ESC
European Society
of Cardiology

Smartphone-based atrial fibrillation screening in the general population: feasibility and impact on medical treatment

Henri Gruwez [1,2,3,*,†], Frederik H. Verbrugge[1,4,5,†], Tine Proesmans[6], Stijn Evens[6],
Peter Vanacker[7,8], Matthieu Pierre Rutgers[9], Geert Vanhooren[10],
Philippe Bertrand[1,3], Laurent Pison [1,3], Peter Haemers [2],
Pieter Vandervoort[1,3], and Dieter Nuyens[3]

[1]Biomedical Research Institute, Faculty of Medicine and Life Sciences, Hasselt University, Hasselt, Belgium; [2]Department of Cardiovascular Sciences, Catholic University Leuven, Leuven, Belgium; [3]Department of Cardiology, Hospital East-Limburg, Genk, Belgium; [4]Centre for Cardiovascular Diseases, University Hospital Brussels, Jette, Belgium; [5]Faculty of Medicine and Pharmacy, Vrije Universiteit Brussel, Brussels, Belgium; [6]Qompium NV, Hasselt, Belgium; [7]Department of Neurology, Antwerp University Hospital and Antwerp University, Antwerp, Belgium; [8]Department of Neurology, Groeninge Hospital, Kortrijk, Belgium; [9]Department of Neurology, Clinique de l'Europe, Brussels, Belgium; and [10]Department of Neurology, Sint-Jan Hospital Brugge-Oostende, Bruges, Belgium

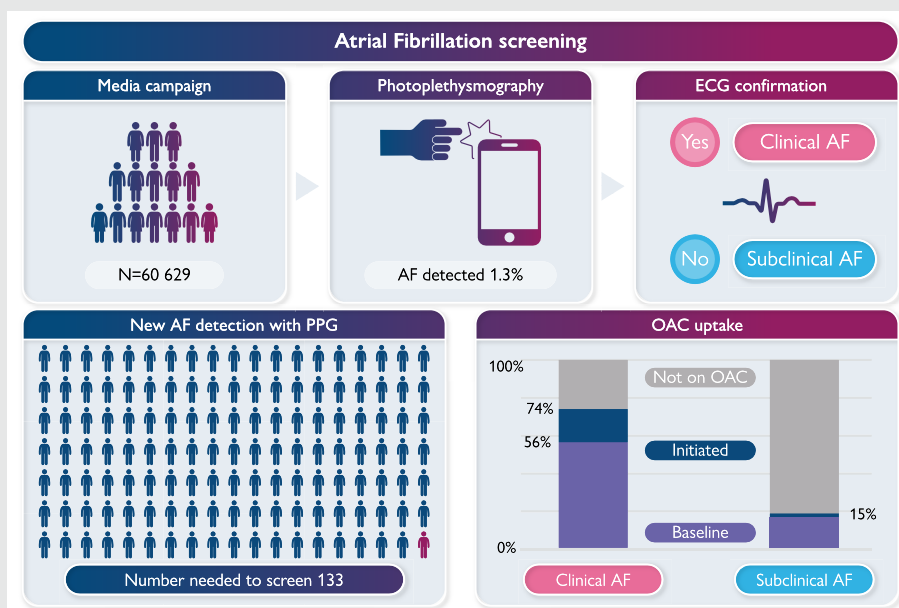|	
Aims	The aim of this study is to determine the feasibility, detection rate, and therapeutic implications of large-scale smartphone-based screening for atrial fibrillation (AF).
Methods and results	Subjects from the general population in Belgium were recruited through a media campaign to perform AF screening during 8 consecutive days with a smartphone application. The application analyses photoplethysmography traces with artificial intelligence and offline validation of suspected signals to detect AF. The impact of AF screening on medical therapy was measured through questionnaires. Atrial fibrillation was detected in the screened population ($n = 60.629$) in 791 subjects (1.3%). From this group, 55% responded to the questionnaire. Clinical AF [AF confirmed on a surface electrocardiogram (ECG)] was newly diagnosed in 60 individuals and triggered the initiation of anti-thrombotic therapy in 45%, adjustment of rate or rhythm controlling strategies in 62%, and risk factor management in 17%. In subjects diagnosed with known AF before screening, a positive screening result led to these therapy adjustments in 9%, 39%, and 11%, respectively. In all subjects with clinical AF and an indication for oral anti-coagulation (OAC), OAC uptake increased from 56% to 74% with AF screening. Subjects with clinical AF were older with more co-morbidities compared with subclinical AF (no surface ECG confirmation of AF) ($P < 0.001$). In subjects with subclinical AF ($n = 202$), therapy adjustments were performed in only 7%.
Conclusion	Smartphone–based AF screening is feasible at large scale. Screening increased OAC uptake and impacted therapy of both new and previously diagnosed clinical AF but failed to impact risk factor management in subjects with subclinical AF.

* Corresponding author. Tel: +32 89 32 2051, Email: henri.gruwez@zol.be
†The first two authors shared first authorship.

Graphical Abstract

Atrial Fibrillation screening

Media campaign

N=60 629

Photoplethysmography

AF detected 1.3%

ECG confirmation

Yes — Clinical AF

No — Subclinical AF

New AF detection with PPG

Number needed to screen 133

OAC uptake

Not on OAC — Initiated — Baseline

100% / 74% / 56% / 0%

15%

Clinical AF — Subclinical AF

Subjects from the general population were recruited through a media campaign to perform AF screening with a smartphone application. The application analyses photoplethysmography traces with artificial intelligence and offline validation of suspected signals to detect AF. The number needed to screen to detect a new case of AF was 133. When AF is confirmed on a surface ECG, it is referred to as clinical AF. In all subjects with clinical AF and an elevated CHA_2DS_2-VASC score, OAC uptake increased from 56% to 74% with AF screening. Subclinical AF refers to AF that is not confirmed with a surface ECG, OAC uptake in this group increased from 15% to 18%. AF, atrial fibrillation; ECG, electrocardiogram; OAC, oral anti-coagulation; PPG, photoplethysmography.

Keywords   Atrial fibrillation • Screening • Stroke • Photoplethysmography • Digital health

Introduction

Atrial fibrillation (AF) is the most frequent heart rhythm disorder treated by cardiologists. An average person's lifetime risk to develop AF is ~25%.[1] Currently, the prevalence of AF in Europe is estimated between 2% and 4%, but expected to double from 2010 to 2060 because of an increasing burden of risk factors such as hypertension, diabetes, and ageing in the population.[2,3]

A diagnosis of AF is associated with a five–fold increased stroke risk and 1.5– to two-fold increased risk of all–cause mortality.[4] Early diagnosis and appropriate treatment, particularly with oral anti-coagulation (OAC) in individuals at high risk for stroke or systemic embolism, may mitigate this substantial morbidity and mortality although current evidence only applies to *clinical AF*.[5–7] *Clinical AF* is defined as AF that is documented on a surface electrocardiogram (ECG). *Subclinical AF* is defined by the contemporary ESC guidelines as 'AF automatically detected by an insertable cardiac monitor or wearable monitor and confirmed by visually reviewed intracardiac electrograms or ECG-recorded rhythm'.[8,9] In recent years, an exponential number of digital devices and wearables have been developed to monitor the heart rhythm without ECG recordings. These devices, such as pulse oximeters, smart rings, smartwatches, and smartphone applications use photoplethysmography (PPG) to monitor the heart rhythm.[10] Alike ECG-based monitors, these devices use automated algorithms to detect AF, and visual confirmation of suspected signals identified by automated algorithms is necessary to filter false positives or artefactual recordings. The 'conventional definition of subclinical AF' does not accommodate for AF detected with PPG, nor is there another term in the
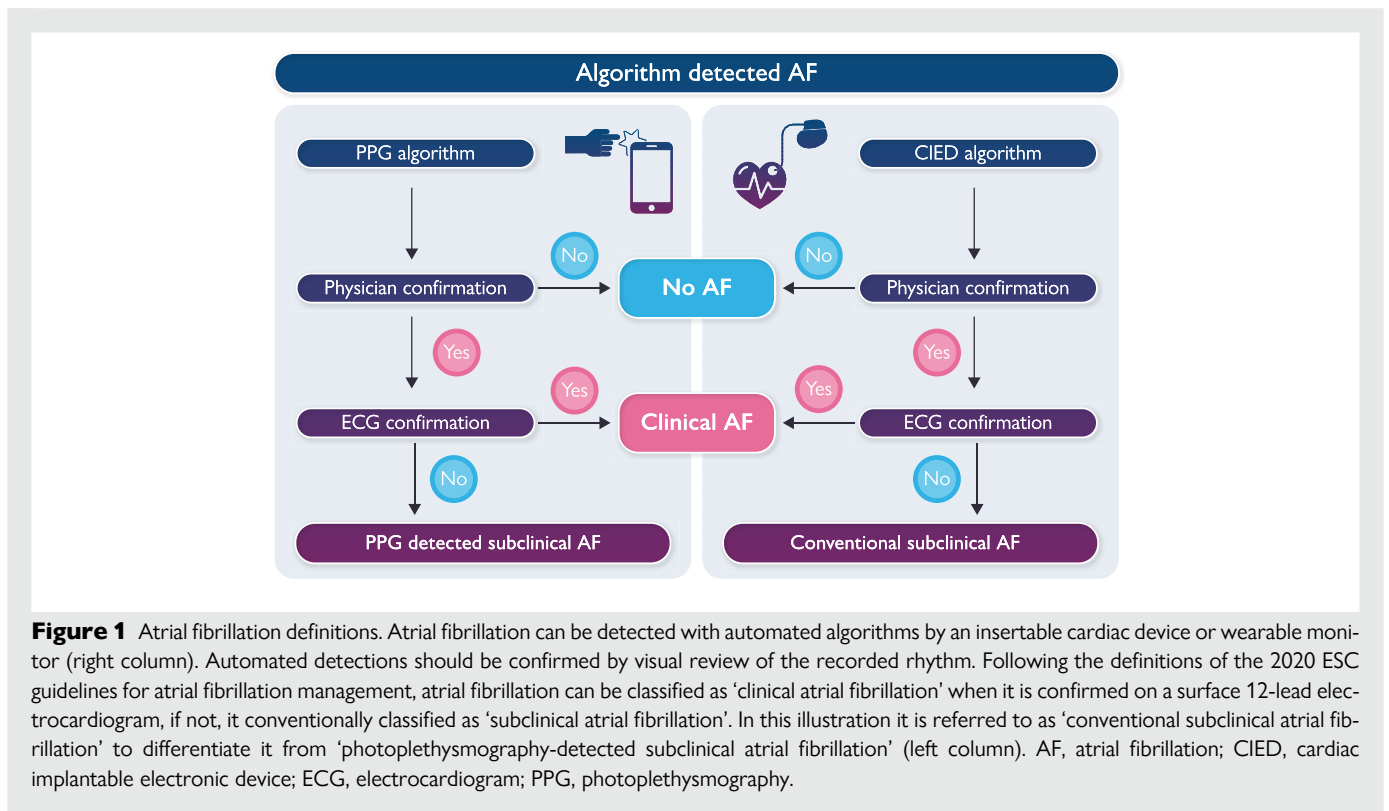
guidelines to describe this. Hence, for the sake of simplicity, in this paper, 'PPG-detected subclinical AF' is concisely referred to as 'subclinical AF' (*Figure 1*). The impact of subclinical AF on clinical outcomes such as stroke and mortality is uncertain.

The US Preventive Services Task Force concluded in 2022 that there is insufficient evidence to recommend for or against screening for AF and clinicians should use their clinical judgment regarding whether to screen and how to screen for AF.[9] Frequent or long-term ECG monitoring is cumbersome and unlikely to be cost-effective, yet recent innovations in AF screening tools and strategies have the potential to increase screening coverage at relatively low cost and efforts.[11] One attractive option uses PPG technology through the build–in camera of a smartphone.[12–14] As no additional hardware is required and smartphone use is nearly ubiquitous, this could facilitate mass screening.[14,15] This study was set up to assess the feasibility, diagnostic yield, and impact on medical therapy of physician–supervised digital screening for AF.

Methods

Study design

This is a prospective cohort study of subjects from the general population undergoing AF screening with a smartphone application based on PPG technology (FibriCheck©, Qompium, Hasselt, Belgium) that received Food and Drug Administration (FDA) 510(k) clearance and Conformité Européenne (CE) certification for AF detection.[16] Readers from three Belgian newspapers with a collective reach of 1.3 million readers were informed on AF through an article that promoted AF screening with a smartphone application using the smartphone camera.[13,14,17] Free access codes

Figure 1 Atrial fibrillation definitions. Atrial fibrillation can be detected with automated algorithms by an insertable cardiac device or wearable monitor (right column). Automated detections should be confirmed by visual review of the recorded rhythm. Following the definitions of the 2020 ESC guidelines for atrial fibrillation management, atrial fibrillation can be classified as 'clinical atrial fibrillation' when it is confirmed on a surface 12-lead electrocardiogram, if not, it conventionally classified as 'subclinical atrial fibrillation'. In this illustration it is referred to as 'conventional subclinical atrial fibrillation' to differentiate it from 'photoplethysmography-detected subclinical atrial fibrillation' (left column). AF, atrial fibrillation; CIED, cardiac implantable electronic device; ECG, electrocardiogram; PPG, photoplethysmography.

to the application were provided for a period of 8 days in December 2018. Additionally, the newspaper article comprised instructions on how to install the application, perform measurements with it, and participate in the screening study. Prior to account activation or any data collection, users were informed on the current study through their smartphone and provided informed consent through electronic signature. Subjects with a positive screening result indicating AF provided a second written informed consent to allow registration of their downstream use of medical resources and therapeutic changes as a consequence of screening. This second consent was part of a questionnaire sent by e-mail (see Supplementary material online, *Supplement S1*). The company collected and analysed the data. All academic authors had full access to the data set and statistical analyses. They vouch for the accuracy and completeness of the report as written. The first authors, who are academics, wrote the first draft of the manuscript, which was subsequently revised by all authors. The company could make suggestions for the writing, but the final decision resided with the academic authors. The study complies with the Declaration of Helsinki and was approved by the ethical review board of Ziekenhuis Oost–Limburg (Genk, Belgium). Study objectives were predefined in the protocol submitted to the ethical review board (see Supplementary material online, *Supplement S2*).

Data collection and heart rhythm assessment through the smartphone application

Smartphone-based assessment of the heart rhythm through the smartphone application (FibriCheck©) has been described before.[14,17] Briefly, by making use of the flashlight and camera of a smartphone, a PPG signal is obtained from placing one's finger on the camera lens. The application checks acquired PPG signals for quality. Compromised signals are not used for analysis to avoid inaccurate results. Study participants with frequent poor–quality PPG measurements received notifications through the application, guiding them on how to perform better measurements. After the measurement, a screen shows up that displays the average heart rate and whether any irregularities were detected by the proprietary algorithm. A text with corresponding colour code was used to communicate results to the user: measurement of insufficient quality (blue), normal

regular rhythm (green), non-AF arrhythmia (orange), or possible AF (red). 'Non-AF arrhythmia' is a category that contains abnormal regular rhythms or irregular rhythms that to do not fit the algorithm's criteria for AF. It is further classified as: bradycardia, tachycardia, frequent extrasystole, bigeminy, or trigeminy. But this is not disclosed to the user.

Study participants were instructed to assess their heart rhythm twice daily, as well as when experiencing any symptoms. Notifications were sent through the application to boost compliance towards the recommended screening frequency. After termination of the screening period, accounts were closed, and users received a summarizing report by e-mail. This summarizing report contained information on the number and quality of heart rhythm measurements performed; the highest, lowest, and average heart rate registered; and arrhythmias that were identified. Raw PPG signals for all arrhythmias (classified as possible AF or non-AF arrhythmia) underwent secondary offline validation by medical technicians.[17] Hence, the screening technique evaluated in this study is not just a smartphone application but rather a supervised digital screening. All participants with confirmed PPG-detected AF after offline validation were advised to see their general practitioner to consider the need for further evaluation and/or treatment.

At the time of account registration, subscribers were required to provide their age and gender. In addition, they were asked to voluntarily provide length, body weight, known history of AF, and co-morbidities to calculate the CHA_2DS_2-VASc score. Other data collected included the timing, results, and raw PPG signals for every use of the smartphone application as described above. Results were automatically sent to a secure server and subsequently anonymized for analysis.

Therapeutic implications in subjects with a positive screening result

Six months after sending the summarizing final report, participants with a positive screening result for AF received a questionnaire by e-mail to register their downstream use of medical resources and therapeutic changes. Questionnaires specifically asked whether individuals had contacted a physician or were planning to do so. Subjects indicated whether they consulted a general practitioner or cardiologist, whether further investigation was performed, and whether treatments was initiated or adapted.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation or median (interquartile range). One-way analysis of variance or the Kruskal–Wallis H–test was used for comparisons as appropriate. Categorical data are expressed as counts (percentages) and compared with Pearson's χ^2 test. Statistical significance was always set at a two-tailed probability level of <0.05. All statistics were performed using IBM SPSS Statistics (version 27.0.1.0, Chicago, IL, USA) and R Studio (version 4.0.2; Boston, MA, USA).

Results

Screened population

A study flowchart is provided in *Figure 2*. During the 2–week onboarding period, 62 807 subjects downloaded the screening application on their smartphone. From this group, 60 629 (97%) performed at least one measurement that rendered a PPG signal of sufficient quality for analysis (i.e. the screened population). The average age of the screened population was 49 ± 15 years and 34 842 were men (57%). In 791 subjects (1.3%), the final screening result was positive for AF. This included both clinical and subclinical AF. The yield of screening for AF increased from 0.5% with a single heart rhythm measurement to 1.3% after the 8–day screening period (*Figure 3*). The yield of screening was higher ($P < 0.001$) in subjects who strictly adhered to the recommended screening protocol (2.5%). *Table 1* shows the characteristics of the subjects. Subjects with clinical vs. subclinical AF were older with more co-morbidities. Symptoms were reported by 44% of the participants during at least one measurement (see Supplementary material online, *Supplement S3*).

Adherence to screening recommendations by study participants

From the screened population, 9538 (16%) performed at least one measurement on each day during the 8-day screening period. Only 4898 (8%) strictly adhered to the recommended screening frequency of at least two measurements every day. On the final day (Day 8) of the screening period, 16 030 participants (26%) were still performing measurements (see Supplementary material online, *Supplement S4*).

Diagnostic yield of the smartphone application

The screened population ($n = 60\,629$) generated 585 614 unique 60-s PPG traces. Photoplethysmography signal quality was sufficient for analysis in 513 821 measurements (88%). The proportion of measurements with insufficient signal quality decreased from 15% on Day 1 to 10% on Day 8 ($P < 0.001$). Insufficient PPG signal quality was observed more frequently in older individuals, increasing from 10% in participants <40 years to 17% in participants ≥70 years ($P = 0.004$).

In 470 559 (80%) measurements, the algorithm classified the heart rhythm as normal, and no further action was performed (see Supplementary material online, *Supplement S5*). In 10 231 measurements (1.7%), AF was suspected, which was confirmed after offline validation in 2998 measurements. A total of 35 130 measurements were classified by the algorithm as non-AF arrhythmia of which 70 were reclassified to confirmed AF after offline validation. The offline validation is an integral part of the smartphone application (FibriCheck©) and is performed by the developer when the application is used outside the context of a clinical study.

Therapeutic implications in subjects with a positive screening result

This was from the 791 subjects with AF confirmed after offline validation. This was a new finding in 456 participants (58%), while 335 had a prior history of AF (42%). The number needed to screen was 133 to detect a new case of AF. A total of 577 subjects with AF (69%) were also found to have normal measurements during the screening period. A total of 436 subjects responded to the questionnaire on their downstream use of healthcare resources and therapeutic changes after screening. From the subgroup with newly detected AF that responded to the questionnaire ($n = 262$), 51% complied with the recommendation to see a physician of whom 77% received further investigation with a 12-lead ECG and/or Holter that confirmed the diagnosis in 59%. From the subgroup with a history of AF that responded to the questionnaire ($n = 174$), 78% visited a physician.

In new AF cases, the first physician contacted was a general practitioner in 56% and a cardiologist in 44%. General practitioners referred
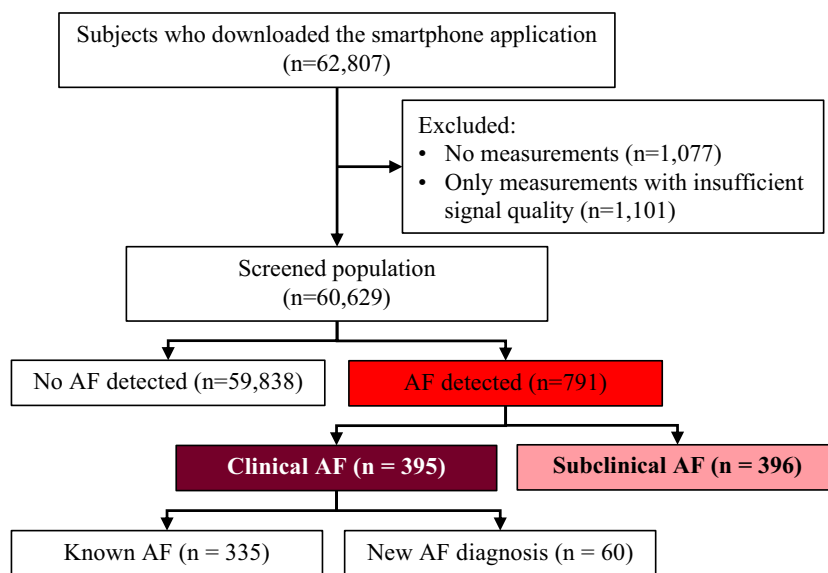
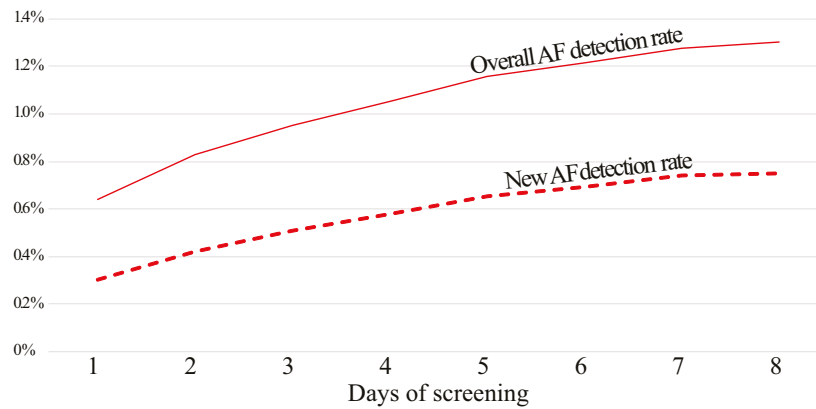**Figure 2** Study flowchart. AF, atrial fibrillation.

Figure 3 Atrial fibrillation screening yield. Overall atrial fibrillation detection rate (solid line) represents the proportion of subjects with a positive screening result regardless of a previous atrial fibrillation diagnosis. New atrial fibrillation detection rate (dashed line) represents the proportion of subjects with a positive screening in whom atrial fibrillation was previously undiagnosed. AF, atrial fibrillation.

to cardiology in 62%. 32% of the participants with a new detection of AF were not planning to take any further action and reported the following reasons: of these, 70% believed that the condition was not serious, 17% disclosed that measurements were not performed by themselves, 7% were asymptomatic, and 6% did not trust the smartphone application.

The therapeutic actions that were taken as a direct consequence of AF detection during screening were different for newly detected clinical AF compared to newly detected subclinical AF (*Figure 4*). Anti-coagulation therapy rate and rhythm control therapy were initiated more often in new clinical AF compared to new subclinical AF (*Figure 4*). In new clinical AF, anti-thrombotic therapy was started in 45%, rate or rhythm control therapy was adjusted in 62%, and lifestyle adjustments were suggested in 3%. However, in new subclinical AF, treatment adjustments were less frequent (*Figure 4*). Moreover, no subjects with new subclinical AF reported that lifestyle adjustments were suggested by their physician.

Screening also impacted the treatment of subjects with a history of AF. In this group, 9% had an adjustment of antithrombotic therapy, 10% had an adjustment of rate control medication, 11% had an adjustment of rhythm control medication, 11% underwent an electrical cardioversion, 19% underwent a catheter ablation, and 11% had a modification in risk factor management. In all, a positive screening result had therapeutic implications in 55% of the subjects, both with new or previously known clinical AF.

The uptake of OAC therapy increased with AF screening. Forth, we describe OAC uptake amongst all subjects who responded to the questionnaire with an indication for OAC treatment in case of AF detection, defined as a CHA_2DS_2-VASC score of ≥ 1 for men and ≥ 2 for women.[18,19] In subjects with clinical AF and an indication for treatment, the OAC uptake increased from 56% to 74% with AF screening. In subjects with subclinical AF, the indication for OAC is unclear; hence, the uptake of OAC in subjects with subclinical AF and 'an indication for treatment' increased only from 15% to 18% with screening.

Discussion

We performed a population–based digital screening for AF using only smartphones as detection devices. A smartphone application was used to make PPG recordings and to search for AF with artificial intelligence software. Suspected traces were supervised by a medical technician. AF was found in 1.3% of 60 629 study participants from the general population during the 8–day study period. The screening identified subjects with clinical AF and (PPG-detected) subclinical AF. A positive screening result had therapeutic implications in over half of the subjects with clinical AF. In subjects with clinical AF and an indication for anti-coagulation, OAC uptake increased with 32% after screening. Interestingly, age and co-morbidities were highest in the clinical AF group, followed by the subclinical AF group, followed by the non-AF group.

The ubiquitous availability of smartphones in the general population enabled this screening approach to reach a large portion of the population at low threshold. In this study, a media campaign attracted 60 629 participants in a period of only 2 weeks. These subjects engaged in a screening trial to voluntarily perform 585 614 PPG measurements over the course of a week, by using a dedicated smartphone application that was provided for free. This would be hardly imaginable without significant logistic challenges through conventional screening methods such as 12-lead ECG or Holter monitoring. Multiple screening trials have been described adopting digital health approaches to screen for AF in large populations with minimal effort using single-lead ECG or a combination of PPG and single-lead ECG. However, the necessitated hardware such as ECG devices or smartwatches are not as widespread as smartphones.[20–25]

Photoplethysmography as a technology has not yet been adopted by the guidelines to diagnose AF. However several validation studies have demonstrated the application's high diagnostic accuracy.[13,16] Following the definition, AF detected with PPG should be confirmed with ECG to make the diagnosis of clinical AF.[8,18] In this study AF detected with PPG screening was confirmed with ECG or Holter monitor in 71% of all cases who underwent confirmational testing. In subjects without a history of AF, the AF confirmation rate with was 59%. Similar digital AF screening trials reported a variety of AF confirmation rates ranging from 34% in the Apple Heart Study, 36% in the eBRAVE study, 60% in the 'Smart in OAC—AFNET 9' study[26] and 87% in the Huawei Heart Study. The eBrave study used a similar smartphone-based screening strategy with PPG.[27] The Apple Heart study and Huawei Heart Study used a smartwatch-based screening with PPG and ECG.[21,28] In both studies subjects with an irregular rhythm on PPG screening underwent subsequent ECG patch readings. There are many possible explanations for the variation in AF confirmation rates

Table 1 Screened population characteristics

	No AF (n = 59 838)		Subclinical AF (n = 396)		Clinical AF (n = 395)		Subclinical AF vs. clinical AF
	n	Value	n	Value	n	Value	P-value
Age (year)		48 ± 15		59 ± 14		65 ± 10	<0.01
≥65 years	59 838	14%	396	39%	395	57%	
≥75 years		2%		10%		13%	
Men	59 829	57%	396	69%	395	82%	<0.01
Body mass index (kg/m^2)	16 295	25 (23–28)	109	26 (24–30)	134	28 (24–31)	0.07
Known AF	54 134	4%	308	0	395	85%	<0.01
Heart failure	54 142	3%	308	7%	387	23%	<0.01
Hypertension	54 187	20%	310	30%	387	51%	<0.01
Diabetes	54 168	4%	308	6%	387	12%	0.01
History of stroke	54 140	3%	308	4%	387	14%	<0.01
Atherosclerotic disease	54 150	6%	308	7%	387	15%	<0.01
CHA$_2$DS$_2$-VASc score	54 122	1 (0–1)	308	1 (0–2)	387	2 (1–3)	<0.01

AF, atrial fibrillation.

amongst these studies. The duration of AF episodes is one such explanation. A smartwatch-based approach performs semi-continuous rhythm measurements, while screening with a smartphone-based approach yields only two rhythm measurements per day. Hence, short AF episodes are more likely to be detected by a smartwatch compared to a smartphone. These short AF episodes are more likely to be missed by confirmational testing. By performing only two daily measurements, a smartphone screens for longer AF episodes that are more likely to be detected by confirmational testing.

The employed screening strategy allowed users to determine when and how frequent heart rhythm assessments were performed. Hence, subjects could prioritize assessments while experiencing symptoms. Even though subjects had to perform these measurements autonomously, 88% of the PPG measurements acquired in the study were of sufficient quality for analysis and a learning-curve was observed with less signals of low quality towards the end of the screening period. On the other hand, compliance quickly waned, and any nighttime AF remained undetected as patients cannot perform measurements while sleeping. Nighttime AF might be more frequent and can be detected with a semi-continuous PPG monitor, such as smartwatches and wristbands.[26] However, the use of smartphones is more widely adopted and may reach more subjects for screening, specifically in the elderly population.

Apart from demonstrating the feasibility of this screening strategy, this study provides insightful information on its diagnostic yield. A positive screening result for AF was found in 791 individuals (1.3%) of the screened population (2.5% of participants who strictly adhered to two daily measurements) and 4.3% in the 65 + population. Positive screening results were a new detection in 0.78% in the overall population and 2.4% in those aged 65 years and older. Other population based AF screening studies reported similar findings: 0.52% (Apple Heart Study),[21] 0.23% (Huawei Heart Study),[28] and 1.0% (FitBit Heart study)[29] in the overall screened population and 3.1, 2.8, and 3.6% in those aged 65 years and older. As would be expected, positive screening for AF was associated with older age and more co-morbidities, confirming that the diagnostic yield is highly dependent of the background risk for AF.[30] The larger proportion of subjects ≥65 years in this study (14%) compared to the Apple Heart Study (6%) and Huawei Heart Study (1.8%) is likely an important driver for the higher AF detection rate.[21,22] Detection rates of newly diagnosed AF depend on the

screening setting, target population, screening duration, and screening device.[31] The following studies targeted an elderly population with co-morbidities to achieve higher AF detection rates: eBRAVE (1.6%), STROKESTOP (3.0%), mSTOPS (3.9%), EAGLE (10.6%), and LOOP studies (31.8%).[9,10,27,32–34] Accordingly, the EHRA practical guide and US Preventive Services Task Force recommendations highlight the importance of risk group selection for AF screening.[9,10]

The diagnostic yield of AF screening increases with the duration, dispersion, and number of screenings.[30] Therefore, it is somewhat concerning that the motivation for repetitive heart rhythm assessments quickly waned during the 8-day study period. Also, only 14% of subjects with known AF had a positive screening result. This suggests that more subjects with AF might be detected with longer or more frequent screening. Theoretically, an increased screening duration would be preferred over an increased screening frequency because an increased screening frequency leads to detection of shorter paroxysmal AF episodes. The LOOP study screened for (short, >6 min) AF episodes with an implantable loop recorder and was not able to demonstrate a significant reduction the primary endpoint of stroke and systemic embolism. Plausible explanations were low event rates in subjects with short AF episodes, lack of power, and high performance in the control group.[34] Although it has been found that AF episodes as short as 6 min might be associated with a higher thrombo-embolic risk, it is still unclear how much AF burden, for which patients, is needed to benefit from anti-coagulation.[35–37] The STOKESTOP study is the only randomized study that demonstrated a small net benefit compared with standard of care.[38]

A particular strength of the current study is that follow-up data were available on how the AF screening impacted on subsequent medical treatment. Screening for AF positively impacted OAC uptake in subjects with clinical AF and an indication for anti-coagulation. Oral anti-coagulation uptake increased not only in subjects with a new diagnosis of AF but also in subjects who were already diagnosed with AF before screening. In the latter, AF screening triggered to re-evaluate the thromboembolic risk and let to initiation of OAC treatment. Only a few subjects with subclinical AF were started on OAC treatment. These are subjects found to have AF on PPG measurements without ECG confirmation. Oral anti-coagulation treatment in this population is debatable and is currently not recommended by the guidelines as it is not supported by evidence. The thromboembolic
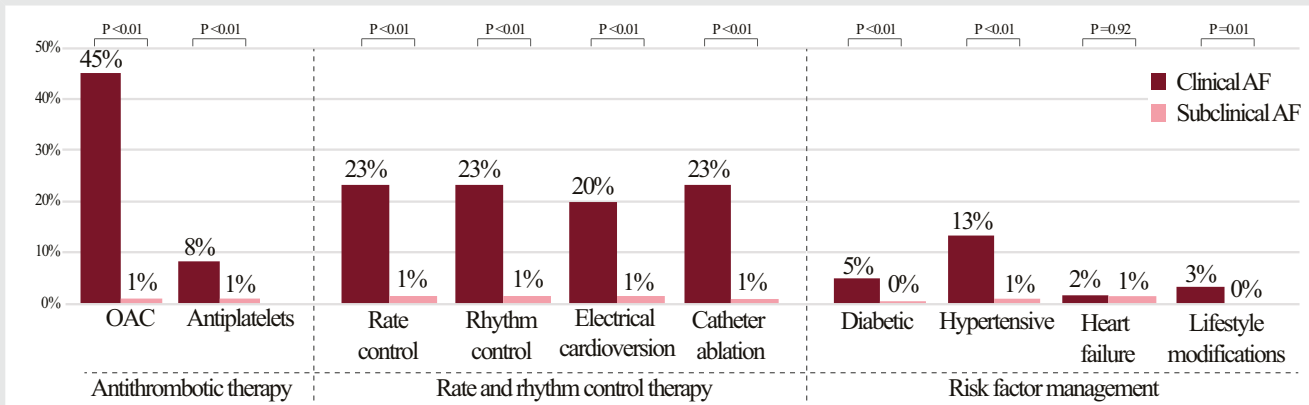
Figure 4 Therapeutic actions in subjects with a new diagnosis of atrial fibrillation. The left-sided bars (burgundy) represent therapeutic actions in subjects with a new diagnosis of clinical atrial fibrillation. The right-sided bars (pink) represent therapeutic actions in subjects with a new diagnosis of subclinical atrial fibrillation. AF, atrial fibrillation; OAC, oral anti-coagulation.

risk in subjects with conventional subclinical AF is unclear, let alone in PPG-detected subclinical AF. Hence, the low rates of OAC initiation in subclinical AF currently seem like a correct attitude, given the lack of evidence. The ARTESiA trial and NOAH-AFNET 6 trials are two on-going randomized studies to determine whether OAC therapy (with apixaban and edoxaban, respectively) reduces the risk of stroke or systemic embolism in patients with subclinical AF and additional risk factors.[39,40]

Interestingly, age and co-morbidities gradually increase from subjects with a negative screening result to subjects with subclinical AF and further increases in subjects with clinical AF detected by the screening programme (*Table 1*). Hence, the subjects identified with subclinical AF by the screening programme are at higher risk for both AF and for thromboembolism compared to subjects with a negative screening result, even if the detection of AF was not confirmed on ECG.[41,42] The eBRAVE AF trial confirmed that subclinical AF (PPG-detect AF not confirmed with ECG) is associated with three times higher risk of major adverse cardiac events.[27] Even if anti-thrombotic therapy has not been proved to be beneficial in this population, subjects with subclinical AF should be targeted for risk factor management far more than they are now. Not only the physician but also the screening application can provide information about lifestyle modifications and AF to sensitize this group.[43–45] This is important as one-third of subjects with new detected AF took no further action despite being advised to contact a physician. The main reason for neglecting the advice was being asymptomatic or feeling that AF is not a serious condition. As opposed to the present pragmatic study design, in which AF confirmation and management were left at the general practitioner or cardiologist, the Huawei Heart Study integrated an AF management programme with a mobile AF application (mAFA) incorporating the Atrial Fibrillation Better Care (ABC) pathway: A, avoid stroke; B, better symptom management; and C, cardiovascular and other co-morbidity risk reduction integrated approach to AF management.[3,44] This approach motivated more participants with PPG-detected AF to contact a physician (62%) and participants with confirmed AF to enrol in the mAFA follow-up programme (95%).[28] This AF management programme reduced the risk for the composite outcome of 'ischaemic stroke/systemic thromboembolism, death, and rehospitalization' compared to usual care.[44,45]

Hence, future AF screening programmes should defer from a pragmatic AF management approach and incorporate a structured AF management programme based on the ABC pathway to better educate on AF, to stimulate compliance, to increase OAC uptake (in patients with an indication for OAC), and to target risk factor management and lifestyle modifications.

Study limitations

The main limitations to this study are drop-out, self-reported data, and selection bias. Drop-out occurred as only 55% of the subjects with a positive screening result for AF responded to the follow-up questionnaire. Self-reported data from questionnaires were used on medical history, medication, and interventions following AF detection. Selection bias was possibly induced as participants were approached through a media campaign and registered voluntarily.

Conclusions

Large–scale screening for AF is feasible using only a smartphone with a dedicated application based on PPG technology. In this study, 60 629 participants were screened within a period of only 2 weeks. With supervised digital screening, 1.3% of the participants had a positive screening result for AF. The number needed to screen to detect a new case of AF was 133. Screening initiated important therapeutic actions such as changes in antithrombotic therapy, rate or rhythm control therapy in over half the subjects with clinical AF, but not in subjects with subclinical AF. The uptake of OAC treatment in subjects with clinical AF and an indication for anticoagulation increased after screening. The thrombo-embolic risk of subjects with subclinical AF remains debated, and there is no consensus on treatment. Interestingly, this study demonstrates that subclinical AF is associated with increased comorbidities that were not addressed with risk factor management. Hence, future screening programmes should defer from a pragmatic AF management approach and incorporate a structured AF management programme to optimize guideline-directed therapy in screen positives with clinical AF and at least initiate risk factor management in screen positives with subclinical AF.

Supplementary material

Supplementary material is available at *European Heart Journal – Digital Health*.

Funding

None declared.

Data availability

The data underlying this article were provided by Qompium NV, Belgium. Data will be shared on reasonable request to the corresponding author with permission of Qompium NV.

References

1. Benjamin EJ, Levy D, Vaziri SM, D'agostino RB, Belanger AJ, Wolf PA. Independent risk factors for atrial fibrillation in a population-based cohort: the Framingham Heart Study. *JAMA J Am Med Assoc* 1994;**271**:840.
2. Krijthe BP, Kunst A, Benjamin EJ, Lip GYH, 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.
3. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-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). *Eur Heart J* 2021;**42**:373–498.
4. Andersson T, Magnuson A, Bryngelsson IL, Frøbert O, Henriksson KM, Edvardsson N, *et al.* All-cause mortality in 272 186 patients hospitalized with incident atrial fibrillation 1995–2008: a Swedish nationwide long-term case-control study. *Eur Heart J* 2013;**34**:1061–1067.
5. 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.
6. Patel MR, Mahaffey KW, Garg J, Pan G, Singer DE, Hacke W, *et al.* Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med* 2011;**365**:883–891.
7. Giugliano RP, Ruff CT, Braunwald E, Murphy SA, Wiviott SD, Halperin JL, *et al.* Edoxaban versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2013;**369**:2093–2104.
8. Noseworthy PA, Kaufman ES, Chen LY, Chung MK, Elkind MSV, Joglar JA, *et al.* Subclinical and device-detected atrial fibrillation: pondering the knowledge gap: a scientific statement from the American Heart Association. *Circulation* 2019;**140**:E944–E963.
9. Davidson KW, Barry MJ, Mangione CM, Cabana M, Caughey AB, Davis EM, *et al.* Screening for atrial fibrillation: US Preventive Services Task Force recommendation statement. *JAMA J Am Med Assoc* 2022;**327**:360–367.
10. Svennberg E, Tjong F, Goette A, Akoum N, Di Biase L, Bordachar P, *et al.* How to use digital devices to detect and manage arrhythmias: an EHRA practical guide. *Europace* 2022;**24**:979–1005.
11. Singh N, Chun S, Hadley D, Froelicher V. Clinical implications of technological advances in screening for atrial fibrillation. *Prog Cardiovasc Dis* 2018;**60**:550–559.
12. Vandenberk T, Stans J, Mortelmans C, Van Haelst R, Van Schelvergem G, Pelckmans C, *et al.* Clinical validation of heart rate apps: mixed-methods evaluation study. *JMIR mHealth uHealth* 2017;**5**:e129.
13. Proesmans T, Mortelmans C, Van Haelst R, Verbrugge F, Vandervoort P, Vaes B. Mobile phone–based use of the photoplethysmography technique to detect atrial fibrillation in primary care: diagnostic accuracy study of the FibriCheck app. *JMIR mHealth uHealth* 2019;**7**:e12284.
14. Verbrugge FH, Proesmans T, Vijgen J, Mullens W, Rivero-Ayerza M, Van Herendael H, *et al.* Atrial fibrillation screening with photo-plethysmography through a smartphone camera. *Europace* 2019;**21**:1167–1175.
15. Turakhia MP, Desai M, Hedlin H, Rajmane A, Talati N, Ferris T, *et al.* Rationale and design of a large-scale, app-based study to identify cardiac arrhythmias using a smartwatch: the Apple Heart Study. *Am Heart J* 2019;**207**:66–75.
16. O'Sullivan JW, Grigg S, Crawford W, Turakhia MP, Perez M, Ingelsson E, *et al.* Accuracy of smartphone camera applications for detecting atrial fibrillation: a systematic review and meta-analysis. *JAMA Netw open* 2020;**3**:e202064.
17. van der Velden RMJ, Verhaert DVM, Hermans ANL, Duncker D, Manninger M, Betz K, *et al.* The photoplethysmography dictionary: practical guidance on signal interpretation and clinical scenarios from TeleCheck-AF. *Eur Hear J Digit Heal* 2021;**2**:363–373.
18. January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC, *et al.* 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association task force on practice guidelines and the Heart Rhythm Society. *J Am Coll Cardiol* 2014;**64**:e1–e76.
19. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C *et al.* 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2021;**42**:373–4985.
20. Gruwez H, Proesmans T, Evens S, Verbrugge FH, Deferm S, Dauw J, *et al.* Atrial fibrillation population screening. *Card Electrophysiol Clin* 2021;**13**:531–542.
21. Perez MV, Mahaffey KW, Hedlin H, Rumsfeld JS, Garcia A, Ferris T, *et al.* Large-scale assessment of a smartwatch to identify atrial fibrillation. *N Engl J Med* 2019;**381**:1909–1917.
22. Fan YY, Li YG, Li J, Cheng WK, Shan ZL, Wang YT, *et al.* Diagnostic performance of a smart device with photoplethysmography technology for atrial fibrillation detection: pilot study (Pre-mAFA II registry). *J Med Internet Res* 2019;**21**:e11437.
23. Svennberg E, Engdahl J, Al-Khalili F, Friberg L, Frykman V, Rosenqvist M. Mass screening for untreated atrial fibrillation the STROKESTOP study. *Circulation* 2015;**131**:2176–2184.
24. Gudmundsdottir KK, Fredriksson T, Svennberg E, Al-Khalili F, Friberg L, Frykman V, *et al.* Stepwise mass screening for atrial fibrillation using N-terminal B-type natriuretic peptide: the STROKESTOP II study. *Europace* 2020;**22**:24–32.
25. Lubitz SA, Atlas SJ, Ashburner JM, Lipsanopoulos ATT, Borowsky LH, Guan W, *et al.* Screening for atrial fibrillation in older adults at primary care visits: VITAL-AF randomized controlled trial. *Circulation* 2022;**145**:946–954.
26. Fabritz L, Connolly DL, Czarnecki E, Dudek D, Guasch E, Haase D, *et al.* Smartphone and wearable detected atrial arrhythmias in older adults: results of a fully digital European case finding study. *Eur Heart Journal Digit Heal* 2022;**3**:610–625.
27. Rizas KD, Freyer L, Sappler N, von Stülpnagel L Spielbichler P, Krasniqi A, *et al.* Smartphone-based screening for atrial fibrillation: a pragmatic randomized clinical trial. *Nat Med* 2022;**28**:1823–1830.
28. Guo Y, Wang H, Zhang H, Liu T, Liang Z, Xia Y, *et al.* Mobile photoplethysmographic technology to detect atrial fibrillation. *J Am Coll Cardiol* 2019;**74**:2365–2375.
29. Lubitz SA, Faranesh AZ, Selvaggi C, Atlas SJ, McManus DD, Singer DE, *et al.* Detection of atrial fibrillation in a large population using wearable devices: the Fitbit Heart Study. *Circulation* 2022;**146**:1415–1424.
30. Diederichsen SZ, Haugan KJ, Kronborg C, Graff C, Højberg S, Køber L, *et al.* Comprehensive evaluation of rhythm monitoring strategies in screening for atrial fibrillation: insights from patients at risk monitored long term with an implantable loop recorder. *Circulation* 2020;**141**:1510–1522.
31. Corica B, Bonini N, Imberti JF, Romiti GF, Vitolo M, Attanasio L, *et al.* Yield of diagnosis and risk of stroke with screening strategies for atrial fibrillation: a comprehensive review of current evidence. *Eur Hear J Open* 2023;**3**:oead031.
32. Steinhubl SR, Waalen J, Edwards AM, Ariniello LM, Mehta RR, Ebner GS, *et al.* Effect of a home-based wearable continuous ECG monitoring patch on detection of undiagnosed atrial fibrillation the mSToPS randomized clinical trial. *JAMA J Am Med Assoc* 2018;**320**:146–155.
33. Noseworthy PA, Attia ZI, Behnken EM, Giblon RE, Bews KA, Liu S, *et al.* Artificial intelligence-guided screening for atrial fibrillation using electrocardiogram during sinus rhythm: a prospective non-randomised interventional trial. *Lancet* 2022;**400**:1206–1212.
34. Svendsen JH, Diederichsen SZ, Højberg S, Krieger DW, Graff C, Kronborg C, *et al.* Implantable loop recorder detection of atrial fibrillation to prevent stroke (the LOOP study): a randomised controlled trial. *Lancet* 2021;**398**:1507–1516.
35. Van Gelder IC, Healey JS, Crijns HJGM, Wang J, Hohnloser SH, Gold MR, *et al.* Duration of device-detected subclinical atrial fibrillation and occurrence of stroke in ASSERT. *Eur Heart J* 2017;**38**:1339–1344.
36. Healey JS, Connolly SJ, Gold MR, Israel CW, Van Gelder IC, Capucci A, *et al.* Subclinical atrial fibrillation and the risk of stroke. *N Engl J Med* 2012;**366**:120–129.
37. Mahajan R, Perera T, Elliott AD, Twomey DJ, Kumar S, Munwar DA, *et al.* Subclinical device-detected atrial fibrillation and stroke risk: a systematic review and meta-analysis. *Eur Heart J* 2018;**39**:1407–1415.
38. 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.
39. Lopes RD, Alings M, Connolly SJ, Beresh H, Granger CB., Mazuecos JB, *et al.* Rationale and design of the apixaban for the reduction of thrombo-embolism in patients with device-detected sub-clinical atrial fibrillation (ARTESiA) trial. *Am Heart J* 2017;**189**:137–145.
40. Kirchhof P, Blank BF, Calvert M, Camm AJ, Chlouverakis G, Diener HC, *et al.* Probing oral anticoagulation in patients with atrial high rate episodes: rationale and design of

the non–vitamin K antagonist oral anticoagulants in patients with atrial high rate episodes (NOAH–AFNET 6) trial. *Am Heart J* 2017;**190**:12–18.

41. Saliba W, Gronich N, Barnett-Griness O, Rennert G. Usefulness of CHADS2 and CHA2DS2-VASc scores in the prediction of new-onset atrial fibrillation: a population-based study. *Am J Med* 2016;**129**:843–849.

42. Lip GYH, Nieuwlaat R, Pisters R, Lane DA, Crijns HJGM. 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**: 263–272.

43. Delesie M, Knaepen L, Dendale P, Vijgen J, Ector J, Verbeeck J, *et al.* Effect of targeted education for atrial fibrillation patients: design of the EduCare-AF study. *Eur J Clin Invest* 2021;**51**:e13442.

44. Guo Y, Lane DA, Wang L, Zhang H, Wang H, Zhang W, *et al.* Mobile health technology to improve care for patients with atrial fibrillation. *J Am Coll Cardiol* 2020; **75**:1523–1534.

45. Guo Y, Guo J, Shi X, Yao Y, Sun Y, Xia Y, *et al.* Mobile health technology-supported atrial fibrillation screening and integrated care: a report from the mAFA-II trial long-term extension cohort. *Eur J Intern Med* 2020;**82**:105–111.