that most of the studies regarding screening programmes for AF detection have a cross-sectional design, without any active comparator, nor including a follow-up phase to establish if the use of the screening programme had an impact on major adverse clinical events.

The present paper supports the concept that using a systematic screening approach is able to reduce significantly the occurrence of stroke. In the general population, taking as reference the current global population of Belgium, using the screening procedure for the all population of Belgium every year will result in more than 34,000 strokes avoided over the lifetime course, with more than 21,000 strokes avoided in the population age \geq 65 years old. In this context, recently the results of a 5-year observation derived from an AF screening programme, despite not providing definitive evidence due to the limited number of subjects, clearly pointed out how using a screening programme reduces the occurrence of stroke²⁷

Related to the costs expenditure, our paper clearly demonstrates that using this population screening programme is cost-effective even in the general population when considering the general threshold of 30,000 GBP per QALY²². When limiting the screening to the subjects age \geq 65 years or those \geq 75 years the programme appears clearly cost-effective, even though it resulted in a slightly higher cost than compared to the few other cost-effectiveness evaluations of AF screening activities²². Conversely, compared to a similar paper recently published, evaluating the cost-effectiveness of a similar population screening in the Netherlands, our programme showed a significantly lower ICER per QALY²⁸. Obviously, the implementation of a nationwide general screening population implies a relevant impact in terms of commitment and still deserves further evidence to be strongly supported.

Limitations

As per each other modelling analyses, being based on assumptions subjectively defined by the authors, this represents an inherited limitation to the study, even though the sensitivity analysis clearly showed that our screening programme would be cost-effective in most of the cases. Secondly, the analysis is based on a Belgian scenario of voluntary subjects attending the screening initiative, that as volunteers may also have been more burdened with vague AF-related symptoms and would have taken advantage of a free screening procedure; hence, the external validity and generalizability of the results presented need to be considered. Furthermore, most patients with undetected AF would be found in the first years of the screening procedure, but the entire 40-years screening procedure was cost-effective indicating

that even a shorter screening programme would be cost-effective. Lastly, we based the weights related to NOACs derived from randomized clinical trials and the patients included in the trials are likely to differ from the overall real-life population.

CONCLUSIONS

The use of a handheld ECG machine in a population screening programme is costeffective in identifying new AF patients and reducing stroke occurrence in the general population, subjects \geq 65 and subjects \geq 75 years. Our results clearly support the use of more systematic screening for AF in patients \geq 65 and \geq 75 years old.

FUNDING

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DECLARATION OF CONFLICTING INTERESTS

MP: Small consultancy fees for Boehringer Ingelheim. GHM: Grants from Boehringer Ingelheim, St Jude Medical, Sanofi, MSD and MSH for the organization of the screening campaign and conduction of the study. GHYL: Consultant for Bayer/Janssen, BMS/Pfizer, Medtronic, Boehringer Ingelheim, Novartis, Verseon and Daiichi-Sankyo. Speaker for Bayer, BMS/Pfizer, Medtronic, Boehringer Ingelheim, and Daiichi-Sankyo. No fees are directly received personally. All other authors have nothing to disclose.

AUTHOR'S CONTRIBUTION

MP, AF, GYHL and GHM conceived the study and planned the analysis. MP and AF performed the analysis, interpreted results and produced the first draft of the manuscript. PG, CS, JV, IB, YV and GHM collected data used for the analysis. PG, CS, JV, IB, YV, GYHL and GHM revised extensively the manuscript for important intellectual content. All authors approved the final version of the manuscript.

REFERENCES

- Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Europace* 2016; 18: 1609–1678.
- Xiong Q, Proietti M, Senoo K, et al. Asymptomatic versus symptomatic atrial fibrillation: A systematic review of age/gender differences and cardiovascular outcomes. *Int J Cardiol* 2015; 191: 172–177.
- 3. Sanna T, Diener H-C, Passman RS, et al. Cryptogenic stroke and underlying atrial fibrillation. *N Engl J Med* 2014; 370: 2478–86.
- Sposato LA, Cipriano LE, Saposnik G, et al. Diagnosis of atrial fibrillation after stroke and transient ischaemic attack: a systematic review and meta-analysis. *Lancet Neurol* 2015; 14: 377–387.
- 5. Fitzmaurice DA, Hobbs FDR, Jowett S, et al. Screening versus routine practice in detection of atrial fibrillation in patients aged 65 or over: cluster randomised controlled trial. *BMJ* 2007; 335: 383.
- 6. Lowres N, Neubeck L, Redfern J, et al. Screening to identify unknown atrial fibrillation. A systematic review. *Thromb Haemost* 2013; 110: 213–22.
- Proietti M, Mairesse GH, Goethals P, et al. A population screening programme for atrial fibrillation: A report from the Belgian Heart Rhythm Week screening programme. *Europace* 2016; 18: 1779–1786.
- Svennberg E, Engdahl J, Al-Khalili F, et al. Mass Screening for Untreated Atrial Fibrillation: The STROKESTOP Study. *Circulation* 2015; 131: 2176–84.
- Lowres N, Neubeck L, Salkeld G, et al. Feasibility and cost-effectiveness of stroke prevention through community screening for atrial fibrillation using iPhone ECG in pharmacies: The SEARCH-AF study. *Thromb Haemost* 2014;

111: 1167–76.

- Desteghe L, Raymaekers Z, Lutin M, et al. Performance of handheld electrocardiogram devices to detect atrial fibrillation in a cardiology and geriatric ward setting. *Europace* 2017; 19: 29–39.
- Aronsson M, Svennberg E, Rosenqvist M, et al. Cost-effectiveness of mass screening for untreated atrial fibrillation using intermittent ECG recording. *Europace* 2015; 17: 1023–1029.
- Proietti M, Mairesse GH, Goethals P, et al. Cerebrovascular disease, associated risk factors and antithrombotic therapy in a population screening cohort: Insights from the Belgian Heart Rhythm Week programme. *Eur J Prev Cardiol*; 24. Epub ahead of print 2017. DOI: 10.1177/2047487316682349.
- Kaleschke G, Hoffmann B, Drewitz I, et al. Prospective, multicentre validation of a simple, patient-operated electrocardiographic system for the detection of arrhythmias and electrocardiographic changes. *Europace* 2009; 11: 1362– 1368.
- Hobbs FDR, Fitzmaurice DA, Mant J, et al. A randomised controlled trial and cost-effectiveness study of systematic screening (targeted and total population screening) versus routine practice for the detection of atrial fibrillation in people aged 65 and over. The SAFE study. *Health Technol Assess* 2005; 9: iii–iv, ix– x, 1-74.
- Lip GYH, Lane DA. Stroke Prevention in Atrial Fibrillation. *JAMA* 2015; 313: 1950–1962.
- 16. Lip GYH, Nieuwlaat R, Pisters R, et al. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest* 2010;

137: 263–72.

- 17. Camm AJ, Kirchhof P, Lip GYH, et al. Guidelines for the management of atrial fibrillation. *Eur Heart J* 2010; 31: 2369–2429.
- Hart RG, Pearce LA, Aguilar MI. Meta-analysis: Antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. *Ann Intern Med* 2007; 146: 857–867.
- Odutayo A, Wong CX, Hsiao AJ, et al. Atrial fibrillation and risks of cardiovascular disease, renal disease, and death: systematic review and metaanalysis. *BMJ* 2016; 354: i4482.
- 20. Ruff CT, Giugliano RP, Braunwald E, 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.
- Kongnakorn T, Lanitis T, Annemans L, et al. Stroke and systemic embolism prevention in patients with atrial fibrillation in Belgium: comparative cost effectiveness of new oral anticoagulants and warfarin. *Clin Drug Investig* 2015; 35: 109–19.
- 22. Mairesse GH, Moran P, Van Gelder IC, et al. Screening for atrial fibrillation: a European Heart Rhythm Association (EHRA) consensus document endorsed by the Heart Rhythm Society (HRS), Asia Pacific Heart Rhythm Society (APHRS), and Sociedad Latinoamericana de Estimulacion Cardiaca y Electrofisiolog. *Europace* 2017; 19: 1–35.
- Freedman B, Camm J, Calkins H, et al. Screening for Atrial Fibrillation: A Report of the AF-SCREEN International Collaboration. *Circulation* 2017; 135: 1851–1867.
- 24. Hobbs FR, Taylor CJ, Jan Geersing G, et al. European Primary Care

Cardiovascular Society (EPCCS) consensus guidance on stroke prevention in atrial fibrillation (SPAF) in primary care. *Eur J Prev Cardiol* 2016; 23: 460–73.

- US Preventive Services Task Force SJ, Curry SJ, Krist AH, et al. Screening for Atrial Fibrillation With Electrocardiography: US Preventive Services Task Force Recommendation Statement. *JAMA* 2018; 320: 478–484.
- Jonas DE, Kahwati LC, Yun JDY, et al. Screening for Atrial Fibrillation With Electrocardiography: Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA 2018; 320: 485–498.
- Engdahl J, Holmén A, Rosenqvist M, et al. A prospective 5-year follow-up after population-based systematic screening for atrial fibrillation. *Europace* 2018; doi: 10.1093/europace/euy045.
- Jacobs MS, Kaasenbrood F, Postma MJ, et al. 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.

FIGURE LEGENDS

Figure 1: Basic description of Markov Model used for this analysis.

Legend: Part 1 refers to the screening procedure. Part 2 refers to treatment and follow-up following the screening phase. Squares indicate clinical choices made by physicians. Circles indicates the clinical events that may occur probabilistically.

Figure 2: Number of patients found in AF among the 1000 subjects simulated in the model.

Legend: Red line indicates no screening procedure performed. Black line indicates screening procedure performed.

Figure 3: Acceptability Curves for Sensitivity analysis.

Parameter	Value	Reference
Age Classes Distribution (%)		
<65 years	69.5%	7
65-74 years	21.8%	
≥75 years	8.6%	
Gender Distribution (%)		
Male	41.4%	7
Female	58.6%	
Unknown AF Prevalence (%)		
General Population	1.1%	7
Subjects ≥65 years	2.0%	
Subjects ≥75 years	3.1%	
CHA ₂ DS ₂ -VASc Distribution (%)		
CHA ₂ DS ₂ -VASc 0	15.5%	
CHA ₂ DS ₂ -VASc 1	33.5%	7
CHA ₂ DS ₂ -VASc 2	18.6%	
CHA ₂ DS ₂ -VASc 3	9.4%	
CHA₂DS₂-VASc ≥4	23.0%	
Stroke Risk for Untreated AF (%/year)		
CHA ₂ DS ₂ -VASc 0	0%	
CHA ₂ DS ₂ -VASc 1	1.3%	
CHA ₂ DS ₂ -VASc 2	2.2%	
CHA ₂ DS ₂ -VASc 3	3.2%	
CHA ₂ DS ₂ -VASc 4	4.0%	17
CHA ₂ DS ₂ -VASc 5	6.7%	
CHA ₂ DS ₂ -VASc 6	9.8%	
CHA ₂ DS ₂ -VASc 7	9.6%	
CHA ₂ DS ₂ -VASc 8	6.7%	
CHA ₂ DS ₂ -VASc 9	15.2%	
Stroke Risk Difference with VKAs (RRR)	-64%	18
Stroke Risk Difference with NOACs (RRR)	-19%	20
Major Bleeding Risk Difference with VKAs (RRR)	+66%	18
Major Bleeding Risk Difference with NOACs (RRR)	-14%	20
Death Risk Difference with VKAs (RRR)	-26%	18

Table 1: Relevant Parameters in the Model

Death Risk Difference with NOACs (RRR)	-10%	20
Utility Weight AF	0.73	21
Utility Weight Stroke	0.56	21
Utility Weight Major Bleeding	0.15	21
Main Costs (Mean)		
ECG Handheld (<i>€ per device/year</i>)	100 €	а
Screening Associated Costs (€ per hour)	34.28€	а
NOAC Cost (€ per day)	3.50€	21
NOAC Routine Care Cost (€ per year)	91 €	21

Legend: ^a= previously unpublished data from BHRW programme; AF= atrial

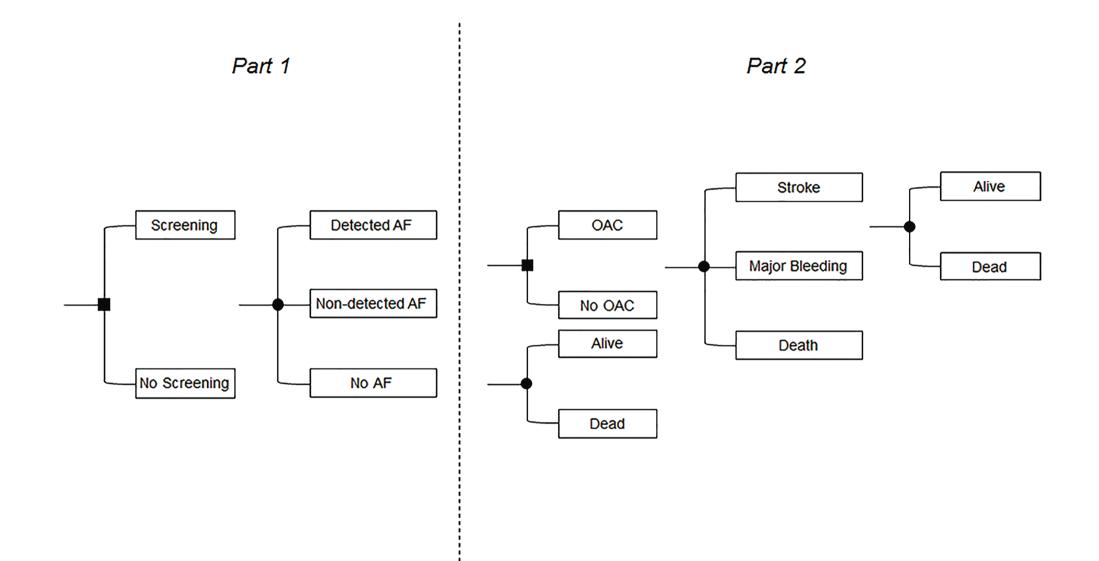
fibrillation; NOAC= non-vitamin K antagonist oral anticoagulant; VKAs= vitamin K

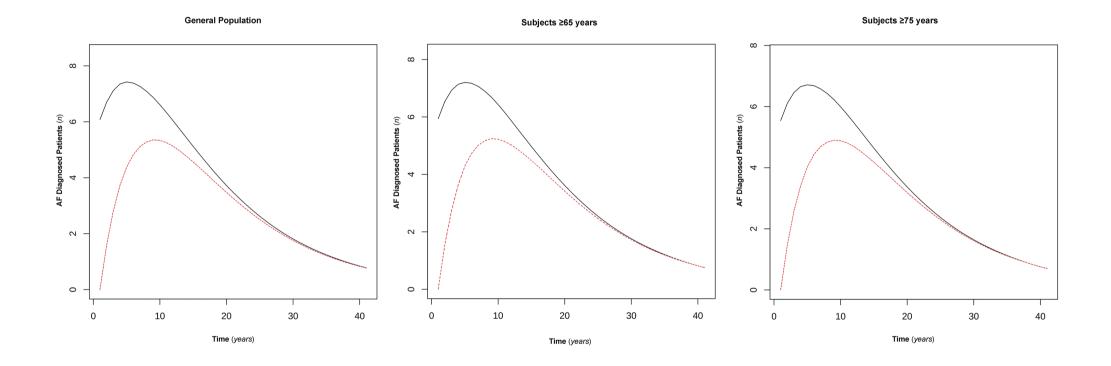
antagonists; RRR= relative risk reduction.

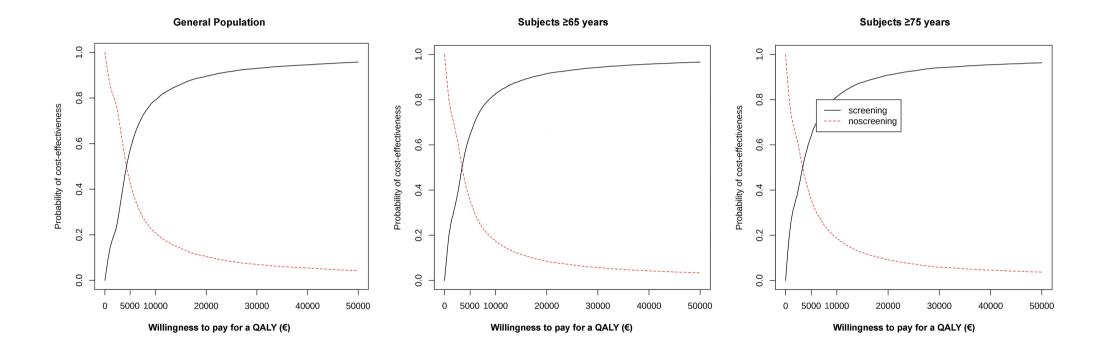
Table 2: Base-case scenario	for 1000 screened individuals
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	Lifetime	Strokes	Life	QALY	ICER per gained	ICER per gained
	Costs		Years		life year	QALY
General Population						
No Screening	178,086.5€	11.1	19,139.1	19,081.4		
Screening	290,071.0€	8.3	19,148.6	19,086.0	11,787.8 €	24,344.5€
<u>Subjects ≥65 years</u>						
No Screening	175,301.2€	10.9	10469.7	9,982.7		
Screening	256,687.2€	8.0	10473.9	9,987.3	19,377.6 €	17,692.6 €
<u>Subjects ≥75 years</u>						
No Screening	163,528.2€	10.1	8,886.5	8,817.9		
Screening	239,323.8€	7.4	8,899.4	8,829.2	5,875.6 €	6,707.6 €

Legend: ICER= incremental cost-effectiveness ratio; QALY= quality adjusted life year.







APPENDIX

Belgian Heart Rhythm Week Investigators

Dr. Wim Huysmans, AZ Herentals, Herentals; Dr. Peter Goethals, BHC Clinique Saint-Jean, Brussels; Dr. Katalien Galle, Onze-Lieve-Vrouw van Lourdes Ziekenhuis, Waregem; Dr. Bernard Deruyter, Cliniques de l'Europe, Site Ste. Elisabeth, Uccle; Dr. Olivier Godefroid, Hôpital de Jolimont - site de Lobbes, Lobbes; Dr. Liliane Jahjah, C.H.U. Saint-Pierre, Brussels; Dr. Janik Van Der Auwera, C.H.I.R.E.C. Braine-l'Alleud, Braine-l'Alleud; Prof. Christophe Scavée, Cliniques Universitaires Saint-Luc, Woluwe-Saint-Lambert; Dr. Mohamed Mira, Centre Médical de Jette, Jette; Dr. Alexandre Delcour, CHU Sart-Tilman, Liège; Dr. Pierre Van Robays, CHA Libramont, Libramont; Dr. Ron Cytryn, Centre Hospitalier Tubize-Nivelles, Tubize and Nivelles; Prof. Dr. Rik Willems, UZ Leuven, Campus Gasthuisberg, Leuven; Dr. Ivan Blankoff, ISPPC – CHU de Charleroi, Lodelinsart, Montigny-le-Tilleul and Charleroi; Dr. Georges Mairesse, Cliniques du Sud Luxembourg, Arlon; Dr. Alberic Van Dorpe, Diagnosecentrum Lommel, Lommel; Dr. Luc De Wolf, Cabinet privé, Tienen; Dr. Vida Firsovaite, AZ Oudenaarde, Oudenaarde; Dr. Ricardo Gil Oliveira, Epicura, site Hornu, Hornu; Dr. Frédéric Dumont, Saint Luc Bouge (SLBO), Bouge; Dr. Antoine de Meester, Hôpital de Jolimont, Haine-Saint-Paul; Dr. Etienne Marchand, CHR Haute Senne, Soignies; Dr. Johan Vijgen, Jessaziekenhuis, Hasselt; Dr. Pierre-Yves Stainier, Clinique Reine Astrid de Malmedy, Malmedy; Dr. Frédéric Deprez, Clinique Sainte-Elisabeth, Namur; Dr. Ann Selleslagh, Sint Jozefkliniek Bornem & Willebroek – Campus Bornem, Bornem; Dr. Suzanne Sini Kengmeni, Polyclinique de France, Brussels; Dr. Frank Martens, Medisch Centrum Aarschot, Aarschot; Dr. Xavier Carryn, CHR de Namur, Namur; Dr. Bruno Schwagten, ZNA Middelheim Ziekenhuis Antwerpen, Antwerp; Dr. Vaes Johan,

Algemeen Ziekenhuis Diest Campus Statiestraat, Diest; Dr. Lars Grieten, Ziekenhuis Oost Limburg, Genk; Dr. Frank Provenier, AZ Maria Middelares Gent, Ghent; Dr. Gaetano Paparella, BHC Site Saint-Pierre Ottignies, Ottignies; Dr. Dirk Bresseleers, ZNA Campus Jan Palfijn, Merksem; Dr. Stefan De Maeseneire, AZ Sint-Elisabeth Zottegem, Zottegem; Dr. Hans Jacobs, RZ Heilig Hart Tienen, Tirlemont; Dr. Nematollah Ahadi, Hôpital Sainte-Thérèse - IFAC - Vivalia, Bastogne; Dr. Dieter De Cleen, AZ Klina, Brasschaat; Dr. Filip De Vlieghere, AZ Zeno campus Blankenberge, Blankenberge; Dr. Jan Vermeulen, AZ Sint Dimpna, Geel; Dr. Philippe Lousberg, Centre Hospitalier Peltzer-La Tourelle, Verviers; Dr. Pierre Dermine, Hôpital GHDC site Notre Dame, Charleroi; Dr. Mehran Talmaseb, A.Z.Sint-Jan AV - campus Oostende, Ostende; Dr. Yves Vandekerckhove, A.Z.Sint-Jan - campus Brugge, Bruges; Dr. Philippe Dasnoy, AZ Jan Portaels, Vilvorde; Dr. Pierre Hausman, GHdC Sainte Joseph - site Gilly, Gilly; Dr. Elif Akseki, Clinique Edith Cavell - CHIREC, Uccle; Dr. Ruben Casado, Hôpital Erasme (ULB), Brussels; Dr. Filip De Kerpel, Sint-Jozefskliniek Izegem, Izegem; Dr. Alain De Caevel, Clinique Notre-Dame de Grâce, Gosselies; Dr. Wim Huybrechts, Sint-Augustinus GZA Ziekenhuizen, Wilrijk; Dr. Tom Rossenbacker, Imeldaziekenhuis, Bonheiden; Dr. André Brammerloo, AZ Vesalius, Tongres; Dr. Dirk Verleyen, AZ St-Lucas, Brugges; Dr. Tom Mulleners, Sint-Franciskusziekenhuis, Heusden-Zolder; Dr. John Thoeng, AZ TURNHOUT -Campus Sint-Elisabeth - Centre de Cardiologie, Turnhout; Dr. Tim Boussy, AZ Groeninge, Courtrai; Dr. Emmanuel Catez, CHU Brugmann, Brussels; Dr. Pascal Godart, CHU Ambroise Paré, Mons; Dr. Katarina Van Beeumen, AZ Sint-Lucas Gent, Gand; Dr. Benedikt Callens, AZ Sint Vincentius Deinze, Deinze; Dr. Imad Baroud, Clinique Edmond-Jacques, Virton; Dr. Philippe Collès, Centre de Santé des Fagnes-Chimay, Chimay; Dr. Marc Delforge, CHR de Huy, Huy; Dr. Frédéric Van

Heuverswyn, UZ Gent, Ghent; Dr. Philippe Evrard, CHC Saint-Joseph Liège, Liège;
Dr. Philippe Purnode, Clinique Ste. Anne - St. Rémi, Anderlecht; Dr. Joeri Voet, AZ
Nikolaas, Sint-Niklaas; Dr. Joost Geraedts, AZ Sint-Blasius, Termonde; Dr. Stefan
Ketels, AZ Damiaan Oostende, Oostende; Dr. Francine Desimpel, SintAndriesziekenhuis, Tielt; Dr. Peter Geelen, OLV Ziekenhuis Ninove, Ninove, Asse
and Aalst; Prof. Dr. Dominique Blommaert, CHU Dinant Godinne UCL Namur, Yvoir;
Dr. Stefan De Groof, A.Z. H. Familie, Rumst; Dr. Tom Herbots, Hôpital Sint-Trudo,
Sint-Truiden; Dr. Stefaan Vandamme, ASZ Campus Geraardsbergen,
Geraardsbergen; Dr. Geert Valgaeren, AZ Monica Campus Deurne, Deurne; Prof.
Dr. Christiaan Vrints, Universitair Ziekenhuis Antwerpen, Edegem; Dr. Bart Wollaert,
ZNA Stuivenberg, Antwerp; Dr. Ann Feys, AZ Jan Palfijn, Ghent; Dr. Erik Dhondt, AZ
St. Rembert, Torhout; Dr. Jean-Manuel Herzet, C.H.R. de la Citadelle, Liège; Dr.
Stephan Chevalier, Centre de Cardiologie, Ottignies; Dr. Wim Anné, AZ Delta
ziekenhuis - Campus Roeselare, Roeselare and Menen; Dr. Mihaela Vasile, C.H. de
Dinant (St.-Vincent), Dinant.