Mobile photoplethysmographic technology to detect atrial fibrillation

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Mobile Health Technology for Atrial Fibrillation Screening Using Photoplethysmography-Based Smart Devices: The HUAWEI Heart study

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Abstract
Background: Low detection and nonadherence are major problems in current management approaches for patients with suspected atrial fibrillation (AF). Mobile health (mHealth) devices may enable earlier AF detection, and improved AF management.
Objectives: To investigate the effectiveness of AF screening in a large population-based cohort using smart device based photoplethysmography (PPG) technology, combined with a clinical care AF management pathway using a mHealth approach.
Methods: AF screening was performed with smart devices using PPG technology (Huawei Technologies Co., Ltd., Shenzhen, China) which were made available for the population aged over 18 years across China. Monitoring for at least 14-days with a wristband (HONOR BAND 4) or wristwatch (HUAWEI WATCH GT, HONOR WATCH), was allowed. The patients with ‘possible AF’ episodes using the PPG algorithm were further confirmed by health providers among the MAFA (mobile AF App) Telecare center and network hospitals, with clinical evaluation, electrocardiogram (ECG), or 24-h Holter.
Results: There were 246,541 individuals who downloaded the PPG screening App, and 187,912 individuals used smart devices to monitor their pulse rhythm between October 26, 2018 and May 20, 2019. Among those with PPG monitoring (mean age 35 years, 86.7% male), 424 (mean age 54 years, 87.0% male) received a ‘suspected AF’ notification (424/187,912, 0.23%). Of those effectively followed up, 227 individuals (227/262, 87.0%) were confirmed as having AF, with the positive predictive value (PPV) of PPG signals being 91.6% (95% confidential interval (CI) 91.5%-91.8%). Both ‘suspected AF’ and ‘identified AF’ markedly increased with age (p for trend <0.001), and individuals in Northeast China had the highest proportion of detected AF of 0.28% (95%CI 0.20-0.39). Of the individuals with identified AF, 216 (216/227, 95.1%) subsequently entered a programme of integrated AF management using a mobile AF application (mAFA); approximately 80% of ‘high risk’ patients were successfully anticoagulated.
Conclusions: Based on the present study, continuous home-monitoring with smart device based PPG technology could be a feasible approach for AF screening. This would help efforts at screening and detection of AF, as well as early interventions to reduce stroke and other AF-related complications.

Condensed Abstract: The study aimed to determine the feasibility of AF screening in a large population-based cohort using smart device based photoplethysmography (PPG) technology, combined with a clinical care AF management pathway. There were 187,912 individuals used smart devices to monitor their pulse rhythm between October 26, 2018 and May 20, 2019. 87.0% were confirmed as having AF, with the PPV of PPG signals being 91.6%. Following entry into a programme of integrated AF management using a mobile AF application, approximately 80% of high risk patients were successfully anticoagulated. Based on the present study, continuous home-monitoring with smart device based PPG technology could be a feasible approach for AF screening. This would help efforts at screening and detection of AF, as well as early interventions to reduce stroke and other AF-related complications.

Keywords: atrial fibrillation, screening, photoplethysmography, integrated care

Abbreviations:
AF = atrial fibrillation
ECG = electrocardiogram

PPG = photoplethysmography
USPSTF = US Preventive Services Task Force
mAF App = mobile atrial fibrillation application
PPV = positive predictive value
CHA2DS2-VASc = congestive heart failure, hypertension, age ≥75, diabetes, stroke, vascular disease, age 65–74, and sex category (female)
HAS-BLED = hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalised ratio, elderly, drugs/alcohol concomitantly
SAMe-T2T2R = sex female, age, medical history, treatment, tobacco use, race

Introduction

Low detection and nonadherence are major problems in current management approaches for patients with suspected atrial fibrillation (AF). AF screening has been advocated with the recognition that this could ultimately reduce AF-related stroke and death, with the initiation of treatments such as oral anticoagulation, and other risk-factor modifications to reduce AF-related complications and arrhythmia progression [1]. Indeed, active screening strategies could improve detection of AF in comparison with routine care. Nonetheless, a systematic screening strategy for AF did not show an obvious advantage to opportunistic screening, using pulse palpation and a 12-lead electrocardiogram (ECG) [2].

Recent advances in mobile and wearable devices provide a possible solution [3]. New technology has been developed to improve the early detection of AF and among these, photoplethysmography (PPG) and single lead ECG recordings are promising methods available to the public for detecting AF [4]. In the STROKESTOP study, a handheld ECG recorder for intermittent ECG recordings over 2 weeks improved AF diagnosis in high-risk population aged 75-76 years old [5]. Another AF screening approach with twice-weekly single-lead ECG recorders among those aged over 65 years identified more incident AF than routine care, but adverse clinical events (including stroke, thromboembolism, death, etc.), were not significantly different over a 52-week follow-up period [6]. Hence, it has been questioned how AF screening could have a more beneficial effect on subsequent AF management, and the U.S. Preventive Services Task Force (USPSTF) recently concluded that the current evidence was insufficient to assess the balance of benefits and harms of screening for atrial fibrillation with ECG [7]. Similarly, current U.K. National Screening Committee policy recommends that population screening for AF should not be offered by the National Health Service [8]. Thus, more evidence on strategies for improving AF screening, detection and subsequent management to reduce AF-related adverse outcomes is needed.

Approaches using random brief ECG screening could possibly miss those individuals with a low burden of (paroxysmal) AF, and long-term continuous screening may overcome the problem. An ECG skin adhesive patch, which could provide 14-day monitoring, resulted in a higher proportion of AF diagnosis compared with delayed monitoring; however, nearly one third of subjects refused to use the ECG patch, and some individuals reported skin irritation, resulting in early discontinuation structured management [9]. A smartwatch strap with single ECG sensor may be a more comfortable method, with 93% sensitivity and 84% specificity of AF diagnosis compared to a 12 lead ECG, but only 66% of monitored signals could be interpretable with the app algorithm alone 10]. Thus, the stability of the signal quality and motion artifacts are additional considerations when considering an ECG-based approach to AF screening.

In contrast, increasing evidence supports PPG-monitoring for AF screening [11,12,13]. Mass screening for AF has been carried out using smartphone cameras with reliable PPG signals [14]. In our previous pilot study, both smartphones and smart bands with PPG demonstrated good performance in detecting AF [15]. Hence, it may be more practical to screen for AF in a large population using a PPG-based smart device, especially if integrated with a structured management program for AF, again based on smart technology. In a pilot study of such a structured management program, we showed that a mHealth technology-supported AF application (mAF App) could be developed and validated, integrating patient clinical decision support tools, guideline-based treatment, educational materials and patient involvement strategies with self-care protocols and structured follow-up [16].

In the Huawei Heart Study, our aim was to screen for AF and report the incidence of AF identified, as well as the proportion of AF patients being anticoagulated. We hypothesized that use of a mobile health PPG technology approach would facilitate AF screening, and the associated App-based integrated AF care approach would result in early AF detection and increased use of oral anticoagulation. The latter could have the potential in reducing AF-related complications such as stroke and mortality [17].

Methods

The Mobile health technology for improved screening, patient involvement and optimizing integrated care in Atrial Fibrillation (MAFA II) study program was developed to verify a screening and integrated care approach to improving AF management. The 'Pre-MAFA' study was the first stage of the MAFA II program, using HUAWEI smart technology (herein referred to as the 'Huawei Heart Study') to test the feasibility of continuous home-monitoring with PPG technology in a large population [18] (Online Figure 1). Identified AF patients were then transferred into a structured program of holistic and integrated care using a smartphone App (mAF App) [18]. The present report only focuses on the 'Huawei Heart Study', which is the AF screening component ('Pre-MAFA') of this programme.

AF screening with smart devices using PPG technology (Huawei Technologies Co., Ltd., Shenzhen, China) were made available for the population aged over 18 years across China. Inclusion criteria included use of the Huawei phone (Android 5.0 or higher), and one of following smart devices: Huawei Watch GT (Version 1.0.3.52 or higher), Honor Watch (Version 1.0.3.52 or higher), and Honor Band 4 (Version 1.0.0.86 or higher). The participants needed to have compatible HUAWEI smart device(s) and phone. Exclusion criteria included age <18 years, and inability to use smart phone or devices. At least 14-day monitoring with smart devices based on PPG (with the PPG algorithm developed by Huawei) was proposed. The study was approved by the Central Medical Ethic Committee of Chinese PLA General Hospital (Approval number: S2017-105-02) and registered at the Chinese Clinical Trial Registry (ChiCTR) website (ChiCTR-OOC-17014138). Subjects could freely download the app in the HUAWEI Appstore. All subjects who were interested in the study were informed of the study design and gave their informed consent before entering the study. Adults downloading the AF screening App across China mainland were enrolled into present Pre-MAFA study analysis between October 26, 2018 to May 20, 2019.

AF detection

An AF screening App was developed based on the Android Operating System (Google, Mountain View, California). The individuals could initiate rhythm monitoring with AF screening App using smart devices. The users could also start directly AF detection with MAFA (**Figure 1**). The irregular pulse wave would be screened with active or periodic measuring using the PPG algorithm. Individuals could initiate active measurements at rest, and 45-second PPG signals would be collected. Periodic measurements would be automatically be taken every 10 minutes, and 60-second PPG signals would continuously be collected. The discrimination rule of the PPG algorithm and notification of 'suspected AF' is shown in **Figure 2.** A notification of 'suspected AF' would be delivered, once the proportion of 'possible AF' episodes was 100%, when ten measurements were initiated. In the case of PPG measurements >10, the threshold T was set to ensure that the positive predictive value of making a decision was over 0.85, and the sensitivity would be as high as possible. The T could be adjusted to a more suitable value with enough study data were collected. The notification of 'suspected AF' would also be delivered once the proportion of ‘possible AF’ episodes over threshold T in the setting of PPG measurements was >10 (**Figure 2)**.

AF *diagnosis* and management

The individuals with ‘suspected AF’ episodes using the PPG algorithm were further confirmed by the health providers using the MAFA Telecare center and network hospitals, with clinical evaluation, ECG, or 24-h Holter (Online Figure 2). Individuals with ‘identified AF’ would be managed according to an App-based AF integrated care pathway approach, based on the ABC (‘A’ Avoid stroke, ‘B’ Better symptom management, and ‘C’ Cardiovascular risk and comorbidity management) pathway [19]. The ABC pathway approach has been associated with improved clinical outcomes in various independent cohorts [20,21,22].

Statistical analysis

Continuous variables were tested for normality by the Kolmogorov-Smirnov test. Data with a normal distribution were presented as a mean (standard deviation, SD). Data with a non-normal distribution were presented as median (interquartile range, IQR) and were analyzed by using Kruskal-Wallis test. $\chi 2$ test was used for categorical variables. Data visualization analysis was utilized for the enrollment across China with ECharts, version 4.2.1 (Apache Software Foundation).

The “irregular pulse rhythm” by PPG algorithm was observed, and the predictive ability of AF with PPG algorithm was analyzed in comparison with the confirmed diagnosis of AF using clinical evaluation, ECG, or 24-h Holter by the health providers from the MAFA Telecare center and network hospitals. The proportion of "identified" AF from the general population screening that were enrolled into the subsequent main MAFA integrated care trial was calculated to explore the feasibility of the approach AF screening combined with integrated care.

The monitoring method for first “suspected” AF was calculated, and “suspected” AF episodes in relation to measurement method, the automatic periodical measurements and active measurements, were analyzed using the Kruskal-Wallis test for the comparations among different measurement approaches. Moreover, the influence of the continuous monitoring time on first detected "suspected" and “identified" AF episodes were investigated, to explore the optimal screening "window". Incident AF was analysed in relation to age strata, sex, and region. Finally, AF management among individuals with "identified" AF enrolled into an App-based AF integrated care structured programme with the mAFA trial, were investigated, including their stroke risk, bleeding risk, and the likelihood for good anticoagulation control. Anticoagulant use classified by risk assessment is reported, while the changes on oral anticoagulant use among different risk strata were compared.

A 2-sided P-value <0.05 was considered as statistically significant. The 95% confidential intervals (CIs) were calculated with Wilson score method without continuity correction [18]. Statistical analysis was performed using IBM SPSS Statistics, version 25.0 (SPSS Inc.).

Results

There were 246541 individuals who downloaded the PPG screening app, and 187912 individuals used smart devices to monitor their pulse rhythm between October 26, 2018 and May 20, 2019. Enrollment and baseline characteristics are summarized in Online Figure 3 **and Table 1.**

Monitoring method and identification

There were 265,139 ‘suspected AF’ episodes for 424 subjects (mean age 54 years, 87.0% male) among 187,912 subjects screened (mean age 35 years, 86.7% male). Of the ‘suspected AF’ subjects, 262 (262/424, 61.8%) were effectively followed up with full medical history, physical examination, ECG, or 24-hour Holter (**Figure 3**). Of those with full assessment, 227 (227/262, 87.0%) subjects were confirmed as having AF. Cardiac rhythms of 'suspected AF' episodes are summarized in Online Figure 4.

There were 186,956 'identified AF' episodes for the 227 subjects and 203,985 episodes for the 262 'suspected AF' subjects. The positive predictive value (PPV) of PPG signals was 91.6% (95%CI 91.5%-91.8%). Individuals with 'suspected AF' episodes were mostly monitored using automatic periodical measurements (periodical vs. active measurements, 37.0% vs. 7.6%, $p<0.001$) (Online Figure 5, Online Table 1). 70.8% of AF episodes were found within 14 days, but nearly one third of AF episodes were recorded after two weeks (**Figure 4**). The distribution of monitoring time in the whole cohort is shown in Online Figure 9. Supplementary material online summarizes user reported adverse events (Online Table 2), a comparison performance of the various smart devices utilized in PPG screening (Online Table 3), and the standby time of the various smart devices with or without PPG screening (Online Table 4). They show generally high specificity (approx. 99%), sensitivity (100%) and accuracy (>99%), irrespective of smart device used.

AF episodes in the general population

Incident 'suspected AF' and 'identified' AF markedly increased with age (p for trend <0.001) (**Figure 5**). The highest proportion of AF episodes was among the elderly, ie. those aged over 65 years, with 2.78% (95% CI 2.28-3.38) being 'suspected AF', and 1.70% (1.31-2.19) being 'identified' AF (**Figure 5**). There was a higher risk of incident AF in individuals aged over 55 years compared to those aged under 55 years (2.62% vs 0.17%; $p<0.001$). The prevalence of detected AF was highest in Northeast China compared to other regions in China ($p<0.001$, Online Figure 6).

AF management

216 (216/227, 95.1%) individuals with 'identified AF' were entered into an App-based AF integrated care structured program with MAFA (**Figure 3**); of these, 29 (29/216,13.42%) who initiated MAFA to monitor the rhythm were subsequently found to have a known AF diagnosis. Clinical decision support tools were provided for doctors and patients (Online Table 5). The patient's personized stroke risk was assessed with the CHA2DS2-VASc score (mean, SD, 1.07, 1.09), while bleeding risk was assessed using the HAS-BLED score (mean, SD, 0.35, 0.52), respectively. Their likelihood for good anticoagulation control was assessed using the SAMe-T2T2R score (mean, SD, 3.71, 0.66). Distribution of subjects according to these scores are shown in Online Table 5.

Overall, 79.6% of patients at high-risk were anticoagulated (Table 3). There was no difference in risk characteristics and anticoagulant use among high-risk individuals comparing individuals with newly detected AF and with known AF (Table 2).

Discussion

In the Huawei Heart Study, we show that PPG-based smart devices were feasible as an easy-to-use screening tool in this population-based, large-scale AF screening study, with a good performance for AF detection (**Central Illustration**). Second, the heterogeneity of incident AF, in relation to regions and age, suggests the need for a different prevention approaches based on local population requirements. Thus, the use of mobile and wearable devices could provide a simple, feasible and practical mHealth approach for AF early detection, that can be followed by guideline-guided app-based intervention.

AF management integrated with AF detection might provide more benefits for patients. Previous studies have demonstrated that smart devices (smartphone, E-patch, handing device, wrist band, etc.) can be used for AF detection [5,6,9,10,11,12,13,14,15]; however, an integration with subsequent clinical management of 'screened AF' was lacking. In the present Huawei Heart Study (Pre-MAFA), 95.1% of individuals with identified AF, who screened from general population, were entered into an AF integrated care program with MAFA, providing guideline-guided intervention and leading to a high proportion of patients being successfully anticoagulated.

The clinical decision support within the MAFA program with CHA_2DS_2-VASc, HAS-BLED, and SAMe-TT_2R_2 scores on the MAFA platform provides risk-assessment advice for doctors, and facilitates sharing decision making for the patients. In this study, approximately 80% of 'high risk' AF patients in MAFA received oral anticoagulants (OACs), which is a marked improvement over prior reports of suboptimal thromboprophylaxis in prior Chinese cohorts [23,24,25]. Thus, AF screening, combined with a clinical integrated care program for detected AF, may translate to better treatment and prevention of AF-related major complications, such as stroke and death.

The continuity, comfort and the stability of monitoring signals, that are not influenced by motion, are challenges for a good predictive ability for AF using smart devices. A lower accuracy in ambulatory than sedentary patients has been observed with a Cardiogram app using a wristwatch [26]. Indeed, only 66% of monitoring signals could be interpretable with a single-lead ECG wristwatch by App algorithm alone [10]. In the present study, 91.6% of PPG positive signals by algorithm were confirmed as AF. The improved screening ability of AF with the present PPG-based smart devices possibly stems from frequent, continuous monitoring and the good quality of monitoring signals. With a single battery life (average standby time with HUAWEI smart devices is 6.7 days with PPG screening), periodic measurements could be taken automatically every 10 minutes in this study, which was far more frequent than obtained from the Apple watch in the Apple Heart Study, with measurements only taken every two hours at baseline, which was then increased to every 16 minutes once an irregular tachogram was detected [27]. In addition, the discrimination of the PPG algorithm could possibly contribute to the better detection of AF, as shown in this study.

Our study found that most AF episodes were found within 14 days, but nearly one third of AF episodes were detected on monitoring after 2 weeks. In the case of paroxysmal AF, the time to the first detection has been inversely related to AF burden [28,29]. Automatic periodic PPG measurements have the advantage of active measurements in the search for AF episodes in this study, suggesting that a continuing monitoring approach was better than single-point intermittent monitoring. Our study also supports the possibility that PPG-based wrist-worn wearables (watches, bands) would be the good choices for AF screening [30,31].

In this study, the prevalence of 'suspected AF' of 0.2% in the general population was lower than the 0.5% reported in Apple Heart Study [27]. There are possibly several reasons for this. This was much younger population with 1.8% who were aged over 65 years old in the present study, compared to 6% being aged over 65 years old in Apple Heart Study [27]. There is also a lower incidence and prevalence of AF in the Chinese population compared to the Western population [32,33]. The strict discrimination rule of the PPG algorithm may also contribute to the low prevalence of detected AF.

However, a trend for increasing detected AF with aging was evident in the Chinese population, with a fifteen-fold (2.62/0.17) greater AF risk in those aged >55 years compared to those aged < 55 years; this difference was only eight-fold (4.5/0.53) in the Apple Heart Study. AF screening might be much more beneficial for those at high-risk of AF, (e.g., population with age >55 years). The cost effectiveness of AF screening related to different population risks would need to be ascertained in future studies. In addition, we noted a geographical difference in incident AF in the present study, with the highest prevalence of AF in Northeast China that was consistent with the distribution of clinical risk factors for AF (Online Table 6). The heterogeneity of risk factors incident AF may suggest the need for different prevention approaches in different settings based on local clinical risk profiles.

Strengths and limitations

There were several limitations in this study. We were not doing a trial of the efficiency of AF screening since the current study relates to the "yield" with the current technology and the specificity of the diagnosis, rather than sensitivity. Although we had strict follow-up procedures for ‘suspected AF’, there were 38% of individuals with ‘suspected AF’ who could not be effectively followed up, which would decrease the proportion of identified AF. For the PPV calculation with PPG signals, we did not have real-time 12-lead ECG data synchronized with PPG-based smart devices. Indeed, it would be difficult to make all individuals have a 14-day 12-lead Holter examination with a mass population screening study. However, the diagnosis of AF was confirmed with medical history, physical examination, ECG or 24-Holter by healthcare providers. While we aimed to focus on newly diagnosed or detected AF, 29 subjects were subsequently found to have known AF, as was also seen in the Apple Heart Study, where 15% with known AF entered that study [27]. Also, incident AF detection in present study might be impacted by the availability of smart phones and devices. In the present study, 24% of subjects downloaded the App but were without compatible smart devices. The underlying reason(s) may be multifactorial; however, 187,912 individuals were entered into the study, suggested the PPG-based smart device could still be a feasible screening strategy. Finally, we did not report on hard outcomes (stroke, death, etc) impacted with AF screening approach in the present Pre-MAFA study and would be further reported in the future from the ongoing MAFA II trial [18].

Conclusion

Continuous home-monitoring with smart device-based PPG technology is a feasible approach for screening and early detection of AF in a large population. This could help efforts at screening and detection of AF, as well as early interventions to reduce stroke and other AF-related complications.

Perspectives

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: We demonstrate the feasibility of AF screening in a large population-based cohort using smart device based photoplethysmography (PPG) technology, combined with a clinical care AF management pathway. Following entry into a program of integrated AF management using a mobile AF application, approximately 80% of high-risk patients were successfully anticoagulated.

TRANSLATIONAL OUTLOOK: Continuous home-monitoring with smart device-based PPG technology could be a feasible approach for AF screening. This would help efforts at screening and detection of AF, as well as early interventions to reduce stroke and other AF-related complications. This integrated approach should be verified in randomized trials.

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Figure Legends

Figure 1: AF screening flow diagram. *MAFA: mobile Atrial Fibrillation Application.

Figure 2: The notification of “suspected” AF by algorithm. *N>10, 0<T<1, seen AF detection in the Method in the text.

Figure 3: AF screening, confirmation, and transference into MAFA. Inclusion: Adult ≥18 years; Huawei phone (Android 5.0 or higher); Smart devices: Huawei Watch GT (Version 1.0.3.52 or higher), Honor Watch (Version 1.0.3.52 or higher), Honor Band 4 (Version 1.0.0.86 or higher). Exclusion: Adult <18 years; Inability to use smart phone or devices.

Figure 4: Monitoring time to first AF episode. The monitoring time to first detected AF episode were classified by 0-7 days, 8-14 days, 15-21 days, 22-30 days, and >31 days.

Figure 5: Incident “suspected” and “identified” AF among 187,912 population. The incident "suspected" and "identified" AF were shown in relation to age- and sex-proportions.

Central Illustration: Mobile health devices could be a feasible approach for AF screening, and into subsequent AF integrated management. MAFA: mobile Atrial Fibrillation Application.

Table 1: Baseline characteristics.

	Overall Cohort (n=187,912)	Notification (n=424)	Individuals with clinical evaluation (n=262)	Identified AF (n=227)
Suspected AF episodes, n	265,139	265,139	203,985	186,956
Female, n (%)	24938 (13.3)	55(13.0)	43(16.4)	42(18.5)
Age, mean (SD)	34.7(11.5)	54.1(14.3)	54.9(14.0)	56.1(13.7)
≥65, n (%)	3419 (1.8)	95(22.4)	62(23.7)	58(25.5)
55-64, n (%)	7491 (4.0)	112(26.4)	71(27.1)	69(30.4)
40-54, n (%)	44432 (23.6)	136(32.1)	82(31.3)	64(28.2)
20-39, n (%)	132570 (70.5)	81 (19.1)	47(17.9)	36(15.9)
Location				
East China, n (%)	57,177 (30.4)	116 (27.4)	67 (25.6)	58 (25.6)
North China, n (%)	32,488 (17.3)	98 (23.1)	71 (27.1)	63 (27.8)
Central China, n (%)	26,033 (13.9)	42 (9.9)	25 (9.5)	19 (8.4)
South China, n (%)	21,333 (11.4)	36 (8.5)	23 (8.8)	20 (8.8)

Southwest China, n (%)	17,156 (9.1)	30 (7.1)	15 (5.7)	13 (5.7)
Northwest China, n (%)	12,762 (6.8)	30 (7.1)	15 (5.7)	14 (6.2)
Northeast China, n (%)	12,805 (6.8)	62 (14.6)	42 (16.0)	36 (15.9)
Others, n (%)	8,158 (4.3)	10 (2.4)	4 (1.5)	4 (1.8)

Table 2: Risk assessments and anticoagulant use of the 216 patients entered into the MAFA programme.

(n,%)	Individuals with newly detected AF (n=187)	Individuals with known AF (n=29)	p
CHA_2DS_2-VASc score			
(mean, SD)	1.04(1.05)	1.24 (1.35)	0.365
(median, interquartile range)	1(0-2)	1(0-2)	
HAS-BLED score			
(mean, SD)	0.33(0.52)	0.48(0.57)	0.141
(median, interquartile range)	0(0-1)	0(0-1)	
SAMe-T_2T_2R score			
(mean, SD)	3.72 (0.63)	3.66 (0.85)	0.644
(medican, interquartile range)	4(3-4)	4(3-4)	
*Individuals at high risk (n,%)	46 (24.60)	8 (27.59)	0.730
Anticoagulant use amongst patients at high risk	35(76.09)	8 (100%)	0.266

* Individuals at high risk: CHA_2DS_2-VASc ≥3 in females, ≥2 in males.

See Figure 3 for patient flow.

Table 3: Oral anticoagulant use in AF patients.

	Low risk	Intermediate risk	High risk
N (%)	91 (42.1)	71(32.9)	54 (25.0)
Anticoagulant use at baseline, n%	5 (5.49)	9 (12.68)	43 (79.63)
Anticoagulant use at 3 months, n%	3 (3.30)	29 (40.85)	42 (77.78)
p	0.372	<0.001	0.673

* Low risk: CHA_2DS_2-VASc of 0 in males, or 1 in females; Intermediate risk: CHA_2DS_2-VASc of 2 in female, 1 in male; High risk: CHA_2DS_2-VASc ≥3 in females, ≥2 in males. McNemar's test was used for testing the difference.

The reasons for patients with or without oral anticoagulants (OACs) on baseline:

- Low risk patients with OACs at baseline: 2 patients undergoing AF ablation, with OAC used after discharge, 2 patients with current onset acute AF episodes, and 1 patient with rheumatic valvular heart disease.
- High risk patients without OACs at baseline: six patients who were unwilling to accept anticoagulants, four patients with antiplatelets (aspirin or clopidogrel), and one patient anticoagulated with traditional Chinese medicine.

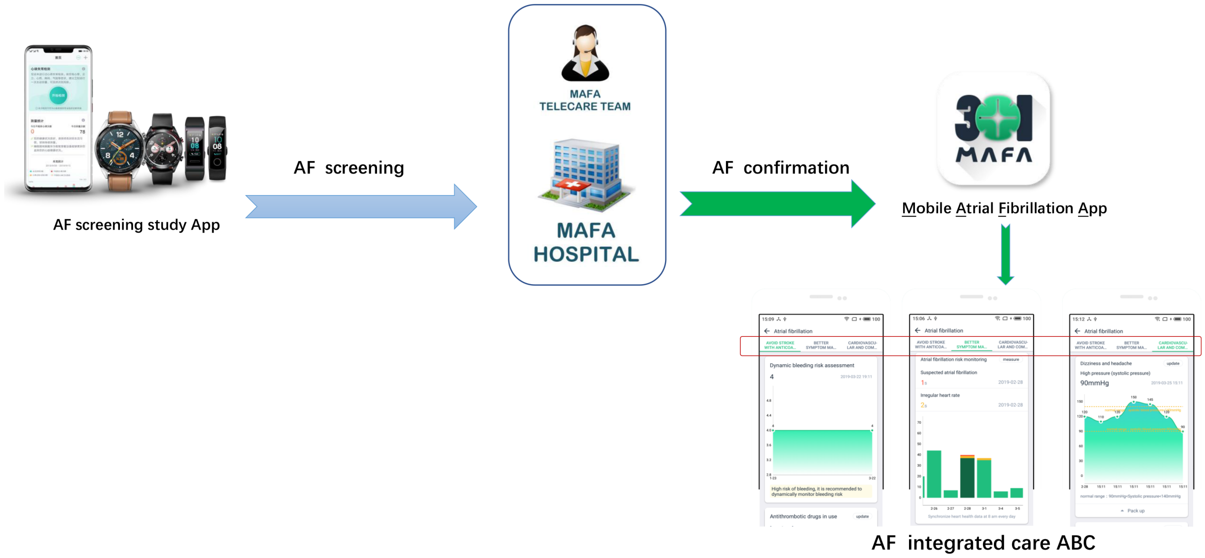


Figure 1 AF screening flow diagram

*MAFA: mobile Atrial Fibrillation Application

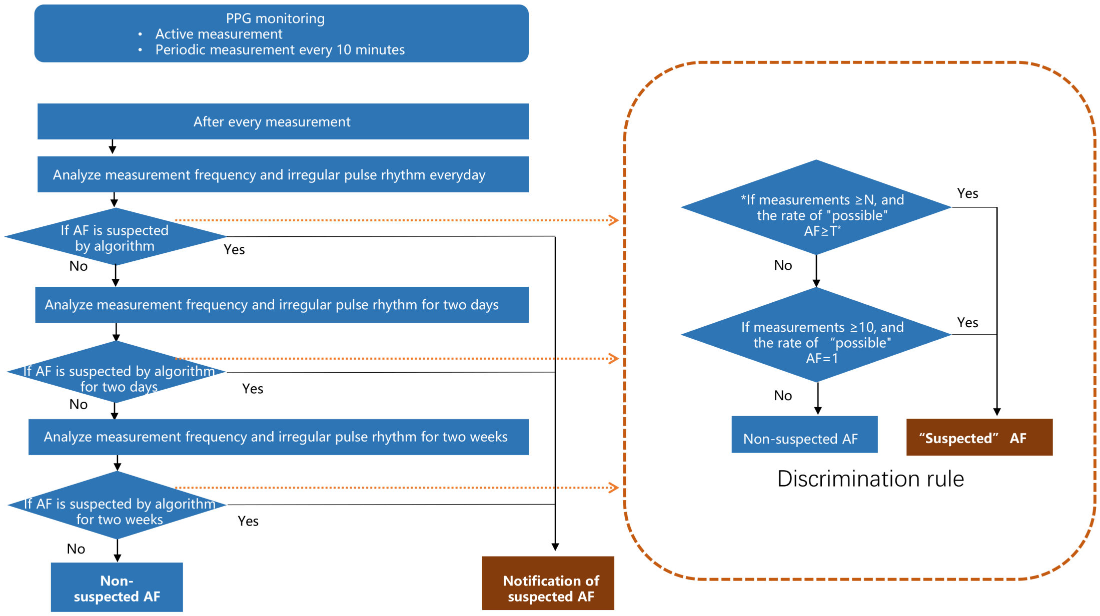


Figure 2 The notification of "suspected" AF by algorithm *N>10, 0<T<1, See AF detection in the Method in the text.

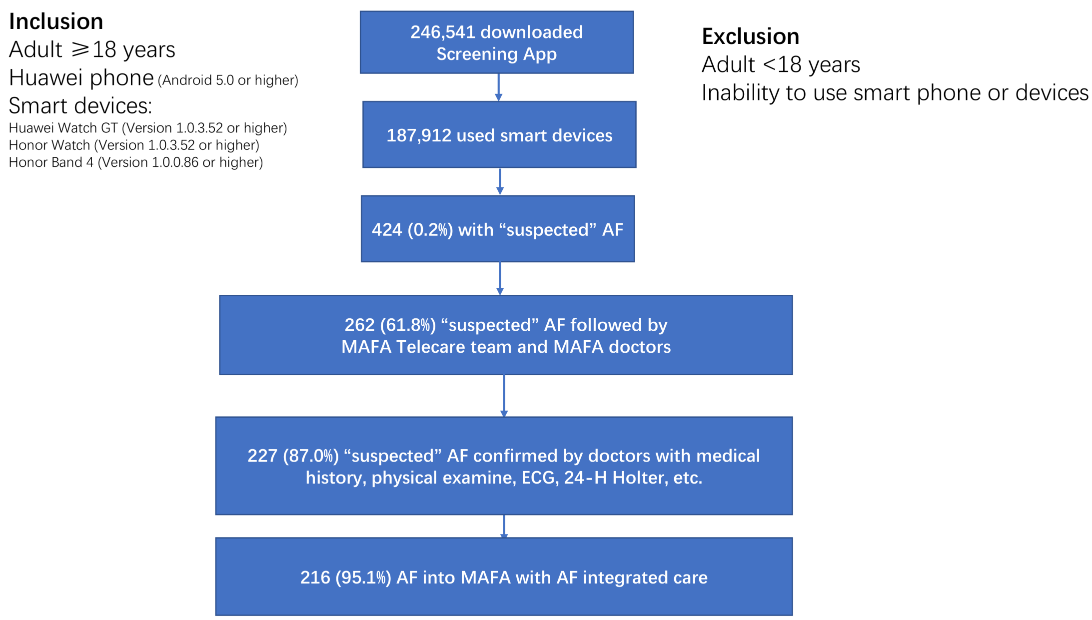


Figure 3 AF screening, confirmation, and transference into MAFA

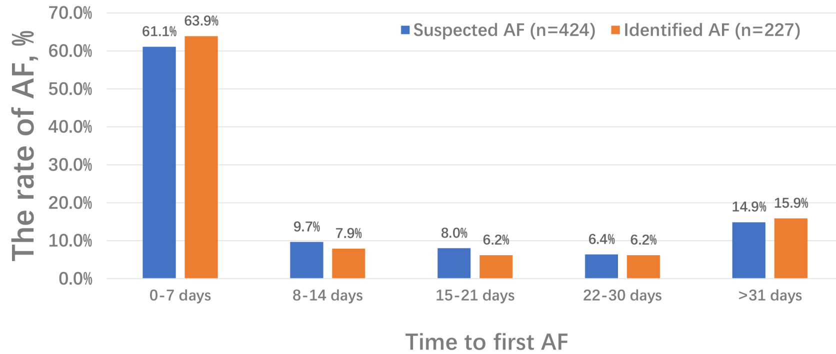
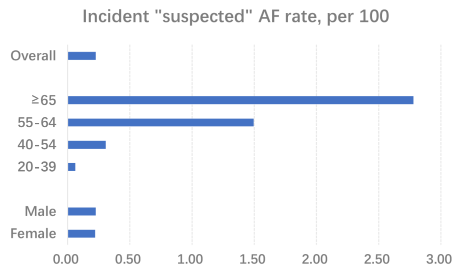


Figure 4 Monitoring time to first detected AF episode

	Suspected AF	Total	%	95%CI
Overall	424	187912	0.23	(0.21-0.25)
⩾65	95	3419	2.78	(2.28-3.38)
55-64	112	7491	1.50	(1.24-1.80)
40-54	136	44432	0.31	(0.26-0.36)
18-39	81	132570	0.06	(0.05-0.08)
Male	369	162972	0.23	(0.20-0.25)
Female	55	24938	0.22	(0.17-0.29)



	Identified AF	Total	%	95%CI
Overall	227	187912	0.12	0.11-0.14
⩾65	58	3419	1.70	(1.31-2.19)
55-64	69	7491	0.92	(0.73-1.16)
40-54	64	44432	0.14	(0.11-0.18)
18-39	36	132570	0.03	(0.02-0.04)
Male	185	162972	0.11	(0.10-0.13)
Female	42	24938	0.17	(0.12-0.23)

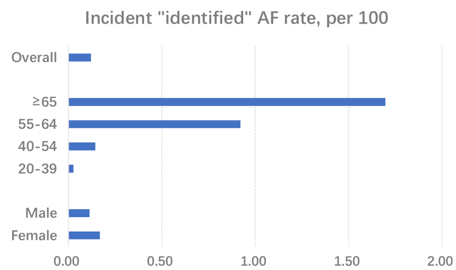
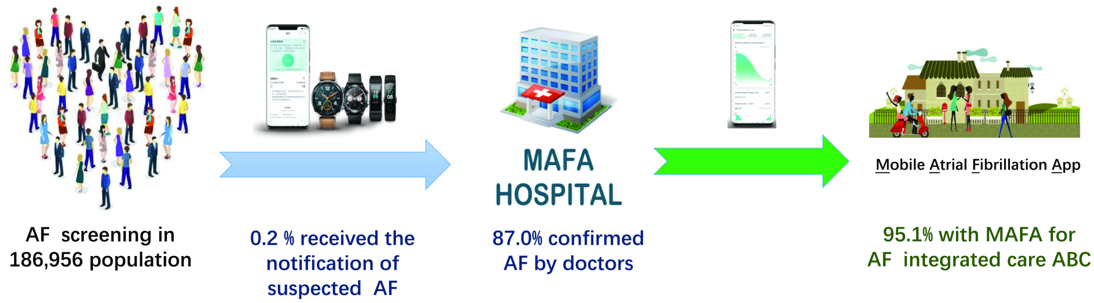
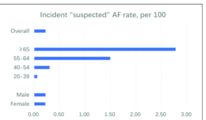


Figure 5 Incident“suspected”and“identified”AF among the screened population (n=187912)



Incident“suspected”and“identified”AF

	Suspected AF	Total	%	95%CI
Overall	424	187912	0.23	(0.21-0.25)
⩾65	95	3419	2.78	(2.28-3.38)
55-64	112	7491	1.50	(1.24-1.80)
40-54	136	44432	0.31	(0.26-0.36)
18-39	81	132570	0.06	(0.05-0.08)
Male	369	162972	0.23	(0.20-0.25)
Female	55	24938	0.22	(0.17-0.29)



	Identified AF	Total	%	95%CI
Overall	227	187912	0.12	0.11-0.14
⩾65	58	3419	1.70	(1.31-2.19)
55-64	69	7491	0.92	(0.73-1.16)
40-54	64	44432	0.14	(0.11-0.18)
18-39	36	132570	0.03	(0.02-0.04)
Male	185	162972	0.11	(0.10-0.13)
Female	42	24938	0.17	(0.12-0.23)

Oral anticoagulant use in AF patients with MAFA

	Low risk	Intermediate risk	High risk
N (%)	91 (42.1)	71(32.9)	54 (25.0)
Anticoagulant use at baseline, n%	5 (5.49)	9 (12.68)	43 (79.63)
Anticoagulant use at 3 months, n%	3 (3.30)	29 (40.85)	42 (77.78)
p	0.470	<0.001	0.814

* Low risk: CHA_2DS_2-VASc of 0 in males, or 1 in females; Intermediate risk: CHA_2DS_2-VASc of 2 in female, 1 in male; High risk: CHA_2DS_2-VASc ≥3 in females, ≥2 in males.

CENTRAL ILLUSTRATION:
Mobile health devices could be a feasible approach for AF screening, and into subsequent AF integrated management. MAFA: mobile Atrial Fibrillation Application

SUPPLEMENTARY APPENDIX

Mobile Health technology for atrial fibrillation screening using photoplethysmography-based smart devices: The HUAWEI Heart study

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Online Table 1 "Suspected" AF episodes in relation to measurement method

	Total subjects with "suspected" AF (n=424)	Subjects with "suspected" AF followed up (n=262)	Subjects identified with AF (n=227)
Active measurement (median, IQR)	172.0 (56.5-396.0)	200.5(53.7-518.7)	210.0 (86.0-518.7)
Automatic periodic measurement (median, IQR)	232.5 (57.5-690.2)	286.0 (66.0-860.0)	319.0 (65.0-900.0)
Active and periodic measurement (median, IQR)	1219.5 (263.7-2092.0)	1427.0(362.0-4416.0)	1430.0 (594.0-4461.0)
P	<0.001	<0.001	<0.001

* IQR: interquartile range.

Kruskal-Wallis test was used for the comparation among different measurement approaches.

When the subjects downloaded App and had matched smart devices, periodic measurements were automatically taken every 10 minutes, and 60-second PPG signals would be continuously collected, per measurement. In addition, subjects could initiate (additional) active measurements as needed.

Online Table 2 Users reported adverse events

	Overall cohort
Total	**186**
Any device connection and data synchronization issues	**123**
Login and experience issues (any)	**63**
Skin irritation, anxiety, pressure	**0**

Online Table 3 Comparison of the performance of smart devices utilized in PPG screening

Smart devices	Planned enrolled subjects	Enrolled subjects	AF	Sinus rhythm	Specificity	Sensitivity	Accuracy
HONOR BAND 4	200	264	27	237	99.2%	100%	99.2%
HONOR WATCH	200	265	24	241	99.2%	100%	99.2%
HUAWEI WATCH GT	200	212	22	190	98.9%	100%	99.1%

Online Table 4: Comparison of the standby time of smart devices with or without PPG screening

Smart devices	Battery(mAh)	Standby time without PPG screening (days)	Standby time with PPG screening (days)
HUAWEI WATCH GT	420	30	12
HONOR WATCH	178	14	5.5
HUAWEI BAND 3/3PRO	100	12	4.5
HONOR BAND 4/5	100	14	5

OnlineTable 5: Clinical decision support for 216 identified AF entering the MAFA programme

Risk scores	**n**	**%**
CHA_2DS_2-VASc		
0	81	37.5
1	69	31.9
2	45	20.8
3	14	6.5
4	5	2.3
5	2	.9
HAS-BLED		
0	146	67.6
1	66	30.6
2	3	1.4
3	1	.5
SAMe-T_2T_2R		
2	6	2.8
3	69	31.9
4	124	57.4
5	16	7.4
6	1	.5
Total	216	100

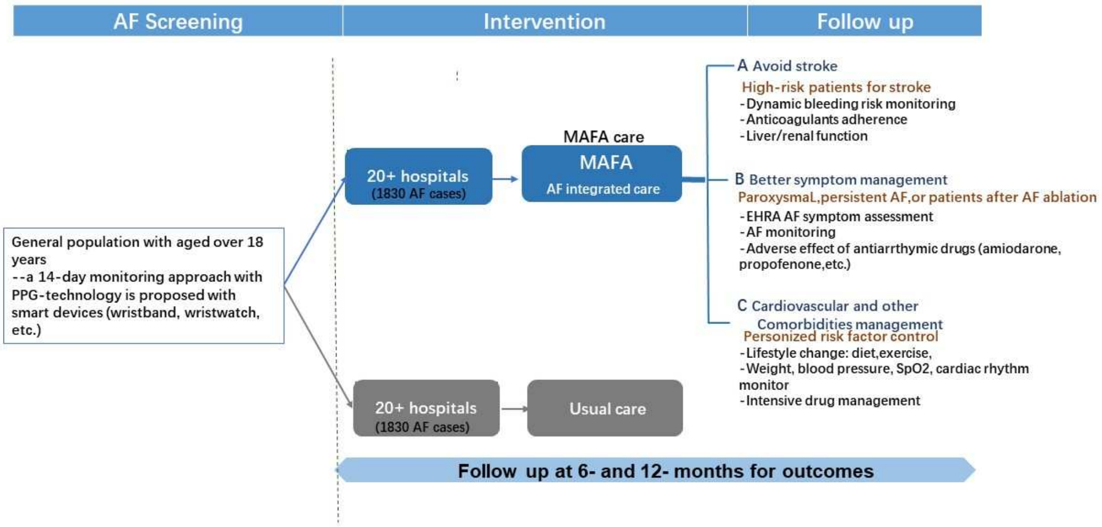
OnlineTable 6 Risk factors of 66573 individuals with C2HEST scores

	East China (n=20095)	North China(n=11574)	South China (n=9224)	Central China (n=7651)	Southwest China (n=6077)	Northwest China (n=4573)	Northeast China (n=4517)	Others (n=2862)
Hypertension, n (%)	3166 (15.76%)	1829(15.80%)	1490(16.15%)	1245(16.27%)	956(15.73%)	691(15.11%)	753(16.67%)	475(16.60%)
Diabetes, n (%)	723(3.60%)	424(3.66%)	330(3.58%)	267(3.49%)	222(3.65%)	155(3.39%)	162(3.59%)	110(3.84%)
COPD/Night snoring, n (%)	6701(33.35%)	3833(33.12%)	3069(33.27%)	2561(33.47%)	2071(34.08%)	1569(34.31%)	1578(34.93%)	891(31.13%)
HF, n (%)	273(1.36%)	168(1.45%)	138(1.50%)	106(1.39%)	91(1.50%)	61(1.33%)	85(1.88%)	37(1.29%)
Hyperthyroidism, n (%)	262(1.30%)	156(1.35%)	138(1.50%)	101(1.32%)	73(1.20%)	71(1.55%)	86(1.90%)	37(1.29%)
CAD, n (%)	569(2.83%)	364(3.14%)	266(2.88%)	228(2.98%)	183(3.01%)	124(2.71%)	137(3.03%)	84(2.94%)

* C2HEST score: C2: CAD/COPD (1 point each); H: hypertension (1 point); E: elderly (age ⩾ 75 years, 2 points); S: systolic HF (2 points); and T: thyroid disease (hyperthyroidism, 1 point). The C2HEST score was developed to assess the individual risk of developing AF in the Asian population. (Li YG, et al. Chest. 2019). COPD: chronic obstructive pulmonary disease. HF: heart failure. CAD: coronary artery disease.

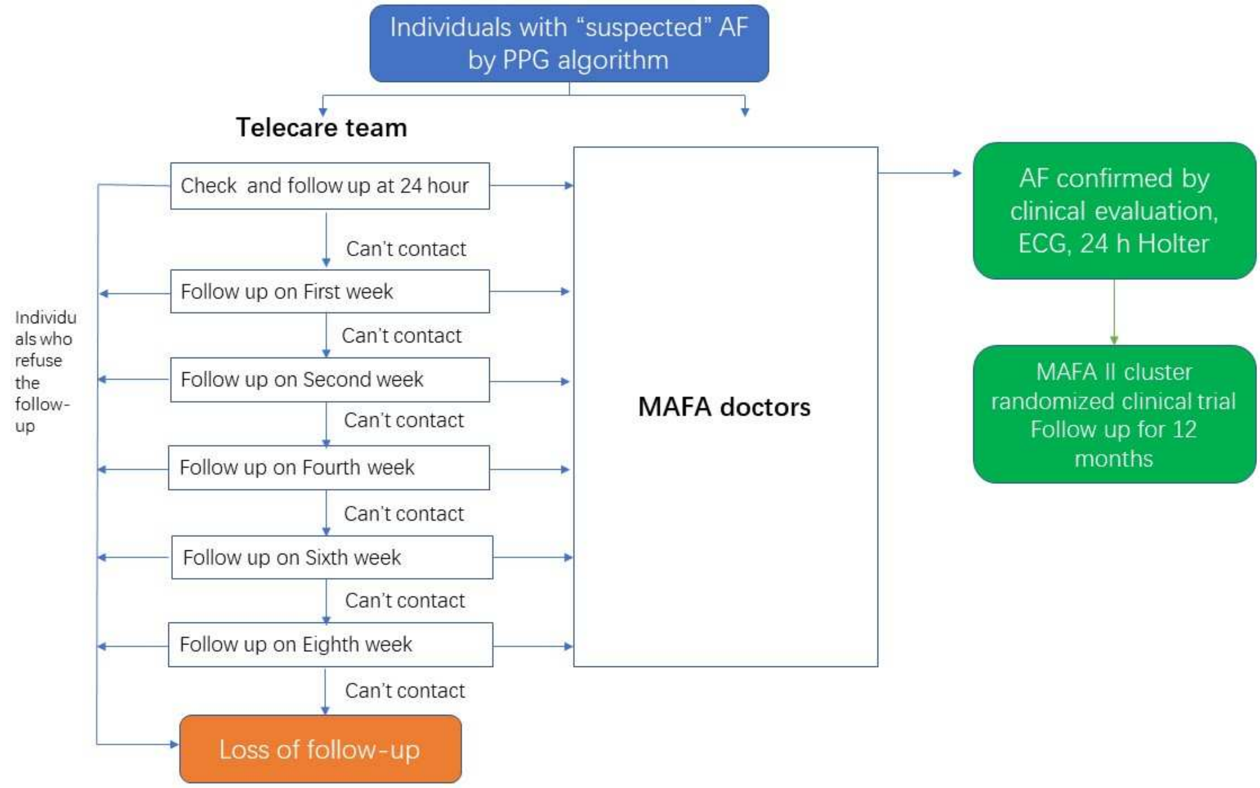
Online Figure 1: Flow chart of AF screening and the mAFA II project

*



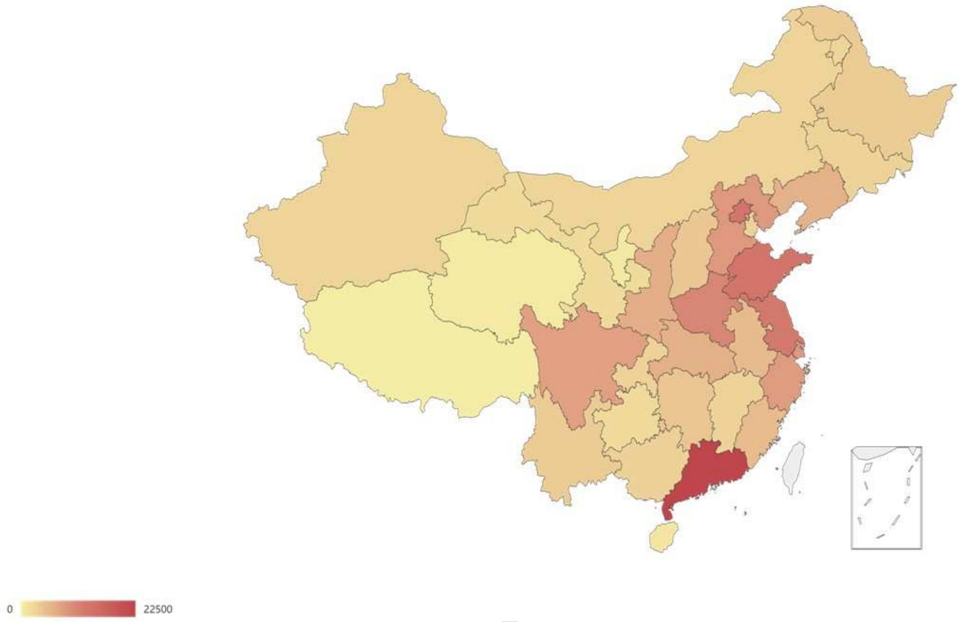
MAFA: mobile Atrial Fibrillation Application. PPG: Photoplethysmography (Guo Y, et al. Int J Clin Pract. 2019 Apr 19:e13352.)

Online Figure 2: The confirmation and follow-up of individuals with "suspected" AF



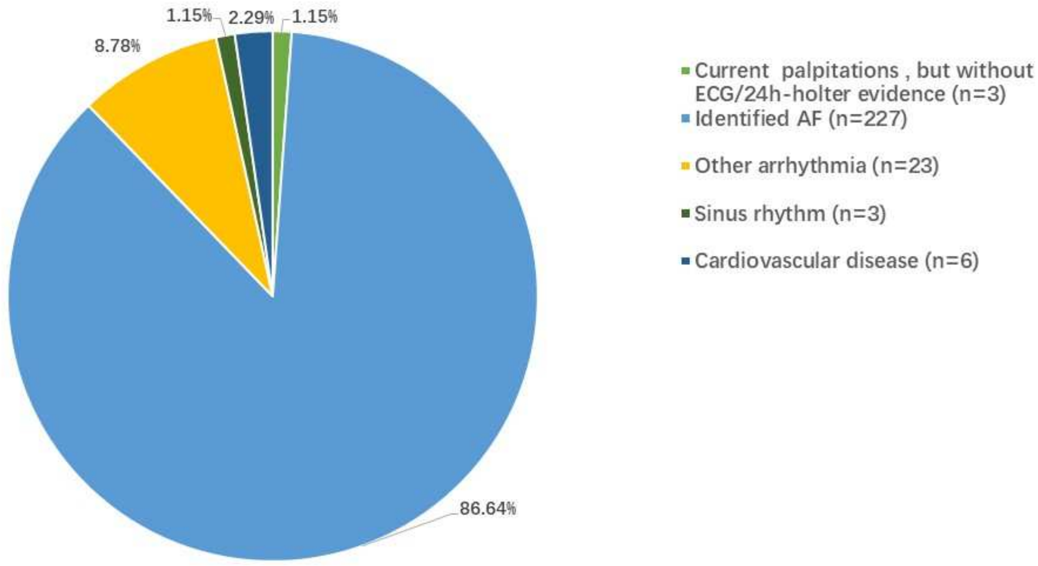
***** Once the notification of "suspected" AF was delivered, the participants could choose the MAFA hospitals nearby, book the doctors, then go to hospitals, receive clinical evaluation. The clinical evaluation included that the evaluation of cardiovascular risk factors, medical history, physical examination, ECG or 24-hour Holter.

Online Figure 3: Enrolment across China (n=187912)

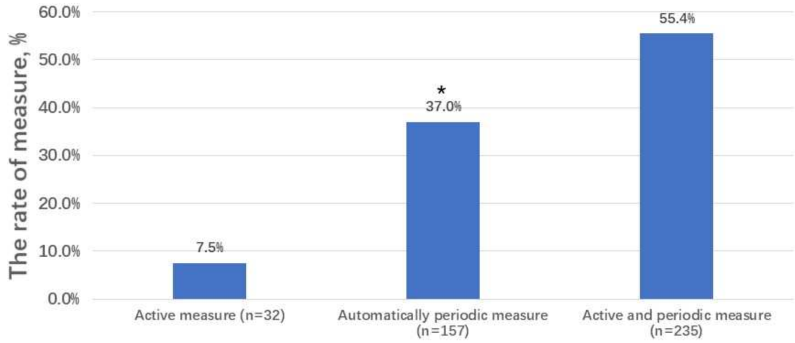


Data visualization analysis was utilized for the enrolment across China with ECharts.
Enrolment: October 26, 2018 to May 20, 2019.

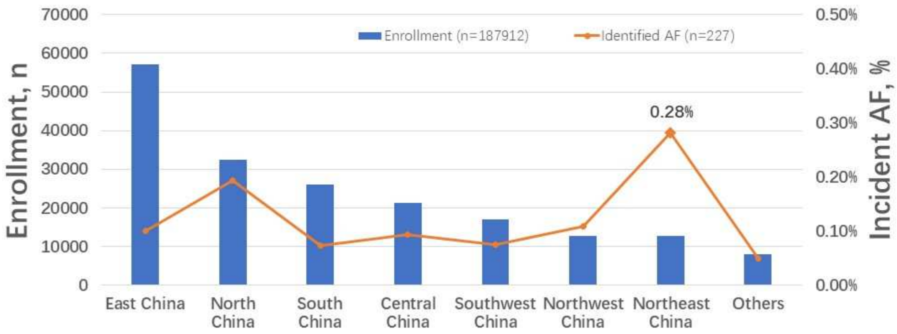
Online Figure 4: Cardiac rhythm of those with "suspected" AF



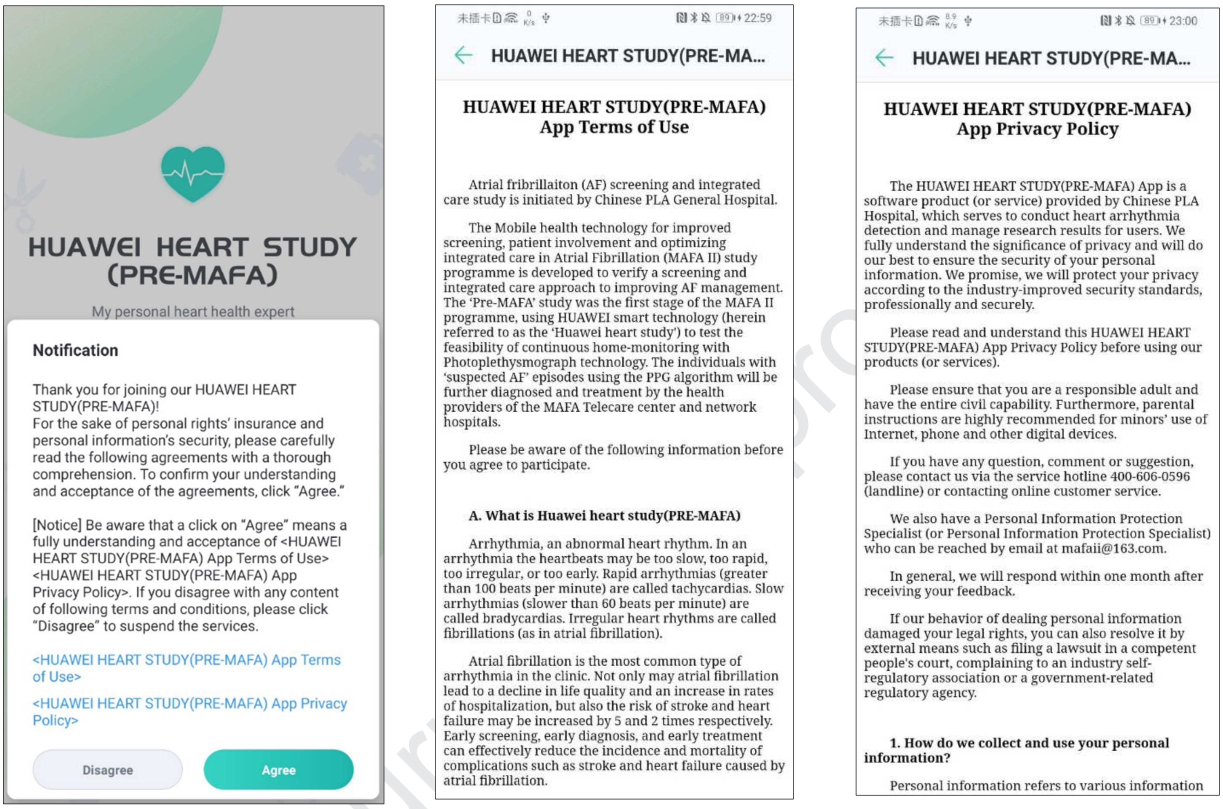
Online Figure 5: Monitoring method for first "suspected" AF



Online Figure 6: The prevalence of detected AF across China



Online Figure 7: The informed consent of AF screening and MAFA II study



HUAWEI HEART STUDY
(PRE-MAFA)

My personal heart health expert

Notification

Thank you for joining our HUAWEI HEART STUDY(PRE-MAFA)!
For the sake of personal rights' insurance and personal information's security, please carefully read the following agreements with a thorough comprehension. To confirm your understanding and acceptance of the agreements, click "Agree."

[Notice] Be aware that a click on "Agree" means a fully understanding and acceptance of <HUAWEI HEART STUDY(PRE-MAFA) App Terms of Use> <HUAWEI HEART STUDY(PRE-MAFA) App Privacy Policy>. If you disagree with any content of following terms and conditions, please click "Disagree" to suspend the services.

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Disagree Agree

22:59

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HUAWEI HEART STUDY(PRE-MAFA)
App Terms of Use

Atrial fribrillaiton (AF) screening and integrated care study is initiated by Chinese PLA General Hospital.

The Mobile health technology for improved screening, patient involvement and optimizing integrated care in Atrial Fibrillation (MAFA II) study programme is developed to verify a screening and integrated care approach to improving AF management. The 'Pre-MAFA' study was the first stage of the MAFA II programme, using HUAWEI smart technology (herein referred to as the 'Huawei heart study') to test the feasibility of continuous home-monitoring with Photoplethysmograph technology. The individuals with 'suspected AF' episodes using the PPG algorithm will be further diagnosed and treatment by the health providers of the MAFA Telecare center and network hospitals.

Please be aware of the following information before you agree to participate.

A. What is Huawei heart study(PRE-MAFA)

Arrhythmia, an abnormal heart rhythm. In an arrhythmia the heartbeats may be too slow, too rapid, too irregular, or too early. Rapid arrhythmias (greater than 100 beats per minute) are called tachycardias. Slow arrhythmias (slower than 60 beats per minute) are called bradycardias. Irregular heart rhythms are called fibrillations (as in atrial fibrillation).

Atrial fibrillation is the most common type of arrhythmia in the clinic. Not only may atrial fibrillation lead to a decline in life quality and an increase in rates of hospitalization, but also the risk of stroke and heart failure may be increased by 5 and 2 times respectively. Early screening, early diagnosis, and early treatment can effectively reduce the incidence and mortality of complications such as stroke and heart failure caused by atrial fibrillation.

23:00

HUAWEI HEART STUDY(PRE-MA...

HUAWEI HEART STUDY(PRE-MAFA)
App Privacy Policy

The HUAWEI HEART STUDY(PRE-MAFA) App is a software product (or service) provided by Chinese PLA Hospital, which serves to conduct heart arrhythmia detection and manage research results for users. We fully understand the significance of privacy and will do our best to ensure the security of your personal information. We promise, we will protect your privacy according to the industry-improved security standards, professionally and securely.

Please read and understand this HUAWEI HEART STUDY(PRE-MAFA) App Privacy Policy before using our products (or services).

Please ensure that you are a responsible adult and have the entire civil capability. Furthermore, parental instructions are highly recommended for minors' use of Internet, phone and other digital devices.

If you have any question, comment or suggestion, please contact us via the service hotline 400-606-0596 (landline) or contacting online customer service.

We also have a Personal Information Protection Specialist (or Personal Information Protection Specialist) who can be reached by email at mafaii@163.com.

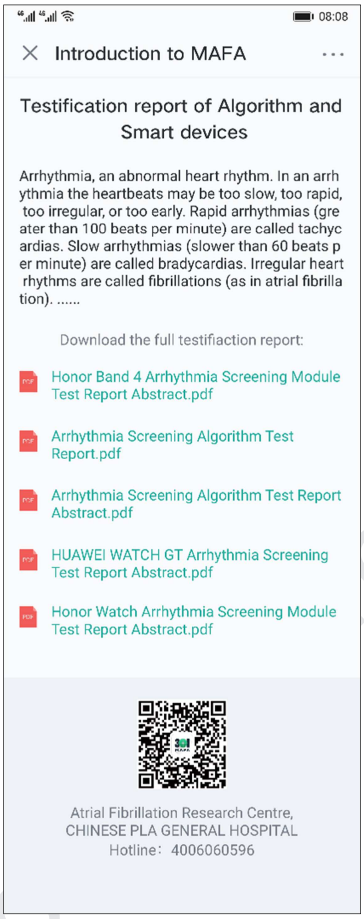
In general, we will respond within one month after receiving your feedback.

If our behavior of dealing personal information damaged your legal rights, you can also resolve it by external means such as filing a lawsuit in a competent people's court, complaining to an industry self-regulatory association or a government-related regulatory agency.

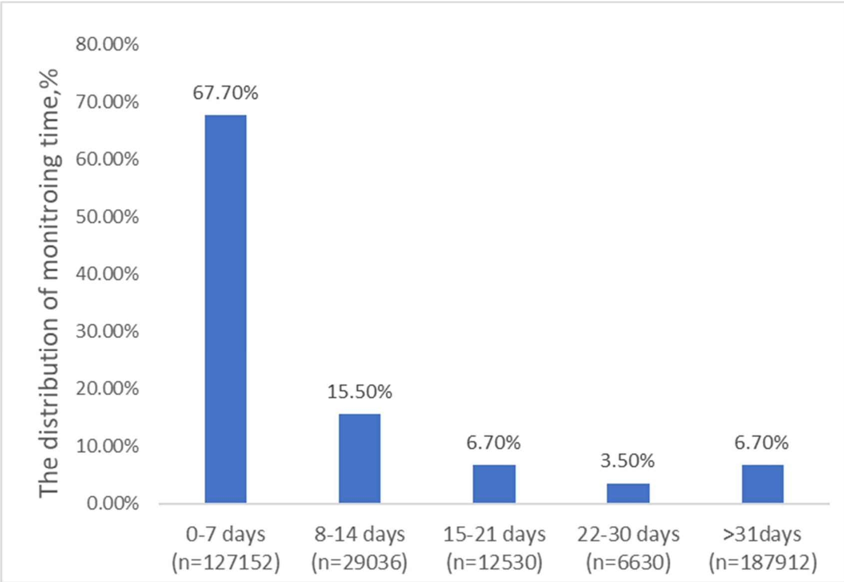
1. How do we collect and use your personal information?

Personal information refers to various information

Online Figure 8: Verification report of the PPG algorithm and smart devices



Online Figure 9: The distribution of monitoring time in the whole cohort



Online Figure 10 Verification report of PPG algorithm
There were four stages to develop, verify, and validate the PPG algorithm.
The pilot work has been published as follows: *Fan YY, et al. JMIR Mhealth Uhealth. 2019 Mar 5;7(3):e11437.*
The development and testification of PPG algorithm has been presented in the 2019 Cardiac Imaging & Cardiac Intervention Summit (http://www.cici.net.cn/2019/), and the validation of PPG algorithm (developed by HUAWEI) with 14-day monitoring, "Photoplethysmographi-based smart device for continuous detection of atrial fibrillation in a real-world setting", presented at the 2019 European Society of Cardiology Congress in Paris, France.

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心律失常筛查算法测试报告摘要

临床心电图是一套被医学界广泛接受和认可的心律失常筛查和诊断方法，该方法的有效性已被众多文献和临床实践证实。本院以临床心电图检测结果为对照标准，测试基于华为智能穿戴设备数据的心律失常筛查算法的有效性。

房颤是最常见的心律失常疾病。2018年6月~9月，本院招募372位受测者（234位男性，138位女性；年龄18-93岁，中位数63岁；165名房颤患者，207名窦性心律人群；共3268例样本）。测试时，受试者佩戴华为智能穿戴设备并保持安静状态，由穿戴设备采集受试者的生理信号作为实测数据，由心律失常筛查算法给出分析结果。同时记录受试者的心电图，两位医师独立判读心电图，若判读结果一致，则将该结果作为金标准，若不一致则排除。对比金标准，基于华为智能穿戴设备数据的心律失常筛查算法的测试结果如下：

灵敏度：95.6%；特异性：99.4%；综合准确率：97.8%。

结果显示，基于华为智能穿戴设备数据的心律失常筛查算法给出的测试结果与临床心电图检测结果高度一致，对心律失常筛查有效。

Arrhythmia Screening Algorithm Test Report Abstract

Clinical electrocardiogram (ECG) is widely accepted by medical field as a gold standard to screen and diagnose the arrhythmia, and has been validated by literatures and clinical practices. The test result of ECG is used by the Chinese PLA General Hospital as the standard for the verification of arrhythmia screening algorithm based on the data collected by HUAWEI smart wearable devices.

Atrial fibrillation is one of the most common arrhythmia diseases. 372 subjects (234 males, 138 females; aged from 18 to 93 with the median 63; 165 atrial fibrillation patients, 207 sinus rhythm subjects, 3268 samples in total) were recruited in the arrhythmia screening algorithm test from June to September, 2018. The subjects were asked to wear HUAWEI smart wearable devices at rest state during the test. The photoplethysmography (PPG) signals were collected by the wearable devices and analysis results were given by the arrhythmia screening algorithm. The ECG was collected and interpreted by two independent physicians at the same time. If the interpreted results are consistent, then they are used as the gold standard, otherwise the results are excluded. Compared with the gold standard, the test results of arrhythmia screening algorithm based on the data collected by HUAWEI smart wearable devices are as bellows:

Sensitivity: 95.6%, specificity: 99.4%, accuracy: 97.8%.

The result shows that the screening results of arrhythmia screening algorithm based on the data collected by HUAWEI smart wearable devices are highly consistent with those ECG based interpretations and effective in arrhythmia screening.

中国人民解放军总医院　心内科主任医师

（签名）郭豫涛

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Online Figure 11 Verification report of smart devices used

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荣耀手环4心律失常筛查测试报告摘要

临床心电图是一套被医学界广泛接受和认可的心律失常筛查和诊断方法，该方法的有效性已被众多文献和临床实践证实。本院以临床心电图检测结果为对照标准，测试了基于荣耀手环4数据的心律失常筛查算法的有效性。

房颤是最常见的心律失常疾病。2018年9月18日~9月25日，本院招募264位受测者（129位男性，135位女性；年龄16-89岁，中位数51岁；27名房颤患者，237名正常人群，共264例样本）。测试时，受试者佩戴荣耀手环4并保持安静状态，由智能手表采集受试者的生理信号作为实测数据，由心律失常筛查算法给出分析结果。同时记录受试者的心电图，两位医师独立判读心电图，若判读结果一致，则将该结果作为金标准，若不一致则排除。对比金标准，基于荣耀手环4数据的心律失常筛查算法的测试结果如下：

灵敏度：100%；特异性：99.16%；综合准确率：99.24%。

结果显示，基于荣耀手环4数据的心律失常筛查算法给出的测试结果与临床心电图检测结果高度一致，对心律失常筛查有效。

Honor Band 4 Arrhythmia Screening Module Test Report Abstract

Clinical electrocardiogram (ECG) is widely accepted by medical field as a gold standard to screen and diagnose the arrhythmia, and has been validated by literatures and clinical practices. The test result of ECG is used by the Chinese PLA General Hospital as the standard for the verification of arrhythmia screening module based on the data collected by Honor Band 4.

Atrial fibrillation is one of the most common arrhythmia diseases. 264 subjects (129 males, 135 females; aged from 16 to 89 with the median 51; 27 atrial fibrillation patients, 237 sinus rhythm subjects, 264 samples in total) were recruited in the arrhythmia screening module test from Sept. 18, 2018 to Sept. 25, 2018. The subjects were asked to wear Honor Band 4 at rest state during the test. The photoplethysmography (PPG) signals were collected by the smart watch and analysis results were given by the arrhythmia screening module. The ECG was collected and interpreted by two independent physicians at the same time. If the interpreted results are consistent, then they are used as the gold standard, otherwise the results are excluded. Compared with the gold standard, the test results of arrhythmia screening module based on the data collected by Honor Band 4 are as bellows:

Sensitivity: 100%, specificity: 99.16%, accuracy: 99.24%.

The result shows that the screening results of arrhythmia screening module based on the data collected by Honor Band 4 are highly consistent with those ECG based interpretations and effective in arrhythmia screening.

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HUAWEI WATCH GT智能手表心律失常筛查测试报告摘要

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美国心脏学学会荣誉委员，欧洲心脏病协会荣誉委员，美国心脏病协会/卒中协会专业会员，中华老年保健研究会心血管专业委员会秘书长、青委副主任委员，中华医学会心血管分会预防医学组委员，中华医师协会高血压委员会第二届青年委员，中国老年医学会基础与转化医学分会委员，中国生物医学工程学会心律分会女性心律失常工作委员会委员。

临床心电图是一套被医学界广泛接受和认可的心律失常筛查和诊断方法，该方法的有效性已被众多文献和临床实践证实。本院以临床心电图检测结果为对照标准，测试了基于HUAWEI WATCH GT智能手表数据的心律失常筛查算法的有效性。

房颤是最常见的心律失常疾病。2018年9月18日~9月25日，本院招募212位受试者（123位男性，89位女性；年龄16-89岁，中位数45岁；22名房颤患者，190名正常人群，共212例样本）。测试时，受试者佩戴HUAWEI WATCH GT智能手表并保持安静状态，由智能手表采集受试者的生理信号作为实测数据，由心律失常筛查算法给出分析结果。同时记录受试者的心电图，两位医师独立判读心电图，若判读结果一致，则将该结果作为金标准，若不一致则排除。对比金标准，基于HUAWEI WATCH GT智能手表数据的心律失常筛查算法的测试结果如下：

灵敏度：100%；特异性：98.95%；综合准确率：99.06%。

结果显示，基于HUAWEI WATCH GT智能手表数据的心律失常筛查算法的测试结果与临床心电图检测结果高度一致，对心律失常筛查有效。

HUAWEI WATCH GT Arrhythmia Screening Test Report Abstract

Clinical electrocardiogram (ECG) is widely accepted by medical field as a gold standard to screen and diagnose the arrhythmia, and has been validated by literatures and clinical practices. The test result of ECG is used by the Chinese PLA General Hospital as the standard for the verification of arrhythmia screening module based on the data collected by HUAWEI WATCH GT.

Atrial fibrillation is one of the most common arrhythmia diseases. 212 subjects (123 males, 89 females; aged from 16 to 89 with the median 45; 22 atrial fibrillation patients, 190 sinus rhythm subjects, 212 samples in total) were recruited in the arrhythmia screening module test from Sept. 18, 2018 to Sept. 25, 2018. The subjects were asked to wear HUAWEI WATCH GT at rest state during the test. The photoplethysmography (PPG) signals were collected by the smart watch and analysis results were given by the arrhythmia screening module. The ECG was collected and interpreted by two independent physicians at the same time. If the interpreted results are consistent, then they are used as the gold standard. Or the results are excluded. Compared with the gold standard, the test results of arrhythmia screening module based on the data collected by HUAWEI WATCH GT are as bellows:

Sensitivity: 100%, specificity: 98.95%, accuracy: 99.06%.

The result shows that the screening results of arrhythmia screening module based on the data collected by HUAWEI WATCH GT are highly consistent with those ECG based interpretations and effective in arrhythmia screening.

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