

Atrial fibrillation screening with photo-plethysmography through a smartphone camera

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Aims

This cross-sectional study was set up to assess the feasibility of mass screening for atrial fibrillation (AF) with only the use of a smartphone.

Methods and results

A local newspaper published an article, allowing to subscribe for a 7-day screening period to detect AF. Screening was performed through an application that uses photo-plethysmography (PPG) technology by exploiting a smartphone camera. Participants received instructions on how to perform correct measurements twice daily, with notifications pushed through the application's software. In case of heart rhythm irregularities, raw PPG signals underwent secondary offline analysis to confirm a final diagnosis. From 12 328 readers who voluntarily signed up for screening (49 ± 14 years; 58% men), 120 446 unique PPG traces were obtained. Photo-plethysmography signal quality was adequate for analysis in 92% of cases. Possible AF was detected in 136 individuals (1.1%). They were older ($P < 0.001$), more frequently men ($P < 0.001$), and had higher body mass index ($P = 0.004$). In addition, participants who strictly adhered to the recommended screening frequency (i.e. twice daily) were more often diagnosed with possible AF (1.9% vs. 1.0% in individuals who did not adhere; $P = 0.008$). Symptoms of palpitations, confusion, and shortness of breath were more frequent in case of AF ($P < 0.001$). The cumulative diagnostic yield for possible AF increased from 0.4% with a single heart rhythm assessment to 1.4% with screening during the entire 7-day screening period.

Conclusion

Mass screening for AF using only a smartphone with dedicated application based on PPG technology is feasible and attractive because of its low cost and logistic requirements.

Keywords

Atrial fibrillation • Mass screening • Photo-plethysmography • Smartphone

Introduction

The lifetime risk for atrial fibrillation (AF) development in the general population is estimated at $\sim 25\%$.¹ By 2030, 14–17 million AF patients are anticipated in the European Union, with 120–215 thousand new diagnoses per year.² Atrial fibrillation is independently associated with a two-fold increased risk of all-cause mortality in women and a 1.5-fold increase in men.³ Early diagnosis and appropriate treatment, particularly with oral anticoagulation in persons at high risk for stroke

or systemic embolism, may mitigate this risk and prevent substantial morbidity.¹

In the general population, current European Society of Cardiology guidelines recommend opportunistic screening by pulse taking or electrocardiogram (ECG) rhythm strip in individuals >65 years of age (Class I, Level B).¹ In addition, systematic screening with an ECG may be considered in patients >75 years or those at high stroke risk (Class IIb, Level B).¹ Because such screening efforts are cumbersome

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What's new?

- This study represents one of the largest population screening efforts for atrial fibrillation (AF) using a non-conventional screening method.
- The results strongly suggest that more intensive screening for AF is associated with a substantially higher diagnostic yield.

and expensive when implemented on a large scale, they are unlikely to be cost-effective in population groups at lower risk.

Interestingly, recent innovations in AF screening strategies and development of new screening devices have the potential to increase screening coverage at relatively low cost and efforts.⁴ Blood pressure devices with algorithms based on pulse irregularity, dedicated AF screening devices based on single- or multiple-lead ECG, and smartphone applications have all shown promise in this respect. Smartphone applications using photo-plethysmography (PPG) technology through their build-in camera are particularly attractive as no additional hardware is needed and smartphone use is likely to become—if not already is—ubiquitous in the real-world setting, paving the way for mass screening. Small studies on PPG-based screening for AF have already demonstrated excellent sensitivity of 87–100% with an acceptable specificity of 90–97% against the 12-lead ECG as gold standard.^{5–11} The current study was set up to assess the feasibility of mass screening for AF through a smartphone-based algorithm using PPG technology by the only CE approved application that has been recently developed.¹²

Methods

Study design

This cross-sectional screening study was set up by Qompium N.V. (Hasselt, Belgium) in cooperation with the academic authors. The aim was to assess the feasibility of mass screening for AF through a smartphone-based algorithm using PPG technology. A local newspaper in Layman's press agreed to cover an article to create awareness and inform its readers on AF and the potential value of screening for this arrhythmia. With 92 638 subscribers in 2017, this newspaper served ~10.8% of the local community at the time the article was published in print as well as online (September 2017). Readers were enlightened about the possibility of screening for AF by making use of the camera in their smartphone. A QR-code was provided to give free access to the screening application for a 7-day period (Figure 1). Additionally, the article comprised instructions on how to install the application, perform measurements with it, and participate in the screening programme. Prior to account activation or any data collection, users were informed and asked to agree with the privacy policy and terms of service of the company. Study participants were instructed to assess their heart rhythm twice daily, as well as in case of 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, as well as any irregularities identified. All participants with episodes other than a normal regular heart rhythm were advised to see their

general practitioner to consider the need for further evaluation and additional testing. The study complies with the Declaration of Helsinki. All authors had full access to the data and vouch for its accuracy and completeness. The first author (F.V.) wrote the first draft of the manuscript, which was subsequently revised by all authors.

Smartphone-based photo-plethysmography signal acquisition

To assess the heart rhythm in this study, PPG technology was applied. Photo-plethysmography is a technique whereby a volumetric measurement is optically obtained. A classic application is the pulse oximeter, which illuminates the skin and measures changes in light absorption with blood volume pulse variation, using this information to determine oxygen saturation and heart rhythm.¹³ The same principle can be applied by using the flashlight of a smartphone and measuring the amount of reflected light through its build-in camera. A CE and FDA approved application has been developed for this purpose and can be used with most commercially available devices.¹² To obtain a high-quality PPG signal with a smartphone, subjects should adopt a sitting position with both arms resting on a firm surface, holding the smartphone in a vertical position with their dominant hand. Subsequently, the index finger of their non-dominant hand should cover the flashlight and backside camera horizontally, without putting firm pressure (Figure 1). The measurement time to acquire the PPG signal is ~1 min, with a countdown clock visible on the smartphone screen when the application is running (Figure 1).

Smartphone application to assess the heart rhythm

The smartphone application used in this study firstly checks acquired PPG signals for their quality. Insufficient quality is identified using a machine-learning algorithm based on a recurrent neural network. Compromised signals are not used for analysis to avoid inaccurate diagnostic results. In this study, the number of insufficient quality measurements was closely monitored. Study participants with frequent poor-quality PPG measurements received notifications through the application, guiding them on how to perform better measurements. After every measurement, the user is asked to indicate his/her well-being on a 5-point Likert scale and comment on the potential presence of symptoms (i.e. light headedness, confusion, fatigue, palpitations, chest pain, shortness of breath, and/or other symptoms). Afterwards, a screen shows up that displays the average heart rate and any irregularities detected. A text with corresponding colour code is used to communicate results to the user: measurement of insufficient quality (blue), normal heart rhythm (green), or possible irregularities (orange). The last category is divided by the algorithm in suspected premature or missed beats (i.e. ≥ 3 during the 1-min registration) vs. suspected AF or atrial flutter with variable heart block. The AF algorithm is a random tree classifier using a combination of different features that analyse inter and intra beat-to-beat characteristics and time resolved and dimensionless patterns.

The distinction between irregular measurements was only communicated to the study participant through the final report after all divergent PPG signals had undergone offline secondary analysis by medical technicians, to ensure data quality and avoid concern about potentially false positive alarms (Figure 1). Notably, as PPG signals reflect pulse pressure, atrial flutter with constant heart block, or regular atrial tachycardia cannot be distinguished from sinus rhythm by the application, unless the presence of arrhythmia is clear because of the high ventricular rate.

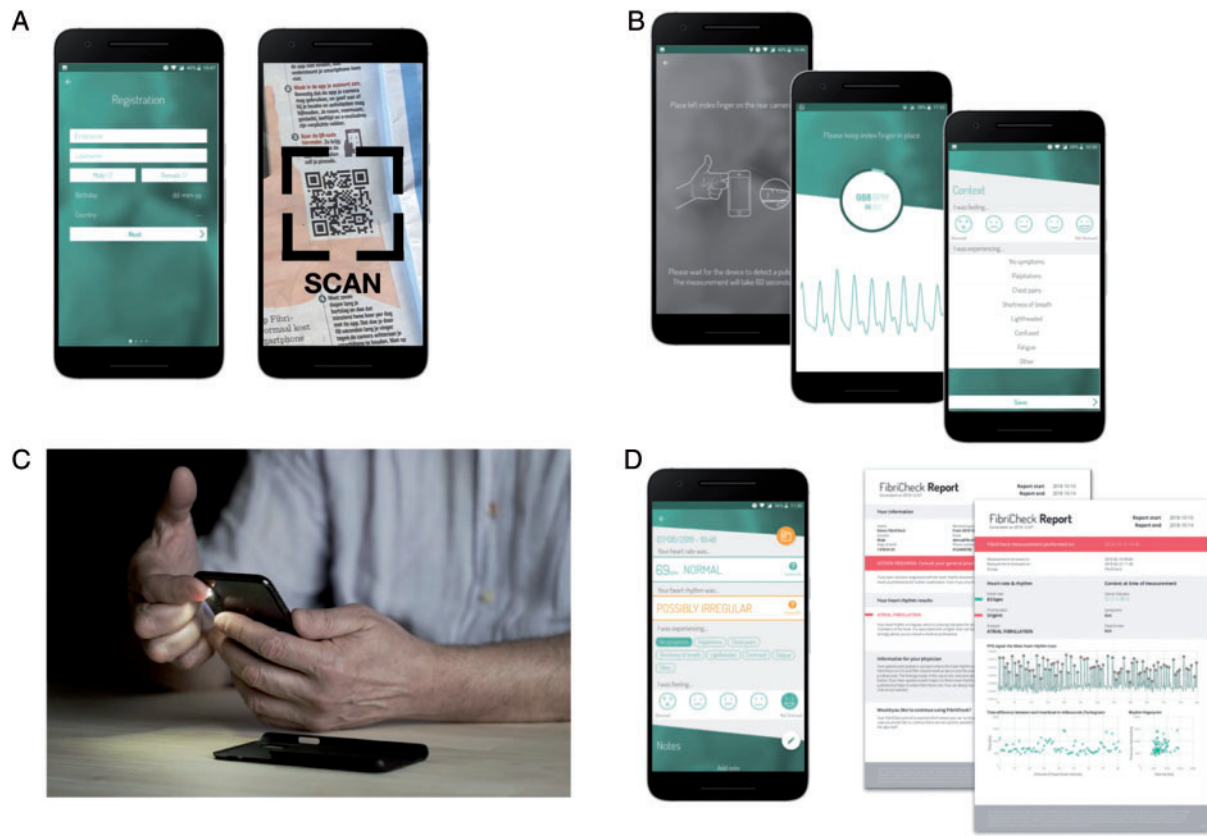


Figure 1 (A) Scanning of the QR-code and registration. (B) On-screen instructions guide the user to perform high-quality measurements. During the measurement, a screen is displayed with a countdown clock and a real-time photo-plethysmography trace. After each measurement, well-being and symptoms can be annotated. (C) Correct position to acquire a reliable photo-plethysmography signal. (D) Each measurement is automatically analysed by the algorithm. Measurements indicative of an irregular rhythm are reviewed by medical technicians under supervision of cardiologists. A summarizing report includes an overview of the measurements and a general conclusion.

Data collection

At the time of account creation for participation to the screening programme, subscribers were required to register age and gender. In addition, it was asked to voluntarily provide length and body weight. Other data collected include the timing, results, and raw PPG data for every use of the smartphone application for heart rhythm assessment as described above. Results were automatically sent to a secure server by the application and subsequently de-identified for all analyses. Raw PPG data for all suspected irregularities underwent secondary offline review by medical technicians under the supervision of cardiologists experienced in PPG analysis. The final diagnosis was confirmed by consensus.

Patient-reported outcomes

Four months after communicating the results and call-to-action in the end-report, screen-positive participants were contacted by phone to collect clinical outcome data.

Statistical analysis

Continuous variables are expressed as mean \pm standard deviation. The independent Student's *t*-test was used for comparison between

individuals with vs. without AF. Categorical data are expressed as counts (%) 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 R Statistical Software (version 3.5.1) and RStudio (version 1.1.447) (Boston, MA, USA).

Results

Screening coverage

After publication of the article on smartphone-based AF screening in the layman's press, 12 328 individuals registered for voluntarily participation to the screening programme and completed at least one measurement with a PPG signal of sufficient quality for analysis within the 7-day study period. A group of 480 subscribers (3.7%) was excluded, because they either had performed no heart rhythm measurements or did only achieve measurements of insufficient quality because of an incompatible smartphone. With the local community served by the newspaper as the denominator, the screening coverage of the overall population was 1.43%. Screening uptake was highest in individuals 40–69 years of age and substantially decreased below 20 years

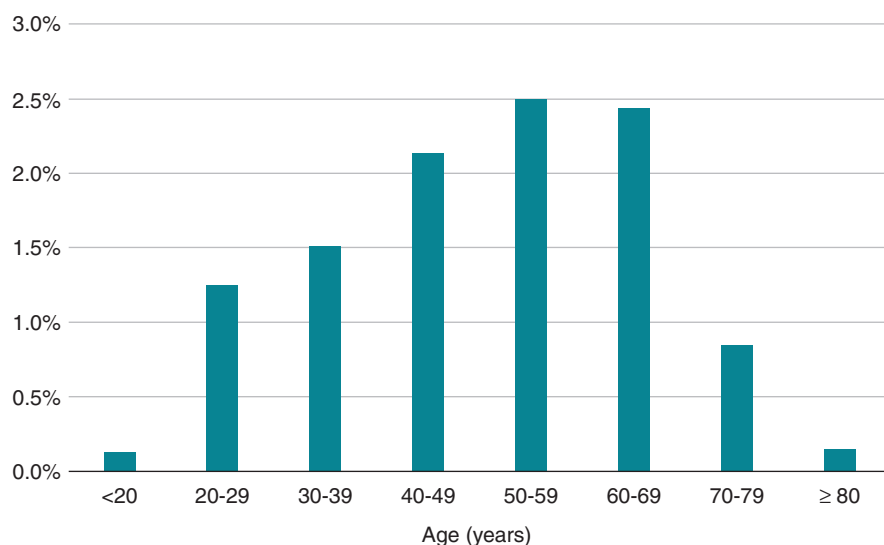


Figure 2 Screening coverage of the overall population after the publication of one local newspaper article (print + online) providing free access for atrial fibrillation screening through a smartphone-based application during a 7-day period.

and above 70 years (Figure 2). Among study participants, 1179 (10%) strictly adhered to the recommended screening protocol of at least two measurements per day. Premature drop-out from screening, defined as compliance with the screening protocol on Day 1, but no measurements on Day 7 was observed in 3328 (27%).

Screened population and diagnostic yield for possible atrial fibrillation

The average age of the screened population was 49 ± 14 years with 7184 male genders (58%). Possible AF was detected by the application's algorithm and confirmed by offline analysis of the corresponding raw PPG signals in 136 participants for an overall prevalence of 1.1%. Population characteristics according to the potential presence of AF are presented in Table 1. The prevalence of possible AF increased from 0.1% in the age group <40 years to 11.1% in individuals ≥ 80 years (Figure 3). Individuals with a diagnosis of possible AF were more frequently men compared with women ($P < 0.001$) and had a higher body mass index ($P = 0.004$). The proportion of study participants diagnosed with AF was 1.9% vs. 1.0% in individuals who did vs. did not adhere to the recommended screening frequency, respectively ($P = 0.008$). The cumulative diagnostic yield for possible AF increased from 0.4% with a single heart rhythm assessment performed to 1.4% with screening during the entire 7-day screening period (Figure 4).

Photo-plethysmography signal quality

Measurements by study participants generated 120 446 unique PPG traces of 60 s duration. PPG signal quality was sufficient for analysis in 110 713 cases (92%). The frequency of measurements with insufficient quality for analysis decreased significantly during the screening period, from 17% on Day 1 to 2% on Day 7 ($P < 0.001$; Figure 5).

Heart rhythm analysis by the smartphone application

A flowchart of the results of heart rhythm screening by the smartphone application's algorithm and confirmation by secondary offline analysis of the raw PPG data is provided in Figure 6. In 98 586 measurements (89%), the algorithm classified the heart rhythm as normal and no further action was performed. In 12 127 cases (11%), possible irregularities were identified of whom 615 (5%) were confirmed as possible AF by confirmatory offline analysis of the raw PPG data. The average revision time per irregular measurement was 7 s. Examples of different PPG measurements are given in Figure 7.

The average result on the 5-point Likert scale for well-being was 2.6 ± 2.3 in cases with confirmed AF vs. 2.6 ± 2.2 in cases where the heart rhythm was classified as normal ($P = 0.556$). Associated symptoms during measurements are presented in Figure 8. Symptoms of palpitations, confusion, and shortness of breath were more frequent in measurements that were indicative for AF ($P < 0.001$). Palpitations were the most frequently reported symptom at 11% in individuals with possible AF. Overall, individuals did report symptoms in 139/615 (24%) of measurements indicative for AF.

Patient-reported outcomes

Screen-positive participants were informed of the detection of possible AF in their end-report and referred to a medical professional to confirm diagnosis. Four months after reporting, they were contacted to collect outcome information. One hundred screening-positive subjects consented to provide this information. Forty subjects did not have a prior diagnosis, of which 53% consulted a physician and had the diagnosis confirmed on ECG. Sixty subjects were known AF patients, of which 28% received an adjustment of their current care strategy after consultation of a physician. Persistent or permanent AF was confirmed on 12-lead ECG, paroxysmal AF was confirmed on Holter monitor or implantable loop recorder.

Discussion

This study represents one of the largest population screening efforts for AF making use of a non-conventional screening method (i.e. other than 12-lead ECG, Holter registration, or implantable loop recorder). By making use of PPG technology through a smartphone camera by a dedicated, CE approved application, 12 328 individuals were screened during a 7-day period. Importantly, participants were actively and voluntarily involved in their measurements and it was possible for them to choose the moments of heart rhythm assessment and repeat them an unlimited amount of times. Furthermore, it was possible to register potential symptoms at the same time through the application. The screening technique was simple and required only the use of a smartphone. As a result, 120 446 unique PPG traces were obtained with acceptable quality for analysis in >90%. A possible diagnosis of AF was made in 136 patients (1.1%). One hundred out of 136 patients (74%) had a confirmed AF diagnosis.

The current study provides some important insights regarding AF screening. Firstly, after publication of a single advertising article in a

local newspaper, 1.43% of the overall population could be screened by just providing free access to a smartphone-based screening programme. Screening coverage went up to 2.5% in age categories most relevant for screening. Presumably, more extensive advertisement efforts through diverse media could be exploited to further increase this number with relatively low cost and logistic efforts. Secondly, data from this study strongly suggest that more intensive screening for AF is associated with a substantially higher diagnostic yield. Indeed, participants adhering strictly to the recommended screening frequency of two heart rhythm assessments per day had almost a doubling of their chance to be detected with possible AF. In addition, the cumulative diagnostic yield for possible AF increased continuously from 0.4% with a single heart rhythm assessment to 1.4% with screening during a 7-day period. Importantly, a continuous increase in diagnostic yield is expected with longer screening periods, even beyond 7 days. Thirdly, in the majority of cases where possible AF was detected, there were no specific symptoms and general well-being was similar compared to individuals with a normal regular heart rhythm. This indicates that the screening strategy as outlined in this manuscript is particularly interesting to potentially detect silent, sub-clinical AF, which is associated with more frequent complications.¹⁴ Fourthly, this study provides convincing evidence that the build-in camera of a smartphone can be used to obtain reliable PPG signals in a broad population, also including elderly who might be less familiar with smartphone handling. The frequency of measurements with insufficient PPG signal quality quickly fell from 17% to 6% after 1 day use of the smartphone application and further to 2% after 7 days, indicating a fast learning curve among participant. Fifthly, results of this study suggest the importance of secondary offline analysis of divergent raw PPG signals, both to consider alternative arrhythmia diagnoses and avoid false positive detection of AF. Finally, all screening-positive participants that provided outcome data were confirmed on ECG after consulting a medical professional.

Table 1 Characteristics of the screened population (n = 12 328)

Characteristics	No AF diagnosis	AF diagnosis	P-value
N	12 192	136	
Age (years)	49 ± 14	62 ± 11	<0.001
Male gender	7, 084 (58%)	100 (74%)	<0.001
Length (cm)	174 ± 9	177 ± 9	0.129
Body weight (kg)	79 ± 16	88 ± 16	0.002
Body mass index (kg/m ²)	26 ± 4	28 ± 4	0.004

AF, atrial fibrillation.

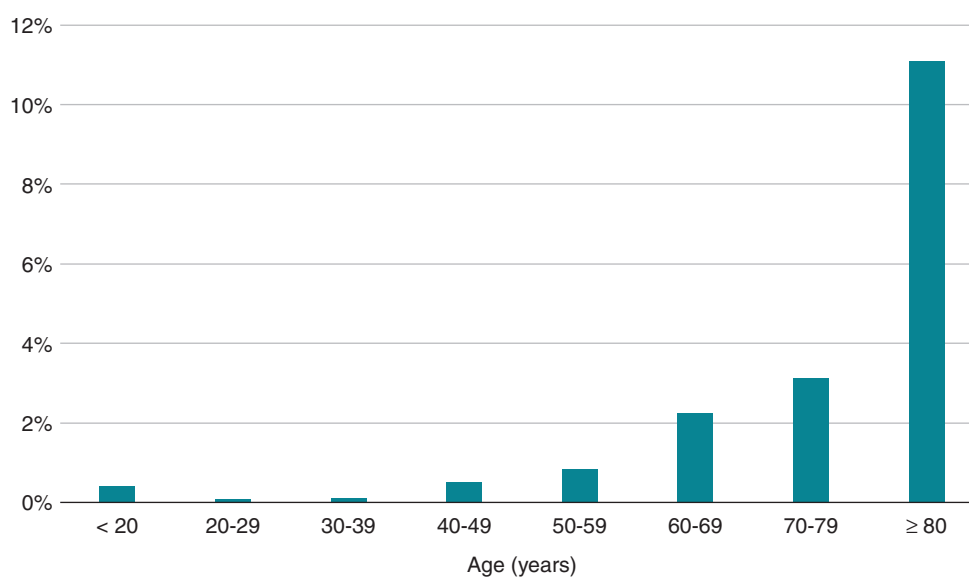


Figure 3 Prevalence of atrial fibrillation in the screened population according to age.

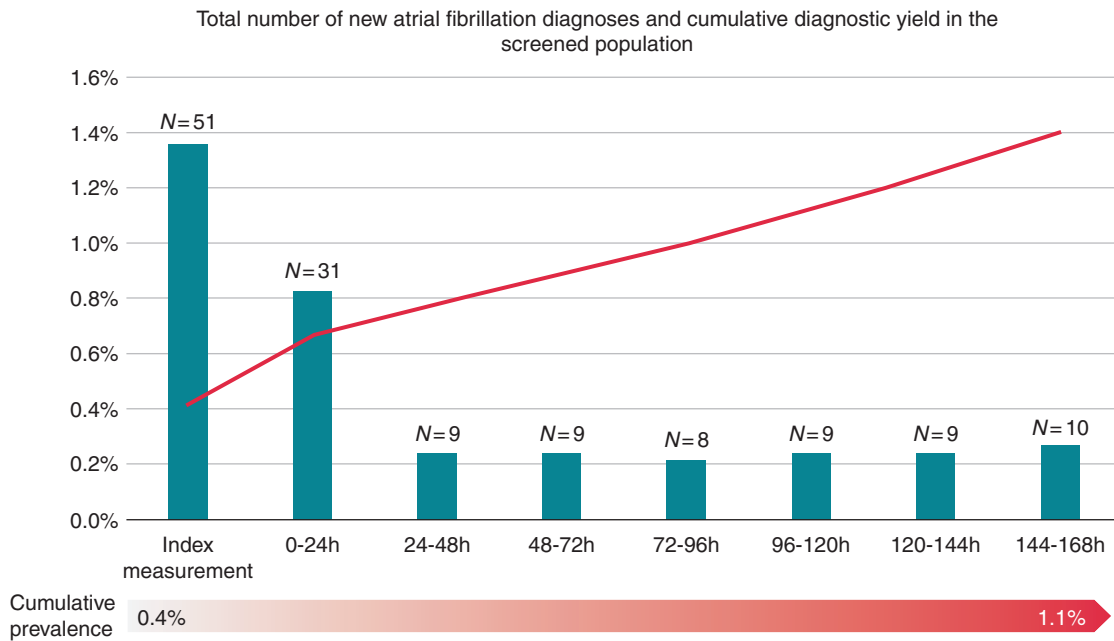


Figure 4 Cumulative diagnostic yield (curve) and prevalence (arrow) for atrial fibrillation during the 7-day screening period. The cumulative diagnostic yield is calculated based on the number of participants performing measurements on the corresponding days. The prevalence is calculated based on the total study population.

Two previous studies have used smartphone-based PPG technology to screen for AF, albeit through a different smartphone application, and have validated findings against an accepted gold standard. McManus *et al.*⁷ obtained 219 PPG traces from 98 participants with AF, 15 with premature atrial beats, and 15 with premature ventricular beats. They found 97% sensitivity and 93.5% specificity for detecting AF by comparing to a 12-lead ECG or 3-lead telemetry. Krivoshei *et al.*⁹ compared 5-min PPG signals between 40 patients with AF and 40 individuals in sinus rhythm and found a somewhat lower sensitivity of 87.5% with a specificity of 95%. More recently, Proesmans *et al.*¹⁵ validated the FibrCheck application in a primary care convenience sample of 223 patients, of whom 102 were in AF. They reported a sensitivity of 96% and a specificity of 97% for the detection of AF compared to 12-lead ECG.

Alternatively, by adding an additional piece of hardware (i.e. electrode) to a smartphone, acquisition of a single-lead ECG is possible. Such an approach was tested in the Assessment of Remote Heart Rhythm Sampling Using the AliveCor Heart Monitor to Screen for Atrial Fibrillation (REHEARSE-AF) study.¹⁶ In this study, 1001 individuals aged >65 years without a known history of AF or cardiac pacing and with a CHA₂DS₂-VASc score ≥ 2 not receiving anticoagulation therapy were recruited and randomized towards smartphone-based single-lead ECG screening twice weekly over 12 months vs. usual care. With smartphone-based AF screening, the diagnostic yield for AF was significantly higher {hazard ratio [95% confidence interval (CI)] = 3.9 (1.4–10.4); $P = 0.007$ } at a cost of \$10 780 per AF diagnosis. Photo-plethysmography technology and single-lead ECG, both acquired through a smartphone, have been compared against each other, finding similar diagnostic accuracy with a somewhat lower positive predictive value and higher negative predictive value for PPG.^{6,12}

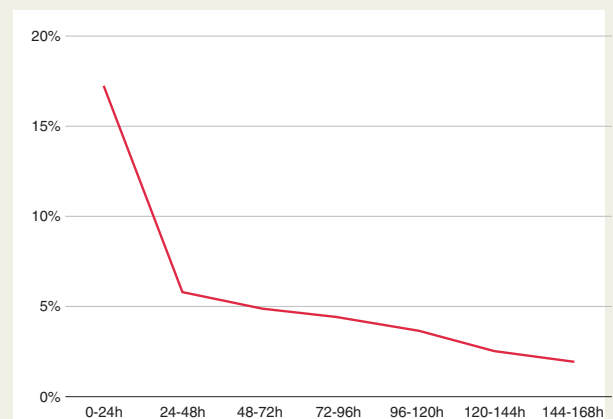


Figure 5 Frequency of smartphone-based photo-plethysmography measurements of insufficient quality for analysis during the study period.

The main benefit of PPG technology over single-lead ECG is that no additional hardware is needed, making the technology cheaper and more readily accessible. Indeed, the current study screened more than 10 times the number of patients recruited in REHEARSE-AF with the smartphone application software and the company's medical technician services as the only potential costs (estimated as €1278 per AF diagnosis; market price provided by the company with data not presented in the Results section). Moreover, recruitment in this study was very fast (within 48 h) with an unlimited amount of heart

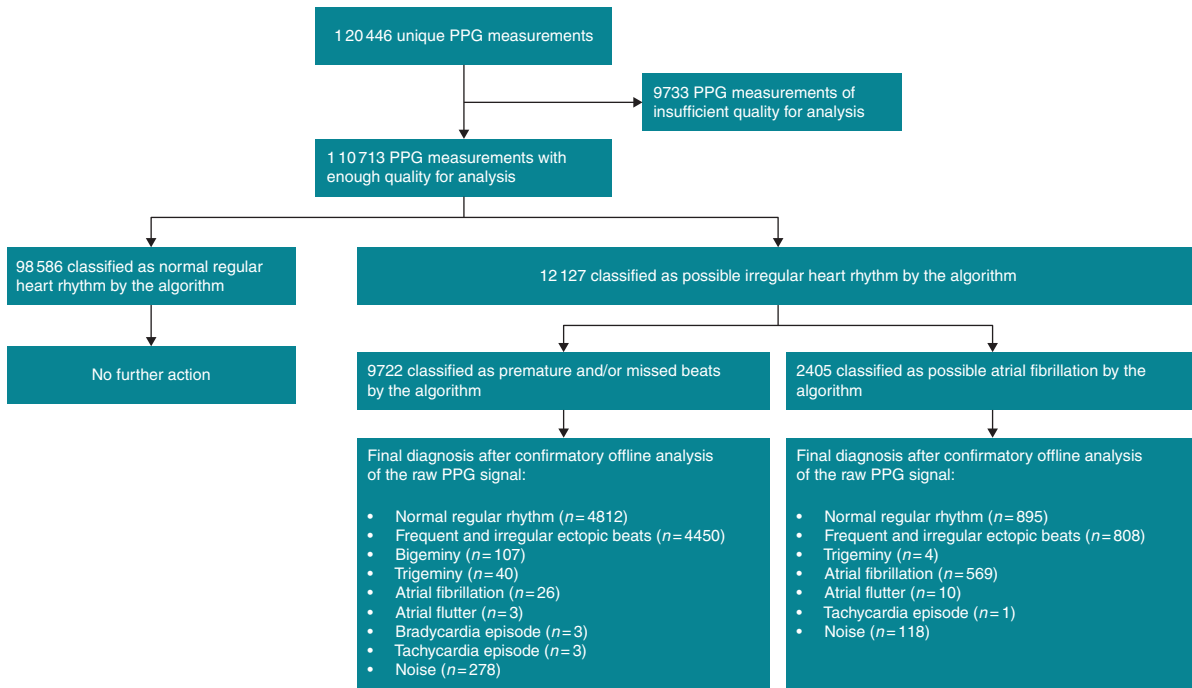


Figure 6 A flowchart of the results of heart rhythm screening by the smartphone application’s algorithm and confirmation by secondary offline analysis of the raw PPG data. PPG, photo-plethysmography.

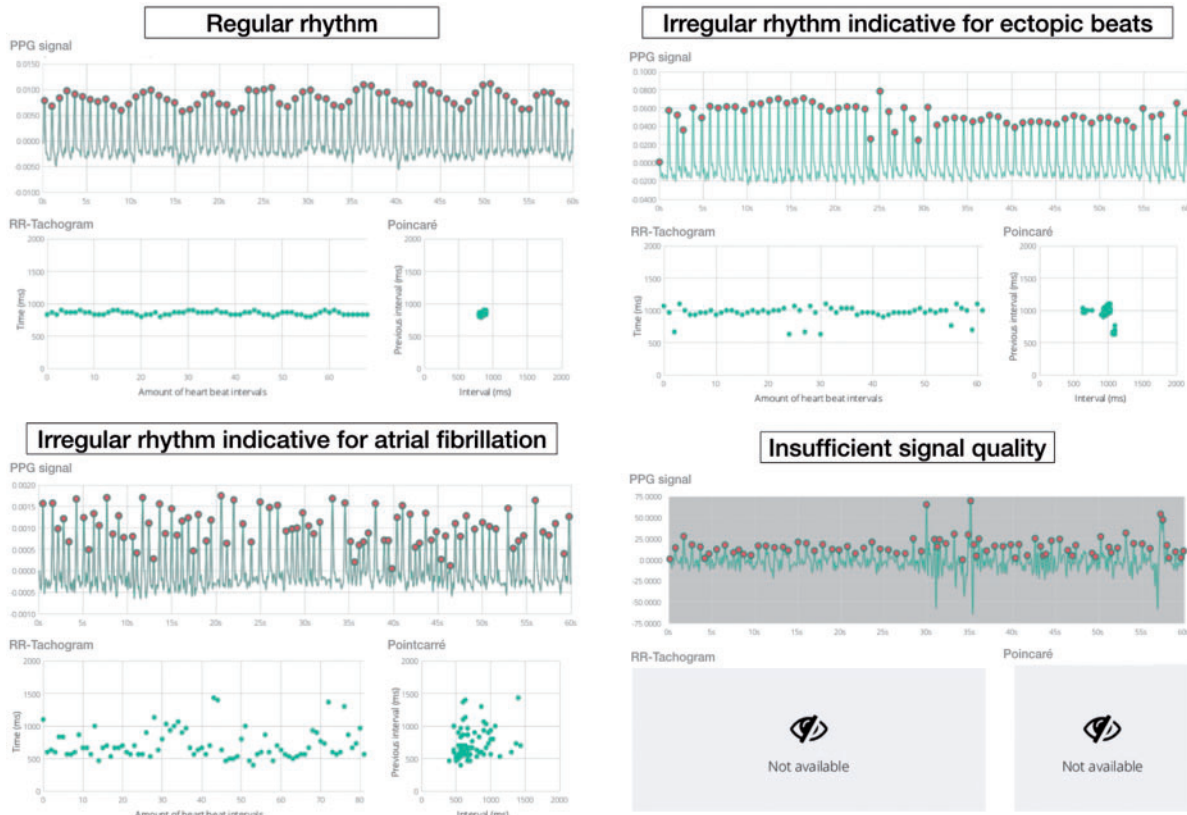


Figure 7 Examples of raw PPG traces and their tachogram and Poincaré plot, representing different rhythms. PPG, photo-plethysmography.

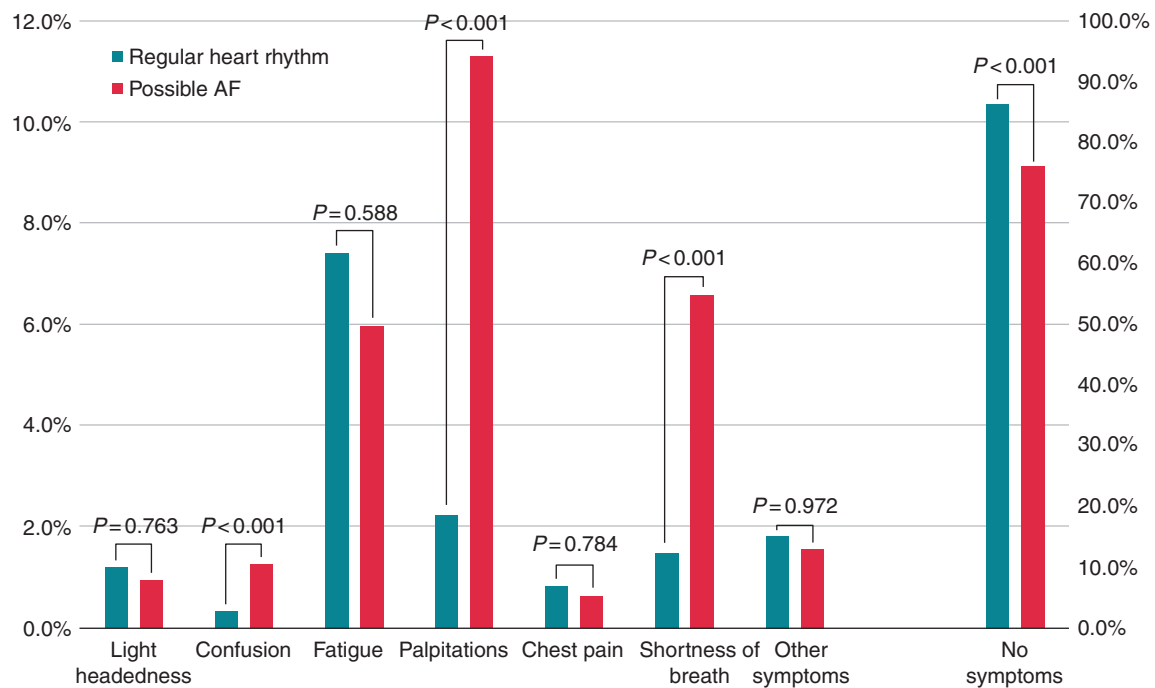


Figure 8 Symptoms associated with heart rhythm assessments according to its result. AF, atrial fibrillation.

rhythm assessments for every subscriber, again indicating the low threshold for screening and absence of significant logistic barriers impeding screening uptake.

Clinical implications

As AF screening through non-conventional screening methods like smartphone-based PPG technology is likely to play a more important role in future clinical practice, some important questions regarding implementation and therapeutic consequences arise. Importantly, all pivotal randomized clinical trials showing benefits of oral anticoagulation in AF patients at high stroke risk have made the AF diagnosis conventionally through 12-lead ECG.^{17–19} With smartphone-based AF screening, there is a potentially earlier diagnosis of AF when its burden is lower. Although it has been found that AF episodes as short as 6 min might be associated with a higher thrombo-embolic risk, ongoing randomized clinical trials are still sorting out just how much AF burden is needed for patients to benefit from anticoagulation.²⁰ A second important question is whether more intensive AF screening should lead to earlier referral for AF ablation procedures in selected populations where those have shown promise to improve clinical outcomes.²¹ Large, randomized clinical trials are urgently needed to address these questions. Thirdly, smartphone-based applications to screen for AF have a potential impact on patient awareness for the disease, which could lead to better education and more extensive follow-up. This has the potential to improve clinical outcomes, although cost-efficiency should be studied further. In this respect, the screening strategy used in the current study is particularly attractive as there is a low burden for both patients and physicians. The former has an easy screening tool at his/her disposal, with stringent quality

checks of PPG signals provided by medical technicians of the company and with feedback going directly to the user of the application. The latter gets only involved when there is a potential concern of a relevant heart rhythm disorder. In this scenario, there is thus no need for the physician to review the irregular measurements. Finally, there may be an important role for smartphone-based AF screening in particular patients' populations. In patients with embolic stroke of undetermined source, serial ECG and Holter screening have important logistic limitations and implantable loop recorders have greater costs. Additionally, smartphone-based heart rhythm assessment could be interesting during the follow-up of patients with known AF and after ablation procedures, to quantitatively assess its burden and correlate it with symptoms, especially when the latter are atypical.

Study limitations

The results of this study should be interpreted in the light of some methodological limitations. Firstly, heart rhythm assessments in the current study were 1 min snapshots. The duration of possible AF episodes could therefore not be quantified and, consequently, there is no prove for long-standing episodes of AF. Secondly, as the screening method implied the use of a smartphone, selection bias might have occurred. Results of the current study may not be applicable to individuals not used to handle a smartphone. Indeed, a lower screening uptake was found in persons above the age of 70 years, potentially for this reason. Yet, as current generations in whom smartphone use is ubiquitous grow older, this should not have a major impact on the external validity of this study. Further, inherent to the study design that relied on a newspaper article to convince people to participate to a screening programme, patients already diagnosed with AF could have been

particularly attracted by this concept to monitor their disease. This could have inflated the population prevalence of AF found in this study. Thirdly, the large bunch of normal PPG signals found with screening were not manually revisited to confirm the diagnosis of a normal regular rhythm, creating the theoretical possibility of missed AF diagnoses. Yet, it has been demonstrated that PPG-based screening for AF has a very high negative predictive value >99%.⁶ Moreover, as there was no limitation for the number of heart rhythm assessments per individual, AF would presumably be detected with subsequent measurements. Fourthly, although every abnormal PPG signal was analysed offline by experienced technicians under supervision of a cardiologist, a 12-lead ECG was not available as gold standard comparison to confirm the diagnosis of AF. Fifthly, as study participants were identified by their smartphone use, the possibility exists that some measurements have been carried out by other persons than the owner of the smartphone him/herself. Finally, no follow-up data were available on therapeutic interventions and outcome in participants with possible AF. Whether participants with screening-detected subclinical AF are eligible for stroke prevention with oral anticoagulation remains to be answered.

Conclusions

Mass screening for AF using only a smartphone with dedicated application based on PPG technology is feasible. In this study, after providing this technology for free and making the public aware by a single advertising article in a local newspaper, screening coverage of the overall population was 1.43%, which was even higher up to 2.5% in age categories most relevant for screening. A potential diagnosis of AF was made in 136 patients (1.1%).

Funding

Qompium N.V. provided free use of the FibrCheck[®] algorithm for every study participant during the 7-day study period. The local newspaper *Het Belang van Limburg* published a free article to inform its readers on this smartphone-based algorithm and encourage people to participate in the screening programme.

Conflict of interest: F.H.V. has received consultancy fees from Qompium N.V., which is the company that holds the exclusive rights on the FibrCheck[®] algorithm.

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