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Original article



Mobile health technology-supported atrial fibrillation screening and integrated care: A report from the mAFA-II trial Long-term Extension Cohort

Yutao Guo^{a,b,*}, Jun Guo^a, Xiangmin Shi^a, Yuan Yao^c, Yihong Sun^d, Yunlong Xia^e, Bo Yu^f, Tong Liu^g, Yundai Chen^a, Gregory Y H Lip^{a,b,**}, On behalf of the mAF-App II Trial investigators

^a Department of Cardiology, Chinese PLA General Hospital, Beijing, China

^b Liverpool Centre for Cardiovascular Sciences, University of Liverpool, Liverpool, United Kingdom; and Aalborg Thrombosis Research Unit, Department of Clinical Medicine, Aalborg University, Aalborg, Denmark

^c Institute for Hospital Management Research, Chinese PLA General Hospital, Beijing, China

^d China-Japan Friendship Hospital, Beijing, China

^e Department of Cardiology, First Affiliated Hospital of Dalian Medical University, Dalian, China

^f Department of Cardiology, First Hospital of China Medical University, Shenyang, China

^g Tianjin Key Laboratory of Ionic-Molecular Function of Cardiovascular Disease, Tianjin Institute of Cardiology, Second Hospital of Tianjin Medical University, Tianjin, China

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ABSTRACT

Background. In the mobile Atrial Fibrillation App (mAFA)-II trial, the use of mobile health (mHealth) technology, incorporating AF screening and integrated management strategy, was associated with improved short-term clinical outcomes. The aim of this study was to report adherence/persistence and long term (≥ 1 year) clinical outcomes of the mAFA-II trial, with mHealth-supported optimised stroke prevention, symptom control and comorbidity management.

Methods. We studied an adult population screened for AF, where identified patients could enter a structured program of holistic and integrated care based on the ABC (Atrial fibrillation Better Care) pathway using mHealth with a mAFA intervention. In this cluster randomised trial, comparing mHealth intervention to usual care, the primary composite outcome was 'stroke/thromboembolism, all-cause death and rehospitalization'.

Results. The 1261 subjects (mean age 67.0 years, 38.0% female) who were followed up over one year (mean follow-up 687 (standard deviation, SD 191) days) in the intervention arm, had a lower risk of the composite outcome of 'ischaemic stroke/systemic thromboembolism, death, and rehospitalization' (hazard ratio, HR 0.18, 95% confidence interval, CI: 0.13–0.25, $P < 0.001$), compared to usual care (1212 subjects, mean age 70.1 years, 42.1% female). Of 842 patients using their smart devices for 'Better symptom management', 70.8% had good management adherence (monitoring time/follow-up since initial monitoring $\geq 70\%$), with the persistence of use of 91.7%.

Conclusion. Amongst AF patients with long term use (≥ 1 year) of mHealth technology for optimising stroke prevention, symptom control and comorbidity management, adherence/persistence was good and associated with a reduction in adverse clinical outcomes.

1. Background

The priorities of atrial fibrillation management include stroke prevention, decisions on rate or rhythm control and proactive management of comorbidities, as well as lifestyle changes. Given that atrial

fibrillation patients can present to a diverse range of health care professionals, including general practitioners, non-cardiologists and cardiologists, there has been proposals to streamline the patient care pathway into a simple holistic and integrated approach that can be followed by all stakeholders and understood by patients.

* Corresponding author at: Department of Cardiology, Chinese PLA General Hospital 28 Fuxing Road, Haidian Street, Beijing 100853 China.

** Corresponding author at: University of Liverpool, Liverpool, UK.

E-mail addresses: dor_guoyt@hotmail.com (Y. Guo), gregory.lip@liverpool.ac.uk (G.Y.H. Lip).

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One such approach to holistic atrial fibrillation care is the ABC (Atrial fibrillation Better Care) pathway, as follows: ‘A’ Avoid stroke. Anticoagulation; ‘B’ Better symptom management with patient-centred symptom directed rate or rhythm control; ‘C’ Cardiovascular risk and Comorbidity management, including lifestyle changes[1,2]. The Atrial fibrillation Better Care pathway has been shown in post-hoc analyses of clinical trial cohorts and observational studies to be associated with improved clinical outcomes and reduces healthcare costs[3–5].

Even before a patient enters the care pathway, we also need improvements in screening, and next, to show how detected atrial fibrillation patients can be entered into structured management programme. We previously reported that photoplethysmography based general-population atrial fibrillation screening approach was feasible, whereby 0.23% with “suspected” atrial fibrillation from a screened population of 246,541 received a notification of suspected atrial fibrillation, of which 87% were confirmed as atrial fibrillation, and 80% of high-risk patients were subsequently anticoagulated[6]. Short term outcomes (mean followup 262 days) of such identified atrial fibrillation patients randomized into the mAFA-II (mobile Atrial Fibrillation App) cluster randomized trial using mobile health (mHealth) based integrated care management found a significant reduction in the composite outcome of ‘ischaemic stroke/systemic thromboembolism, death, and rehospitalization’, compared to usual care[7]. However, the long-term adherence/persistence of mobile health technology use and the impact on clinical outcomes, remains uncertain although the approach has been increasingly proposed for chronic disease management. The mAFA programme is still ongoing (patients can still download and start using the mAF App), but we need to answer the question on ‘long term users’ (ie. using mHealth for >1 year) which is the current specific focus of the present paper.

In the present report from the mAFA-II trial, the objective was to report adherence/persistence and long term (≥ 1 year) clinical outcomes of the mAFA-II trial, with optimised stroke prevention, symptom control and comorbidity management. Hence, the subgroup of atrial fibrillation patients with mobile health technology use and follow up of over one year were included into this ancillary analysis.

2. Methods

The mobile Atrial Fibrillation Application (mAFA) programme, which investigated mobile health (mHealth) technology for improved screening and optimised integrated care in atrial fibrillation, has been described previously[8]. In brief, the programme included the pre-mAFA phase of screening for atrial fibrillation in the general population[6]. Then those with identified atrial fibrillation were considered for entry into the mAFA II cluster randomized trial[9], to validate an integrated care approach based on the Atrial fibrillation Better Care pathway.

The study was approved by the Central Medical Ethics Committee of Chinese PLA General Hospital (Approval number: S2017-105-02) and registered on the WHO International Clinical Trials Registry Platform (ICTRP) [chictr.org.cn; registration number ChiCTR-OOC-17014138 (<http://www.chictr.org.cn/showprojen.aspx?proj=24191>)]. The study was compliant with the Declaration of Helsinki.

2.1. Study population

Subjects aged over 18 years old across China, with compatible smart phone and devices were freely available for continuous photoplethysmography-based pulse monitoring after providing electronically signed study informed consent, between October 26, 2018 and June 16, 2020. The subjects who received the notification of ‘suspected’ atrial fibrillation were further confirmed with the diagnosis of atrial fibrillation (or not) upon the clinical evaluation, electrocardiography (ECG), or 24 hour Holter monitoring by mAFA programme health providers[8]. At least 14-days monitoring was proposed for the subjects;

but they could freely monitor their pulse rhythm beyond 14 days[8]. All ‘identified atrial fibrillation’ in atrial fibrillation screening phase were followed up by mAFA programme telecare team, but in this long-term cohort, we focused on the subgroup of subjects with ‘identified’ atrial fibrillation followed up for over one year.

2.2. mAFA II long-term cohort

Following a pilot feasibility study (mAFA-I)[10], we updated the mobile Atrial Fibrillation App with the Atrial fibrillation Better Care pathway on February 22, 2018 for conducting the mAFA-II clinical trial. The mAFA II trial participants were consecutively recruited from those referred from the initial atrial fibrillation screening programme (‘pre-mAFA’)[6], or from the out-patient and in-patient departments from 40 participating centres in China, between June 1, 2018 and December 1, 2019. This trial was designed as a cluster randomised trial which compared mobile health technology intervention with the mobile Atrial Fibrillation App, against ‘usual care’ at a cluster level[9]. The centre selection, cluster randomization, patient’s enrolment, and hospital type have been reported previously[8]. To report adherence/persistence and long term (≥ 1 year) clinical outcomes, the subgroup of atrial fibrillation patients using mobile health technology intervention with follow up over one year were included, as the mAFA II long-term cohort (Fig. 1).

Atrial fibrillation patients allocated to the mobile health technology intervention could download the mobile Atrial Fibrillation App, to follow an integrated care management approach using the Atrial fibrillation Better Care pathway, as follows [8]:

- **‘A’ Anticoagulation to Avoid stroke** – Anticoagulation with non-vitamin K antagonist oral anticoagulant or well-managed warfarin;
- **‘B’ Better symptom management** with patient-centred symptom-directed shared decisions for rate or rhythm control;
- **‘C’ Cardiovascular risk and comorbidity management** (blood pressure, sleep apnoea, diabetes etc.) plus lifestyle changes (weight reduction, regular exercise, reducing alcohol/stimulants, psychological morbidity, smoking cessation, etc.).

For **‘A’ Anticoagulation to Avoid stroke**, the laboratory parameters (international normalized ratio, renal/hepatic function, etc.) could be tested in local hospitals, with data uploaded by the mobile Atrial Fibrillation App. Anticoagulant quality monitoring, dynamic risk bleeding assessment[11], and guideline-adherent dosage adjustment based on age, renal/liver function changes, etc., were provided by the mobile Atrial Fibrillation App, and management further confirmed/modified by doctors in the mAFA programme network[8,9].

For **‘B’ Better symptom management**, patients could report atrial fibrillation symptoms, compliant with European Heart Rhythm Association classification[12], but also could monitor their pulse rhythm for ‘suspected’ atrial fibrillation, together with the ‘atrial fibrillation burden’ during their monitoring time if they had photoplethysmography-based smart devices. Patient advice (drugs, lifestyle, or behavioural changes, etc.) of rate or rhythm control would be given to the patients by in-built communication function with doctors using mAFA. For

For **‘C’ Cardiovascular risk and comorbidity management**, optimized management targets for risk factors and lifestyle recommendations were based on guidelines, as previously described[9].

Patients allocated to **usual care** received their ‘usual care’ treatments by local health providers according to their local clinical practice [9]. Power calculations for the main mAFA-II trial have been previously published[8,9], and the current ancillary analysis only focuses on the subgroup with long term usage.

2.3. Outcomes

In this mAFA II trial long-term cohort, the subgroup with mobile

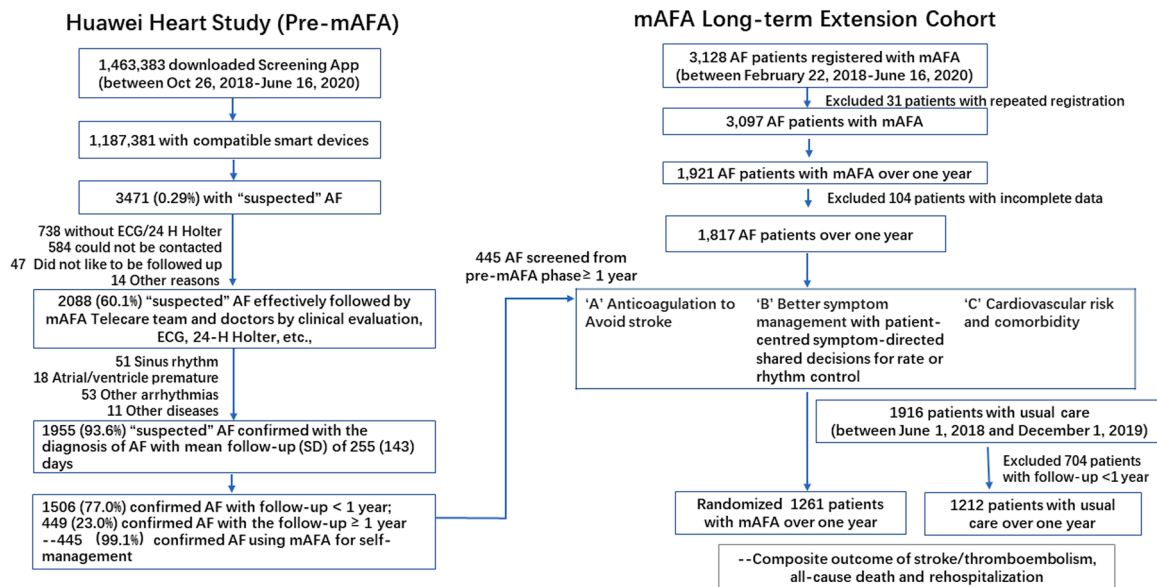


Fig. 1. Flow chart of AF screening and mAFA Long-term Extension Cohort with over one-year follow-up. *mAFA: mobile Atrial Fibrillation Application. App: application. AF: atrial fibrillation. SD: standard deviation.

health technology use and follow up of over one year were enrolled into this ancillary analysis. Of note, all patients within this subgroup were included, and those with clinical outcomes occurring at <1 year, were included into the intention to treat analysis, to report outcomes of mobile health technology intervention vs. usual care.

The *primary endpoint* was the composite of stroke/thromboembolism, all-cause death, and rehospitalization, which reported previously[8,9]. Reasons for rehospitalization included any cause for atrial fibrillation, heart failure, thromboembolism, major bleeding, coronary artery disease, and other cardiovascular disease. The *secondary outcomes* included event rates for the components of the primary endpoint. We also focused on outcomes related to the components of the Atrial fibrillation Better Care pathway as follows:

- **'A' Anticoagulation to Avoid stroke** outcomes were assessed with thromboembolism and bleeding events.
- **'B' Better symptom management** outcomes were evaluated with regard to recurrent atrial fibrillation or related symptoms.
- **'C' Cardiovascular risk and comorbidity management** outcomes for this ancillary analysis were assessed with regard to atrial fibrillation patients with heart failure, and blood pressure management over the follow-up period.

2.4. Adherence and persistence

The adherence and persistence with mobile health technology use was evaluated, as follows: i) the rate of subjects with suspected atrial fibrillation from photoplethysmography-based screening transferred into the mAFA trial programme over one year; and ii) the adherence/persistence of patients using atrial fibrillation on their smart devices.

2.5. Statistical analysis

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). The proportions of 'suspected' and 'confirmed' atrial fibrillation from the general population screening phase was calculated, stratified by gender and age. Subject-reported comorbidities among general population, 'suspected' atrial fibrillation, and 'confirmed' atrial fibrillation were investigated for the underlying risk factors in general population, given this was a large cohort involving

more than one million. For these identified atrial fibrillation from screening approach transferred into mAFA trial programme over one year, the utilization of the mobile Atrial Fibrillation App was evaluated.

The rates of thromboembolism, bleeding events, recurrent atrial fibrillation, heart failure, rehospitalization, and all-cause death for patients using mobile Atrial Fibrillation App were compared with usual care. Rates are expressed as 'events/per 1000 patient-years, but while some patients suffered more than one event, the follow-up survival analysis was only calculated for the time to first event.

Given that atrial fibrillation patients with 'usual care' did not routinely monitor their blood pressure in a systematic manner, blood pressure changes could not be compared between patients allocated to mAFA trial intervention and usual care clusters. Hence, the changes on blood pressure levels were only described for patients with mAFA trial intervention.

Cox proportional hazards models adjusted for cluster effect, and baseline risk factors, were used to analyse the primary composite outcome of stroke/thromboembolism, all-cause death, and rehospitalization over one year. Adjusted baseline risk factors included age, gender, hypertension, coronary artery disease, diabetes mellitus, heart failure, peripheral artery disease, pulmonary disease (chronic obstructive pulmonary disease, obstructive sleep apnoea syndrome, pulmonary hypertension), dilated cardiomyopathy, prior ischaemic stroke, prior other thromboembolism, prior intracranial bleeding, prior other bleeding, liver/renal dysfunction.

The adherence of using mobile health technology was calculated, defined as the rate of the monitoring time using smart devices divided by the follow-up period since initial monitoring. The persistence of mobile health technology use for patients was defined as any of uploading medical materials, consulting with mAFA trial programme health providers, participation/involvement in educational programs, etc. during the follow up period. We also report the rate of subjects with suspected atrial fibrillation from the screening phase, transferred into the mAFA trial over one year, and the adherence/persistence of patients. Finally, the utilisation of the mobile Atrial Fibrillation App over time was observed, to describe use the mobile health technology application during coronavirus disease 2019 outbreak in China, since January 20, 2020.

A two-sided P-value < 0.05 was considered as statistically significant. The 95% confidence intervals (CIs) were calculated with Wilson score method without continuity correction. All statistical analyses were

conducted using IBM SPSS Statistics, version 22.0 (SPSS Inc), and MedCalc version 19. 0.4 (MedCalc Software).

3. Results

3.1. General population-based atrial fibrillation screening

Between October 26, 2018 and June 16, 2020, there were 1463,383 subjects who downloaded the mobile Atrial Fibrillation App for screening, and of these 1187,381 subjects (mean age 35.4, SD 11.5, 17.3% female) had compatible smart devices. Of the latter, 3471 subjects received a notification of 'suspected' atrial fibrillation, and 2088 'suspected' cases (60.1%, 2088/3471; mean age 56.2 (SD 13.8), 16.3% female) were effectively followed up by the mAFA programme health providers (Fig. 1). Those with confirmation of 'suspected' atrial fibrillation are shown in Supplemental Fig. 1.

Sleep apnoea (40.9%) and hypertension (39.8%) were most common self-reported comorbidities in this screening population (Table 1). There were 449 with confirmed atrial fibrillation (23.0%, mean age 55.7, SD 13.6 years; 15.4% female) with follow-up of over one year and >99% ($n = 445$) used the mobile Atrial Fibrillation App for their self-management with the Atrial fibrillation Better Care pathway (Fig. 1).

The proportion of suspected atrial fibrillation among general population increased with age, with the highest prevalence of 5.84% (321/5492, 95% CI, 5.25–6.50) in subjects aged over 75 years old. The proportions of 'suspected' and 'confirmed' atrial fibrillation are shown in Supplemental Fig. 2. The prevalence of 'suspected' atrial fibrillation stratified by age strata, ranged from 0.04%–5.38% in females, and 0.06%–6.28% in males (Supplemental Fig. 3).

3.2. Atrial fibrillation Better Care pathway

Baseline characteristics of the intervention and usual care arms from a total of 40 centres participating in this cluster randomised trial are shown in Supplemental Table 2.

The 'intervention group' consisted of 1261 subjects (mean age 67.0 years, 38.0% female) from 20 clusters who were followed up for over one year (mean follow-up 687 (SD 191) days; median 701 days (IQR 489–841)). These were compared to 1212 subjects (mean age 70.1 years, 42.1% female) managed with 'usual care' with a mean follow-up of 514 (SD 167) days (median 546 (IQR 394–632)) from another 20 research centers.

Rates of clinical outcomes (thromboembolism, bleeding events, recurrent atrial fibrillation and its symptoms, heart failure, and rehospitalization) were lower in patients allocated to intervention, compared

Table 1
Baseline characteristics of AF screening in Pre-mAFA phase.

	Overall Cohort ($n = 1187,381$)	Suspected AF ($n = 3471$)	Confirmed AF ($n = 1955$)
Female, n (%)	205,545 (17.3)	591 (17.0)	324 (16.6)
Age, mean (SD)	35.4(11.5)	56.1(14.3)	56.7 (13.7)
18–39, n (%)	816,794 (68.8)	465 (13.4)	221 (11.3)
40–54, n (%)	290,753 (24.5)	1050 (30.3)	600 (30.7)
55–64, n (%)	53,730 (4.5)	896 (25.8)	535 (27.4)
65–74, n (%)	20,612 (1.7)	739 (21.3)	418 (21.4)
75–84, n (%)	4750 (0.4)	282 (8.1)	156 (8.0)
≥85, n (%)	742 (0.1)	39 (1.1)	23 (1.2)
Subject self-reported comorbidities	Overall Cohort ($n = 468,203$)	Suspected AF ($n = 1861$)	Confirmed AF ($n = 1118$)
Sleep apnoea, n (%)	157,159 (33.6)	762 (40.9)	466 (41.7)
Hypertension	74,431 (15.9)	741 (39.8)	463 (41.4)
Coronary artery disease	13,902 (3.0)	414 (22.2)	268 (24.0)
Heart failure	7288 (1.6)	251 (13.5)	161 (14.4)
Diabetes	17,841 (3.8)	231 (12.4)	137 (12.3)
Hyperthyroidism	6684 (1.4)	71 (3.8)	46 (4.1)

SD: standard deviation. mAFA: mobile Atrial Fibrillation Application.

with usual care (all $P < 0.05$) (Table 2, Supplementary Table 3).

Compared to usual care, patients allocated to intervention had a lower risk of the composite outcome of 'ischaemic stroke/systemic thromboembolism, death, and rehospitalization', adjusted for baseline risk factors (hazard ratio, HR 0.18, 95% CI: 0.13–0.25, $P < 0.001$) (Fig. 2, Supplemental Fig. 4, Supplementary Table 4). Cumulative incidences of all-cause death and rehospitalization are shown in Supplemental Fig. 5. Atrial fibrillation patients allocated to intervention also showed improved blood pressure control over time (Supplemental Fig. 6).

3.3. Adherence and persistence

There were 842 atrial fibrillation patients (mean age \pm SD, 51.8 \pm 14.2; 15.0% female) using mAFA intervention, particularly for the 'B' criterion, ie. Better symptom management. Of these, 70.8% of patients had good management adherence (monitoring time/follow-up since initial monitoring $\geq 70\%$), with the persistence of use of 91.7% (Fig. 3). Younger patients and those with paroxysmal AF showed trends for better adherence with mobile health supported management using smart devices, with adherence of over 70% (see Supplemental Figs. 7 and 8). After coronavirus disease 2019 outbreak on January 20, 2020 in China, the monthly active users of the mobile Atrial Fibrillation App increased over time (Supplemental Fig. 9).

4. Discussion

Amongst atrial fibrillation patients with long term use (≥ 1 year) of mobile health technology for optimising stroke prevention, symptom control and comorbidity management, their adherence/persistence was good and associated with a reduction in adverse clinical outcomes, when compared to those managed with usual care. Second, patients using the mobile Atrial Fibrillation App had a reduced risk for the primary composite outcome of 'ischaemic stroke/systemic thromboembolism, death, and rehospitalization', compared to usual care. Third, >70% of subjects using mobile health technology had good management adherence, with the persistence of use of 91.7%.

As far as we are aware, the mAFA programme is the first mobile health technology based programme for atrial fibrillation screening, followed by a structured patient care pathway based on the principal components of atrial fibrillation management. The present analysis focused on the subgroup of participants enrolled for ≥ 1 year was pre-planned to assess adherence/persistence and long-term outcomes, given that the overall mAFA programme is continually enrolling subjects, using the mobile Atrial Fibrillation App.

Atrial fibrillation confers a significant health, economic, and social burden, with the increased risk of stroke, death, dementia, heart failure and hospitalization[13]. Hence, its early diagnosis with appropriate management would help prevent the main atrial fibrillation-related complications. However, even before the patient with atrial fibrillation enters any management pathway, there is the need to improve the detection of this arrhythmia.

Smart technology is increasingly deployed to help with screening for atrial fibrillation. Indeed, the continuous monitoring of pulse rhythm on home with wearable devices is practical, which has been proven to improve the early identification of atrial fibrillation[6,14]. Following its detection, the next important step is to manage these identified atrial fibrillation patients with a holistic integrated approach, to achieve the main goals of atrial fibrillation management. While much attention has focused on stroke risks of atrial fibrillation, we recognize the high mortality and other adverse outcomes associated with this common arrhythmia. Indeed, of the mortality outcomes associated with atrial fibrillation, only one in 10 is stroke related and > 7 in 10 are cardiovascular[15,16].

Efforts are therefore being directed to streamline the management of atrial fibrillation in an integrated manner, which needs a simple

Table 2

Long-term outcomes in AF patients using mAFA, compared to usual care in mAFA II cluster randomized trial.

	mAFA no./total no.	Usual care no./total no.	mAFA events/per 1000 patient-years	Usual care events/per 1000 patient-years	Hazard ratio (adjusted)* (mAFA vs. Usual care)	95%CI	P
Primary endpoint							
Composite outcome of IS/TE, death, and rehospitalization	87 /1261	165 /1212	0.10	0.26	0.18	0.13–0.25	<0.001
Secondary outcomes							
Thromboembolism							
• Ischaemic stroke	6 /1261	50 /1212	0.01	0.08	0.11	0.05–0.27	<0.001
• Other TE	5/1261	11 /1212	0.01	0.02	0.29	0.09–0.94	0.03
Bleeding events							
• Intracranial bleeding	0 /1261	5 /1212	0.00	0.01	–	–	–
• Extracranial bleeding	20 /1261	41 /1212	0.02	0.07	0.37	0.20–0.70	0.002
Recurrent AF or AF symptom	46 /1261	95/1212	0.05	0.15	0.33	0.23–0.48	<0.001
Heart failure	28 /1261	57 /1212	0.03	0.09	0.40	0.24–0.66	<0.001
Rehospitalization	69 /1261	89 /1212	0.08	0.14	0.69	0.49–0.97	0.03
All-cause death	12 /1261	32/1212	0.01	0.05	0.94	0.39–2.23	0.89

Data are n (%). * The effect of mAFA intervention on the clinical events after adjustment for cluster effect, age, gender, hypertension, coronary artery disease, diabetes mellitus, heart failure, peripheral artery disease, pulmonary disease (chronic obstructive pulmonary disease, obstructive sleep apnoea syndrome, pulmonary hypertension), dilated cardiomyopathy, prior ischaemic stroke, prior other thromboembolism, prior intracranial bleeding, prior other bleeding, liver/renal dysfunction based on the baseline characteristics. IS: ischaemic stroke. TE: thromboembolism. Extracranial bleeding included gastrointestinal, urogenital, skin, mouth bleeding, and other non-major bleeding. For the composite outcome of IS/TE, death, and rehospitalization: (i) in 'usual care', there were 9 patients with all 3 outcomes of ischaemic stroke, rehospitalization, and death, 47 patients with two of three outcomes, and 109 patients with any of the three outcomes; (ii) for patients with mAFA, there were 4 patients with all 3 outcomes of ischaemic stroke, rehospitalization, and death, 2 patients with two of three outcomes, and 81 patients with any of the three outcomes. Other TE and extracranial bleeding events are in [Supplementary Table 3](#).

Reasons for rehospitalization included any cause for AF, heart failure, thromboembolism, major bleeding, artery coronary disease, and other cardiovascular disease. mAFA: mobile Atrial Fibrillation Application. CI: confidence interval.

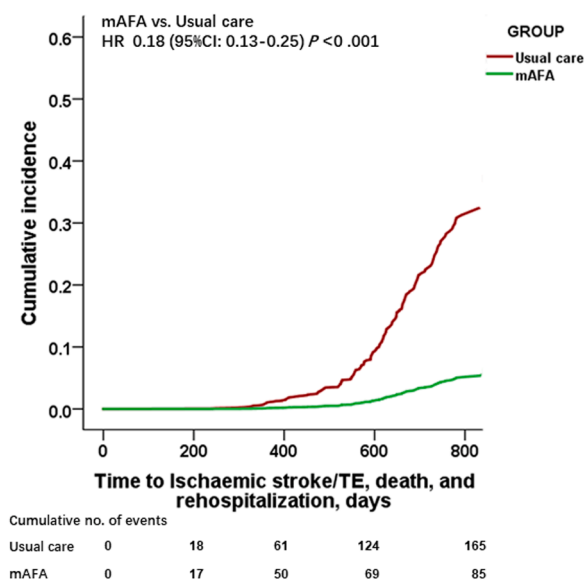


Fig. 2. Cumulative incidence of the composite outcome of ischaemic stroke/TE, death, and rehospitalization. *mAFA: mobile Atrial Fibrillation Application. TE: other systemic thromboembolism. HR: hazard ratio. CI: confidence interval.

approach that can be followed by all healthcare practitioners (general practitioners, non-cardiologists, cardiologists), the patient, and their carers. This has led to the proposal of the ABC (Atrial fibrillation Better Care) pathway, whereby ABC pathway compliance has been associated with improved clinical outcomes and lower healthcare costs[3–5]. Such a uniform message ('Simple as ABC...') applicable to all stakeholders is important given that conflicting information received from different healthcare providers can negatively affect adherence with management

[17].

The benefits of integrated care on atrial fibrillation outcomes are increasingly evident. In the meta analysis by Gallagher et al. demonstrated that the use of an integrated care approach in atrial fibrillation reduced the risk for cardiovascular hospitalisations by 42%[18]. Indeed, an integrated care approach in the present mAFA II trial long term extension cohort reduced the risk for rehospitalisation by 31%. Other nurse-driven (or nurse-led) integrated care approaches have also been demonstrated to be clinically beneficial for atrial fibrillation patients [19–21].

However, there are growing challenges on how best to apply mobile health technology into atrial fibrillation management, with marked heterogeneity of published findings. In the SUPPORT-AF study, the supportive tools based on electronic medical records, supplemented by email notifications, related to anticoagulant prescribing was feasible, but did not increase anticoagulant use in patients with atrial fibrillation. [22] Patient refusal or non-adherence was suggested as the main reason for a patient being non-anticoagulated. Also, it may be inadequate to simply inform physicians with the rate of anticoagulant use by patients under their care, but there is the need to support the physicians to ascertain the underlying barriers to anticoagulant use and assess stroke (and bleeding) risks, while improving patient's knowledge as part of a streamlined integrated care management pathway approach.

In the mAFA-II trial, we previously reported the short term outcomes (mean follow-up of 262 days) associated with mobile health management based on the Atrial fibrillation Better Care pathway, with a significant reduction in the composite outcomes, that was largely driven by hospitalisations[7]. In the present analysis of those (long term) mAFA participants with ≥ 1 year use/followup, there were maintained reductions in the composite outcome and hospitalization using mAFA trial intervention. Importantly, for the individual components of the ABC pathway, there were significant reductions in ischaemic stroke, extracranial bleeding, recurrent atrial fibrillation and atrial fibrillation-related symptoms, as well as heart failure during long term

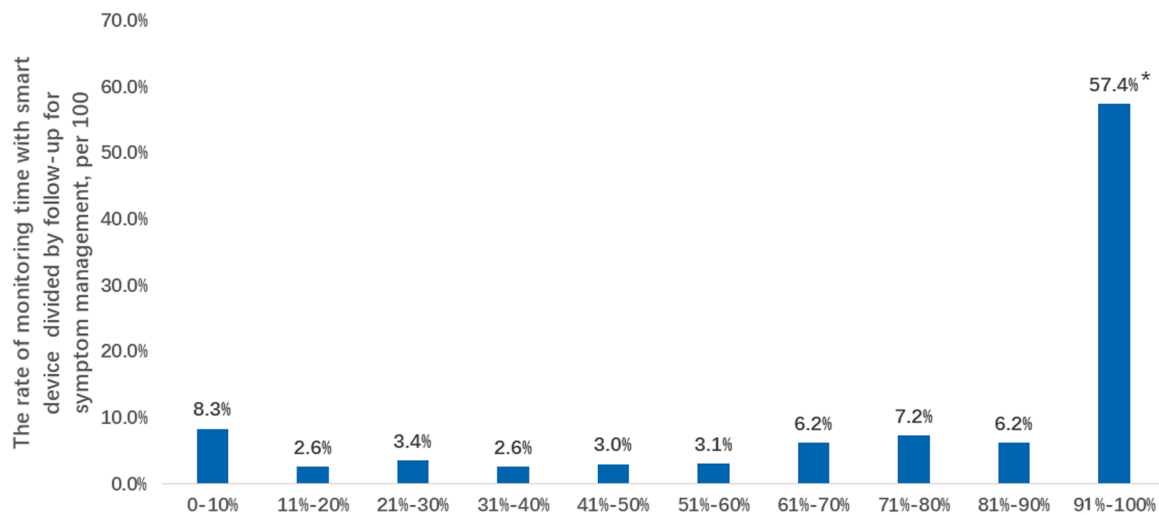


Fig. 3. Adherence of patient-centred symptom-directed rate or rhythm control with smart devices using mAFA (B criterion of ABC pathway).

* $P < 0.001$, compared among the adherence strata. There were 842 atrial fibrillation patients using photoplethysmography-based smart devices focused on 'B' criterion (Better symptom management): 70.8% had management adherence (monitoring time/follow-up since initial monitoring) of $\geq 70\%$, with the persistence of use of 91.7%.

mAFA: mobile atrial fibrillation Application.

followup. This was associated with good adherence and persistence with the mobile Atrial Fibrillation App and the overall mAFA programme.

We did not observe a significant difference in all-cause death alone, perhaps associated with significant reduction in ischaemic stroke over one year in patients on mAFA intervention compared to usual care (Supplementary Fig. 5). Another possibility is that the coronavirus disease 2019 outbreak might have led to suboptimal atrial fibrillation 'usual-care' management (e.g. less anticoagulant monitoring) leading with additional cardiovascular events[23]. Suboptimal 'usual-care' management includes a decline in oral anticoagulant use without mobile Atrial Fibrillation App intervention, as previously reported[11], which could contribute to worse outcomes (including more ischaemic strokes) in those allocated to the 'usual care' arm of the trial.

Uptake and use of the mobile Atrial Fibrillation App increased even more during the recent coronavirus disease 2019 pandemic period in China. Indeed, digital wearables, telehealth/E-visit, remote management, etc. have been proposed for disease management by academic societies since the coronavirus disease 2019 outbreak[24]. A similar program, e.g. TeleCheck-AF programme, is carrying out atrial fibrillation management through teleconsultations, but without any outcome data[25]. The present study provides some descriptive evidence for mobile health technology for atrial fibrillation management during the current challenging coronavirus disease 2019 pandemic.

5. Limitations

Important limitations should be recognized. This study was performed in a healthcare system with widespread smartphone use, and the results may not be generalizable to other healthcare settings. While we conducted a cluster randomized trial and have adjusted for cluster effect and baseline risk factors, residual confounding may still be present. Moreover, there was possibly selection bias with more male, younger subjects during atrial fibrillation screening phase, although the baseline characteristics were balanced in mAFA-II trial phase of the programme.

The present report which focuses on the subgroup of patients using the mobile Atrial Fibrillation App for over one year, so the patients with less than a year of follow-up were excluded from this analysis. Nonetheless, any 'hard' clinical outcomes in all patients from this subgroup (ie. with >1 year use), even those occurring at < 1 year were also recorded, but less censored data could bias the outcome analysis. Of note, we have also compared the baseline characteristics of patients with

mobile Atrial Fibrillation App use < 1 year and ≥ 1 year (Supplementary Table 5). The patients enrolled into mAFA programme for over one year were more likely to have more comorbidities, compared with patients using the mobile Atrial Fibrillation App for < 1 year. Finally, we found generally good adherence and persistence with the mAFA programme, but this may reflect our relatively young mean age of the study cohort. Further analyses from the mAFA II trial would focus on the elderly and those with clinical complexity, such as multimorbidity.

6. Conclusion

Amongst atrial fibrillation patients with long term use (≥ 1 year) of mobile health technology for optimising stroke prevention, symptom control and comorbidity management, adherence/persistence was good and associated with a reduction in adverse clinical outcomes.

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Declaration of Competing Interest

GYHL: Consultant for Bayer/Janssen, BMS/Pfizer, Medtronic, Boehringer Ingelheim, Novartis, Verseen and Daiichi-Sankyo. Speaker for Bayer, BMS/Pfizer, Medtronic, Boehringer Ingelheim, and Daiichi-Sankyo. No fees are directly received personally. Other authors: None declared.

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Supplementary materials

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ejim.2020.09.024.

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