

PPG-based smartphone application vs usual care for atrial fibrillation screening: A European multicenter randomized trial

Jakob Johannes Reichl, MD,^{1,2,3} Khaled Abdel Hamid, MD,¹ Thilo Burkard, MD,^{3,4} Annina Salome Vischer, MD,⁴ Caroline Guzman,⁴ Dariusz Dudek, PhD, MD,⁵ Artur Pawlik, MD,⁵ Bela Merkely, MD,⁶ Janos Marcell László, MD,⁶ Athanasios J. Manolis, MD,⁷ Manolis S. Kallistratos, MD,⁷ Dominik Linz, MD,⁸ Markus Dörr, MD,^{9,10,11} Christine Bahr, MD,¹⁰ Branko Belesin, MD, PhD,¹² Thomas Hübner, PhD,¹³ Nicole König, PhD,¹³ Diana Piper, PhD,¹³ Jens Eckstein, MD, PhD^{1,2}

ABSTRACT

BACKGROUND Atrial fibrillation (AF) is the most frequent arrhythmia worldwide and a major cause of ischemic stroke. Screening tools are becoming increasingly popular to detect AF for stroke prevention, yet data from randomized trials are lacking.

OBJECTIVE The purpose of this study was to analyze AF detection rates using a smartphone application with early intervention (intervention group) compared with no intervention (sham group).

METHODS This is an international, multicenter, prospective, randomized, sham-controlled, double-blinded trial conducted between October 2019 and May 2024. Patients with no prior AF were randomized 1:1 to an intervention group or a sham group. The study application used the smartphone camera to generate photoplethysmography signals. If an arrhythmia was detected, patients in the intervention group received a notification and a 7-day patch electrocardiogram to confirm AF.

RESULTS A total of 1021 patients from 8 centers were randomized. The mean CHA₂DS₂-VASc score was 3.4 ± 0.92 in the intervention group and 3.5 ± 1.02 in the sham group. Arrhythmia was detected in 32 (3.1%) cases: 20 (3.9%) in the intervention group and 12 (2.4%) in the sham group. AF was diagnosed in 13 (1.3%) patients. AF detection rates were numerically higher in the intervention group (10 [1.9%] vs 3 [0.5%]; $P = .094$), especially in cases of asymptomatic AF (4 [0.8%] vs 0 [0%]; $P = .13$). There was no difference in the rate of stroke, transient ischemic attack, or systemic embolism after 6 months.

CONCLUSION In this multicenter trial, application usage in combination with early intervention did not significantly increase overall AF detection rates. However, asymptomatic AF detection was numerically higher in the intervention group, aligning with current guidelines that recommend photoplethysmography-based devices for AF screening.

KEYWORDS Atrial fibrillation; Stroke; Stroke prevention; Wearables; Screening; AF Screening

(Heart Rhythm 2025; ■:1–8) © 2025 Heart Rhythm Society. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Atrial fibrillation (AF) is the most common cardiac arrhythmia, affecting an estimated 30 and 100 million people worldwide. Because of an aging population and increasing risk factors, the prevalence is expected to rise significantly in the coming

decades.¹ Studies have projected that in 2060, ~14.4 million elderly Europeans will be affected.²

AF is associated with increased mortality, higher hospitalization rates due to heart failure, and a higher risk of

From the ¹Departement D&ICT, Innovation Management, University Hospital of Basel, Basel, Switzerland, ²Department of Internal Medicine, University Hospital of Basel, Basel, Switzerland, ³Department of Cardiology and Cardiovascular Research Institute, University Hospital Basel, Basel, Switzerland, ⁴Medical Outpatient Department, University Hospital of Basel, Basel, Switzerland, ⁵Department of Cardiology and Cardiovascular Interventions, University Hospital, Jagiellonian University Medical College of Krakow, Krakow, Poland, ⁶Heart and Vascular Centre, Semmelweis University, Budapest, Hungary, ⁷Cardiology Department, Asklepion Hospital of Athens, Athens, Greece, ⁸Department of Physiology, University Maastricht, Maastricht, The Netherlands, ⁹Department of Internal Medicine B, University Hospital of Greifswald, Greifswald, Germany, ¹⁰Ambulantes Herz-Kreislauf-Zentrum Pasewalk, Pasewalk, Germany, ¹¹German Centre for Cardiovascular Research, partner site Greifswald, Greifswald, Germany, ¹²Cardiology Clinic, Clinical Center of Serbia, Belgrade, Serbia, and ¹³Preventicus GmbH, Jena, Germany..

thromboembolic events such as stroke.³ While common symptoms include dyspnea, chest pain, palpitations, and fatigue,⁴ AF can be asymptomatic or clinically silent. Additionally, patients may experience both symptomatic and asymptomatic episodes, with silent AF occurring in an estimated 12%–45% of cases.^{5–7}

Stroke is the second leading cause of death in Europe, responsible for 13% of all deaths,⁸ and a major cause of complex neurological disability. In 2017, the total annual cost of stroke reached €60 billion, with further increases expected.⁹ Since AF is a major contributor to stroke—present in 20%–30% of patients with ischemic stroke and newly diagnosed in ~10%—early detection is essential.^{10–13} AF-related strokes are often more severe than ischemic strokes without AF, resulting in higher mortality rates, longer in-hospital stays, and higher degrees of functional disability.¹⁴ Early detection of AF and initiation of anticoagulation lead to a drastic decrease in stroke risk.¹³

Consequently, the development of screening strategies for early AF detection has become an important research topic and is recommended in current professional guidelines.^{15,16} Traditional methods such as opportunistic pulse palpation, routine electrocardiograms (ECGs), and 24-hour monitoring often miss paroxysmal AF and are impractical for large-scale screening owing to cost and equipment limitations.

Effective screening requires high predictive accuracy at low cost by using simple, low-risk tools.¹

Recently, digital technologies such as smartphones, smartwatches, and other wearables using photoplethysmography (PPG) have emerged as promising tools for AF screening^{17–19} and are now included in international guidelines.¹⁵

The primary aim of this randomized double-blinded study was to investigate the effect of a smartphone application on the detection rates of AF. We hypothesized higher detection rates in the intervention group.

Methods

Study design

We conducted an investigator-initiated, prospective, double-blinded, randomized, sham-controlled, international multicenter medical device study between October 2019 and May 2024 in a population at risk but with no history of AF. Eight centers in Switzerland, Germany, the Netherlands, Poland, Serbia, Hungary, and Greece participated. The study was conducted in compliance with the Declaration of Helsinki (as revised in 2013), the International Council for Harmonisation (ICH) Good clinical practice (GCP)-guidelines, the International Organisation for Standardisation guidelines (ISO EN 14155), and all applicable national legal and regulatory requirements. Ethics approval was obtained from all local ethics committees, and the study was registered on

ClinicalTrials.gov (NCT04108884). All patients provided written informed consent and were explicitly informed that real-time feedback of monitoring results would vary by group as part of the study design. In the sham-group, abnormal PPG findings were not ignored but were retrospectively reviewed and escalated for clinical follow-up when appropriate. Furthermore, the application was used as an adjunct to usual care, allowing patients in the control group unrestricted access to medical attention at any time. All study sites underwent a site initiation call to review the inclusion and exclusion criteria, study variables, and study-specific definitions. The study team provided ongoing support to sites throughout the data collection process, ensuring that any concerns or questions were addressed.

We included patients with no prior diagnosis of AF and a calculated CHA₂DS₂-VASc score of ≥ 3 for individuals younger than 65 years or ≥ 2 for individuals 65 years or older. All patients were required to provide written informed consent to be included in the study. Exclusion criteria were prior diagnosis of AF, chronic anticoagulation therapy, an implanted cardiac electronic device (pacemaker or intracardiac cardioverter-defibrillator), and an inability to comply with study procedures (eg, language problems, psychological disorders, or dementia). Technical limitations such as inability to use the application properly or smartphone incompatibility were also grounds for exclusion.

Study application

For this study, we used the Preventicus Heartbeats application (Preventicus GmbH). The application uses a validated algorithm to screen for AF by using the patient's pulse wave obtained with the smartphone camera at the fingertip. The application uses the smartphone's light-emitting diode light and camera without requiring any additional accessories, with the camera functioning as a PPG sensor. The user places the camera lens on their fingertip for 1 minute to record a pulse wave extracted from the video signal. The generated pulse wave signals are analyzed and translated by a patented and medical device-certified algorithm into an ECG-comparable report that can be read and evaluated by an ECG technician or cardiologist. Figure 1 depicts an example of arrhythmic pulse waves in a patient who would later be diagnosed with AF. Figure 2 presents a report that normal users of the application receive. In addition to pulse wave analysis and a report of heart rate, patients receive a notification if arrhythmia is suspected. In the study version of the application, patients received no such report or notification. The application has been evaluated in clinical trials before and reached a sensitivity and specificity of >90% in a study group with a high prevalence of AF.^{17–19} Importantly, the application is not intended to provide a definitive diagnosis of AF with its therapeutic implications, but exclusively for AF screening or progress monitoring. The application is compatible with most smartphone platforms, including iOS and Android. Minimum requirements at the time of the trial were iOS 9 or Android 4.4 operating systems.

Abbreviations

AF: atrial fibrillation

ECG: electrocardiogram

EHRA: European Heart Rhythm Association

PPG: photoplethysmography

TIA: transient ischemic attack

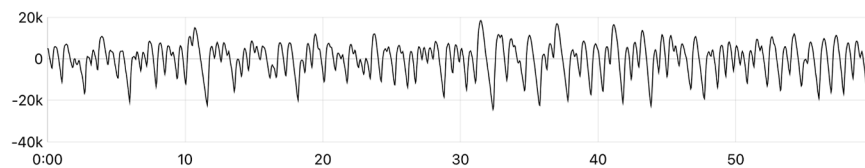


Figure 1

Pulse wave signals of a patient detected by the application. In this case, the infrequent pulse waves suggested arrhythmia. The x-axis shows the time (t) in seconds, and the y-axis shows the pulse wave amplitude.

Study procedures

Eligible patients were randomized into an intervention arm (intervention group) and a standard-of-care arm (sham group). The application was installed on the personal smartphones of all patients. Randomization occurred during the download and installation process in a 1:1 ratio, ensuring that both patients and local investigators remained blinded to group allocation.

All patients in both groups downloaded and installed the same version of the application. They were instructed to use the application twice daily during the first 2 weeks of enrollment and then twice weekly from the third week onward, and additionally whenever experiencing palpitations. For each use, patients were instructed to place a finger over the smartphone camera for ~1 minute. The total observation period lasted 6 months.

In cases of suspected arrhythmia in the application group, the recording was transmitted to the Preventicus Telecare Center, where it was analyzed for the likelihood of AF. For patients in the intervention group, if AF was suspected and confirmed by the telecare center, the principal investigator was notified and an appointment for a 7-day Holter ECG was scheduled. Holter monitoring was conducted using the CardioMem CM 100 XT device (Getemed), a mobile patch ECG loop recorder. Figures 3 and 4 illustrate the

measurement protocol and the evaluation process for suspected arrhythmia.

For patients in the sham group, instead of immediate feedback, a cumulative report was provided at the end of the trial. In addition to the specified measurements, patients in both groups received standard medical care. Furthermore, all patients were free to seek medical counseling, and all diagnostic measures, including ECG monitoring, were available to their treating physicians in case of palpitations. If a patient was hospitalized for any reason, it was recorded whether hospitalization was due to AF, stroke, transient ischemic attack (TIA), myocardial infarction, or systemic embolism. At the end of the trial, a patient survey was conducted to assess patients' knowledge about AF before and after the trial, including its associated health risks. The survey also evaluated any technical difficulties encountered with the application and overall satisfaction. In patients with a confirmed diagnosis of AF, a study visit was conducted by the local investigators. Typical symptoms associated with AF were assessed and documented using the European Heart Rhythm Association (EHRA) score.²⁰ Asymptomatic AF was defined as the absence of typical symptoms such as palpitations, chest pain, dyspnea, lightheadedness, and other symptoms typically associated with AF.²¹

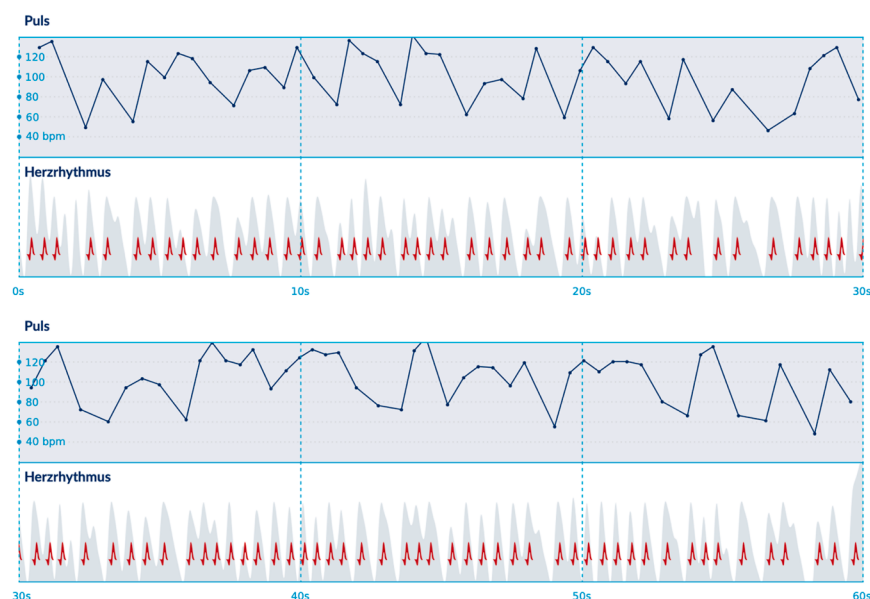
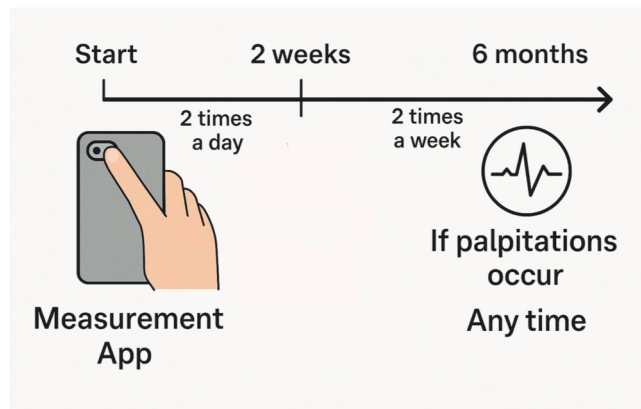


Figure 2

Example of a report that patients receive from the application. In this case, a patient was informed about arrhythmic pulse frequencies (as depicted in Figure 1), and medical consultation with the suspicion of atrial fibrillation (AF) was suggested to him or her. Used with the permission from Preventicus GmbH.

**Figure 3**

Measurement protocol during the study, used by both the intervention group and the sham group.

The primary outcome was the prevalence of AF detected by the 7-day Holter ECG. Secondary outcomes included the total number of arrhythmias detected by the application, detection rates of asymptomatic AF, and the incidence of stroke, TIA, systemic embolism, and myocardial infarction at 6 months. Additionally, patients' overall satisfaction with the application was assessed, as well as the compliance with the measurement protocol. Compliance rates were categorized into 4 categories on the basis of the percentage of the required measurements for both phases: >80%, 60%–80%, 40%–60%, and <40%.

Statistical analysis

Categorical data are presented as frequencies and percentages. For continuous variables, the total number of measurements, means, and standard deviations are reported if

normal distribution was apparent. Normality was tested using the Kolmogorov-Smirnov test. Nonnormally distributed variables are presented as medians with 25th and 75th percentiles. Statistical comparisons were conducted using the *t* test for normally distributed variables and the Mann-Whitney *U* test for nonnormally distributed variables. Differences between ordinal variables were assessed using the Pearson χ^2 test. A *P* value of <.05 was considered significant. All data analyses were performed using R Statistics, version 4.3.3 (The R Foundation). Study data were stored using RedCap (Research Electronic Data Capture).

Sample size calculation

The sample size was determined using a resampling method. Each sample size was evaluated by simulating patient data 999 times ($R = 999$), thereby assuming a detection rate (number of confirmed AF diagnoses/total number of patients) under usual care of 3%. We assumed that the detection rate is 2 times the rate under usual care when using the application (6%). In each sample, the prevalence of detected AF was compared between patients treated according to usual care and patients using the application and it was tested whether these rates differed between the 2 groups using the χ^2 test. An α level of .05 was used (2-sided) for tests. Our sample size calculation resulted in a total number of 1058 patients, assuming no dropouts, in order to achieve a power of at least 60%.

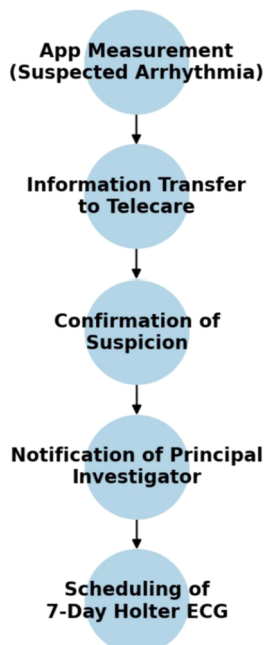
Results

Baseline characteristics

A total of 1021 patients from 8 centers met the inclusion criteria and were randomized. Of these, 510 patients were assigned to the intervention group and 511 patients were assigned to the sham group. The mean age was 65 years for both groups, and the mean CHA₂DS₂-VASc score was 3.4 ± 0.92 for the intervention group and 3.5 ± 1.02 for the sham group. Baseline characteristics are summarized in Table 1. No notable differences in baseline characteristics, such as comorbidities or medications, were observed.

AF and arrhythmia detection

A total of 32 cases (3.1%) of arrhythmia were detected, with 20 (3.9%) cases in the intervention group and 12 (2.4%) in the sham group. Among these patients, AF was diagnosed in 13 (1.3%). Of these, 10 (1.9%) were diagnosed in the intervention group following Holter ECG monitoring after notification from the telecare center. In the sham group, 3 (0.5%) AF cases were diagnosed during the trial in patients where application measurements detected an arrhythmia. At 6 months, there was no significant difference in AF detection rates between the 2 groups (1.9% vs 0.5%; $P = .094$). All patients in the sham group with AF reported typical symptoms, with an EHRA score of 2–3, while in the intervention group, 4 patients with AF were asymptomatic (4 [0.8%] vs 0 [0%]; $P = .133$). This corresponds to an estimated annualized detection

**Figure 4**

Procedure for patients in the intervention group with suspected arrhythmia. ECG = electrocardiogram.

Table 1 Baseline characteristics between patients in the intervention and sham groups

Variable	Intervention group	Sham group	P
No. of patients	510	511	
Age (y)	66.9 ± 8.9	66.9 ± 10.0	>.99
Sex: male	271 (53.1)	255 (50.2)	.381
Ethnicity			
Caucasian	493 (96.7)	495 (96.9)	.995
Asian	7 (1.4)	2 (0.4)	.180
Black	0 (0)	2 (0.4)	.480
Others	3 (0.6)	2 (0.4)	.998
Height (cm)	169.43 ± 11.94	169.60 ± 11.68	.820
Weight (kg)	82.32 ± 44.85	80.95 ± 17.93	.521
CHA ₂ DS ₂ -VASc score	3.43 ± 0.92	3.54 ± 1.02	.091
Estimated GFR (Cockcroft-Gault equation) (mL/min)	74.85 ± 16.41	74.82 ± 17.19	.985
Antihypertensive medication	448 (87.8)	444 (87.1)	.777
Angiotensin receptor antagonist	153 (34.2)	179 (40.3)	.067
ACE inhibitor	208 (46.4)	209 (47.1)	.900
Aldosterone antagonist	32 (7.1)	30 (6.8)	.924
Diuretics	143 (31.9)	148 (33.3)	.705
Alpha antagonist	17 (3.8)	20 (4.5)	.716
Calcium channel blocker	165 (36.8)	159 (35.8)	.805
β-Blocker	273 (60.9)	263 (59.2)	.652
Antiplatelet therapy	359 (70.4)	353 (69.2)	.733
Aspirin	314 (87.5)	309 (87.5)	1.000
Clopidogrel	99 (27.6)	109 (30.9)	.376
Prasugrel	13 (3.6)	15 (4.2)	.812
Ticagrelor	47 (13.1)	51 (14.4)	.677
Other antiplatelet medication	4 (1.1)	7 (2.0)	.525
Statin therapy	369 (93.4)	376 (91.9)	.501
Insulin therapy	38 (9.6)	31 (7.6)	.370
Oral antidiabetics	132 (33.5)	124 (30.4)	.385

Values are presented as mean ± standard deviation or n (%).

ACE = angiotensin-converting enzyme; GFR = glomerular filtration rate.

rate of 15.7 events per 1000 patient-years of asymptomatic AF, based on a total of 255 patient-years of observation. Anticoagulation was initiated in all patients with newly diagnosed AF, except for 1 patient, for whom the treating cardiologist decided against anticoagulation because of the AF episodes being short (<30 minutes) and the patient already being on dual antiplatelet therapy.

AF burden and results from Holter ECGs

The AF burden differed significantly between patients, with 10% AF burden being the longest AF duration. The longest single episode in this case was 637 minutes, tachycardia episodes with a maximal heart rate of 140 beats/min, and consequently, the patient showed symptoms correlating to EHRA score 3. In contrast, in the 4 patients with asymptomatic

AF, the burden was low, ranging from 0.14% to 3.97%, with 57 minutes being the longest episode in the latter case, with a maximal heart rate of 115 beats/min. In cases where AF was not confirmed, the Holter ECG showed sinus rhythm with a high burden of premature atrial contractions, but there were also 2 cases that showed sinus rhythm without any arrhythmia.

Stroke, TIA, and systemic embolism

By the end of the trial, stroke or TIA occurred in 4 patients: 2 in the intervention group and 2 in the sham group. Additionally, systemic embolism was observed in 4 patients: 1 in the intervention group and 3 in the sham group. To our knowledge, these events were unrelated to AF. Myocardial infarction occurred in 3 cases: 1 in the intervention group and 2 in the sham group. A total of 64 patients were hospitalized during the study; 26 patients in the intervention group and 38 patients in the sham group. Death occurred in 1 patient in each group: one due to respiratory failure and the other due to terminal lung cancer. The results are presented in Table 2.

Patient questionnaire

In the patient survey, 438 participants (42.9%) reported being unaware of AF before joining the study. A total of 652 patients (63.8%) reported a better understanding of AF and its associated health risks. Technical difficulties were reported by 75 patients (7.3%), with the main issue being poor signal quality, which necessitated repeated measurements. Overall, 93.9% of patients were very satisfied or satisfied with the application and the frequency of screening. Fifty-eight patients (5.6%) did not complete the study per protocol. Of these, 6 patients withdrew their consent, 11 were lost to follow-up, 12 had noncompliance issues, and 22 reported technical problems. Five patients terminated the study early owing to personal reasons, and health issues were the reason for early termination in 2 patients.

Table 2 Outcomes and findings

Variable	Intervention group	Sham group	P
No. of patients	510	511	
Arrhythmia	20 (3.9)	12 (2.4)	.210
Atrial fibrillation	10 (1.9)	3 (0.5)	.094
Symptomatic	6 (1.2)	3 (0.5)	.997
Asymptomatic	4 (0.8)	0 (0)	.133
Cerebrovascular accident (stroke/TIA)	2 (0.4)	2 (0.4)	1
Systemic embolism	1 (0.2)	3 (0.6)	.615
Hospitalization	26 (5.1)	38 (7.4)	.153
Hospitalization related to AF	2 (0.4)	2 (0.4)	1
Myocardial infarction	1 (0.2)	2 (0.4)	.998
Death (all-cause)	1 (0.2)	1 (0.2)	1

Values are presented as n (%).

AF = atrial fibrillation; TIA = transient ischemic attack.

Compliance

During the first 2 weeks, 83.74% of patients recorded >80% of all required measurements; 5.78% recorded 60%–80%, while 10.48% recorded 40%–60% of measurements. During the rest of the study, 68.27% recorded >80% of measurements, 9.07% did 60%–80%, 5.36% 40%–60%, and 17.56% recorded <40% of all required measurements.

Discussion

In this large, randomized, double-blind, multicenter European trial, we aimed to investigate the potential of a smartphone application for improving AF detection rates. The study did not confirm our initial hypothesis but contributed to the growing body of evidence on device-based cardiovascular diagnostics, especially in the context of an aging population and the increasing use of wearable devices.

Large observational trials, such as the Apple Heart Study, the Huawei Heart Study, and Fitbit Heart Study, have demonstrated the feasibility of screening for AF by using wearable devices for large populations.^{22–24} The mean ages in the Apple and Huawei heart studies were 41 and 35 years, respectively. Consequently, the proportion of patients 65 years or older was low, with only 5.9% in the Apple Heart Study and 1.8% in the Huawei Heart Study. Our study differs from these aforementioned studies because of the randomized double-blinded approach and inclusion criteria tailored to include only participants in whom the diagnosis of AF would possibly result in anticoagulation therapy. As a result, our study included a significantly older population, with a mean age of 67 years in both groups. By using a smartphone application, we aimed to reach more people throughout Europe, as smartwatches and other devices are less widespread, especially in lower-income countries. Our estimated asymptomatic AF diagnosis rate of 15.7 per 1000 patient-years falls between rates reported in the aforementioned studies. The Apple Heart Study found a lower rate of ~1.14 per 1000 patient-years in a general population, while the Huawei Heart Study reported a higher rate of 32 per 1000 patient-years. These findings emphasize the importance of tailored screening strategies. Even though our study was performed in patients at higher risk for AF, determined by a CHA₂DS₂-VASc score of ≥ 2 , the overall event rates were surprisingly low. Finding the correct screening protocols for the right population will be an important topic for future studies.

We found that the applied screening method can assist in the diagnosis of AF, especially in the context of asymptomatic AF. Although we did not find significant differences in detection rates between both groups, there was a numerical difference, especially regarding asymptomatic AF cases, of which we found 4 in the intervention group and none in the sham group. Patients with asymptomatic AF are more difficult to diagnose, putting these patients at an especially high risk for AF complications such as stroke or systemic embolism.²⁵ While symptomatic AF may be detected through a variety of conventional means, the primary clinical value of

the wearable-smartphone system lies in its ability to identify asymptomatic or unrecognized episodes, which are unlikely to prompt medical attention without continuous or semicontinuous monitoring. Importantly though, the AF burden measured by our Holter ECGs was low in our asymptomatic patients.

In the context of asymptomatic or subclinical AF, clinical risk prediction scores such as the HARMS2-AF score or the CHARGE-AF score play an important role in identifying individuals at risk of developing AF.^{26,27} These tools could guide decision making on whom to screen more extensively. However, they estimate risk rather than confirm arrhythmia presence. PPG-based smartphone applications offer complementary benefits by offering real-time detection of possible arrhythmia, enabling a prompter confirmation using standard-of-care-diagnostics. When used together, both approaches may enhance AF screening and early diagnosis, although this has yet to be proven in prospective trials.

The results of our study differ from recently published studies, such as the Assessment of Remote Heart Rhythm Sampling Using the AliveCor Heart Monitor to Screen for Atrial Fibrillation (REHEARSE-AF) - study by Halcox et al,²⁸ who detected significantly more AF cases using a WiFi-enabled iPod to obtain ECGs from high-risk patients. They obtained ECGs twice weekly for 1 year. Reasons for this difference in AF detection rates might lie in the longer observational period of 12 months compared with 6 months in our trial; additionally, their study population included older patients, with the mean age being 6 years higher than in our study. The eHealth-based Bavarian Alternative Detection of Atrial Fibrillation (eBRAVE-AF) trial demonstrated a significant benefit of a smartphone application for AF detection rates.²⁹ However, in contrast to their study, which mainly included policy shareholders of a large insurance company, our population was recruited from a real-world setting in multiple European health care systems.

Notably, the overall incidence of AF in our study population was low, with only 1.3% of newly diagnosed cases—significantly below our estimated incidence of 3%–6%. While the reasons for this low incidence in our high-risk study population are not fully clear, a possible explanation may lie in differences in European health care systems, with a majority of patients being enrolled from countries in which the sensitivity for the diagnosis of AF in their respective health care systems has increased in recent years.³⁰ Another explanation may lie in the overall short study duration of 6 months. Additionally, it is important to consider that participation in the trial itself may have heightened patients' awareness of cardiac symptoms in both groups, potentially prompting earlier diagnostic evaluations outside the structured trial procedures. This phenomenon, commonly referred to as the Hawthorne effect, could have contributed to the absence of a statistically significant difference in AF detection rates between the intervention and sham groups.³¹

Overall, the role of prolonged cardiac monitoring for stroke reduction remains unclear. Prior studies have clearly demonstrated the utility of prolonged cardiac monitoring

technologies in unmasking AF in patients with stroke.^{32–34} However, a clear clinical benefit has yet not been proven for patients after stroke.³⁵ In this context, an important consideration in interpreting our findings is the likely large number needed to monitor to prevent a single stroke event, particularly given the relatively low incidence of newly diagnosed AF observed in our study (2.0%). Moreover, while an early detection of AF may provide opportunities for stroke prevention through anticoagulation, our study was not powered to directly assess stroke reduction, and the 2 cerebrovascular events observed were unrelated to AF. Additionally, it has suggested that low-burden AF may not carry the same stroke risk as symptomatic high-burden AF.³⁶

Last, while frequent monitoring may facilitate the early detection of AF, it also carries inherent risks. These include the possibility of unnecessary follow-up investigations, over-treatment, and increased anxiety or psychological distress among patients confronted with asymptomatic or uncertain rhythm abnormalities.^{37,38} The extent of these potential harms remains challenging to quantify and was not systematically assessed in our study, yet these points have to be considered when developing future screening strategies. Defining the appropriate screening population, optimal screening duration, and the threshold of AF burden that significantly increases stroke risk will be key objectives for future clinical trials.

Limitations

Our study has a number of limitations. First, as the study was conducted only in Europe, the results may not be applicable to health care systems in other regions. Second, as a specific smartphone application was used, the transferability to other PPG-based technologies and smartphone applications may be limited. Another key limitation of our trial was that it was underpowered, primarily because of a lower-than-anticipated incidence of newly diagnosed AF. This limitation likely reduced our ability to detect statistically significant differences between the study arms. Additionally, the relatively short follow-up duration of 6 months may not have been sufficient to capture meaningful differences in critical clinical outcomes such as stroke or systemic embolism.

Conclusion

In this multicenter trial, the application usage in combination with early intervention did not lead to significantly higher detection rates of AF. However, usage of the application was considered feasible by a large patient cohort, with good compliance over 6 months, and it led to a numerically higher detection rate of asymptomatic AF, supporting the AF screening strategies in the present guidelines.

Acknowledgments

We thank Christina Schumacher for her extraordinary recruitment support and Ada Winterhalter and Ulrike Schmitt for coordination and monitoring of the trial.

Funding Sources: This trial was funded by a grant of the European Union's Horizon 2020 SME programme (829639 - RedStroke) to Dr Hübner (main applicant) and Dr Eckstein (coapplicant).

Disclosures: Dr Hübner is the founder and CEO of Preventicus. Dr König and Dr Piper are employees of Preventicus. Dr Eckstein and Dr Dörr each holds 0.5% virtual shares of Preventicus. Dr Burkard received grants from the Swiss National Science Foundation, Cardiovascular Research Foundation Basel, AstraZeneca, Daiichi Sankyo, Medtronic, Roche Diagnostics, Novartis, Menarini, Sanofi, Novo Nordisk, and Collabree (outside the submitted work) and lecture and/or travel fees paid to institution by Servier, Medtronic, Sanofi, Novartis, Novo Nordisk, and Daiichi Sankyo (outside the submitted work). Preventicus had no role in the analysis of all data acquired for this study. All other authors confirm that they do not have any conflicts of interest regarding this trial and manuscript.

Address reprint requests and correspondence: Dr Jens Eckstein, Department of Internal Medicine, University Hospital Basel, Petersgraben 4, CH-4031 Basel, Switzerland. E-mail address: jens.eckstein@usb.ch

References

1. 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 Estimulación Cardíaca y Electrofisiología (SOLAECE). *Europace* 2017;19:1589–1623.
2. Di Carlo A, Bellino L, Consoli D, et al. Prevalence of atrial fibrillation in the Italian elderly population and projections from 2020 to 2060 for Italy and the European Union: the FAI Project. *Europace* 2019;21:1468–1475.
3. Ball J, Carrington MJ, McMurray JJV, Stewart S. Atrial fibrillation: profile and burden of an evolving epidemic in the 21st century. *Int J Cardiol* 2013;167:1807–1824.
4. Heidt ST, Kratz A, Najarian K, et al. Symptoms in atrial fibrillation: a contemporary review and future directions. *J Atr Fibrillation* 2016;9:1422.
5. Verma A, Champagne J, Sapp J, et al. Discerning the incidence of symptomatic and asymptomatic episodes of atrial fibrillation before and after catheter ablation (DISCERN AF): a prospective, multicenter study. *JAMA Intern Med* 2013;173:149.
6. Strickberger SA, Ip J, Saksena S, Curry K, Bahnson TD, Ziegler PD. Relationship between atrial tachyarrhythmias and symptoms. *Heart Rhythm* 2005;2:125–131.
7. Piccini JP, Simon DN, Steinberg BA, et al. Differences in clinical and functional outcomes of atrial fibrillation in women and men: two-year results from the ORBIT-AF registry. *JAMA Cardiol* 2016;1:282.
8. Soto Á, Guillén-Grima F, Morales G, Muñoz S, Aguinaga-Ontoso I. Trends in mortality from stroke in the European Union, 1996–2015. *Eur J Neurol* 2021;28:182–191.
9. Luengo-Fernandez R, Violante M, Candio P, Leal J. Economic burden of stroke across Europe: a population-based cost analysis. *Eur Stroke J* 2020;5:17–25.
10. Grond M, Jauss M, Hamann G, et al. Improved detection of silent atrial fibrillation using 72-hour Holter ECG in patients with ischemic stroke: a prospective multicenter cohort study. *Stroke* 2013;44:3357–3364.
11. Henriksson KM, Farahmand B, Asberg S, Edvardsson N, Terént A. Comparison of cardiovascular risk factors and survival in patients with ischemic or hemorrhagic stroke. *Int J Stroke* 2012;7:276–281.
12. Kishore A, Vail A, Majid A, et al. Detection of atrial fibrillation after ischemic stroke or transient ischemic attack: a systematic review and meta-analysis. *Stroke* 2014;45:520–526.
13. 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.
14. Lip GHY. Stroke and bleeding risk assessment in atrial fibrillation: when, how, and why? *Eur Heart J* 2013;34:1041–1049.
15. Hindricks G, Potpara T, Dagres N, 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.
16. Joglar JA, Chung MK, Armbruster AL, et al. 2023 ACC/AHA/ACCP/HRS Guideline for the diagnosis and management of atrial fibrillation: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2024;149:e1–e156.
17. Krivoshei L, Weber S, Burkard T, et al. Smart detection of atrial fibrillation. *Europace* 2017;19:753–757.

18. Koenig N, Seecle A, Eckstein J, et al. Validation of a new heart rate measurement algorithm for fingertip recording of video signals with smartphones. *Telemed E-Health* 2016;22:631–636.
19. Brasier N, Raichle CJ, Dörr M, et al. Detection of atrial fibrillation with a smartphone camera: first prospective, international, two-centre, clinical validation study (DETECT AF PRO). *Europace* 2019;21:41–47.
20. Wynn GJ, Todd DM, Webber M, et al. The European Heart Rhythm Association symptom classification for atrial fibrillation: validation and improvement through a simple modification. *Europace* 2014;16:965–972.
21. Noseworthy PA, Kaufman ES, Chen LY, 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.
22. Turakhia MP, Desai M, Hedlin H, 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.
23. Lubitz SA, Faranesh AZ, Atlas SJ, et al. Rationale and design of a large population study to validate software for the assessment of atrial fibrillation from data acquired by a consumer tracker or smartwatch: the Fitbit Heart Study. *Am Heart J* 2021;238:16–26.
24. Guo Y, Lip GY. Mobile health for cardiovascular disease: the new frontier for AF management: observations from the Huawei Heart Study and mAFA-II randomised trial. *Arrhythm Electrophysiol Rev* 2020;9:5–7.
25. Wallenhorst C, Martinez C, Freedman B. Risk of ischemic stroke in asymptomatic atrial fibrillation incidentally detected in primary care compared with other clinical presentations. *Thromb Haemost* 2022;122:277–285.
26. Goudis C, Daos S, Dimitriadis F, Liu T. CHARGE-AF: a useful score for atrial fibrillation prediction? *Curr Cardiol Rev* 2023;19:e010922208402.
27. Segan L, Ho WW, Crowley R, et al. Combining polygenic and clinical risk scores in atrial fibrillation risk prediction: implications for population screening. *Heart Rhythm* 2025;22:1906–1914.
28. Halcox JPJ, Wareham K, Cardew A, et al. Assessment of remote heart rhythm sampling using the AliveCor heart monitor to screen for atrial fibrillation: the REHEARSE-AF study. *Circulation* 2017;136:1784–1794.
29. Rizas KD, Freyer L, Sappeler N, et al. Smartphone-based screening for atrial fibrillation: a pragmatic randomized clinical trial. *Nat Med* 2022;28:1823–1830.
30. Vad OB, Paludan-Müller C, Diederichsen SZ, Olesen MS. Tackling a growing healthcare challenge: atrial fibrillation epidemiology, prevention, and underlying causes. *Lancet Reg Health Eur* 2024;37:100827.
31. McCambridge J, Witton J, Elbourne DR. Systematic review of the Hawthorne effect: new concepts are needed to study research participation effects. *J Clin Epidemiol* 2014;67:267–277.
32. Gladstone DJ, Spring M, Dorian P, et al. Atrial fibrillation in patients with cryptogenic stroke. *N Engl J Med* 2014;370:2467–2477.
33. Sanna T, Diener HC, Passman RS, et al. Cryptogenic stroke and underlying atrial fibrillation. *N Engl J Med* 2014;370:2478–2486.
34. Sposato LA, Cipriano LE, Saposnik G, Ruiz Vargas E, Riccio PM, Hachinski V. Diagnosis of atrial fibrillation after stroke and transient ischaemic attack: a systematic review and meta-analysis. *Lancet Neurol* 2015;14:377–387.
35. Tsiogoulis G, Triantafyllou S, Palaodimou L, et al. Prolonged cardiac monitoring and stroke recurrence. *Neurology* 2022;98:e1942–e1952.
36. Kim AS, Kamel H, Bernstein RA, Manchanda M, Caprio FZ. Controversies in stroke: should patients with embolic stroke of undetermined source undergo intensive heart rhythm monitoring with an implantable loop recorder? *Stroke* 2022;53:3243–3247.
37. O’Keeffe M, Barratt A, Maher C, et al. Media coverage of the benefits and harms of testing the healthy: a protocol for a descriptive study. *BMJ Open* 2019;9:e029532.
38. Predel C, Steger F. Ethical challenges with smartwatch-based screening for atrial fibrillation: putting users at risk for marketing purposes? *Front Cardiovasc Med* 2021;7:615927.