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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 are asymptomatic. The usefulness and cost-effectiveness of atrial fibrillation screening programmes are debated. We evaluated whether an atrial fibrillation screening programme with a handheld electrocardiogram (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 who 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 atrial fibrillation than not screening. In the base-case scenario, the screening procedure resulted in 106.6 more atrial fibrillation patient-years, resulting in three fewer strokes, 10 more life years and five more quality-adjusted life years (QALYs). The number needed-to-screen (NNS) to avoid one stroke was 361. In subjects ≥65 years old, we found 80.8 more atrial fibrillation patient-years, resulting in three fewer strokes, four more life-years and five more QALYs. The NNS to avoid one stroke was 354. Similar results were obtained in subjects ≥75 years old, 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 atrial fibrillation was cost-effective in the general population, as well as in subjects ≥65 and subjects ≥75 years old.

Keywords

Atrial fibrillation, screening, outcomes, cost-effectiveness analysis

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Introduction

Atrial fibrillation is the most incident and prevalent heart rhythm condition.[1] Despite this, atrial fibrillation 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 atrial fibrillation only after the first stroke occurrence.[4]

In the 2016 European Society of Cardiology (ESC) guidelines, screening procedures for atrial fibrillation early detection are recommended opportunistically for subjects ≥65 years old (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 (≥75 years) or those at high risk of stroke.[1]

The debate about whether to use opportunistic or systematic screening approaches remains controversial. Opportunistic screening is more cost-effective than systematic.[5] A large systematic review reported that opportunistic and systematic screening programmes reported a similar number of new atrial fibrillation diagnoses.[6] Several studies using population-wide or systematic screening programmes, using handheld electrocardiogram (ECG) machines or new technologies-based systems, have reported that these programmes are feasible to identify a significant number of new atrial fibrillation 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 study 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 atrial fibrillation 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 analysed 1000 hypothetical individuals who matched the population of the BHRW screening programme.[7] Simulations have been performed for the overall population of adults, as well as for subgroups of subjects ≥65 years and ≥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 study[7] and additionally supplemented with data from the available scientific literature. The main parameters used to build the model are reported in Table 1.[7,12–15] 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.[7,16] Briefly, the BHRW screening programme is a Belgian national campaign on awareness about atrial fibrillation, designed along with an untargeted voluntary screening programme organized by the Belgian Hearth Rhythm Association held one week per 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 to be filled in independently and anonymously by each subject. From 2010 to 2014 a total of 82,569 Belgian citizens were screened.[7]

ECG tracings were collected through a handheld one-lead ECG machine (Omron, HeartScan HCG-801) with a 30-s long recording. Use of this handheld machine has been previously validated as highly accurate to detect the presence of atrial fibrillation compared with a standard 12-lead ECG.[17] All the procedures were nurse-led.

Atrial fibrillation prevalence and distribution of thromboembolic risk

According to previously published results, the overall prevalence of atrial fibrillation detected in the BHRW screening programme was 1.4%[7] and after the exclusion of patients with a previously reported history of

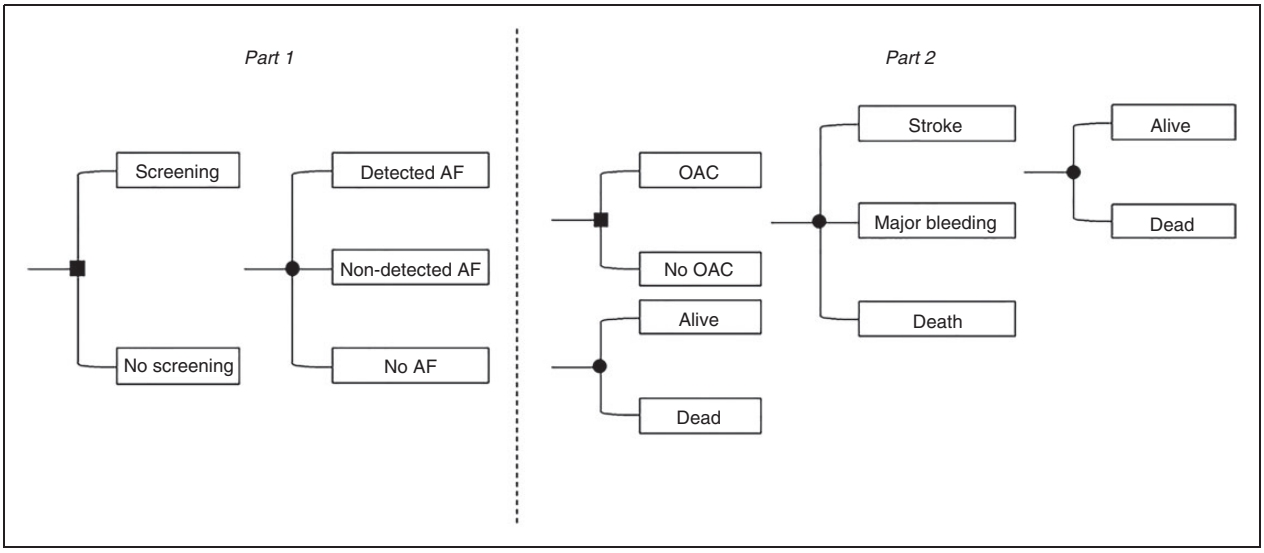

Figure 1. Basic description of the Markov model used for this analysis.
Part 1 refers to the screening procedure. Part 2 refers to treatment and follow-up following the screening phase. Squares indicate clinical choices made by physicians. Circles indicate the clinical events that may occur probabilistically.
AF: atrial fibrillation; OAC: oral anticoagulation

atrial fibrillation, a final prevalence of unknown atrial fibrillation was 1.1%. Stratifying patients per age subgroups, in patients older than 65 years unknown atrial fibrillation was found in 2.0% of patients, while those subjects $\geq$75 years had a final prevalence of 3.1% for detected unknown atrial fibrillation. Prevalence of newly detected atrial fibrillation based on occasional pulse check was evaluated according to previously published data.[18]

In the general cohort of subjects enrolled in BHRW, programmed median (interquartile range) CHA_2DS_2-VASc was 2 (1–3), with 15.5% of subjects with CHA_2DS_2-VASc 0, 33.5% with CHA_2DS_2-VASc 1 and 51% with CHA_2DS_2-VASc $\geq$2. Meanwhile, 86.0% of subjects $\geq$65 years old had a CHA_2DS_2-VASc $\geq$2.

Risk of adverse events and thromboembolic risk treatment

The primary aim of a screening programme for atrial fibrillation is ultimately to reduce the occurrence of thromboembolic events, namely ischaemic stroke. Atrial fibrillation is an independent risk factor for stroke occurrence, increasing up to five-fold the risk of stroke.[19] Concomitant presence of other risk factors, that is, age, hypertension, congestive heart failure, diabetes mellitus, et cetera, increases this risk exponentially.[19] Nowadays, thromboembolic risk is routinely evaluated at baseline and is pivotal in the clinical decision-making process of prescribing oral anticoagulation (OAC) therapy.[1] Thromboembolic risk stratification is made using a clinical scoring system, the CHA_2DS_2-VASc score,[20] largely evaluated and validated in several atrial fibrillation cohorts.[19]

Thromboembolic risk in atrial fibrillation patients untreated with OAC, to compute the model presented, was considered as progressively increasing according to CHA_2DS_2-VASc score, as previously reported in ESC 2010 Guidelines.[12] To simplify the model, patients were considered eligible for OAC prescription for a CHA_2DS_2-VASc score $\geq$2. Death risk for patients without atrial fibrillation was based on epidemiological data about the general Belgian population, and changes in mortality risk due to atrial fibrillation presence, as well as relative risk reduction in death rates, have been considered according to available literature.[13,14,21]

Recently released ESC guidelines for treatment of atrial fibrillation patients recommended for thromboembolic risk reduction the use of non-vitamin K antagonist oral anticoagulants (NOACs) over vitamin K antagonist, namely warfarin.[1] Considering that no indication exists to preferentially use one NOAC over the others[1] and according to the class-effect in reduction of both thromboembolic and bleeding risk that NOACs presented,[14] 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 atrial fibrillation a generic NOAC was prescribed, considering the overall ability in reduction of both thromboembolic and bleeding risk demonstrated by all NOACs.[14]

Table 1. Relevant parameters in the model.

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 old	2.0	
Subjects ≥75 years old	3.1	
CHA_2DS_2-VASc distribution (%)		
CHA_2DS_2-VASc 0	15.5	7
CHA_2DS_2-VASc 1	33.5	
CHA_2DS_2-VASc 2	18.6	
CHA_2DS_2-VASc 3	9.4	
CHA_2DS_2-VASc ≥4	23.0	
Stroke risk for untreated AF (%/year)		
CHA_2DS_2-VASc 0	0	12
CHA_2DS_2-VASc 1	1.3	
CHA_2DS_2-VASc 2	2.2	
CHA_2DS_2-VASc 3	3.2	
CHA_2DS_2-VASc 4	4.0	
CHA_2DS_2-VASc 5	6.7	
CHA_2DS_2-VASc 6	9.8	
CHA_2DS_2-VASc 7	9.6	
CHA_2DS_2-VASc 8	6.7	
CHA_2DS_2-VASc 9	15.2	
Stroke risk difference with VKAs (RRR)	–64%	13
Stroke risk difference with NOACs (RRR)	–19%	14
Major bleeding risk difference with VKAs (RRR)	+66%	13
Major bleeding risk difference with NOACs (RRR)	–14%	14
Death risk difference with VKAs (RRR)	–26%	13
Death risk difference with NOACs (RRR)	–10%	14
Utility weight AF	0.73	15
Utility weight stroke	0.56	15
Utility weight major bleeding	0.15	15
Main costs (mean)		
ECG, handheld (€/device per year)	100	[a]
Screening associated costs (€/h)	34.28	[a]
NOAC cost (€/day)	3.50	15
NOAC routine care cost (€/year)	91	15

[a]Previously unpublished data from Belgian Heart Rhythm Week programme.

AF: atrial fibrillation; ECG: electrocardiogram; NOAC: non-vitamin K antagonist oral anticoagulant; VKA: vitamin K antagonist; RRR: relative risk reduction

Resources and costs

Handheld ECG machines cost €500 and could be reused over five years (annual cost €100). We considered 2.5 mean devices for each centre, for a total of 90 centres throughout Belgium, as reported in the main BHRW paper.[7] As stated above, all screening procedures were nurse-led, with an estimated time of 5 min/test and an overall cost of €34.28/h 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 atrial fibrillation in Belgium.[15] 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 to atrial fibrillation diagnosis and adverse events occurrence were calculated from specific utility weights according with previously published data for CEA modelling analysis in the Belgian population.[15]

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 atrial fibrillation are reported in Figure 2. We found that the number of patients diagnosed with atrial fibrillation is consistently and steadily higher when the population screening procedure is applied, in the overall population, in patients ≥65 years old and in patients ≥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 atrial fibrillation. Consequently, three fewer strokes were obtained with 10 more life years and five more QALYs. The number needed-to-screen (NNS) to avoid one stroke was 361 patients screened.

In patients ≥65 years old use of the screening procedure identified 80.8 more patients with new atrial fibrillation diagnosis, resulting in three fewer strokes, four more life years and five more QALYs. The NNS to avoid one stroke was 354. Furthermore, in patients ≥75 years old the screening procedure resulted in 71.1 more patients diagnosed with atrial fibrillation, resulting in three 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, while the ICER for any gained QALY was €24,344.5. Furthermore, in patients ≥65 years old and ≥75 years old the ICER for any gained life year was €19,377.6 and €17,692.6, respectively, and the ICER for any gained QALY was €5875.6 and €6707.6, 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 old and subjects ≥75 years old.

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 atrial fibrillation, in the general population and in both subjects ≥65 years old and subjects ≥75 years old. Identification of an increased number of patients with atrial fibrillation, if properly treated with OAC, ultimately leads 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 gain in quality of life in subjects ≥65 years and ≥75 years old, while providing a limited advantage when considered among the general population, with ICER for gained QALY barely below €25,000.

In recent years, research regarding use of screening strategies to identify patients with asymptomatic atrial fibrillation has developed, building up an increasing amount of evidence.[22,23] Two recently published expert consensuses from international experts and scientific societies strongly support and recommend performing atrial fibrillation screening in all subjects ≥65 years old, though it is not suggested as a systematic and compulsory strategy, but, rather, one to be implemented in an opportunistic way.[22,23] This approach matches that suggested by International atrial fibrillation guidelines[1] as well as by consensus guidance stemming from the primary care environment.[24] Furthermore, use of a systematic atrial fibrillation screening is suggested to be considered for subjects ≥75 years old,[22] even though guidelines underline how the evidence supporting this type of

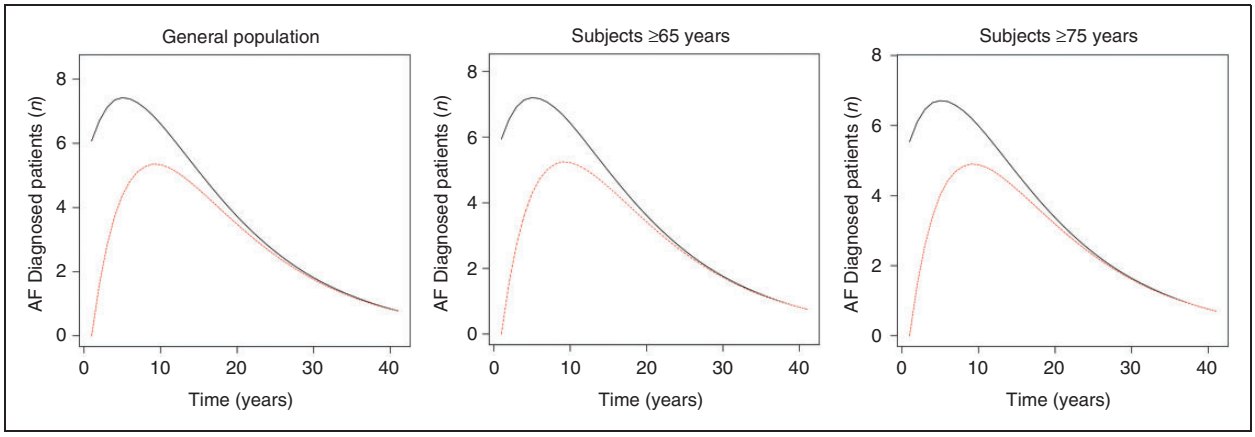

Figure 2. Number of atrial fibrillation patients found among the 1000 subjects simulated in the model. Red line indicates no screening procedure performed. Black line indicates screening procedure performed. AF: atrial fibrillation

Table 2. Base-case scenario for 1000 screened individuals.

	Lifetime costs	Strokes	Life years	QALY	ICER per gained life year	ICER per gained 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
Subjects ≥65 years old						
No screening	€175,301.2	10.9	10,469.7	9982.7		
Screening	€256,687.2	8.0	10,473.9	9987.3	€19,377.6	€17,692.6
Subjects ≥75 years old						
No screening	€163,528.2	10.1	8886.5	8817.9		
Screening	€239,323.8	7.4	8899.4	8829.2	€5875.6	€6707.6

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

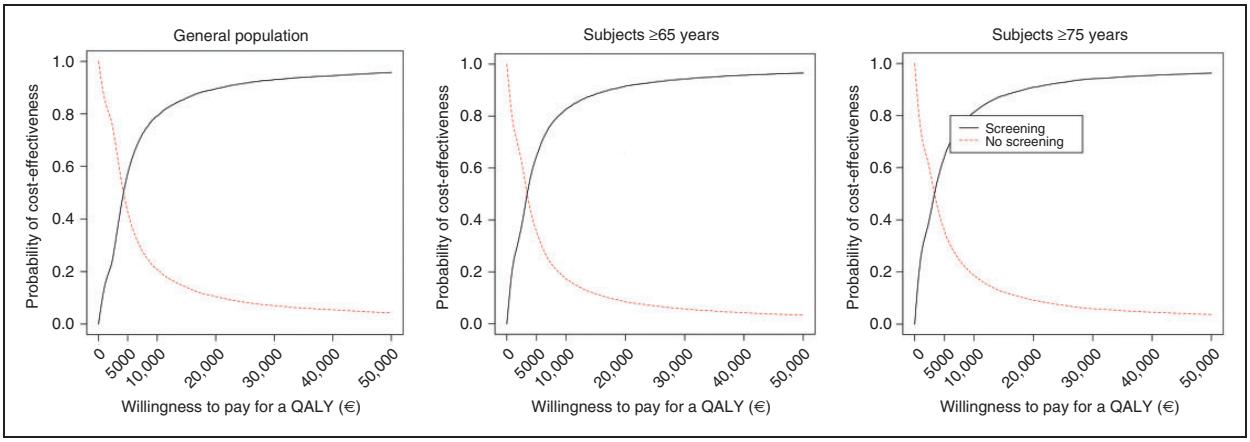

Figure 3. Acceptability curves for sensitivity analysis.

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 subjects ≥75 years old, providing evidence that such a programme will result in a significant increase of atrial fibrillation diagnosis and reduction of events, while remaining cost-effective. Regarding this aspect, we would comment on the evidence that while a lower NNS was found for subjects ≥65 years old, compared with the general population, in the subjects ≥75 years old we found, contrary to what was expected, a slightly higher NNS compared with those ≥65 years old. We can postulate that since the risk of atrial fibrillation progressively increases with age, being greater in subjects ≥75 years old, the likelihood that atrial fibrillation is diagnosed incidentally would be higher than in younger subjects, 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 old considered compared with the other age strata, which could have partially influenced this aspect.

Recently the US Preventive Services Task Force (USPSTF) released a recommendation regarding the use of ECG screening for atrial fibrillation in older (≥65 years) adults.[25] After a systematic revision of the current literature,[26] which concluded that there is not enough evidence to establish the balance between benefits and harms of ECG screening,[26] USPSTF did not make any recommendation regarding the use of ECG screening, claiming the need for further evidence.[25] The summary of evidence and the subsequent statement are limited by the fact that most of the studies regarding screening programmes for atrial fibrillation detection have a cross-sectional design, without any active comparator, nor including a follow-up phase to establish whether 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 whole 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 ≥65 years. In this context, recently the results of a five-year observation derived from an atrial fibrillation 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 stroke.[27]

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 per QALY.[22] When limiting the screening to the subjects aged ≥65 years or those ≥75 years the programme appears clearly cost-effective, even though it resulted in a slightly higher cost compared with the few other cost-effectiveness evaluations of atrial fibrillation screening activities.[22] Conversely, compared with 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 QALY.[28] Obviously, the implementation of a nationwide general population screening implies a relevant impact in terms of commitment and still deserves further evidence to be strongly supported.

Limitations

As per 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. Second, the analysis is based on a Belgian scenario of voluntary subjects attending the screening initiative, who, as volunteers, may have been more burdened with vague atrial fibrillation-related symptoms and may 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 atrial fibrillation 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. Last, we based the weights related to NOACs on those 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 cost-effective in identifying new atrial fibrillation patients and reducing stroke occurrence in the general population, subjects ≥65 years old and subjects ≥75 years old. Our results clearly support the use of more systematic screening for atrial fibrillation in patients ≥65 and ≥75 years old.

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The Belgian Heart Rhythm Week Investigators are listed in the Supplementary Material online.

Author contribution

GYHL and GHM are joint senior authors. 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.

Declaration of conflicting interests

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