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Atrial Fibrillation

Atrial fibrillation: epidemiology, screening and digital health

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Summary

Atrial fibrillation (AF) is highly prevalent with a lifetime risk of about 1 in 3–5 individuals after the age of 45 years. Between 2010 and 2019, the global prevalence of AF has risen markedly from 33.5 million to 59 million individuals living with AF. Early detection of AF and implementation of appropriate treatment could reduce the frequency of complications associated with AF. International AF management guidelines recommend opportunistic and systematic screening for AF, but additional data are needed. Digital approaches and pathways have been proposed for early detection and for the transition to early AF management. Mobile health (mHealth) devices provide an opportunity for digital screening and should be part of novel models of care delivery based on integrated AF care pathways. For a broad implementation of mHealth-based, integrated care for patients with chronic diseases as AF, further high quality evidence is necessary. In this review, we present an overview of the present data on epidemiology, screening techniques, and the contribution of digital health solutions to the integrated management of AF. We also provide a systemic review on current data of digital and integrated AF management.

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Keywords: Atrial fibrillation; Epidemiology; Screening; Digital health; Mobile health

Introduction

Atrial fibrillation (AF) is the most common clinically significant cardiac rhythm disorder and is considered a 21st century cardiovascular disease epidemic.[1] AF is associated with increased morbidity and mortality resulting in high burden of healthcare system. Timely detection of AF coupled with appropriate intervention holds the potential to curtail AF-associated complications.[2]

Digital health refers to the use of information and communication technologies in medicine and other health professions to manage illnesses and health risks and to promote wellness.[3] Digital health has a broad scope and includes the use of wearable devices, mobile health (mHealth), telehealth, health information technology, and telemedicine. Previously, digital health solutions have emerged as promising tools for early AF detection and initiation of prompt management.[4] Nonetheless, the widespread adoption of digital integrated care necessitates further high-quality evidence to strengthen its foundation.

In this review, consisting of two main parts, we presented, in the first part, a narrative, comprehensive summary of the current data regarding epidemiology, screening methods and the role of digital health

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Key messages

- The prevalence of atrial fibrillation (AF) continues to increase globally, justifying the term 21st century cardiovascular disease epidemic.
- This multifactorial AF is intertwined with age, sex, race/ethnicity and common concomitant cardiovascular diseases.
- Timely detection and treatment of AF holds the potential to curtail AF-associated complications.
- Digital health solutions have emerged as promising tools for early AF detection and initiation of prompt management.
- Countries should invest in existing cost-effective public health programs and clinical interventions to increase equal access to digital devices to facilitate AF screening and management.

solutions in integrated AF management. In the second part, we provided the results of a systematic review in which we summarized the current data of digital, integrated AF management based on available publications.

Epidemiology

The Global Burden of Disease (GBD) 2019 study demonstrated that more than 59 million individuals lived with AF in 2019 (Fig. 1).[5] The prevalence has risen markedly since 2010 when the number was 33.5 million.[6] However, the true prevalence of AF is higher because many individuals have undiagnosed AF until they develop symptoms or present with an ischemic stroke. Projection studies show that the prevalence of AF will rise to 15.9 million in 2050 in America[7] and 17.9 million in 2060 in Europe.[8] Increased availability of different heart rhythm recording devices and increased awareness of AF undoubtedly had a significant contribution in the overall increase in detection of AF.[4] However, age-standardized prevalence reported in the GBD study remained stable between 1990 and 2019[5] (Fig. 1). This finding indicates that the increasing prevalence is a consequence of longer average life expectancy globally. In contrast, the Framingham Heart Study established a 4-fold increase in the age-standardized prevalence over a 50-year follow-up period.[9]

The incidence of AF varies depending on race/ethnicity, with white individuals exhibiting a higher risk of AF when compared to black, asian, or hispanic individuals.[10–12] The lifetime risk (LTR) of AF was 1 in 4 among white individuals at ≥40 years in the nineties based on data from America and Europe.[13,14] A decade later, the risk over the lifespan appears to rise to 1 in 3 white individuals at >45 years.[15–17] Accordingly, the LTRs among African American and Chinese individuals have been reported lower, approximately 1 in 5[18] and 1 in 10 at ≥40 years.[16]

The prevalence and incidence of AF not only rises with advancing age but also exhibits a higher occurrence in men compared to women[13,14] (Fig. 2). Those disparities may be attributed to sex-specific variations in AF risk factors.[15] Nevertheless, LTR for AF development appeared to be approximately equivalent in both sexes in North American and European populations,[13,14] possibly mirroring the longer life expectancy observed in women,[14] who reach the cumulative incidence for AF observed in men during later decades.[15]

In addition to race/ethnicity and sex, the LTR is about 1 in 5 among individuals with an optimal risk factor profile and it rises to over 1 in 3 if at least 1 elevated risk factor is present.[17] Therefore, addressing modifiable risk factors like hypertension, diabetes, sleep apnea, hyperlipidaemia and lifestyle risk factors (alcohol overconsumption, smoking, lack of physical activity) are crucial for preventing new-onset and recurrent AF. For example, in the Liraglutide Effect in Atrial Fibrillation (LEAF) study, pre-ablation weight loss (≥3–10% vs <3%) through risk factor management with or without liraglutide therapy provided greater percentage of freedom from AF off antiarrhythmic drugs at 6 months (85% vs 57%), particularly in patients with persistent AF (93% vs 59%).[19] On the other hand, in a randomized controlled trial (RCT) of 140 AF patients who were regular drinkers (>10 drinks/week), an almost 8-fold reduction in alcohol consumption over 6 months resulted in lower AF burden (0.5% vs 1.2%) compared with controls who were allowed to continue their usual level of consumption.[20]

Atrial fibrillation screening

AF carries multiple risks, including a 2-fold increase in myocardial infraction,[21] 5-fold increase in stroke[22] and heart failure,[23] as well as dementia and cognitive decline.[24] Coexistence of the aforementioned conditions is associated with a higher mortality compared to each condition alone.[25] Incident AF is associated with an increased risk of non- and sudden cardiac death by 3.0- and 2.5-fold, respectively.[26] Over approximately 30 years, the global deaths attributed to AF saw a significant rise, with a median of 117,038 deaths in 1990 and 315,337 deaths in 2019.[27] The mean number of life-years lost to AF at 10 years has improved significantly, but in contemporary practice, a two-year gap compared with individuals without AF remains.[28] The total number of disability-adjusted life-years increased from 3.79 million in 1990 to 8.39 million in 2019.[5] AF is associated with high utilization of healthcare and costs.[29,30] Danish data from 2017 showed that the average three-year societal costs per patient attributable to AF were

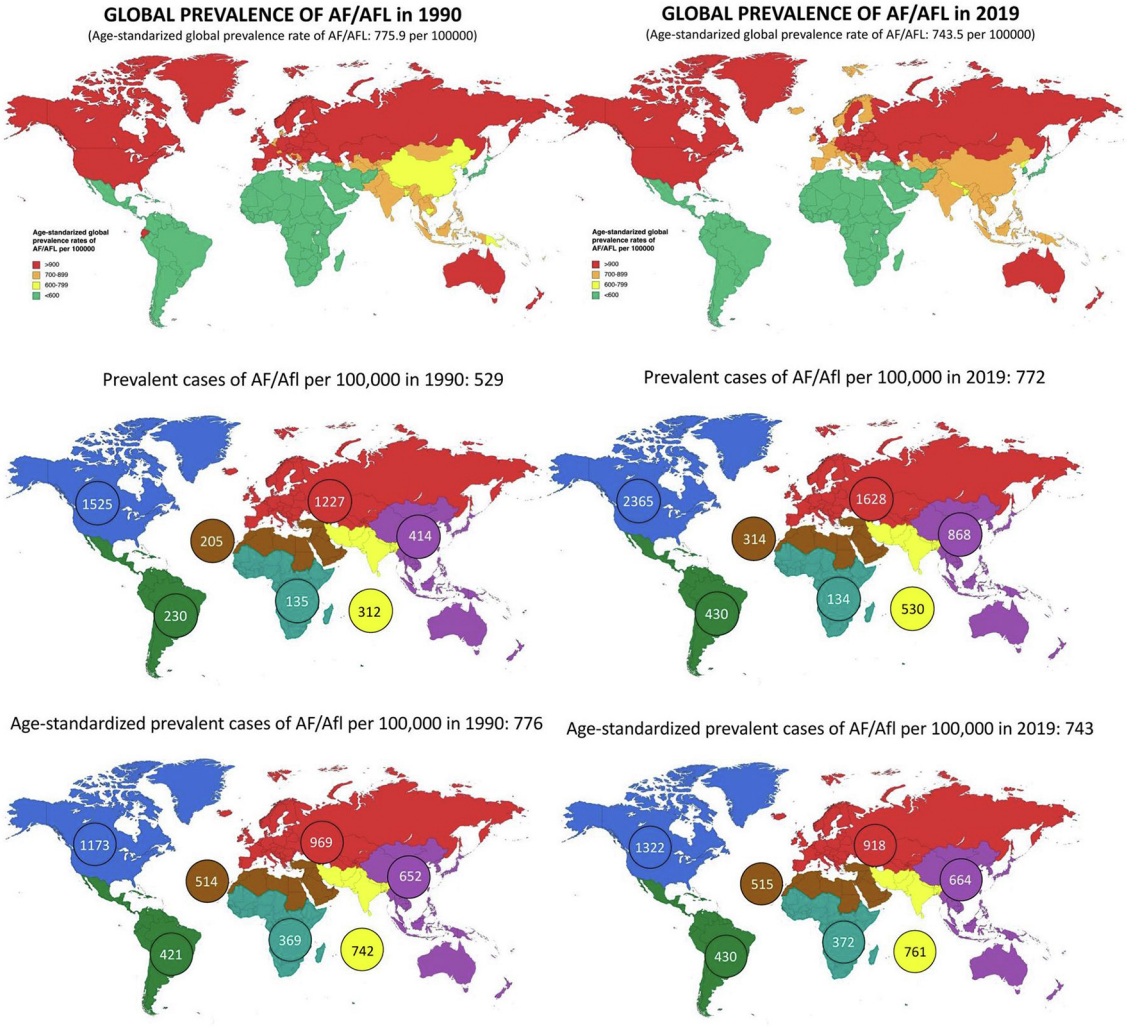

Fig. 1: Prevalence of atrial fibrillation/atrial flutter. Legend. North America is marked in blue, Latin America and Caribbean in dark green, Europe and Central Asia in red, Middle-East and North Africa in brown, Sub-Saharan Africa region in light green, South Asia in yellow, East Asia and Pacific in purple.

~€20,000–27,000,[31] and a recent Scottish study found the annual cost to be ~£3800 per patient.[32]

Considering all the above AF related complications, efforts have been made to reduce the healthcare burden by use of screening focused on high risk populations,[33] or targeted at community based screening programmes.[34] Importantly, while early AF diagnosis is intended to detect AF among individuals with AF-related symptoms, screening invites individuals without AF-related symptoms to undergo testing.[35] A recent meta-analysis of 4 RCTs (REHEARSE-AF, SCREEN-AF, LOOP and STROKESTOP) with a total of 35,836 participants indicated that AF screening was associated with a reduction in stroke as compared with no screening, (RR 0.91, 95% CI 0.84–0.99).[36] However, the meta-analysis results should be interpreted with caution, as the wide-ranging heterogeneity among the included studies and the notably high standard score (z-score) suggest that the inclusion of further studies could potentially alter the overall estimate.

The 2020 European Society of Cardiology (ESC) guidelines on AF management recommend opportunistic screening for AF in persons aged ≥65 years (Class I, Level B) and in hypertensive patients (Class I, Level B) and should be considered in patients with sleep apnea (Class IIa, Level C). Systematic screening for AF should be considered in individuals aged ≥75 years, or at high risk of stroke (Class IIa, Level B).[37] All the different screening strategies and their definitions in the different risk groups are summarized in Table 1. Completed and ongoing prospective trials on AF screening using digital tools are summarized in Tables 2 and 3, respectively.

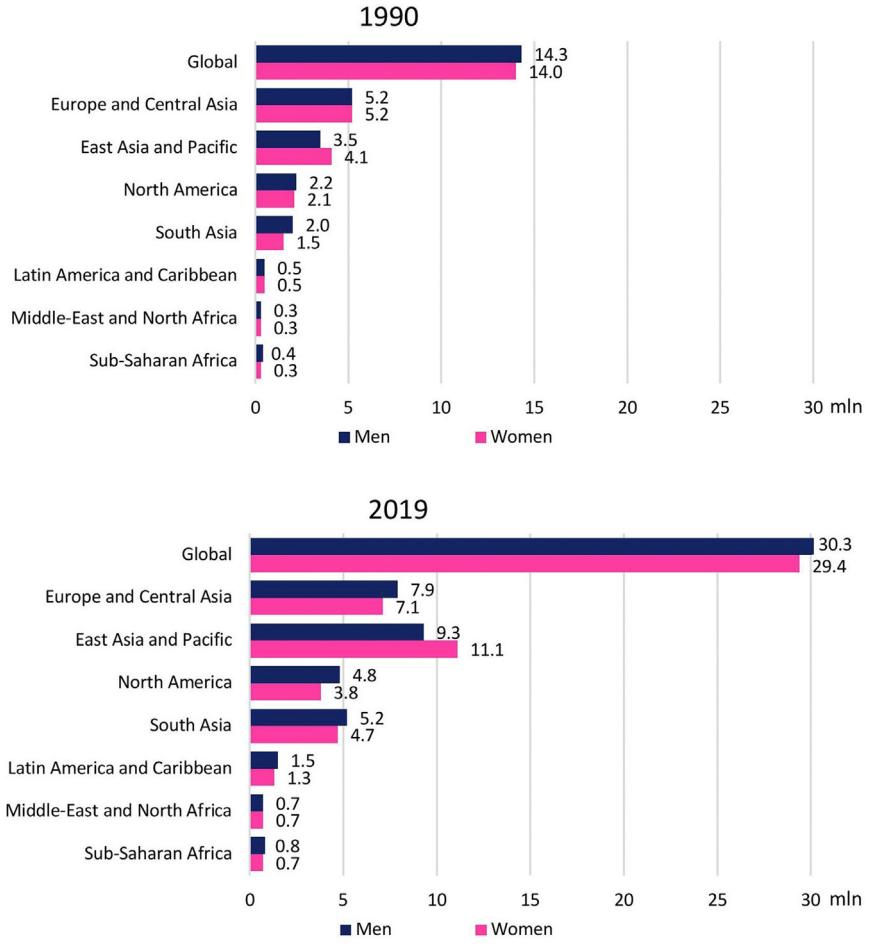

Fig. 2: Prevalence of atrial fibrillation/atrial flutter in both men and women.

Different approaches for atrial fibrillation screening

All existing evidence showing effectiveness of AF therapies in the setting of AF screening is based on trials enrolling patients with electrocardiogram (ECG)-diagnosed AF, including paroxysmal AF. This also accounts for the STROKESTOP study,[38] which randomized (1:1) 75–76-year-olds to be invited to screening for AF by a handheld ECG 2x/day for 2 weeks or to a control group. Treatment with oral anticoagulants was offered if AF was detected or untreated, which reduced the primary combined endpoint of ischaemic or haemorrhagic stroke, systemic embolism, bleeding leading to hospitalisation, and all-cause death (HR 0.96, 95% CI 0.92–1.00). In contrast, studies initiating anticoagulation based on AF detection by continuous rhythm monitoring by implantable cardiac monitors in the LOOP study[39] or based on AHRE's detected by implantable cardiac devices in the NOAH-AFNET 6[40] study did not reduce hard endpoints. In general, detection of asymptomatic AF in a screening program will occur frequently, but data supporting the benefit of having the subject entering the Atrial fibrillation Better Care (ABC) pathway is limited. Ongoing clinical trials are currently testing the impact of implementation of the ABC pathway in Europe (AFFIRMO) and in rural China (MIRACLE-AF) and will determine for which groups of patients ABC pathway is the most optimal to improve the prognosis.

During the 8th Atrial Fibrillation NETwork (AFNET)/European Heart Rhythm Association (EHRA) consensus conference,[41] a systematic screening pathway for AF with an entry of consumer-led screening was introduced (Fig. 3). The document was created by a multidisciplinary group of experts and advocates for a systematic screening approach in all individuals aged ≥75 years and those between 65 and 74 years who possess additional risk factors such as heart failure, hypertension, diabetes, previous stroke or transient ischemic attack, myocardial infarction, lower extremity artery disease, elevated levels

Screening			
Opportunistic	Systematic	Consumer-led	In specific risk groups
Performed as part of clinical contacts for any reason than screening • During routine GP consultation • Pharmacy customers • During vaccination appointments • During healthcare personnel consultation (when pulse palpitation might be performed)	Performed continuously irrespectively of medical contact or needs • Population based • During health campaigns	Performed by individuals in case of symptoms • In out-of-hospital settings (when ECG/PPG-based heart rhythm monitoring might be performed)	Performed in individuals who sustained a prior stroke or transient ischemic attack • In-hospital setting • Post-discharge setting

Table 1: **Types of atrial fibrillation screening.**

NCT	Acronym	Device	Brand	Technology	Age	Enrolment	Study type	Location
Hand-held placement								
NCT02990741	AF-CATCH	Handheld device	AliveCor Kardia	ECG	≥65	4348	Observational	China
NCT04700865	AFstudien	Handheld device	ECG247	ECG	≥65	1500	Interventional	Norway
NCT02006524		Handheld device	MyDiagnostick	ECG	All	3269	Interventional	The Netherlands
NCT03440762		Handheld device	ND	ECG	≥18	83	Interventional	United States
NCT02960334		Handheld device	MyDiagnostick	ECG	≥65	505	Observational	The Netherlands
NCT03860246		Handheld device	AliveCor Kardia	ECG	All	245	Observational	United States
NCT03004859	AF-Stroke	Handheld device	MyDiagnostick	ECG	≥65	7606	Observational	Germany
NCT03740477	SAFARI	Handheld device	AliveCor Kardia	ECG	50–100	1019	Interventional	United States
NCT05067114	SAFE	Handheld device	AliveCor Kardia	ECG	≥18	650	Observational	United States
NCT02409654		Handheld device	AliveCor Kardia	ECG	≥65	500	Interventional	Hong Kong
NCT01160406		Handheld device	Zenicor	ECG	All	250	Observational	Sweden
NCT02270151	IDEAL-MD	Handheld device	MyDiagnostick	ECG	≥65	16,000	Interventional	The Netherlands
NCT04375241	DETECT AF	Handheld device	ND	ECG	≥65	2168	Observational	The Netherlands
NCT02401451	SL-AF	Handheld device	RhythmPadGP	ECG	≥18	750	Interventional	United Kingdom
Hand-held + wearable placement								
NCT03188484	AFRICAT	Handheld device + BP monitor	MyDiagnostik, AliveCor and WatchBP	ECG + Pulsometr	65–75	492	Observational	Spain
NCT02262351	PIAAF-FP	Handheld device + BP monitor	HeartCheck + Watch BP	ECG + Pulsometr	≥65	2174	Interventional	Canada
Wearable placement								
NCT02392754	SCREEN-AF	Patch + BP monitor	Zio®XT + Watch-BP	ECG + Pulsometr	≥75	856	Interventional	Canada, Germany
NCT05818592		Handheld device	ND	ECG	≥18	526	Interventional	United States
NCT05599308		BP monitor	OMRON BP + Watch BP	Pulsometr	≥22	574	Interventional	United States
NCT03313167		Patch + BP monitor	MyBeat + OMRON BP	ECG + Pulsometr	≥65	1316	Observational	Japan
NCT02506244	mSToPS	Patch + wrist-worn device	Zio®XT + Amiigo	ECG + PPG	≥55	6135	Interventional	United States
NCT02875106	BAYathlon	ELR + wrist-worn device + belt	Faros 360 + Adidas miCoach Smart Run + Polar V800, TomTom HR	Pulsometr	≥18	165	Observational	Germany
NCT04176926		Wrist-worn device	FitBit	PPG	≥22	472	Observational	United States
NCT05366803	WHISH STAR	Patch	ND	ECG	65–100	1257	Interventional	United States
NCT03221777	AFOTS	Patch	Zio®XT	ECG	≥18	281	Observational	Canada
NCT02898545	Recurrent AF	ELR	SEEQ	ECG	≥18	1	Interventional	United States
NCT04699812		Patch	ND	ECG	≥22	573	Interventional	United States
NCT04104191		Wrist-worn device	LIVMOR	ECG	≥18	271	Interventional	United States
NCT04842123		Wrist-worn device	Garmin	ECG	≥22	568	Interventional	United States
NCT03721601		Patch + wrist-worn device	ND	ECG + PPG	All	220	Observational	Finland
NCT03477734		Wrist-worn device	Cardiac-Sense1	ECG + PPG	18–85	53	Interventional	Israel
NCT03753139		ELR + wrist-worn device	Faros 360, Suunto Movesense + Empatica E4, Samsung Gear S3	ECG + PPG	≥18	260	Observational	Finland
NCT03335800		Wrist-worn device	Apple Watch	ECG	≥22	419,927	Interventional	United States
NCT04546763		Patch	Zio®XT	ECG	≥22	117	Observational	United States
Invasive placement								
NCT02036450	LOOP	ILR	LINQ	ECG	≥18	6000	Interventional	Denmark
NCT02041832		ILR	REVEAL	ECG	65–90	82	Interventional	Denmark
NCT01727297		ILR	REVEAL	ECG	≥18	446	Interventional	United States

Table 2: **Completed prospective trials on atrial fibrillation screening using digital tools listed currently under clinicaltrials.gov.**

NCT	Acronym	Status	Device	Brand	Technology	Age	Enrolment	Study type	Location
Hand-held placement									
NCT04593498	ESA-AF	Recruiting	Handheld device	Zenicor	ECG	70–89	250	Observational	Sweden
NCT04204330	FECAS-AFS	Active, not recruiting	Handheld device	CardioQvark	ECG	18–96	5000	Interventional	Russia
NCT05784766	SARIC	Not yet recruiting	Handheld device	AliveCor Kardia	ECG	65–90	480	Interventional	United States
NCT04545723		Not yet recruiting	App	FibriCheck	PPG	≥65	8765	Interventional	Belgium
NCT04523649	HUA-TUO	Not yet recruiting	Handheld device	Comfit HealthCare	ECG	≥18	1740	Interventional	Hong Kong
NCT01593553		Unknown	Handheld device	Zenicor	ECG	75–76	7173	Interventional	Sweden
NCT02743416	STROKESTOP II	Unknown	Handheld device	Zenicor	ECG	75–76	6868	Observational	Sweden
NCT02893215		Unknown	Handheld device	Zenicor	ECG	≥65	1622	Observational	Austria
NCT03515057	VITAL-AF	Unknown	Handheld device	AliveCor Kardia	ECG	≥65	35,308	Interventional	United States
NCT04536870	STAREE-HEART	Unknown	Handheld device	AliveCor Kardia	ECG	≥70	500	Interventional	Australia
NCT03524625		Unknown	Handheld device	imPulse	ECG	≥18	200	Observational	United Kingdom
NCT03713333	ASE-INNOVATE	Unknown	Handheld device	AliveCor Kardia	ECG	≥18	500	Interventional	United States
Hand-held + wearable placement									
NCT04108884	RedStroke	Recruiting	App + Patch	Preventicus Heart Beats + ND	PPG + ECG	All	2100	Interventional	Greece
NCT04250220	eBRAVE-AF	Recruiting	App + Patch	Preventicus Heart Beats + CardioMem	PPG + ECG	≥50	4400	Interventional	Germany
Wearable placement									
NCT03911986	R-BEAT	Recruiting	ELR	Novacor R-Test 4	ECG	≥55	755	Interventional	Ireland
NCT05196412		Recruiting	Wrist-worn device	PulseOn Arrhythmi	PPG + ECG	50–99	200	Interventional	Finland
NCT05437926		Recruiting	Wrist-worn device	Huawei	PPG	18–100	102	Observational	The Netherlands
NCT05337202	GERAF	Recruiting	ELR	HeartSDK	ECG	≥65	1250	Observational	The Netherlands
NCT05565781	SMARTTHUNDER	Recruiting	Wrist-worn device	ND	ECG	≥55	100	Interventional	Spain
NCT04624646	CANDLE-AF	Recruiting	Patch	ND	ECG	20–80	600	Interventional	South Korea,
NCT05119725		Recruiting	Patch	S-Patch Cardio	ECG	≥19	2450	Observational	South Korea,
NCT05351775	CARE-DETECT	Recruiting	Wrist-worn device	Phillips	PPG	≥18	300	Interventional	Finland
NCT04884100	enHEART	Recruiting	Wrist-worn device	ND	PPG	≥18	99	Interventional	Switzerland
NCT04932798	GeneAF	Enrolling by invitation	Wrist-worn device	Apple Watch	ECG	≥18	726	Observational	Canada
NCT05444335	SAFE-W	Active, not recruiting	Patch	Zio®XT	ECG	70–100	120	Interventional	United States
NCT04126486	GUARD-AF	Active, not recruiting	Patch	Zio®XT	ECG	≥70	11,931	Interventional	United States
NCT04715555		Not yet recruiting	Patch + wrist-worn device	ND	ECG + PPG	≥65	130	Observational	United Kingdom
NCT04519190		Not yet recruiting	Patch	ND	ECG	18–85	300	Observational	China
NCT05838781	CONSIDERING-AF	Not yet recruiting	Patch	ND	ECG	≥65	2960	Interventional	Sweden
NCT05830578		Not yet recruiting	Wrist-worn device	ASUS Vivowatch	ECG	≥22	602	Observational	Taiwan
NCT00846924	EMBRACE	Unknown	Belt	AccuHeart	ECG	≥55	564	Interventional	Canada
NCT04092985		Unknown	Wrist-worn device	Apple Watch	ECG	≥22	500	Observational	Germany
NCT03301662	TEASE	Unknown	Handheld device (thumb/chest)	Coala Heart	ECG	≥18	100	Observational	Sweden
Invasive placement									
NCT05326828	MINOCA	Recruiting	ILR	CONFIRM Rx	ECG	18–85	60	Observational	Switzerland
NCT04830774	unCOVer-AF	Recruiting	ILR	ILR	ECG	≥18	200	Interventional	United States
NCT05717504	STARGATE	Not yet recruiting	ILR	ND	ECG	≥18	25	Interventional	Canada
NCT01550042	SCARF	Unknown	ILR	ILR	ECG	≥18	50	Observational	The Netherlands
Unknown placement									
NCT03710902	CARDIOSTROKE	Recruiting	ND	ND	ECG	≥40	405	Interventional	Finland

Table 3: **Ongoing prospective trials on atrial fibrillation screening using digital tools listed currently under clinicaltrials.gov.**

of natriuretic peptides ≥125 ng/L, or receive a positive alert from a digital device using photoplethysmography (PPG) or ECG. Systematic AF screening can be facilitated through electronic medical records or population registries that can identify eligible participants by age.[41] Individuals without detected arrhythmias should be reassured. In these individuals, a timeframe for repeated screening/monitoring needs to be established. Whether novel digital approaches for AF screening are effective warrants further study.

Opportunistic vs systematic screening

Meta-analysis of 9 studies (HECTOR-AF, SCREEN-AF, STROKESTOP, D2AF, SAFE, EARLY, REHEARSE-AF,

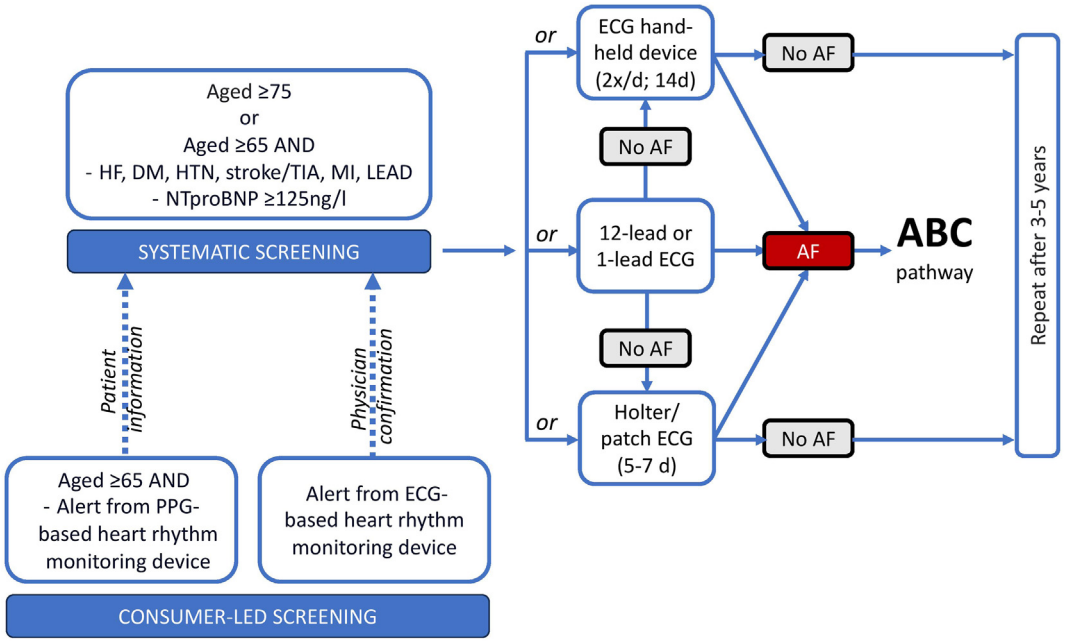

Fig. 3: Systematic screening pathway for atrial fibrillation and entry of consumer-led screening into the systematic screening pathway (suggested by the 8th Atrial Fibrillation NETwork (AFNET)/European Heart Rhythm Association (EHRA) consensus conference[41]). Abbreviations: AF, atrial fibrillation; d, days; DM, diabetes mellitus; ECG, electrocardiogram; HF, heart failure, HTN, hypertension; LEAD, lead lower extremity arterial disease; MI, myocardial infraction; PPG, photoplethysmography; TIA, transient ischemic attack.

Kaasenbrood and Morgan studies), involving 80,665 participants, indicated that systematic screening proved to be effective when compared to standard care (RR 2.11, 95% CI 1.48–3.02) and opportunistic screening (RR 1.86, CI 1.23–2.82).[42] However, there was no significant difference observed between opportunistic screening and standard care (RR 1.13, 95% CI 0.79–1.63). Notably, systematic screening emerged as the most effective approach for detecting AF in individuals aged ≥65 years. In contrast, opportunistic screening did not exhibit a higher level of effectiveness compared to standard care. It's important to note that the quality of evidence was compromised due to potential bias in the included studies and imprecise results, which weakened the overall findings. In another meta-analysis of 9 studies and overall 85,209 patients, which differed by one study from the previous meta-analysis (mSTOPS instead of HECTOR-AF), any AF screening (either systematic or opportunistic) was associated with higher initiation of oral anticoagulation (RR 3.26; 95% CI 1.15–9.23), compared with no screening.[43] There was no significant difference between any AF screening vs no screening in all-cause mortality (RR 0.97; 95% CI 0.93–1.01) or acute cerebrovascular accident (RR 0.92; 95% CI 0.84–1.01). Only systematic screening was associated with higher initiation of oral anticoagulation (RR 5.67; 95% CI 2.68–11.99), compared with no screening. In meta-analysis of 5 studies (SAFE, STROKESTOP, EARLY, DOFA-AP, Morgan study), opportunistic (vs systematic) screening was more likely to be cost-effective.[44] A screening strategy with an initial screening age of 65 years and repeated screens every 5 years until age 80 years was likely to be cost-effective, provided that compliance with treatment does not decline with increasing age.

Photoplethysmography vs electrocardiography

Although the 2020 ESC Guidelines for the diagnosis and management of AF require an ECG documentation for AF diagnosis, PPG its widespread accessibility and low cost making it an interesting tool for remote heart rate and rhythm monitoring, particularly in patients with known AF. Challenges of PPG recordings include underestimation of the heart rate in AF due to a pulse deficit, artefacts in case of for example poor skin contact, activity and variations in skin tone.[45]

For both PPG-based and single-lead ECG devices, diagnosis of regular tachyarrhythmias from the atria can be challenging, based on the lack of (PPG) or difficulty to detect (ECG) P-waves. The distinction between AF, typical atrial flutter, atrial tachycardia, and junctional tachycardia can be difficult to make.

Atrial fibrillation management supported by digital devices

Peri-cardioversion

Achieving optimal rate control in patients with AF on the waiting list prior to elective cardioversion or in

patients with AF using a wait-and-see strategy at the emergency department (ED), can be challenging. Regular assessment of rate control and the use of a simple preprocedural medication adjustment protocol is effective in optimizing peri-cardioversion rate control. The TeleWAS-AF approach supports the management of patients with AF peri-cardioversion via remote rate and rhythm monitoring using digital devices, allowing for remote adjustment of rate control medication and detection of spontaneous conversion to sinus rhythm.[46] In general, all stable patients who present to the ED with recent-onset symptomatic AF planned for a wait-and-see approach who can use digital solutions for remote heart rate and rhythm monitoring are eligible for this approach. Whether the implementation of digital devices can facilitate the management of AF in the ED and reduce the burden on the ED system is currently investigated in ongoing studies.

Post-ablation

Holter-ECG is frequently used to monitor rhythm at 3, 6, and 12 months after AF ablation to test for AF recurrence. During the COVID-19 pandemic, several centers collected experience on using on-demand digital devices for follow-up after AF ablation.[47] In a pilot study from a single-center patients using digital devices 3 months after AF ablation had similar AF detection rates and a reduced need for additional ECG-monitoring compared to standard-of-care.[48] A caveat here is that validation of most devices has not been performed in the post-ablation population, which might be more prone to atrial tachycardias other than AF, which is notably more difficult to diagnose with digital devices using single-lead ECG or PPG. Prior studies have shown that 2 weeks of long-term intermittent monitoring by digital devices more effectively detected AF recurrences and had a higher patients' usability than short continuous Holter monitoring.[49]

Long term atrial fibrillation management

During the COVID-19 pandemic, an on-demand digital approach for the remote management of AF through teleconsultation was used in 40 centres in Europe.[47] The TeleCheck-AF approach implements remote PPG rate and rhythm monitoring in patients managed through teleconsultation. Patients are instructed to use the PPG app 3 times daily and in case of symptoms 1 week prior to teleconsultation. This information is then used during teleconsultation. Data indicate a positive center and patient experience.[50] The effect of this intervention on clinical outcomes will be investigated in a RCT. A structured follow-up packages guiding the rehabilitation at home have been updated for mAFA (mAFA III) and are suitable for patients receiving drug treatment only or left atrial appendage occluder.[51]

Integrated digital atrial fibrillation management: a systematic review

To summarize the current status of digital, integrated AF management, we performed a systematic review of relevant publications.

Search strategies and selection criteria

This screening was conducted in accordance with the preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines (Fig. 4).

The electronic databases PubMed (NCBI), Cochrane (including database of reviews on effectiveness DARE, Current Controlled Trials (CCT), as well as NHS Economic Evaluation Database (NHS-EED) and Health Technology Assessment Database (HTA)) were systematically searched for articles published until February 2023. Search terms included: (1) (atrial fibrillation or AF or Afib) and (2) (digital management or digital care or digital treatment or digital health or remote management or remote care or remote treatment or e-health or ehealth or e health or m-health mhealth or m health or mobile health or mobile-health or telemedicine or app-based or application-based or integrated care). All identified studies were screened based on their title and abstract against search criteria by 2 reviewers (M.G. and K.B.). Full-text manuscripts were independently assessed by both reviewers and manuscripts were included if eligibility criteria were met. Disagreements were resolved through assessment by a third reviewer (D.L.). The final reference list was generated based on originality and relevance with regard to the scope of this review on integrated digital AF management.

A total of 33 publications were considered relevant. Of those, 14 publications reported on integrated e-health enhanced management of AF,[47,52–64] 5 on remote AF management platforms,[65–69] 3 publications on mHealth-based heart rate/rhythm monitoring,[70–72] 6 publications on mHealth supported patient self-care and medication adherence tools[73–78] and 5 publications reported on clinical decision making support tools.[79–83]

All studies with their descriptions and limitations are presented in Table 4. Most of these studies are small observational studies, with short follow up, therefore not achieving a sufficient number of outcomes, which results in the failure to obtain statistically significant differences between analyzed groups. Many studies lack control groups and focus on before-and-after changes, which may be confounded by the Hawthorne effect. When it comes to RCTs, a significant number of them have a cluster design, therefore some differences in baseline characteristics and medical treatment were also evident. Moreover, a biased selection approach might likely influence some results. For example, recruited patients might be more enthusiastic about the use of new technology, and they, consequently, demonstrate a greater likelihood of daily use than a more generalizable

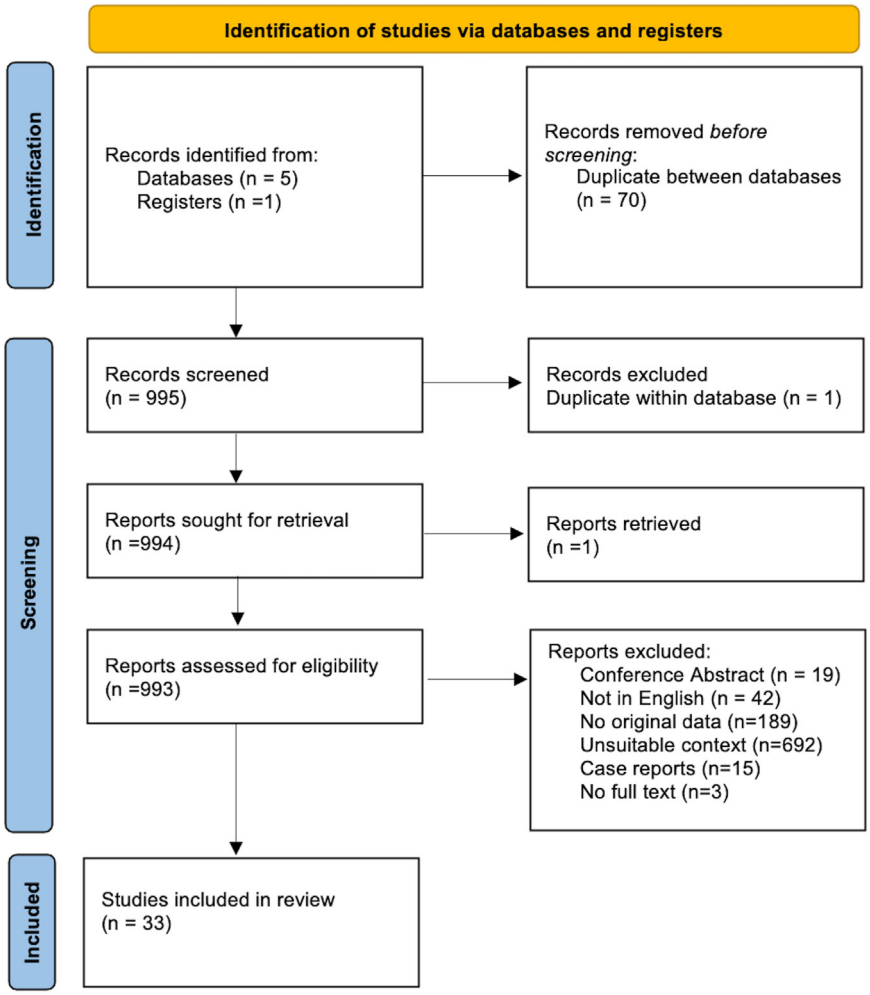

Fig. 4: PRISMA flow diagram for systematic reviews on effects of mobile health solutions designed to integrated atrial fibrillation management.

cohort. Therefore, the results of those studies should be interpreted with caution.

E-health enhanced management of atrial fibrillation

The mAFA-II trial evaluated the efficacy of an mHealth-supported AF management model with integrated clinical decision support tools and guideline-based treatment and patient involvement (mAFA intervention). Results from multiple mAFA-II trial analyses showed that the mAFA intervention (vs usual care) improved patient knowledge on AF, quality of life[52] and oral anticoagulation adherence,[52,56] as well as reduced the risk of bleeding events (2.1% vs 4.3%)[56] and composite outcome of recurrent AF, heart failure and acute coronary syndrome, however, only in patients without heart failure (HR 0.26, 95% CI 0.14–0.48).[55] The mAFA intervention decreased rate of the composite primary endpoint of ischemic stroke/systemic thromboembolism, all-cause death and re-hospitalization over a mean of 286 days (HR 0.39, 95% CI 0.22–0.67)[53] and it reduced the rate even more in the long-term follow-up (mean 697 days; HR 0.18, 95%, CI 0.13–0.25)[54] compared to the usual care group. This superior effect held true for patients with multimorbidity[57] and both in males and females.[58] In a hypothetical cohort within the mAFA-II trial, the base-case analysis indicated cost-effectiveness of applying mHealth-based integrated care for AF with cost-effective ratio of US $14,936 per quality-adjusted life years, which was below the willingness-to-pay (US $33,438 per quality-adjusted life years).[59] However, these findings should be interpreted cautiously due to the model-based approach, short follow-up, region-specific factors, and multiple cost inputs (including expert opinions).

Hendriks et al. randomized 712 patients with newly diagnosed AF to receive an integrated care approach which included nurse-driven, physician supervised AF treatment guided by software based on the AF guidelines or to receive an usual care by a cardiologist.[61] The

Study/ country	Design	Intervention	No. of patients	Age (years)	Women	Study duration	Results	Limitations
E-health enhanced management of atrial fibrillation								
Guo et al.[53] China	RCT		1646(IC) 1646(UC)	67 + 15 70 + 12	38% 38%	291 days	• Death/ischemic stroke/systemic thromboembolism, rehospitalization (IC vs UC): HR 0.39, 95% CI 0.22–0.67 • Rehospitalization: HR 0.32, 95% CI 0.17–0.60)	• Cluster design • Differences in baseline characteristics, OAC between groups • High-level hospital and specific-region setting • Low rates of outcomes • Costs retrieved from multiple sources • Lack of phenotyping of HF at baseline
Guo et al.[56] China	RCT		1077 (IC) 1136(UC)	ND ND	ND ND	12 months	• Bleeding events (IC vs UC): 2.1% vs 4.3%, p < 0.01 • OAC use decreased by 25% in UC	
Guo et al.[52] China	RCT		113 (IC) 96 (UC)	67 + 11 71 + 17	43% 45%	3 months	• Patient AF knowledge: improved (all p < 0.05) • Patient QoL (IC vs UC): 86.5–87.2 vs 71.3–69.9, p < 0.05 • Patient drug adherence: 0 (0–4)–2 (0–4) vs 4 (0–11)–4 (0–11); p < 0.001 • Patient OAC satisfaction: p = 0.013 • App usability: 90% reported app	
Guo et al.[54] China	RCT	mAFA infrastructure - AF education - CDSS (CHA2DS2-VASc, HAS-BLED, SAMe-TT2R2 scores) - Thromboprophylaxis guidance - Patient event tracker - Heart rhythm monitoring - BP monitoring - Symptom tracker - Lifestyle tracker - Medication adherence - Self-care protocols - Structured follow-up	1261 (IC) 1212 (UC)	67 (mean) 70 (mean)	38% 42%	≥12 months	• Death/ischemic stroke/systemic thromboembolism, rehospitalization (IC vs UC): HR 0.18, 95% CI 0.13–0.25 • App usability: persistence of use of 92%	
Yao et al.[57] China	RCT		833 (IC) 1057(UC)	72 ± 12 73 ± 13	33% 42%	≥12 months	• Death/ischemic stroke/systemic thromboembolism, rehospitalization (IC vs UC): HR, 0.37; 95% CI, 0.26–0.53 • Rehospitalizations alone: HR 0.42; 95% CI 0.27–0.64 • Stroke/thromboembolism alone: HR 0.17; 95% CI 0.05–0.51 • MI/HF/uncontrolled BP: HR 0.29; 95% CI 0.19–0.45	
Guo et al.[58] China	RCT		2062 (men) 1262 (women)	68 ± 14 70 ± 13	0% 100%	≥12 months	• Death/ischemic stroke/systemic thromboembolism/rehospitalization (IC vs UC): HR 0.30, 95% CI 0.17–0.52 (men), HR 0.50, 95% CI 0.27–0.92 (women) • Thromboembolism: NS • Death: HR 0.32, 95% CI 0.12–0.87 (men) • Rehospitalization: HR 0.29, 95% CI 0.15–0.57 (men), HR 0.31, 95% CI 0.14–0.68 (women) • Bleeding): NS • RAF/HF/MI: HR 0.32, 95% CI 0.18–0.56 (men)	
Luo et al.[59] China	Cost benefit analysis		NA	NA	NA	30 y	• Costs (IC vs UC): US $35,691 vs US $34,601 • QALY gain: 7.2749 vs 7.2019 • ICER below WTP: US $14,936 vs US $33,438 per QALY	
Guo et al.[55] China	RCT		360 (IC) 354 (UC)	73 ± 13 73 ± 14	45% 35%	12 months	• Death/ischemic stroke/systemic thromboembolism, rehospitalization (IC vs UC): HR 0.40, 95% CI 0.21–0.76 (no HF) • RAF/HF/MI: HR 0.26, 95% CI 0.14–0.48 (no HF) HR 1.99, 95% CI 1.08–3.69 (HF)	

(Table 4 continues on next page)

Study/ country	Design	Intervention	No. of patients	Age (years)	Women	Study duration	Results	Limitations
(Continued from previous page)								
Gawalko et al.[47] Europe	RC	TeleCheckAF infrastructure - AF education - Heart rhythm monitoring - Symptom tracker - Teleconsultations	1480	64 (55–71	38%	NA	• Patient experience: ease to use (94%), safe feeling (74%), willingness to use in the future (58%) • Physician experience: no problems with cloud access (91%), patient recruitment (91%), quality of recordings (91%), patient compliance with heart rate/rhythm monitoring (83%) number and time to include patients, independent of the centers' mHealth experience	• Retrospective design • Differences in mHealth reimbursement system • Course of the study during the pandemic
Hermans et al.[60] Europe	RC		994	65 (57–71)	38%	NA	• Self-reported vs electronic health record agreement: the highest for pacemaker, OAC; lowest for vascular disease, heart attacks, arrhythmias • Patients with (vs without) AF awareness had more likely 100% agreement (27 vs 14%, p = 0.001)	
Hendriks et al.[61] The Netherlands	RCT	CardioConsultAF infrastructure - CDSS - Teleconsultations	356 (IC) 356 (UC)	66 + 13 67 + 12	45% 38%	22 months	• Mortality: HR 0.44, 95% CI 0.23–0.85 • CV-mortality: HR 0.28, 95% CI 0.09–0.85 • Non-CV mortality: NS	• Outside NOAC era • Differences in OAC between groups relatively young and "less severe" clinical profile population
Woo et al.[62] Singapore	RC	- CDSS - AF education - Teleconsultations	43	69 (64–74)	33%	6 months	• CV hospitalization (baseline vs FU): NS • Stroke: NS • Quality of life: AFEQT 90 + 12 vs 95 + 5.4, p < 0.001 • AF knowledge: SGAFKS 4.5 + 2.5 vs 6.9 + 1.8, p < 0.001 • Medication adherence: 1.5 + 0.5 vs 1.3 + 0.4, p = 0.008 • Patient satisfaction: PSQ 3.9 + 0.4 vs 4.1 + 0.3, p = 0.020 • Patient depression: PHQ-9 1.1 + 1.6 vs 0.5 + 1.4, p = 0.004	• Retrospective design • Low sample size • Lack of control group • Hawthorne effect before-and-after study design
Jiang et al.[63] China	PC	HCFT-AF infrastructure - AF education - Health record - Symptom tracker - Heart rhythm monitoring - BP monitoring - Teleconsultations	73	68 ± 10	48%	4 months	• Patient satisfaction 5.2 ± 1.4; ease of use 4.8 ± 1.6, usefulness 5.5 + 1.4; usability 5.1 ± 1.5 • Self-monitoring of BP: 26–72% (p < 0.001), heart rate 8–52% (p < 0.001), heart rhythm 7–48% (p < 0.001) • Moderate physical activity: 22–42% (p = 0.09), quitting or reducing alcohol 51–73% (p = 0.005), quitting or reducing smoking 62–72% (p = 0.04) • Low-salt, low-fat diet: 42–61% (p = 0.04), more fruits or vegetables consumption: 25–76% (p < 0.001) • 94% of indicated patients received OAC	• Small sample size • Lack of control group • Hawthorne effect before-and-after study design

(Table 4 continues on next page)

Study/ country	Design	Intervention	No. of patients	Age (years)	Women	Study duration	Results	Limitations
(Continued from previous page)								
Peleg et al.[64] Italy	PC	MobiGuide's infrastructure - AF education - Health record - Symptom tracking - Lifestyle tracking - CDSS - Medication adherence - Heart rhythm monitoring - BP monitoring	10	ND	ND	127 ± 69 days	• Patient compliance to ECG (0.7 ± 0.3) and BP measure (0.8 ± 1.3) • AF episodes (patient vs system–initiated measurements was higher than that found in system-initiated requests (p = 0.01) • Patient QoL (baseline vs FU): improved/deteriorated in 50%/38% based on EuroQoL; improved/deteriorated in 25%/63% based on AFEQT • Clinician compliance to DSS recommendations (0.3) • Patient compliance to DSS recommendations (>0.9) • Patient satisfaction: system increased patient's confidence (in 50% of patients), made ability to adapt to context (86%), improved patients' peace of mind during travel (88%), improved their interaction with clinicians (>50%); was recommend to others (100%), was intended to use it in the future (89%); not complicated patients' lives (33%) • Clinician satisfaction: system helped to identify priorities and increases patient safety (100% of clinicians), made it easier to manage patients (100%)	• Small sample size • Lack of control group • Hawthorne effect • Before-and-after study design
Remote atrial fibrillation management platforms								
Manimaran et al.[65] United Kingdom	PC	Ortus-iHealth - Virtual arrhythmia clinic appointment via video call	46	62 (23–86)	36%	3 months	• Patient activation: high satisfaction with installation and registration process (in 62% patients), sense of reminders (100%) and clinical letters (83%) usefulness, sense of cost- and time-effectiveness (80%)	• Small sample size • Short FU • Lack of control group
Mitrani et al.[66]	PC	AF-HEART - Heart rhythm, weight and BP tracking, televisitations (dietician), referrals for sleep apnea and hypertension treatment	20	62 ± 8.0	35%	6 months	• Weight loss mean 3.5 kg (p = 0.005) or 3.3 ± 4.4% • Patient QoL (baseline vs FU): improved based on SF-12 (p = 0.01), AFSS (p = 0.01), EQ-5D (p = 0.006), AFEQT (p = 0.03) • Correlation between weight loss and decrease in symptom severity (absolute r = −0.45, p = 0.05 and % r = −0.49, p = 0.03)	• Small sample size • Single-center setting
Stegman et al.[67] Germany	RCT	- Daily transmission of body weight, BP, heart rate/rhythm, oxygen saturation, and self-rated health status	282 (IC) 289 (UC)	74 ± 8.0 74 ± 8.1	32% 30%	12 months	• Days lost due to unplanned CV death or hospitalization (IC vs UC): OR 0.60, 95% CI 0.25–0.95 • All-cause mortality: HR 0.60, CI 0.36–1.00	• Unpowered results • Specific-region setting • New-diagnosed AF not considered in the analyses
Weng et al.[68]	PC	Kinduct AF - Online educational and treatment platform	93	63 ± 12	42%	6 months	• Patient QoL (baseline vs FU): improved (OR 0.45, 95% CI 0.28–0.71) based on CCS-AF; NS changes based on AFSS, EQ-5D • Patient satisfaction: user friendly (83% of patients), easy to navigate (85%), good source for AF information (73%)	• Underpowered results • Log in with credentials may have deterred users
	RCT	- Heart rhythm tracker (KardiaMobile)	36 (IC) 71 (UC)	61 61	33% 40%	6 months	• AFSS score (IC vs UC): mean difference 2.52, 95% CI −4.48 to −0.25 • ED visits, hospitalization: NS	• No data on frequency of AHM use • Low usage rate

(Table 4 continues on next page)

Study/ country	Design	Intervention	No. of patients	Age (years)	Women	Study duration	Results	Limitations
(Continued from previous page)								
Lazaridis et al.[69]	Usability	myAlgos - Physician oriented platform, patient oriented mobile app	5 (physician) 33 (patient)	57 ± 36	37%	4 weeks	• Physicians rating: PSSUQ score of 2.5 ± 0.4; mean satisfaction 75% • Patients rating: MAUQ score of 79.9%; arrangement of the app's interface: 56 ± 8.1 out of 70 (80%); app's predicted usefulness in the self-management of AF: 45 ± 6.3 out of 56 (81.5%)	• Small sample size
	RCT	randomization: full/control version	80	58 ± 9	34%	6 months	• No major CV events or deaths • Median AFEQT change at 6 months + 2.63% in full, vs −1.63% in control version groups (p > 0.001) with highest sub-domain differences in treatment satisfaction and treatment concern • EQ-5D-5L stable in control and minor increase in full version group (+3.5 ± 9%)	• Single center setting • Patient selection bias (mHealth enthusiasts; young population) • Lack of UC
Mobile-Health-based heart rate/rhythm monitoring								
Lambert et al.[70]	RCT	Self-monitoring after early successful AF ablation using smartphone ECG (Kardia Mobile) with an cloud-based platform (KardiaPro) including alerts on AF detection	51 (IC) 48 (UC)	64 ± 10	29%	6 months	• Similar healthcare utilization between groups • More ambulatory ECG and heart rhythm monitors in UC (27.1%) vs IC (5.9%) p = 0.004 • AF detection: 12.5% in UC vs 23.5% in IC (no statistically significant difference)	• Single-center setting • Small sample size • Underpowered for definitive conclusions between groups • Patient selection bias (mHealth enthusiasts) • Cross over between study groups
Caceres et al.[71]	CC	iHeart: Smartphone (IPhone) equipped with the AliveCor Kardia mobile ECG system with transmission of recordings to AliveCor cloud, where staff conducted daily review and interpretation. Additionally, participants in IC received text messages 3/week about AF management and lifestyle factors associated with AF risk.	115 (IC) 123 (UC)	61 ± 12 61 ± 12	23% 23%	6 months	• HRQOL: Increased global AFEQT at 6 months (18.5 points and 11.2 points for IC and UC, respectively) • IC improved scores on physical component summary of SFHS (mean change 3.0, p < 0.05) • EuroQol-5D unchanged with no significant difference in IC vs UC • AFSS significantly decreased (5.4 and 4.5 points in IC and UC, respectively	• Missing data in IC and UC groups at follow-up • Single center • Sample size limited detection of statistically significant differences between groups • Impact of text messages towards patient engagement and AF burden
Hickey et al.[72]	CC	Pilot study of iHeart intervention (see above) Patients received smartphone ECG monitoring (AliveCor) after successful rhythm control strategies; Use of the ECG device daily (and when symptomatic)	23 (IC) 23 (UC)	55 ± 10 55 ± 10	29% 29%	6 months	• AF/AFL detection: HR 2.55, 95% CI 1.06–6.11 • QoL (n = 13): Increased PCS scores at 6 months (50.3 ± 7.6 to 55.9 ± 5.3 (p = 0.02), no significant change in MCS scores • Patient satisfaction: 92% of respondents thought the device was beneficial, 58% said that they were more health conscious after participating in the study • No significant difference in hospitalization	• Lack of UC • Small study group

(Table 4 continues on next page)

Study/ country	Design	Intervention	No. of patients	Age (years)	Women	Study duration	Results	Limitations
(Continued from previous page)								
Mobile-Health supported patient self-care and medication adherence tools								
Desteghe et al.[73] Belgium	PC	Health Buddies - Medication tracker - AF education - Healthy challenge tracker - Teleconsultations - OAC reminders	15 + grandchildren (n = 46)	69 ± 3.7	33%	3 months	• AF knowledge: NS • Medication adherence: NS; lower taking and regimen adherence than self-reported on app • Motivation to use app: decreased in patients (p = 0.009) and grandchildren (p < 0.001); completed the contract (87%) • Mean days using app: higher in patients vs grandchildren (58 ± 30% vs 24 ± 24%, p = 0.002) • App experience: clarity (1.500), novelty (0.942), stimulation (0.923), attractiveness (0.859), efficiency (0.577), dependability (0.481)	• Small sample size • Single-center setting • Lack of UC
Toscos et al.[74]	RCT	Educational program (MyChart) - AF education - Medication adherence	80 (IC) 80 (UC)	71 ± 9 71 ± 9	37% 37%	6 months	• AF knowledge (IC vs UC): improved (p = 0.01) • Medication adherence: NS	• Patient selection bias • Limited degree of accuracy with medication tracking method • No assessment of clinical outcomes
Hsieh et al.[75]	RCT	Web-based management program - AF education - Medication adherence - Symptom tracker - Teleconsultation	115 (IC) 116 (UC)	72 ± 12 75 ± 9.9	55% 46%	24 months	• Coping strategies (IC vs UC) β = 1.90, 95% CI 0.88–2.92 at 6-month • Medication adherence: β = 0.61, 95% CI 0.25–0.96 at 6-month • HRQoL:EQ-5D scores: β = 0.19, 95% CI 0.13–0.25 at 6-month • Readmission events: OR 0.41, 95% CI 0.18–0.93 at 24 months	• Mild-moderate AF severity in most participants • Single-center setting • Lack of inclusion socioeconomic factors for medication adherence/readmission
Guhl et al.[76] United States	RCT	Educational program (animated character with speech, body gesture, facial expression) - AF education - Symptom tracker - Heart rhythm monitoring (AliveCor Kardia)	61 (IC) 59 (UC)	72 ± 11 73 ± 7.3	53% 51%	1 month	• Patient QoL (IC vs UC): mean difference 4.5; 95% CI 0.6–8.3 • Patient daily activity: mean difference 7.1; 95% CI 1.8–12.4 • Patient medication adherence: mean difference 16.6%; 95% CI 2.8%–30.4% • Qualitative assessments of acceptability identified that participants found the relational agent useful, informative, and trustworthy	• Self-reported measures • Small sample size • Patient selection bias
Trymbulak et al.[77] Poland	PC	Mobile phone app based geriatric assessment including wrist-based wearable activity monitor (Fitbit)	40	71 ± 5	38%	6 months	• Adherence: 90% of patients completed baseline survey, 76% all day 30 surveys, 62% day 30 6 min walk test (6MWT) • 65% called 2 times or less, 75% 3 times or less, for support • Primary reasons for calls: assistance with Fitbit devices (26%), account login help (17%), confusing with text message system prompting 6MWT	• No data on acceptability • Small sample size • Patient selection bias (mHealth enthusiasts) • Differences in patient characteristics
Magnani et al.[78] United States	PC	Mobile app (animated character with speech, body gesture, facial expression) - AF education - Symptom tracker - Medication adherence - Heart rhythm monitoring (AliveCor Kardia)	31	68 ± 11	39%	1 month	• Patient QoL: improved from 64.5 ± 22.9 to 76.3 ± 19.4 (p < 0.01) • Patient drug adherence: improved from 7.3 ± 0.9 to 7.7 ± 0.5 (p = 0.01) • Most of the participants found the relational agent useful, informative, and trustworthy	• Lack of UC • Small sample size • Patient selection bias (mHealth enthusiasts)

(Table 4 continues on next page)

Study/ country	Design	Intervention	No. of patients	Age (years)	Women	Study duration	Results	Limitations
(Continued from previous page)								
Clinical decision-making support systems								
Kapoor et al.[79]	PC	AFib 2gether - OAC optimization	37	46% (≥75 y)	30%	ND	• MARS combined average functionality score: 4.51 (SD 0.61) • MARS esthetics category: 4.26 (SD 0.51) • MARS star usability rating: 4.24 (SD 0.89) • Patient satisfaction: improved OAC knowledge (40%), helped clarify provider OAC preferences (62%), helped to decide whether to go on OAC (54%) • Provider ratings: functionality (4.2 ± 0.5), esthetics (4.0 ± 0.5), quality (3.8 ± 0.4) • Provider satisfaction: helped clarify preferences of patients (79%), saved time (82%), helped patients make decision about OAC (59%)	• Lack of UC • Small sample size • Interruption by restrictions COVID -19 pandemic • Limited information for not being on OAC
Karlsson et al.[80] Sweden	RCT	- OAC optimization	7764 (IC) 6370 (UC)	58% (>75 y) 58% (>75 y)	43% 43%	12 months	• Adherence to guidelines (IC vs UC): increased from 70 to 73% vs 70–71%, p = 0.013 • Stroke, transient ischemic attack, or systemic thromboembolism: NS • Bleeding: 12 vs 16 per 1000 patients, p = 0.04	• Cluster design • Single-center setting (publicly funded healthcare) • Closedown of 1 of the primary care clinics in UC
Eckman et al.[81] United Kingdom	RCT	- OAC optimization	801 (IC) 692 (UC)	70 70	44% 48%	12 months	• Rate of discordant therapy decreased from 63% to 59% (p = 0.02).	• Cluster design
Schott et al.[82]	RCT	IDeA Health Decision - Health record - OAC optimization - Medication options - CHA2S2-VASc and HAS-BLED assessment	33 (IC) 33 (UC)	72 ± 8.0 75 ± 11	36% 60%	6 months	• AF knowledge (IC vs UC): OR 3.88, 95% CI 1.39–10.78 • Decision conflict: NS • Patient satisfaction (n = 12): ease of use, acquisition of knowledge regarding stroke; limited ability to ask questions • Clinician satisfaction (n = 9): helped center patient conversation, improved confidence in decision-making, saved time on calculating risk scales	• Cluster design • Small sample size • Single-center setting • Differences in the provision of information by physicians
Cox et al.[83] Canada	RCT	- AF education - Health record -Thromboprophylaxis guidance - Heart rhythm control guidance - Symptom tracker	590 (IC) 543 (UC)	73 ± 10 72 ± 9.9	60% 65%	12 months	• Unplanned emergency department visit/CV hospitalization (IC vs UC): NS • Major bleeding: NS	• Cluster design • Differences in OAC between groups

Abbreviations: AF, atrial fibrillation; AFl, atrial flutter; BP, blood pressure; CC, case–control; CDSS, clinical decision support system; CI, coincidence interval; CV, cardiovascular; ECG, electrocardiogram; ED, emergency department; FU, follow up; HF, heart failure; HR, hazard ratio; IC, intervention care; NA, not applicable; ND, no data; NS, not significant; OAC, oral anticoagulation; OR, odd ratio; PC, prospective cohort; QoL, quality of life; RC, retrospective cohort; RCT, randomized controlled trial; RR, risk ratio; UC, usual care; y, year.

Table 4: **Mobile applications and platforms supporting management of atrial fibrillation.**

study showed a significant reduction in all-cause mortality (HR 0.44, 95% CI 0.23–0.85) during mean follow up of 22 months in intervention (vs control) group.

The impact of another Nurse-Led Integrated Chronic Care E-Enhanced Atrial Fibrillation (NICE-AF) clinic was evaluated in a retrospective cohort study of 43 participants.[62] At 6-month follow up, participants reported significantly higher levels of quality of life, AF knowledge and medication adherence as well as lower levels of depression (all p value < 0.05) than before. No significant differences in cardiovascular hospitalizations and incidence of stroke were observed.

TeleCheck-AF is a mHealth infrastructure dedicated comprehensive AF management through teleconsultations supported by an on-demand PPG-based heart rate and rhythm monitoring app.[47] With expansion of the infrastructure, the feasibility and scalability of TeleCheck-AF was proven by showing the ease of implementing the infrastructure in >80% participating centres and the ease of use of the mobile app by patients (94%). Also, the ability to integrate mHealth data in clinical-decision making processes was demonstrated.[60]

A prospective cohort study of 73 participants evaluated the effectiveness of an integrated AF care via the Hospital-Community-Family-based Telemedicine (HCFT-AF) program including an AF management infrastructure providing care according to the ABC pathway.[63] Patient drug adherence improved significantly over 4 months and patients gave good feedback on the intervention.

Another prospective cohort study by Peleg et al. reported the feasibility of AF MobiGuide patient-centered mobile decision support system for 10 patients with AF and care providers.[64] Analysis of the patients' quality of life questionnaires for the patients with AF was inconclusive. While most patients reported an improvement in their quality of life in the EuroQoL questionnaire, most patients with AF reported a deterioration in the Atrial Fibrillation Effect on QualiTy-of-life (AFEQT) questionnaire.

Remote atrial fibrillation management platforms

The e-medicine Platform for Optimizing the Workflow in hEaRt Diseases (emPOWERD-AF) RCT assessed the usability of myAlgos, an mHealth management system consisting of a physician-oriented platform and patient-oriented smartphone app.[69] Via the platform, physicians received all patient reported data (vital signs, blood pressure, heart rate, body weight, blood glucose levels, oxygen saturation, medication adherence statistics). The platform received a mean 75% satisfaction score by 5 physicians and a mean 75% ease of use and satisfaction score by 80 patients. Over a follow up of 6 months, control and full app version group experienced a similar number of AF-related hospitalizations. However, the full version group (vs control) experienced a significant increase in quality of life.

A prospective cohort study conducted by Manimaran et al. assessed the feasibility of virtual post-ablation clinic appointment in 39 patients.[65] By using the Ortus-iHealth app, patients uploaded vital signs (heart rate, blood pressure, blood glucose, weight, and temperature) onto the platform, to which a trained clinical nurse specialist had an access. Eighty percent of patients reported significant travel cost savings and 93% reported time savings.

In the Atrial Fibrillation Helping Address Care with Remote Technology (AF-HEART) prospective cohort study, 20 patients with AF undergoing antiarrhythmic therapy, cardioversion, and/or catheter ablation underwent an intervention including heart rhythm tracking (AliveCor, Kardia), risk factor reduction by weight reduction, blood pressure monitoring, alcohol reduction, and sleep apnea reduction through referrals.[66] During the 6-month follow up period, the quality of life improved and symptom severity decreased.

Telemedical Interventional Management in Heart Failure II (TIM-HF2) was a RCT that randomized patients with heart failure to non-invasive remote patient management (daily transmission of body weight, blood pressure, heart rate/rhythm, peripheral capillary oxygen saturation, and self-rated health status) and usual care.[67] In a post-hoc analysis, AF status at randomization was assessed and present in 571 patients. Patients with AF in the intervention arm had significantly less days lost due to unplanned cardiovascular hospital admissions or all-cause death.

A prospective cohort study by Weng et al. evaluated an AF-dedicated online educational and treatment platform among 96 participants, with a randomized substudy of 71 participants examining the use of an ambulatory single-lead ECG heart monitoring (AliveCor, Kardia).[68] Patients were encouraged to routinely use the platform to enter the information regarding their weight, exercise, diet, AF symptoms. During 6-month observation, there was an improvement in AF symptom severity (based on Canadian Cardiovascular Society Severity in Atrial Fibrillation (CCS-SAF) scale), with no change in Atrial Fibrillation Severity Score (AFSS) and EQ-5D scores. In the sub-study, the remote heart monitoring also received high satisfaction scores and was associated with improved of quality of life. Patients reported that it helped them avoid AF-related ED visits.

Mobile-health-based heart rate/rhythm monitoring

A RCT by Lambert et al. assessed the impact of mobile heart rhythm monitoring (AliveCor, Kardia) during 6-month follow up and self-management in 100 patients after AF ablation.[70] Number of hospitalizations and ED visits as well as change in anxiety level were similar between intervention and control group. However, more patients in the control group required additional ambulatory heart rhythm monitors compared to those in intervention arm (27% vs 5.9%).

In the iPhone Helping Evaluate Atrial fibrillation Rhythm through Technology (iHEART) case–control study, authors evaluated differences in detection of AF or atrial flutter recurrences in a post-ablation period in 23 patients undergoing daily smartphone ECG monitoring (AliveCor, Kardia) and 23 age and gender matched controls.[72] During the 6-month follow up, patients in intervention group were more than twice as likely to have an episode of recurrent AF/atrial flutter detected (HR 2.55, 95% CI 1.06–6.11). In addition, 92% of respondents thought the device was beneficial and 58% said that they were more health conscious after participating in the study. Significant improvements in physical functioning, role physical, vitality and mental health domains were observed. However, in a sub-analysis of the iHeart study, no statistically significant differences in quality-adjusted life-years or AF symptom severity between intervention (n = 115) and control (n = 123) groups were reported.[71]

Mobile-health supported patient self-care and medication adherence tools

Guhl et al. randomized 120 patients to an intervention arm that consisted of a smartphone based relational AF agent (animated character with speech, body gesture, facial expression) and heart rate/rhythm monitoring (AliveCor Kardia) vs usual care.[76] The intervention group demonstrated significantly higher improvement in quality of life (mean difference 4.5, 95% CI 0.6–8.3), daily activity (7.1, 95% CI 1.8–12.4) and adherence to anticoagulation (16.6%, 95% CI 2.8%–30.4%) compared to the control group during 30-day observation.

One RCT (n = 231) examined the effects of a web-based integrated AF management program and showed significant improvement in coping mechanisms (β = 1.90, 95% CI 0.88–2.92), medication adherence (β = 0.61, 95% CI 0.25–0.96) and quality of life (β = 0.19, 95% CI 0.13–0.25) as compared to usual care.[75] Additionally, fewer readmission events were seen in the intervention (vs control) group within 2 years.

In another RCT of 160 participants, use of patient portal (MyChart) to send educational messages and medication reminders, resulted in improved AF knowledge with marginal effect on medication adherence as compared to a control group.[74]

A small prospective cohort study evaluated feasibility and usability of the HealthBuddies app, developed to increase anticoagulation adherence in elderly patients with AF by providing a contract with their grandchildren (n = 46).[73] Three-month study duration resulted in increase, however not statistically significant, in AF knowledge level of 5.8%, whereas anticoagulation adherence was as high as 99%. However, only 13% of eligible patients were willing to participate in the trial.

Another small prospective cohort study including 31 participants with AF used a similar intervention approach[78] as study by Guhl et al.[76] In line, 30-day smartphone-based intervention significantly improved self-reported medication adherence and quality of life.

A prospective cohort study by Trymbulak et al. evaluated an mHealth application (M-SAGE) intended to monitor the health condition of 40 elderly people with AF.[77] The application consisted of a 6-component geriatric assessment (frailty, cognitive function, social support, depressive symptoms, vision, hearing) and a 6-min walk test that was completed using a Fitbit wristband. It was feasible to use a mobile health app and wearable activity monitor. Participants, on average, required less than 10 min of telephone support over the 6-month period.

Clinical decision-making support systems

In a Swedish RCT (including approximately 14,100 patients with AF), over 12 months, significant increase in adherence to guidelines (from 70% to 73% vs 71%) and lower incidence in significant bleeding (12 vs 16 per 1000 patients) were observed in intervention group managed with clinical decision support tool for stroke prevention as compared to control group.[80] In contrary, another RCT of 590 patients randomized to treatment supported by a computerized clinical decision tool, showed no significant difference in cardiovascular hospitalizations, ED visits and major bleeding as compared to 543 patients randomized to usual care arm over 12 months.[83] In line, in RCT analyzing the impact of a computerized clinical decision support tool for anticoagulation, in nonstratified analyses, changes in discordant care were not significantly different between the intervention group (n = 801) and control (n = 692) groups over 1 year.[81] On the other hand, in a small RCT including 6 clinicians and 66 patients, use of clinical decision-making support system (HealthDecision) improved patients' knowledge about stroke risk (OR 3.88, 95% CI 1.39–10.78) as compared to usual care.[82]

In a small prospective cohort study, among 37 patients with AF, 41% agreed that AFib2gether app for a shared decision-making process regarding anticoagulation improved their AF knowledge.[79] On the other hand, among 34 providers, 79% agreed that the app helped clarify their patients' preferences and 82% agreed that the app saved them time.

Conclusions

AF is highly prevalent with a lifetime risk of about 1 in 3–5 individuals after the age of 45 years. Between 2010 and 2019, the prevalence of AF has risen markedly from 33.5 million to 59 million individuals worldwide. International AF management guidelines recommend opportunistic and systematic screening for AF, but additional data are needed. mHealth devices provide an opportunity for digital screening and should be part of novel models of care delivery based on integrated AF care pathways. For a broad implementation of mHealth based, integrated care for patients with chronic diseases as AF, further high-quality evidence is necessary.

Contributors

All authors contributed equally in manuscript conceptualisation, data curation, formal analysis, investigation, methodology, project administration, resources, software, supervision, validation, visualisation, writing—original draft, writing—review & editing.

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Declaration of interests

None declared.

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