Integrating a heart rate monitoring app in routine general practice:
- Protocol for a cluster randomized trial
- Pilot study

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The effect of a case-finding app on the detection rate of atrial fibrillation compared with opportunistic screening in primary care patients: protocol for a cluster randomized trial

Abstract

Background: Atrial fibrillation is a cardiac arrhythmia commonly encountered in a primary care setting. Current screening is limited to pulse palpation and ECG confirmation when an irregular pulse is found. Paroxysmal atrial fibrillation will, however, still be difficult to pick up. With the advent of smartphones, screening could be more cost-efficient by making use of simple applications, lowering the need for intensive screening to discover (paroxysmal) atrial fibrillation.

Methods/Design: This cluster randomized trial will examine the effect of using a smartphone-based application such as FibriCheck® on the detection rate of atrial fibrillation in a Flemish general practice population. This study will be conducted in 22 primary care practices across the Flanders region of Belgium and will last 12 months. Patients above 65 years of age will be divided in control and intervention groups on the practice level. The control group will be subjected to standard opportunistic screening only, while high-risk patients in the intervention group will be prescribed the FibriCheck® app on top of this opportunistic screening. The difference in detection rate between control and intervention groups will be calculated at the end of the study.

We will use the online platform INTEGO for pseudonymized data collection and analysis, and risk calculation.

Discussion: Smartphone applications might offer a way to cost-effectively screen for (paroxysmal) atrial fibrillation in a primary care setting. This could open the door for the update of future screening guidelines.

Background

Incidence and prevalence of atrial fibrillation

Atrial fibrillation (AF) is one of the most common cardiac arrhythmias. Consequently, it is also frequently encountered in primary care. According to the INTEGO database (containing routinely collected general practice data of over 280.000 patients in Flanders (1), see *Participants* section), the incidence of AF in a Flemish general practice population was 3.3 per 1000 patients in 2015 (2). Estimates around the globe vary widely depending on the source. Current prevalence estimates range from 1 to 4% for Western countries (3), with a generally rising prevalence (4–6).

AF carries a significantly elevated risk of stroke. Relative risk varies between 2.6 and 4.5 for patients over 60 years old, compared to patients without AF (7). The high morbidity and mortality of stroke is evident, and it is often the first presentation of silent AF (8). It therefore seems useful to invest in screening strategies to identify those patients who have a higher risk of AF and need more intense monitoring, which may reduce healthcare costs brought about by hospitalizations for stroke (9,10). Furthermore, because some patients with AF will present with infrequent episodes – so-called paroxysmal atrial fibrillation (PAF) – the need for effective screening measures becomes clear (11). For example, in a Portuguese population aged 40 and older, who were referred for 24-hour continuous Holter monitoring, the prevalence of PAF was 2.5%, compared to 9.4% for persistent AF (12).

Still, many patients go undiagnosed. A recent study in the USA put the proportion of ‘silent’ AF at 2.4% of the adult population (13).

Screening

Stroke risk in AF is commonly calculated using the CHA_2DS_2-VASc score (congestive heart failure, hypertension, age, diabetes, stroke, vascular disease, sex) (14). Originally devised as a tool to predict the risk of stroke in AF, it may be less applicable to AF risk prediction in general (14). Various other scoring systems have been developed over the years, and more

recently the CHARGE-AF score has come to the foreground. For this score, data from three large cohorts in the US was used to predict AF risk in primary care settings (15).

The CHARGE-AF score is sufficiently validated to be used in AF stroke risk prediction and seems to perform better than the CHA_2DS_2-VASc score (16). Furthermore, the CHARGE-AF score uses variables that are readily available from patient files in a primary care setting (15). The variables of the (simple) CHARGE-AF score include age, race, height, weight, systolic and diastolic blood pressure, smoking status, antihypertensive medication use, diabetes, heart failure and myocardial infarction (15).

Opinions on the best approach to screening for AF in general practice are not unanimous. There are various ways to go about it: pulse palpation, which, when revealing an irregular pulse, can lead to a clinical diagnosis of AF, or by performing an electrocardiogram (ECG) to confirm AF after palpation of an irregular pulse. These methods could be used in either specific at-risk populations, or generally in every patient above a certain age, a risk category on its own. Both methods are available in a primary care setting, but performing an ECG is especially time-consuming. The most cost-effective strategy at this moment is likely to involve opportunistically screening every patient 65 years and older by pulse palpation or heart auscultation (17), taking an ECG only in those who have an irregular pulse (18). However, systematic full screening of older patients is not cost-efficient (18,19).

Patients who present with persistent AF are unlikely to be missed using the strategy outlined above. However, patients with the paroxysmal variant might still slip through and never be picked up using these methods. Holter registrations or even longer-term event recorders (in symptomatic patients) could partially solve this issue, but neither are very practical in general usage and their interpretation is very time-consuming.

Other options for screening

In recent years, various devices have been marketed as workarounds to solve the issue of detecting PAF in the general population. In addition, most offer a very user-friendly and easily accessible interface. Examples are heart rate and blood pressure monitors (20), one-lead ECG devices or smartphone apps (21,22), or event recorder patches (23).

The global advent of smartphones might offer a unique opportunity to mediate the problem of detecting PAF (22,24). Apps carry the extra advantage of not needing additional hardware. The FibriCheck® app (Qompium, Hasselt, Belgium) has recently been developed to aid in the detection of PAF. It is based on the photoplethysmography technique, using only the phone's built-in camera and flash (25). The app has been shown to accurately detect AF in a primary care setting (26). An ECG will still be necessary for diagnosis, but there will be less need for continuous ECG or event recording and the data can be easily visualized and interpreted by a general practitioner or cardiologist.

Research question

Implementing the FibriCheck® app in a primary care setting could solve the problem of screening for AF and, specifically, detecting PAF. Therefore, the aim of this study is to investigate the effect of a case-finding strategy with the FibriCheck® application on the detection rate of AF in comparison with opportunistic screening (i.e. pulse palpation, followed by an ECG) in patients with a high risk of AF in general practice.

Methods

Design

The study will be conducted in Flemish primary care practices. By design, it will be a cluster randomized trial: primary care practices will be randomized and divided into a control and intervention group.

Allocation of control and intervention groups will be done by simple balanced randomization (1:1). Enrolment of practices based on the in- and exclusion criteria described below, will be performed by researcher A, who is part of the trial. This will generate a numbered list of the eligible practices. Researcher B will, independently, assign numbers (denoting a specific practice) to either the control or intervention groups by means of a computer-generated list of random numbers, i.e. simple randomization. Researcher B will also prepare sealed, opaque envelopes containing a paper that assigns a specific practice number to a study group, based on this randomly generated number sequence. The process of the envelope preparation up until sealing and storage in a locked compartment, will be videotaped by researcher B, who will thereafter be excluded from every other aspect of the trial. Allocation papers should never be visible, only the envelopes and the numbers on them. The video will be stored on an external device, which will be put in the locked compartment.

After practice enrolment, researcher A will access the locked compartment with the envelopes and review the accompanying video to ensure proper envelope preparation. Without opening or tampering with the letters, researcher A will write the appropriate mailing address on the respective envelope, based on their numbered list of practices. The envelopes will only be opened by the practices if they have an unbroken seal. This protocol is adapted from Radford *et al*. (27).

All Flemish primary care practices conforming to the inclusion criteria will be contacted to be included in the study. Then, they will be randomly subdivided into intervention and control practices. In every practice, patients will be selected according to the previously defined in- and exclusion criteria. Later, high-risk patients in the intervention groups will be identified using the CHARGE-AF score, to be prescribed the FibriCheck® app (see *Intervention group*). High risk is defined as a 5-year risk of AF of at least 10% according to this score.

Due to the nature of the study it is not possible to blind at the practice level. Physicians will always be aware to which group they belong, as will the patients.

Ethics

We will use two different consent forms in this study; practices will be given a study leaflet, outlining the study procedure and required data, together with their own consent form. Patients will be given one week to decide whether they want to participate. Those who want to be included will be given a separate consent form.

Participants: practices and patients

- To be eligible for inclusion in the study, **practices** must conform to the following conditions:

1. It is a Flemish primary care practice in the INTEGO network.

2. The practice uses an electronic health record (EHR), automatically linked to the INTEGO database.

3. ECG devices used for diagnosis (i.e. confirmation of AF) must be 12-lead.

4. The physician signs a specific study consent form.

- To be eligible for inclusion in the control or intervention groups of the study, **patients** must conform to the following conditions:

1. The patient is 65 years or older.

2. The patient has an electronic medical record (EMR) in the practice. This EMR contains all the patient information, for instance regarding medical history and medication and is managed by the general practitioner.

3. If the patient will be prescribed the FibriCheck® app, he/she signs the relevant patient consent form.

- Exclusion criteria for both the control and intervention group will be defined as follows:

1. The patient has already been diagnosed with AF.

2. The patient is already under anticoagulant therapy.

3. The patient has a pacemaker. Active pacing during measurements influences the results obtained with the FibriCheck® app (26).

4. The patient is unable to use the FibriCheck® application independently due to cognitive disorders, functional limitations, visual impairments…

Data collection and analysis

INTEGO database

The INTEGO network is a morbidity registry containing coded contents of the electronic health records of some 285.000 patients from 90 general practitioners all over Flanders. The information is automatically collected during daily practice and contains diagnoses, year of birth, gender, prescriptions, lab results and various biomedical parameters such as blood pressure, height, weight, etc. (1). The INTEGO procedures have been validated by the Belgian Privacy Commission. The registry is hosted on the Healthdata platform (www.healthdata.be) (28).

FibriCheck®

The data gathered during the study of the patients that are prescribed the FibriCheck® app, will be collected on the FibriCheck® platform, a cloud-based storage space. The research team (headed by the authors of this protocol) will be given credentials to access this platform and extract the data for interpretation and analysis, as will authorized employees of Qompium, the general practitioners of the selected practices and a cardiologist specifically assigned to the study. Only the research team will perform extraction and analysis of these data. Measurements of the app are color-coded, indicating normal versus aberrant heart rhythm and their likelihood (from green over orange to red), or measurement errors (blue, indicating insufficient signal quality for analysis).

After collection, the data will be pseudonymized before access is granted to the FibriCheck® platform.

Intervention group

In every cluster designated as an intervention group, patients aged 65 or older will be selected according to the criteria outlined above. Within this group, high-risk patients will be identified using the CHARGE-AF score, and will be prescribed the FibriCheck® app. An integrated tool in the medical software package will calculate this score from the available parameters in the EHR. If needed, physicians will be asked to input missing data at the first consultation. Data for this score will be automatically extracted from the EHR from INTEGO. All high-risk patients will thus be flagged as such on the INTEGO platform. Physicians will also need to inform and educate patients about their high-risk status, as we consider this good clinical practice.

These high-risk patients will subsequently be informed about the study and possible enrolment and be given a study information letter describing the study procedure and purpose in detail.

Interested patients will be prescribed the FibriCheck® application after informed consent is given. Patients not in possession of a smartphone, will be supplied one for the duration of the study. The application needs to be downloaded and patients will be asked to create a numbered account (in the format ‘patient00x’, etc.) and supply general details such as age and gender. A specific QR code links the patient’s account to the physician’s dashboard, so the latter can easily follow up.

The study will be conducted over the course of 12 months in general practices in the Flanders region of Belgium. Patients will be followed for a total of 4 weeks. Measurements and other data will be collected and interpreted at the end of this period. Positive measurements will be given immediate attention. A minimum of 20 measurements in total per patient in the intervention group is necessary to be considered for inclusion in the study. Patients will be expected to measure at least twice a day (morning and evening, see below).

To be able to track patients in the intervention group who were prescribed the FibriCheck® app, physicians will be asked to flag the specific patient file with a note saying ‘FC’ or ‘FibriCheck’. This will be displayed when the data is later collected from the INTEGO platform.

Every participant will be asked to measure at least twice a day (in the morning and in the evening) and if there are complaints such as dizziness or palpitations. After the measurement, the patient will be asked for his activities up to the measurement and certain symptoms.

Measurements are available for the treating physician and a cardiologist, who will interpret the results within 24 hours. Additionally, an electronic notification will be sent immediately to the interpreting physicians in case of an abnormal result. Physicians will be asked to review these results at least once every 24 hours. At the end of every participant’s study period, a summarizing report will be sent to the treating physician.

When a positive result (red) has been found (indicating the possibility of AF), the patient will be contacted within 48 hours for a formal 12-lead ECG. If this ECG is inconclusive, a 2-week Holter measurement will be ordered. If AF is confirmed, rate or rhythm control and anticoagulant therapy will be started, or the patient will be referred to a cardiologist for further workup. The CHA_2DS_2-VASc score will be used to calculate the risk of thrombosis, and together with the HAS-BLED score (29), indicating the risk of bleeding, it will guide anticoagulant therapy (30).

If a positive FibriCheck® screening cannot be confirmed with 12-lead ECG or 2-week Holter, the patient files will be marked with a special code in the EHR and flagged for future, more intensive screening (with both the application and an ECG at consultation).

Control group

In every cluster designated as a control group, patients aged 65 or older will be selected according to the criteria outlined above. The difference here is that patients will be given the standard opportunistic screening instead: pulse palpation and a 12-lead ECG when an irregular rhythm is found. This is current best practice (31).

Data collected on demographics and clinical characteristics

To be able to compare both groups in terms of clinical similarity, we will provide relevant data that allows reasonable comparison between the intervention and control groups. The data will be extracted from the medical software each practice uses by using the INTEGO procedures. The results will be analyzed and presented on the level of the practice. Baseline group characteristics relevant for the study will be assessed at the start of the study (**Table 1**).

Table 1: Collected data on group characteristics (for control and intervention groups)

Group characteristics (n = 22)
Mean age
Gender distribution
Mean BMI
Mean systolic/diastolic blood pressure, heart rate
Smoking status (current, former, never)
Antihypertensive medication
Type II diabetes
Heart failure
Myocardial infarction

If not already present in the patient file, missing data will be collected during this first interview. For example, if there is no mention of a patient's blood pressure or height and weight, the participating physician will measure these parameters and put them into the EHR.

The general group characteristics schematized in **Table 1** will be used to calculate the cardiovascular CHARGE-AF risk score of patients in the intervention group.

Primary outcome measures

- **Detection rate of AF in patients 65 years and older**: The detection rate of AF in both the control and intervention group will be calculated after 4 weeks. A significant difference in both groups will be noted. Compared with previous studies of similar design (32–34), we will realistically assume a 2-fold increase in the detection rate of AF in the intervention group to be significant.

Secondary outcome measures

- **Thromboembolic complications**: We will track incidence of transient ischemic attack or ischemic stroke during the study period, in addition to the eventual difference between both study populations.

- **Death**: We will keep track of all-cause mortality during the study period, as well as difference in mortality between control and intervention populations.

- **Compliance**: We will keep track of patient compliance during the study period (e.g. minimum number of measurements with FibriCheck®).

Sample size calculation

The calculation hereafter is similar to that of an earlier paper, comparable to ours (34). We used an online calculator, which can be found at http://www.sample-size.net/sample-size-proportions. The sample size calculation was performed for the primary outcome (AF detection rate at practice level). In INTEGO we found a baseline AF incidence of 13.65/1000 patients, 65 years or older, in 2015. As stated above, we estimated a realistic absolute increase of 24.57 AF cases per 1000 patients per year in the intervention group. The sample size calculation, with a power of 0.80 and an α of 0.05, for a two-sided two-sample *t* test, with the incidence of AF per 1000 patients per year as the outcome variable, led to a sample size

of 1835 patients in each arm of the study.

As we will view the results on the practice level, the number of practices needs to be determined, considering the intra-cluster correlation coefficient (ICC). A similar study found an ICC of 0.0027 (18). As we plan to let this study run for 12 months, we wish to include 400 patients (= *m*) per practice/physician. Calculating the variance inflation factor (1 + ICC (m – 1)) leads us to a value of 2.077. To accommodate the expected variance, we will have to include 1835 x 2.077, or 3811 patients per arm. We will assume a loss to follow-up of 15% (34). This brings us to a total study population of 8765 patients, or approximately 11 control and 11 intervention practices.

Statistical analysis

We will analyze our data on an intention-to-screen basis, evaluating the outcomes on the practice (cluster) level. There will be no subgroup analyses.

This means we will include all participants of both the control and intervention groups in the final analysis, regardless of whether they did receive the stated screening intervention or dropped out before they could do so. This ensures that no bias is introduced by looking at the data on the practice level, for example by erroneously overestimating the effect of the intervention (screening with FibriCheck® on top of standard screening). This approach is valid as long as the studied population is appropriately randomized (35).

We will analyze the results on the cluster level, as the study is also randomized at the cluster level. Statistical efficiency should be sufficient with the cluster sizes being equal, as outlined above. As the unit of inference will be the cluster, and not the participant, we will apply standard *t* tests with inverse-variance weighting (36).

Loss to follow-up and missing outcomes

For sample size calculation, we already assumed a loss to follow-up (LTFU) of 15%. The barrier to entry in this study is very low and takes place in the context of a normal doctor's

appointment. Also, results will be read from the practice level, so all information will be collected in a coded fashion and patient confidentiality will be automatically ensured. This will also be outlined in the patient study information leaflet. We anticipate that these factors will reduce LTFU as much as possible.

We will keep track of LTFU – for any reason – during the study and compare LTFU between control and intervention group at the end. Any significant difference will be discussed.

For missing data, we will use multiple imputation to obtain complete datasets.

Harms

This is a purely screening-based trial; there are no adverse effects to be expected solely because of screening in the intervention group.

Discussion

To our knowledge, this will be the first study to evaluate the influence of a stand-alone smartphone application on the detection rate of AF compared to a control group. There are certain indispensable elements on which the study will hinge. Certain issues can be expected here.

Most importantly, the availability of correctly coded data is essential for the study to be conducted. Physicians must code diligently and completely. Without coded data and diagnoses, this study will be difficult to perform on a large basis.

To screen high-risk patients, we will use the sufficiently validated CHARGE-AF score. Certain EMD software packages, however, do not allow custom searches based on every parameter in this score. Ideally, a tool could be developed that automatically calculates the CHARGE-AF score across platforms for every individual patient and notifies the physician if a patient needs to be screened.

There are certain limitations to this study as well. For the data to be correctly sent to the cloud, patients must have a working internet connection. Also, patient compliance is

important. This will have an impact on the detection rate of AF that we will find in both study groups.

Trial status

This study protocol with registration number B3222020000036 was approved by the Ethics Committee of University Hospitals Leuven, Belgium on May 14, 2020.

Funding requested.

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Integrating a heart rate monitoring app in routine general practice: a pilot study

Abstract

Introduction: Atrial fibrillation (AF) is a major risk factor for stroke. The current opportunistic screening procedure consists of pulse palpation and an ECG when an irregular rhythm is found. Smartphone applications that measure heart rhythm could be useful in increasing detection of AF in a primary care setting. We conducted a pilot study with the smartphone application FibriCheck® to assess whether the introduction of such an application is feasible.

Subjects/Methods: Four general practices across Flanders provided patient data for the study. Inclusion criteria for participants were: 65 years or older and a CHARGE-AF score of at least 10%. We excluded patients with known AF or a pacemaker. Participants were asked to measure at least twice a day with FibriCheck®, during at least 14 days. They were provided the SF36 questionnaire both before and after the study, as well as different surveys concerning their user experience and general perception of technology.

Results: There were 92 participants, of which 36 women and 56 men. The study population was relatively homogenous concerning risk factors and medication use at baseline. During the study period, 5.8% of the participants were found to have AF. The average study period was 23 days and the average number of measurements per day was 2.1. Patient compliance was variable, but high. There was no significant change in quality of life after the study. The overall user experience and satisfaction was very high.

Conclusion: FibriCheck® is a relatively easy-to-use application to complement AF screening in primary care. Its implementation in this setting is certainly achievable, and one can expect high rates of patient compliance.

Introduction

Atrial fibrillation (AF) has long been known as an independent risk factor for stroke (1). It is highly prevalent among older patients in primary care, and the incidence is seemingly on the rise (2,3). Hospitalizations for stroke are an important financial burden to society, so a strategy for early and cost-effective screening interventions seems useful (4). Current best clinical practice points to an opportunistic screening approach to detect AF, in which at-risk patients undergo routine pulse palpations and electrocardiograms (ECGs) when an irregular rhythm has been found (5,6). Taking an ECG in routine general practice, however, is quite time-consuming. Furthermore, given the sometimes paroxysmal nature of AF, it could be missed by an opportunistic screening method during a routine consultation (7). A significant proportion of these patients remain undiagnosed (8). Holter measurements and event recorders could partially remedy this issue, but interpretation is again very time-consuming and unlikely to be very cost-effective (9).

Portable heart rate monitoring applications have recently been introduced to provide an on-the-go way to check for arrhythmias in general practice (10–12). They could provide a convenient add-on to current opportunistic screening. Since the advent of smartphones, efforts have been made to use the phone's inbuilt camera to register heart rhythm via photoplethysmography (13). Today, there are various smartphone applications available (14,15). They all perform well in terms of diagnostic accuracy and yield.

In Belgium, the Hasselt-based firm Qompium has developed such a smartphone app, named FibriCheck®. The diagnostic accuracy has already been studied previously (16). An upcoming cluster-randomized controlled trial will study its efficacy as a diagnostic tool to facilitate screening. This pilot study aimed to assess the ease-of-use and implementation of the FibriCheck® app in a primary care setting.

Subjects and methods

This feasibility study ran from January to December 2017. Four general practices across Flanders were recruited in this study (**Table 1**). Every practice used different medical software to code diagnoses and parameters: a deliberate choice to test the ease with which data could be derived from each software package.

Table 1: Overview of recruiting practices

Name of practice	Place	Team	Medical software
Huisartsencentrum Millegem	Mol, Antwerp	4 GPs	MediDoc®
Groepspraktijk Hoeilaart	Hoeilaart, Flemish Brabant	6 GPs, 2 GP trainees	CareConnect®
Huisartsenpraktijk Keerbergen	Keerbergen, Flemish Brabant	2 GPs, 1 GP trainees	Windoc®
Praktijk Gilissen	Riemst, Limburg	2 GPs, 1 GP trainees	Prodoc®

Participants

We opted to only include patients at high risk for AF to test the suitability of the FibriCheck® application. There was no control group. The 5-year risk of AF is commonly indicated using the CHARGE-AF score (17). This score was calculated manually for each potential participant, by extracting the necessary data from the patient file. Frailty score was calculated according to Tocchi *et al*. (18). A score of 0 means no frailty, a score of 1 to 3 increasing risk of frailty and a score of 4 or more indicates definite frailty.

The inclusion criteria were as follows:

- A CHARGE-AF score of 10% or more
- 65 years or older

Exclusion criteria were as follows:

- Known or already diagnosed AF
- Patient has a pacemaker
- Patient takes oral anticoagulants
- Patient is unable to use a smartphone application due to physical, visual, or cognitive impairment

Upon selection of appropriate participants, they were asked to sign a consent form to be included in the study. Before the study commenced, participants were asked whether they had used a smartphone before or had the ability to use a smartphone correctly.

Each participant was given a coded account number, linked to the specific FibriCheck® application on their smartphone. Smartphones were provided in case participants did not own one themselves, others just had to install the application.

At recruitment and at the end of the study, an ECG and a FibriCheck® measurement were taken.

The time the physician spent to explain the study to the participant and on educating them how to use the FibriCheck® application, was registered.

In addition, physicians were asked to indicate what they would have done if the FibriCheck® app were *not* available (i.e. if they were not included in the study). There were two options: no action (and wait for the patient to consult on his own), advise a follow-up consultation. Physicians could also indicate how many consultations they normally anticipated during a 1-year period.

Measurements

At the start of the study, participants were asked to measure at least twice a day with the FibriCheck® app and to indicate if they experienced any symptoms preceding the measurement. Minimum required measuring time was 2 weeks, the individual participant's

study period ended after a maximum of 4 weeks. Patients were considered incompliant and excluded when there were no measurements for 2 weeks or more during the study period, or if they were lost to follow-up.

After measuring, the FibriCheck® application reviewed every measurement immediately afterwards, with four possible outcomes: normal measurement (no tachycardia, no extrasystole, no irregular rhythm; indicated in green), inadequate signal (indicated in blue), measurement requiring urgent attention (possible AF; not signaled to participants), warning (usually more than 4 extrasystoles, or brady- or tachycardia: indicated in orange). Participants were also able to indicate their stress levels with each measurement. The score ranged from 0 (low stress) to 10 (highest stress) with step intervals of 2.5.

Quality of life

Patients were asked to fill in the SF36 questionnaire, to get an impression of their quality of life at baseline. This survey contains 36 questions from various health domains, such as physical functioning or emotional health. It uses graded responses: answers corresponding to more favorable health states receiving higher scores (the minimum and maximum being 0 and 100, respectively). The scores for the questions of a specific health domain are then averaged to compile a subtotal score. Each participant was asked to complete the questionnaire again at the end of the study period.

Technology perception – application usability

Lastly, participants were provided questionnaires at the beginning of the study, concerning their perception and familiarity of current technology. At the end of the study, a general questionnaire about their use of the FibriCheck® app was provided. Answers were graded on a 5-step scale, ranging from ‘completely disagree’ to ‘fully agree’.

Statistics and calculations

A two-proportion, two-tailed *Z*-test was used to analyze the difference in risk factors and medication between male and female participants in the study. To compare the scores on the various domains of the SF36 questionnaire, we used a two-tailed Wilcoxon signed ranks test, as we did not assume normality. The value for any missing item was imputed as the mean value for non-missing items.

We refrained from calculating the total average score of the SF36 questionnaire. This is often done to form an idea about the general health of study participants. However, this supposes a 50/50 equilibrium between the mental and physical aspects of health, and this practice is generally discouraged (19).

The minimal clinically important difference (MCID) for the health-related SF36 questionnaire, was calculated according to earlier studies for similar populations (20,21). We used a distribution-based method, as an anchor-based method was not feasible for this pilot study. A cut-off value of 1 standard error of measurement (SEM) was used to define a meaningful improvement or deterioration, in line with previous studies (21).

The following formula was used to calculate the SEM, with σ being the standard deviation of a particular test, and *r* the reliability coefficient or Cronbach's alpha of the same test (20):

$$\sigma\sqrt{1-r}$$

Data for this formula, as applicable to the SF36 questionnaire, was gathered from the Medical Outcomes Study (22).

The answers to the questionnaires concerning technology perception and usability of the FibriCheck® app, were weighted according to importance: for instance, 'completely agree' (or a similar answer) was assigned a value of 2, 'agree' a value of 1, 'completely disagree' a value of -2, and so on.

For other data, we used descriptive statistics throughout.

Results

Participants

Ninety-two participants in total were recruited from the 4 practices listed in **Table 1**:

- Huisartsencentrum Millegem: 17 patients
- Groepspraktijk Hoeilaart: 35 patients
- Huisartsenpraktijk Keerbergen: 20 patients
- Praktijk Gilissen: 20 patients

There were 36 female and 56 male participants in the study population. The mean age was 76 years (range: 45 to 94; standard deviation (SD): 11.4). The mean BMI was 28.1 kg/m^2 (range: 17.3 to 42.7; SD: 4.6). In our study population, the mean frailty score was 2.6 with 22.8% having a score of 4 or more.

Before the study commenced, participants were asked whether they had used a smartphone before or had the ability to use a smartphone correctly. There was a response rate of 95.7%. In total, 15.9% had a smartphone and knew how it worked, 31.8% did not have an idea what to do with a smartphone, 12.5% had used a smartphone before and could manage, while 39.8% had used a smartphone but found they needed help.

At recruitment and at the end of the study, an ECG and a FibriCheck® measurement were taken. Before commencement, 93.5% of participants were in sinus rhythm, 5.4% had ectopic beats and 1 patient had atrial flutter.

On average, physicians spent around 15 minutes to get participants started with the smartphone and the application (range: 5 to 40 minutes), and another 21 minutes to fill in the necessary administrative paperwork (consent forms, patient education leaflets…; range: 10 to 40 minutes).

The risk factors of the participants, as well as the different medications they were taking at baseline, are listed in **Table 2**.

Table 2: Risk factors and medication of participants at baseline, for men and women

Risk factors	**Men (n = 56)**		**Women (n = 36)**		***p*-value (two-proportion, two-tailed *Z*-test; 95% confidence)**
Diabetes	23	41.1%	9	25%	$p = 0.11$
Arterial hypertension	48	85.7%	26	72.2%	$p = 0.11$
Heart failure	2	3.6%	4	11.1%	$p = 0.15$
Stroke/TIA	5	8.9%	5	13.9%	$p = 0.45$
Cardiac ablation	3	5.4%	1	2.8%	$p = 0.56$
Other cardiac surgery	10	17.9%	2	5.6%	$p = 0.09$
Cardioversion	0	0%	1	2.8%	$p = 0.21$
Thrombosis (DVT/PE)	14	25%	2	5.6%	$p = 0.02$
Hypercholesterolemia	23	41.1%	14	38.9%	$p = 0.83$
Peripheral vascular disease	22	39.3%	6	16.7%	$p = 0.02$
Obesity	15	26.8%	8	22.2%	$p = 0.62$
Smoking	8	14.3%	1	2.8%	$p = 0.07$
CHARGE-AF score					
0-10 (“low”)	16	28.6%	15	44.1%	$p = 0.13$
11-20(“medium”)	18	32.1%	12	35.3%	$p = 0.76$
21-30 (“high”)	11	19.6%	4	11.8%	$p = 0.33$
31+ (“very high”)	11	19.6%	3	8.8%	$p = 0.17$
Medication					
Beta-blockers	26	46.4%	14	38.9%	$p = 0.48$
ACE-I/ARBs	17	30.4%	16	44.4%	$p = 0.17$
CCBs	8	14.3%	6	16.7%	$p = 0.76$
Diuretics	10	17.9%	6	16.7%	$p = 0.88$
No CV	*16*	*28.6%*	*13*	*36.1%*	$p = 0.45$
1-2 CV	*32*	*57.1%*	*16*	*44.4%*	$p = 0.23$
>2 CV	*8*	*14.3%*	*7*	*19.4%*	$p = 0.52$

Abbreviations: TIA = transient ischemic attack, DVT = deep venous thrombosis, PE = pulmonary embolism, ACE-I = angiotensin-converting-enzyme inhibitors, ARB = angiotensin II receptor blockers, CCB = calcium channel blocker, CV = cardiovascular medication.

Physicians would have chosen the ‘wait and see’ approach for 73% of patients, if the FibriCheck® app would not have been available. In this scenario, they anticipated on average between 2 and 3 consultations over a 1-year period. The mean CHARGE-AF score for participants in the “follow-up” group was 20.89, whereas the mean score in the “wait and see” group was 18.60.

Measurements

There were 24 consultations with 18 patients (19.6%) purely because of a FibriCheck® finding, as well as 3 hospital admissions (3.3%) indirectly resulting from a finding on the app. All the aberrant rhythms detected during and at the end of the study, are summarized in **Table 3**.

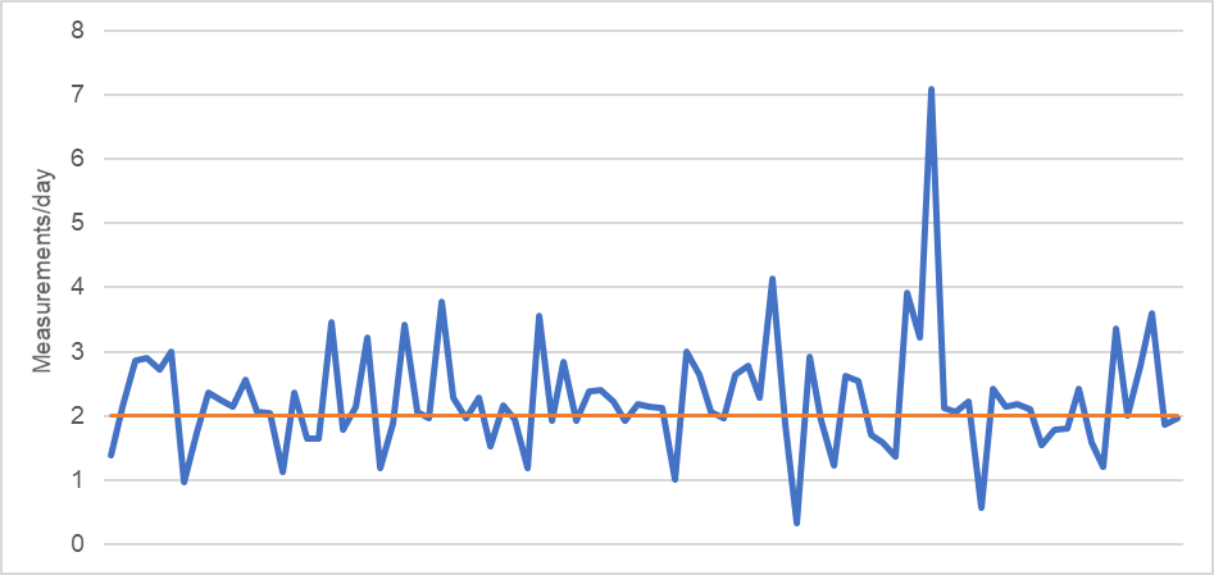
*Table 3: Rhythms detected during the study (n=86)**

Heart rhythm	**Number of patients**	
Ectopic beats (SVES, VES)	10	11.6%
Tachycardia	2	2.3%
Atrial fibrillation	5	5.8%

Abbreviations: SVES = supraventricular extrasystoles, VES = ventricular extrasystoles.
(*) 6 dropouts: 4 exclusions by patient request, 2 excluded due to incompliance.

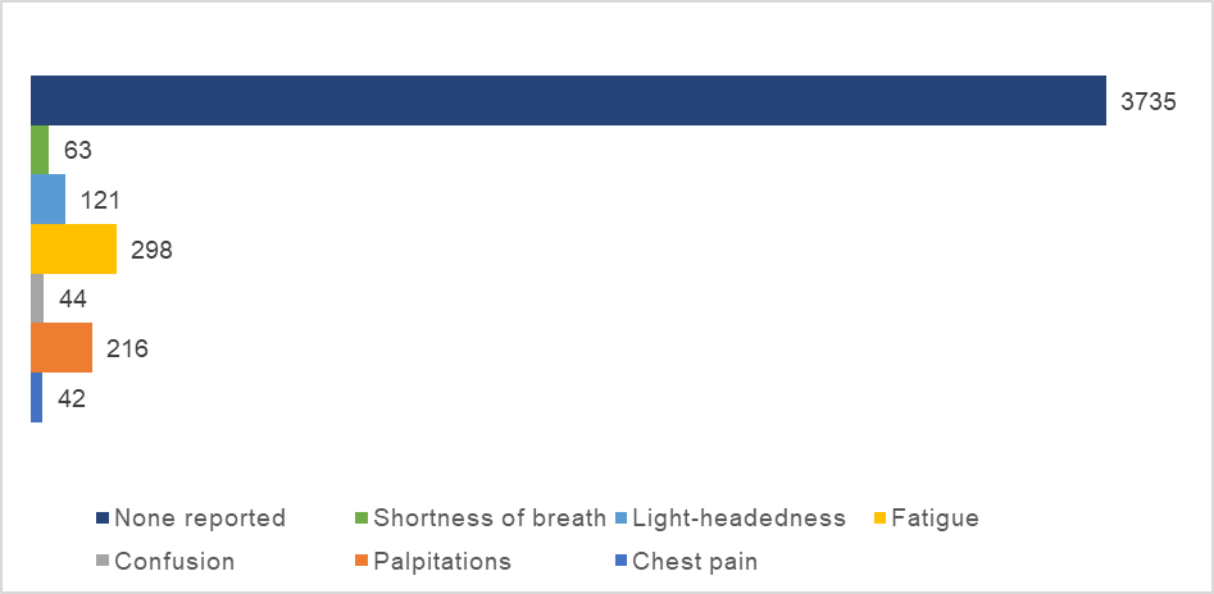
The average participant study period was 23 days. Participants conducted an average of 49.5 measurements during that time, which amounts to 2.1 measurements per day. **Figure 1** shows the average number of measurements for each participant as a line.
The ‘2 measurements per day’ criterion is highlighted, which gives an idea about participant compliance. Approximately 70% of participants had 2 or more measurements per day.

Figure 1: Average number of measurements per day, per participant



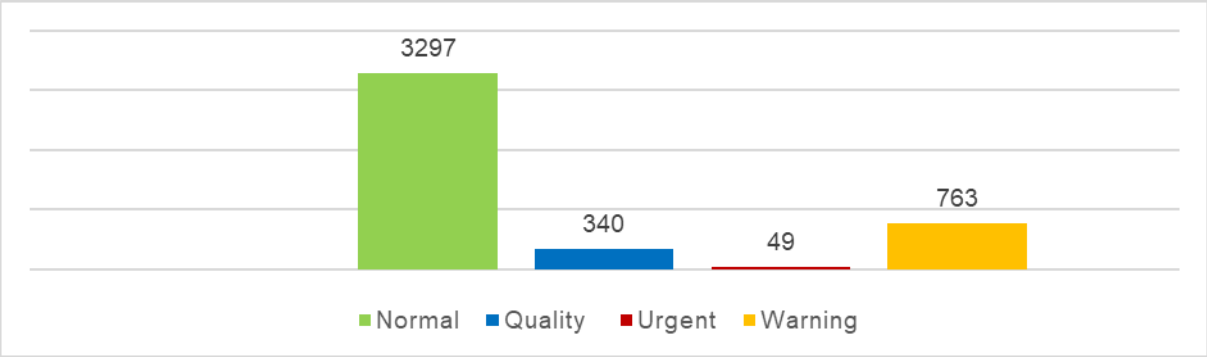
A total of 4489 validated measurements were taken, for 90 participants in total. A summary of the most common symptoms accompanying the measurements is displayed in **Figures 2 and 3**. Most measurements did not report a symptom and per measurement multiple symptoms could be reported. There was a total of 3313 measurements that had a stress level registered. The mean stress level was 2.29.

*Figure 2: Proportion of reported symptoms (n = 4449)**



(*) 40 measurements were not validated by the algorithm, due to connection errors.

*Figure 3: Number of different FibriCheck® measurements (n = 4449)**



(*) 40 measurements were not validated by the algorithm, due to connection errors.

Quality of life

In total, 54 participants filled in the SF36 questionnaire at the start of the study. We excluded 4 patients from the final analysis, because they failed to complete the questionnaire at the end of the study. **Table 4** shows the results for the 50 participants who completed the questionnaire.

Table 4: Comparison of SF36 domain scores, at start and end of study (n = 50)

SF36 domains	Mean score (start)	Mean score (end)	MCID (= 1 SEM)	*p*-value (Wilcoxon signed-rank test, two-tailed; 95% confidence)
Emotional well-being	50.4 (9.6)	42.6 (6.9)	7.0	*p* = <0.001
Energy/fatigue	51.1 (11.7)	51.0 (11.2)	8.4	*p* = 0.76
General health	49.5 (10.9)	48.4 (9.4)	10.0	*p* = 0.64
Pain	71.5 (23.3)	74.3 (23.9)	12.0	*p* = 0.35
Physical functioning	57.9 (24.2)	58.7 (25.2)	7.3	*p* = 0.79
Role limitations/emotional	77.0 (31.8)	84.9 (30.1)	16.8	*p* = 0.10
Role limitations/physical	69.4 (37.1)	73.4 (35)	16.3	*p* = 0.20
Social functioning	83.8 (17.4)	83.8 (20.5)	9.9	*p* = 0.96

Notes: A higher value indicates a more favorable health status (minimum: 0, maximum: 100). Bracketed values are standard deviations.
Abbreviations: MCID = minimal clinically important difference, SEM = standard error of measurement.

Table 4 (cont.)

SF36 domains	Score increase (proportion of participants)	Score reduction (proportion of participants)	No significant change (= 1 SEM)	Ratio I/R
Emotional well-being	10%	62%	28%	0.16
Energy/fatigue	16%	24%	60%	0.67
General health	18%	18%	64%	1.00
Pain	22%	12%	66%	1.83
Physical functioning	24%	20%	56%	1.20
Role limitations/emotional	20%	8%	72%	2.50
Role limitations/physical	20%	10%	70%	2.00
Social functioning	22%	14%	64%	1.57

Abbreviations: SEM = standard error of measurement, I/R = increase/reduction.

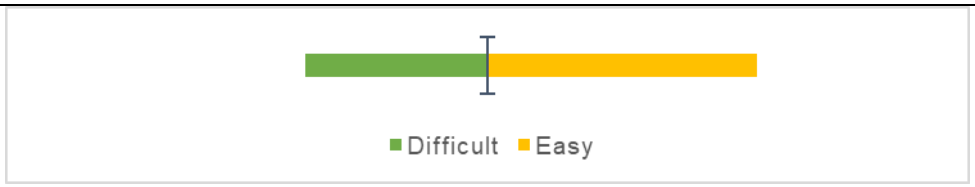
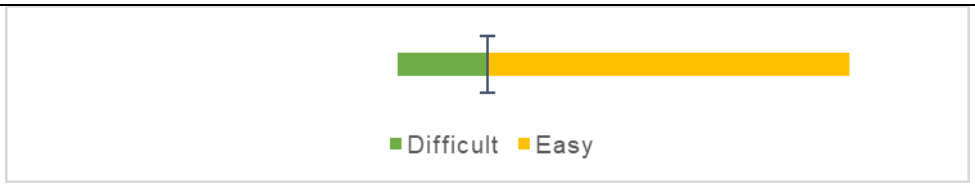
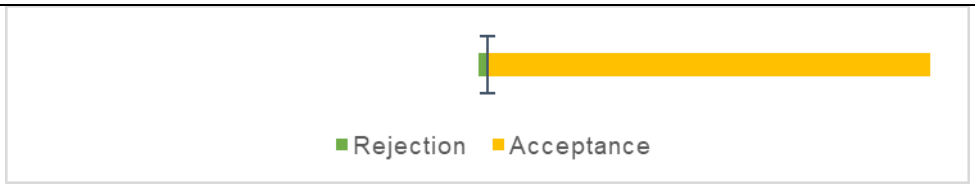
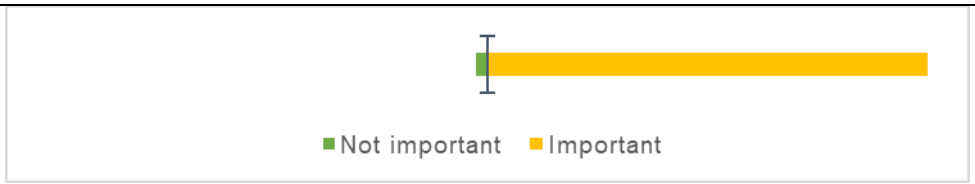
Technology perception and application usability

The data on the technology perception, gathered at the beginning of the study, and the data on the use of the FibriCheck® application, are summarized in **Table 5**. The specific questions belonging to each category, together with their weighting, can be found in **Addendum**. Results are weighted according to the different response categories: more positive or more negative responses are thus weighted accordingly. For purposes of readability, we did not plot the neutral answers. The response rates for the technology and FibriCheck® surveys was 97.2% and 87.4%, respectively.

Participants were most satisfied with the following aspects of the application: simplicity (79%), on-the-go heart rhythm analysis (79%) and the possibility to be followed remotely (73%).

Table 5: Questionnaires concerning technology perception and FibriCheck® usage

Technology perception

Ease of smartphone usage	 Neutral: 14.9%
Smartphone accessibility	
Technology acceptance	 Neutral: 7.6%
Data protection	 Neutral: 9.3%

FibriCheck® usage

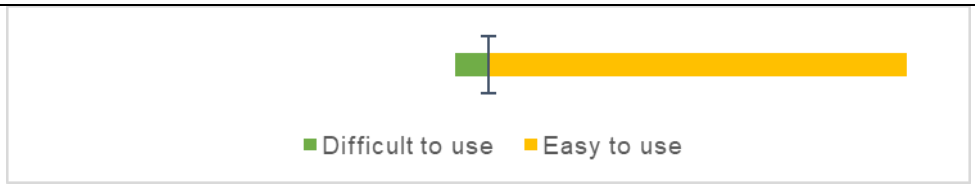
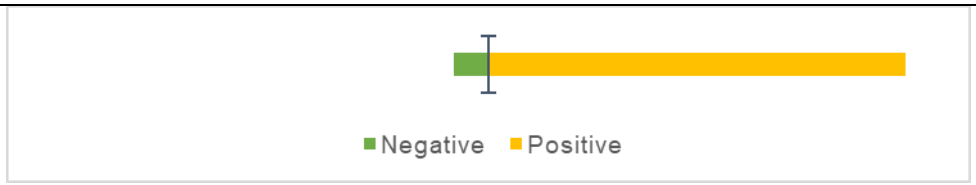
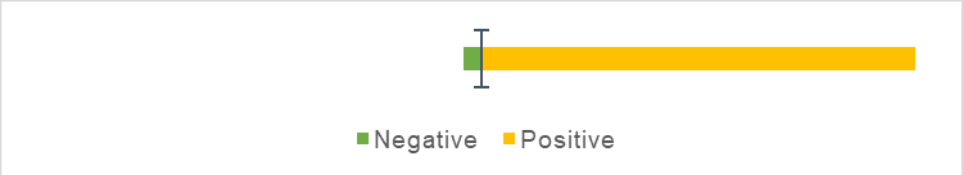
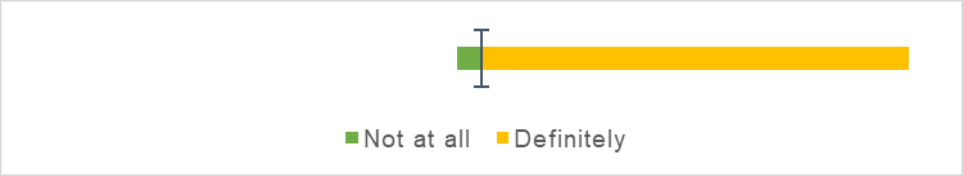
Difficulty	 Neutral: 12.9%
General satisfaction	 Neutral: 11.7%

Table 5 (cont.)

Feeling of safety / Reassurance	 Neutral: 8.8%
Physician relationship	 Neutral: 21.2%

Discussion

This pilot study concerned the easy-of-use and implementation of the AF case-finding app FibriCheck® in primary care. The study population was rather homogenous, and smartphone familiarity at baseline relatively poor. We found a high measurement compliance, with most participants finding the application easy to use. AF was detected in 5.8% of participants. Overall, user experience was positive, and most participants agreed the application gave them a feeling of reassurance and could benefit their doctor-patient relationship.

Participants

This pilot study merely focused on the feasibility of the introduction of an AF case-finding app in a primary care setting. As we were testing the app itself rather than its effect on the detection rate of AF, we did not add a control group and focused only on those patients we thought would benefit the most from such an app.

The study population of 92 participants was predominantly male, but there were no significant differences between men and women regarding risk factors and medication use at baseline. However, the proportion of men with a history of thrombosis or peripheral vascular disease was significantly greater.

Smartphone familiarity was rather poor in our study. Use of smartphones does tend to be lower in older populations, for reasons such as a lack of interest in current technologies, visual impairments, or financial problems (23,24). However, most participants in our study had no problems using the FibriCheck® application. There was some preliminary work involved in acquainting participants with the app, which took around 15 extra minutes in our study. This is not extraordinary, though quite significant in the daily schedule of a GP.

Measurements

An important feature of this pilot study was patient compliance. At the start of the study, participants were asked to measure at least twice a day, for 14 days or more. As this was a preliminary study in anticipation of a larger cluster-randomized trial, we set the bar for non-compliance quite low: only participants with no measuring activity for 2 weeks or more, were excluded from the study.

The 2-week mark proved easy to reach: the average study period was 23 days. This timeframe was chosen deliberately, as 14 days seems to be a sufficient time to detect most AF cases (25). The average number of measurements per day was 2.1, with a large spread (see **Figure 1**). Around 70% of participants measured twice a day or more. Methodologically similar studies found compliance rates ranging from 75% to 95% (14,25), whereas in other studies the measurements were performed in the presence of trained personnel (11,15).

The proportion of participants with AF in this study was 5.8%, higher than other comparable studies or the general population (14,25,26), most likely because we only included high-risk patients. Other studies differed significantly in the device used or the study design, which makes comparison difficult (11,12,15). The most indicated symptoms when conducting a FibriCheck® measurement (if there were any) were fatigue and palpitations, in line with findings from similar studies (14).

Quality of life

We asked participants to complete the SF36 questionnaire both before and after the study, to see if there were any appreciable changes in quality of life. There were no significant changes in any of the SF36 health domains, expect for Emotional Well-being, which showed a significant decrease. This could be due to any number of factors: added stress due to the enrolment in the study in general, or anxiety because of preoccupation with heart disease in particular, possibly amplified by having to test the heart rhythm at least twice a day. Patient anxiety could potentially be diminished when the device does not give direct feedback about the results, as in an ECG app (14).

Technology perception and application usability

The participants in our study were very accepting of the current technology and very open to try the FibriCheck® app, as most could see its benefit if data protection was properly ensured. Another study found that technology acceptance among the elderly seems to be increasing, provided certain barriers (privacy issues, design) are well taken care of (27). The FibriCheck® app was found to be easy to use, and it gave most participants a feeling of reassurance and safety. They also believed it improved their doctor-patient relationship.

Strengths and limitations

This was the first study to assess the feasibility of integrating the FibriCheck® app in a primary care setting. The study population was sufficiently homogenous to be able to draw some relevant conclusions. There was no control group, as this was merely a feasibility study. A comparison with routine care was thus not possible.

Overall, there were varying amounts of missing data, though generally not very much (up to 11% for the demographic data) and at acceptable levels for the different surveys. We decided to ignore missing data when reporting descriptive statistics but opted for mean value imputation in the surveys.

The proportion of participants with AF that was found in this pilot study was decidedly higher than in other similar studies or in the general population, because we only included high-risk patients.

Conclusions and implications for practice

Integrating a smartphone application such as FibriCheck® in primary care, seems to be an easy way to complement routine screening. We found high rates of patient satisfaction, reassurance, and compliance. Smartphone familiarity might still be an issue, although most participants of this study had no problem using the app.

The findings in this study could pave the way for the routine use of new technology in a general practice setting. Given the widespread use of smartphones, screening apps could be a cost-efficient way of complementing routine care with smart technology. As technology acceptance among the elderly will continue to increase, so will the relevance of screening apps.

More research is needed to compare the diagnostic yield of such apps with usual care. Cost-benefit issues and potential barriers to large-scale implementation should be identified.

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Addendum

Table A1: Technology perception questionnaire with weighting

Subject	Question	Response categories				
		Fully agree	Agree	Neutral	Disagree	Fully disagree
Ease of smartphone usage	I think I need help to install the application	+2	+1	0	-1	-2
	I had to train myself to use a smartphone for this project	-2	-1	0	+1	+2
		Yes			No	
	I worked with a smartphone before	+1			-1	
		Never used	Once	I can use it	Useful	Very useful
	How easily can you operate a smartphone?	-2	-1	0	+1	+2
		Yes			No	
Smartphone accessibility	I already have a smartphone	+1			-1	
	I have internet access	+1			-1	
		Yes		No internet	No children	
	I have (grand)children who use a smartphone	+1		-1	0	
		Fully agree	Agree	Neutral	Disagree	Fully disagree
Technology acceptance	Are you open for changes or new innovations?	+2	+1	0	-1	-2
	Do you trust that your smartphone can accurately register measurements?	+2	+1	0	-1	-2
	Healthcare should get more initiatives to follow patients with mobile technology	+2	+1	0	-1	-2
		Fully agree	Agree	Neutral	Disagree	Fully disagree
Data protection	Protection of personal information and privacy is important in general	+2	+1	0	-1	-2
	My privacy is important	+2	+1	0	-1	-2

Table A2: FibriCheck® usage questionnaire with weighting

Subject	Question	Response categories				
		Fully agree	Agree	Neutral	Disagree	Fully disagree
Difficulty of the app	I am convinced that other users have no problems with the application	+2	+1	0	-1	-2
	The application was easy to use	+2	+1	0	-1	-2
	I need help to conduct measurements	-2	-1	0	+1	+2
	The application is complex to use	-2	-1	0	+1	+2
	The different functions of the application were clear	+2	+1	0	-1	-2
	I can use the application independently	+2	+1	0	-1	-2
	The result screen was clear	+2	+1	0	-1	-2
		Fully agree	Agree	Neutral	Disagree	Fully disagree
General satisfaction	I was satisfied about the FibriCheck® product	+2	+1	0	-1	-2
	I would like to continue to use the application after this project	+2	+1	0	-1	-2
	FibriCheck® delivers an added value for the patient	+2	+1	0	-1	-2
	The application was not well designed	-2	-1	0	+1	+2
	The application was bad and not developed properly	-2	-1	0	+1	+2
	I found it positive to register my symptoms	+2	+1	0	-1	-2
		Fully agree	Agree	Neutral	Disagree	Fully disagree
Feeling of safety / Reassurance	FibriCheck® made me feel safe	+2	+1	0	-1	-2
	Did you feel safe using FibriCheck®?	+2	+1	0	-1	-2
	Do you feel reassured knowing that you can always receive support?	+2	+1	0	-1	-2

Table A2 (cont.)

Feeling of safety / Reassurance	Do you feel reassured knowing that your physician can remotely follow your results?	+2	+1	0	-1	-2
	I find it positive that all my data is automatically sent to my healthcare provider	+2	+1	0	-1	-2
		Fully agree	Agree	Neutral	Disagree	Fully disagree
Physician relationship	I feel that FibriCheck® benefits the relation with my healthcare provider	+2	+1	0	-1	-2
	The communication with my healthcare provider has improved	+2	+1	0	-1	-2
	Do you expect that the communication with your healthcare provider will improve?	+2	+1	0	-1	-2