

REVIEW

World Heart Federation Roadmap on Atrial Fibrillation – A 2020 Update

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The World Heart Federation (WHF) commenced a Roadmap initiative in 2015 to reduce the global burden of cardiovascular disease and resultant burgeoning of healthcare costs. Roadmaps provide a blueprint for implementation of priority solutions for the principal cardiovascular diseases leading to death and disability. Atrial fibrillation (AF) is one of these conditions and is an increasing problem due to ageing of the world's population and an increase in cardiovascular risk factors that predispose to AF. The goal of the AF roadmap was to provide guidance on priority interventions that are feasible in multiple countries, and to identify roadblocks and potential strategies to overcome them.

Since publication of the AF Roadmap in 2017, there have been many technological advances including devices and artificial intelligence for identification and prediction of unknown AF, better methods to achieve rhythm control, and widespread uptake of smartphones and apps that could facilitate new approaches to healthcare delivery and increasing community AF awareness. In addition, the World Health Organisation added the non-vitamin K antagonist oral anticoagulants (NOACs) to the Essential Medicines List, making it possible to increase advocacy for their widespread adoption as therapy to prevent stroke. These advances motivated the WHF to commission a 2020 AF Roadmap update. Three years after the original Roadmap publication, the identified barriers and solutions were judged still relevant, and progress has been slow.

This 2020 Roadmap update reviews the significant changes since 2017 and identifies priority areas for achieving the goals of reducing death and disability related to AF, particularly targeted at low-middle income countries. These include advocacy to increase appreciation of the scope of the problem; plugging gaps in guideline management and prevention through physician education, increasing patient health literacy, and novel ways to increase access to integrated healthcare including mHealth and digital transformations; and greater emphasis on achieving practical solutions to national and regional entrenched barriers. Despite the advances reviewed in this update, the task will not be easy, but the health rewards of implementing solutions that are both innovative and practical will be great.

Keywords: atrial fibrillation; AF; cardiology; WHF; NOACs; digital technology

Introduction, Context, and Background

About five years ago, the World Heart Federation (WHF) launched a Roadmap initiative to reduce death and disability from non-communicable diseases (NCDs), focusing on the increasing global burden of cardiovascular disease. This rise in cardiovascular disease disproportionately affects people in low- and middle-income countries (LMICs). The aim of this WHF initiative is to reduce death and disability through effective interventions targeting prevention, early detection, and treatment. One of the main problems in achieving the desired outcomes is that the health system resources required to make an impact are most challenging for LMICs, which vary enormously between and within countries in availability of cardiovascular health resources, so it is difficult to generalize. Even in high-income countries (HICs), areas of health inequalities, socioeconomic deprivation, and often poverty are present in many areas and in minorities including first nation peoples (e.g., native Americans and Aboriginal Australians), migrants and different ethnic or racial groups, and may co-exist with greater cardiovascular burdens including atrial fibrillation (AF) and its complications.

The WHF Roadmap for AF was published in December 2017 [1]. The aim of the Roadmap was to 'provide guidance on priority interventions on a global level that can be adapted to regional contexts' [1]. The interventions in the Roadmap are intended to be evidence-based, feasible in multiple countries, affordable, and cost-effective. That is a difficult set of conditions to achieve, but one that must be achieved if we are to realise the potentials for prevention of death and suffering related to AF globally. The roadmap identified ideal patient-care pathways with the potential of widespread adoption in multiple national settings. It also identified barriers to implementation of interventions and potential strategies to overcome them.

Much has happened in the three years since publication, including technological advances that will change our ability to detect AF early before it becomes symptomatic, and to better predict those who have silent AF or are likely to soon develop it. There have also been technological advances in reducing AF symptoms through more effective ablation of the arrhythmia, and in prevention of cardio-embolism, but the relevance of these technological advances for LMICs is uncertain. The widespread adoption of mobile technology, particularly smartphones, has also facilitated new approaches to healthcare delivery, which could impact general community awareness of the condition and increase patient knowledge, in turn facilitating adherence to effective lifestyle and pharmacological approaches. Finally, an important outcome of the WHF Emerging Leaders Programme was preparation of a successful submission to the World Health Organization to add the non-vitamin K antagonist (VKA) oral anticoagulants (NOACs) to the Essential Medicines List [2]. These developments prompted the WHF to undertake an update of the AF Roadmap in 2020, focusing on new developments, and an assessment of the status of roadblocks and barriers identified in the original Roadmap.

To accomplish this, an international panel of AF experts was assembled to summarize the areas of the original Roadmap requiring updating – what is new and important for the ideal AF patient-care pathway – and to place this information in perspective. Additionally, an online consultation of national society and foundation representatives was carried out, with respondents from 23 countries. The majority stated that the previously identified roadblocks and the suggested solutions were still relevant in their countries, but it was uncertain how much progress had been made. This update will serve as a vehicle to restate the roadblocks and strategies to overcome them and to examine whether the advances reviewed might provide novel ways to more effectively prevent, detect, treat, and reduce complications associated with AF.

1. Global AF Burden and Country Estimates

AF remains the most clinically significant arrhythmia seen in clinical practice [1, 3–5]. Prevalence is about 1–3% in the general population but rises with age (up to 9%, aged ≥ 65 years; up to 17%, ≥ 80 years), presence of comorbidities and male sex, and varies with ethnicity, region, and screening method used [3–10]. Lifetime risk of developing AF also varies with age and ethnicity and is up to 36% for men and 30% for women at age 40–45 and significantly higher in Whites than African Americans [9, 11, 12]. The burden of AF has been on the increase since 1990 with a doubling of prevalent cases from 1990–2019 [13]. Age-standardized prevalence is similar, suggesting that increases are largely due to ageing of the population and population increase. It is projected that by 2030, 14–17 million people in the EU will be living with AF, representing a doubling of the 2010 global data. For the USA, estimated increase is 12 million [14–16]. This increase is attributable to the aging population, increasing AF risk factors and increased screening [13, 17–19]. Genetic differences affect AF occurrence and may contribute to regional differences in prevalence. European ancestry has been linked to a higher burden of AF [20–22], and AF burden is lower in Asians, Hispanics, and Blacks compared to Caucasians [23]. The last global burden of disease surveys showed that AF disability burden was higher in HICs than LMICs [13]. However, this may well be a problem of lower AF ascertainment in many LMICs, as recent studies from Asia using smartphone handheld-electrocardiogram (ECG) technology for community screening have reported increased prevalence compared to earlier studies and some have reported prevalence similar to Europe and USA, **Table 1** [19, 24–28].

AF burden is lowest in sub-Saharan Africa [29], possibly due in part to under-detection and non-recognition. However, it is associated with increased risk of stroke and heart failure [3, 30] and recently, an increase in disability-adjusted life years (DALYs) from AF [31]. African Americans, however, have a lower AF risk than other US ethnic groups despite a higher burden of AF risk factors [21, 32]. There are few population screening studies for AF across the whole African continent, and these have reported relatively low AF burden, coupled with a very significant stroke and heart failure burden, but large-scale screening is lacking in this region, representing an important knowledge gap [30, 33]. Similarly, comparative data are somewhat limited for South and Central America [34–37]. In one 2020 publication with 153,152 participants from 20 countries aged 35–70 (mean 52), using population sampling between 2004–2012, there was a 12-fold variation in prevalence between regions, highest in North America, Europe, then China and South-East Asia, lower in South

Table 1: Temporal trends in country burden of AF detected by AF screening.

Country	2001–2010 publications*		2011–2020 publications*		Prevalence
	Cohort	Burden	Cohort	Burden	
Belgium [225]			≥40 years	2.2% (1.3%–3.0% 95% CI)	
China [226, 227]	General population	0.65% (0.66% men, 0.63% women)	General population	1.14% unadjusted. 0.71% age adjusted (0.72% men, 0.70% women) 34% newly detected AF	
England [228, 229]	≥65 years	8.9% (7.9% to 9.7%) control; 8.4% (7.6% to 9.4%) opportunistic arm; 8.4% (7.6% to 9.3%) systematic arm.	≥45 years	2.0% over all (2.4% men; 1.6% in women) 8% ≥75 years. ≈29.5% newly detected AF	
Germany [230]				2.5% age weighted. 0.7% 35–44 years 10.6% 65–74 years. 15.5% newly detected AF	
Hong Kong [28]			General population	1.8% overall. (95% CI 1.6% to 2%) 2.8% men (95% CI 2.3% to 3.3%) 1.4% women (95% CI 1.2% to 1.6%). 42.2% newly detected AF	
India [25–27]	General population	0.1–0.5%	General population	1.6% 5.6% (for ≥75years.)	
Italy [231, 232]	≥65 years	7.4%	≥65 years	7.3% overall (95% CI 6.6–8.1) 8.6% men. (95% CI 7.5–9.8) 6.2% women (95% CI 5.3–7.2) 16.7% >85years. 8.1% 2016 population adjustment (95% CI 5.9–11.1)	

(Contd.)

Country	Prevalence			
	2001–2010 publications*		2011–2020 publications*	
	Cohort	Burden	Cohort	Burden
Netherlands [9]	≥55 years	5.5% overall (0.7% for 55–59 years; 17.8% ≥85years)		
Portugal [233, 234]	≥40 years	2.5% over all (2.2–2.8%: 95% CI) 6.6% (70 –79 years) 10.4% (≥80years)	≥65 years	9% overall (8.9% men; 9.1% women) 35.9% newly detected
Spain [235, 236]	25–74 years	0.7% 1.1% men. 0.3% women	≥40 years	4.4% (3.8–5.1 95% CI) 4.4% men 4.5% women (3.6–5.3 95% CI) 17.7% ≥80 years (14.1–21.3 95% CI) 10% newly detected AF
Sweden [237, 238]	General population	2.5% overall 2.8% in men 2.1% women 3.9 ≥35 years 6.3% ≥50 years 13.8% ≥80 years	75/76-year-old	14.3%. (95% CI 12.1–16.8) 5.2% newly detected AF (3.8–7.7 95% CI)
Ghana [239]	Rural		≥50 years	0.3% overall (95% CI 0.1–1.0)
Tanzania [240]	Rural		≥70 years	0.67% overall (95% CI 0.33–1.01) 0.96% women (95% CI 0.42 – 1.49) 0.31% men (95% CI 0.04 – 1.24)
Ethiopia [241]	Urban		≥40 years	4.3% overall

Legend: * Publication date may be somewhat later than date of cohort data collection.

America, and lowest in the Middle East, Africa and South Asia [38]. There was also a continuous gradient of AF prevalence from low- to middle- and high-income countries. Notably, the AF-related stroke risk did not differ between regions based on income, but anticoagulation rate was low in LMICs and remains lower than in HICs [39], which may in part explain the similarity in AF-related stroke risk.

Additionally, AF occurs at a relatively younger age in some LMICs [40–43], though this may be explained by more rheumatic AF or an effect from lower general survival in LMICs. However, an integrated oral anticoagulant (OAC) program and service is likely to reduce the burden of AF-related strokes in the young cost-effectively [6]. AF is associated with increased risk of morbidity (up to five-fold increase in stroke, and lesser increases in heart failure, and cognitive impairment) and two-fold and 1.5-fold increase in all-cause mortality in women and men, respectively [44–47]. AF management imposes huge financial burdens on health systems with an estimated annual direct cost of \$26 billion in the USA and AU\$874 million in Australia [48, 49]. The financial impact of AF management is most likely worse in LMICs with fragile health systems, but data are scarce [29]. The embolic complications and cost of AF-related stroke care may be mitigated by early diagnosis using systematic or opportunistic screening and effective anticoagulation for patients with actionable (unrecognized or undertreated) AF [50].

2. Primordial and Primary AF Prevention

Prevention of AF is of paramount importance given its rising incidence, associated disease burden, and cost. As a condition closely associated with ageing and co-morbidity, AF also demonstrates distinct race and sex trends not yet fully understood [51]. There is, however, a well-recognised constellation of underlying risk factors including obesity, diabetes, and hypertension pre-disposing to cardiovascular disease generally and AF in particular [52–54]. The main risk factors for incident AF are summarized in **Table 2**. Although robust data comparing underlying risk factors for AF between different regions of the world are sparse, some studies showed a relatively lower prevalence of older age, diabetes, and hypertension among African AF patients, though hypertension, heart failure, and valvular heart disease remain major risk factors for AF in sub-Saharan Africa [29]. Observational studies suggested links between AF incidence and markers of social deprivation, including lower socioeconomic status (SES), lower educational attainment, and single partnership status, while prevalence data are variable, most likely from lower AF screening and diagnosis in populations with social deprivation [55]. While higher cardiovascular risk factor burden in individuals with social deprivation may drive AF risk, the association is not fully explained. Lower formal education, lower neighborhood SES, and unmarried patients with AF have a higher risk of AF-related complications such as stroke, myocardial infarction, heart failure, and mortality [56, 57].

Successful primordial and primary prevention requires a sustained long-term effort. Effective AF prevention will require primordial prevention of modifiable predisposing risks such as diabetes and rheumatic heart disease. Lifestyle modifications including weight loss to reduce obesity [58–60], no or moderate alcohol intake [56–58], as well as regular physical activity [61–64] may reduce the risk for developing AF. In addition, detection and diagnosis of sleeping disorders [65, 66] and prevention of rheumatic heart disease by improved sanitation and housing as well as prompt treatment of streptococcal infections, may also effectively reduce global AF burden. While all this is well-recognised, there is limited clinical trial evidence to support specific primary prevention interventions for AF. EUROASPIRE V confirms that control of blood pressure, lipids, and diabetes among patients with high risk for cardiovascular disease remains poor [67], suggesting that current strategies for primary prevention of AF and cardiovascular disease are insufficient.

For optimal benefit, individuals should actively participate in shared decision making and a team-based approach to deliver care, which promotes self-management and provides adequate support [5, 68, 69]. The use of individualized risk-assessment models and structured approaches to communication, such as motivational interviewing, could help to engage patients more effectively and enhance outcomes [70]. To achieve this globally is an ongoing challenge across all cardiovascular diseases with many shared risk factors and is the first part of our revised ideal AF pathway (**Figure 1, Table 2**).

Table 2: Main risk factors for incident AF.

Demographic and socioeconomic factors [242–248]	Age, male sex, Caucasian ethnicity, lower socioeconomic status and social deprivation, family history of AF
Lifestyle [242–244, 249–251]	Smoking/tobacco use, alcohol intake, sedentary lifestyle, or vigorous exercise
Cardiovascular conditions [51, 242–244, 252–257]	Heart failure, coronary artery disease, vascular disease, rheumatic heart disease and valvular disease, congenital heart disease, heart rhythm disorders
Health factors and other risk factors [242–244, 258–263]	Hypertension, dyslipidemia, diabetes mellitus, renal dysfunction, obesity, sleep-disordered breathing, chronic obstructive pulmonary disease, inflammatory diseases, surgery

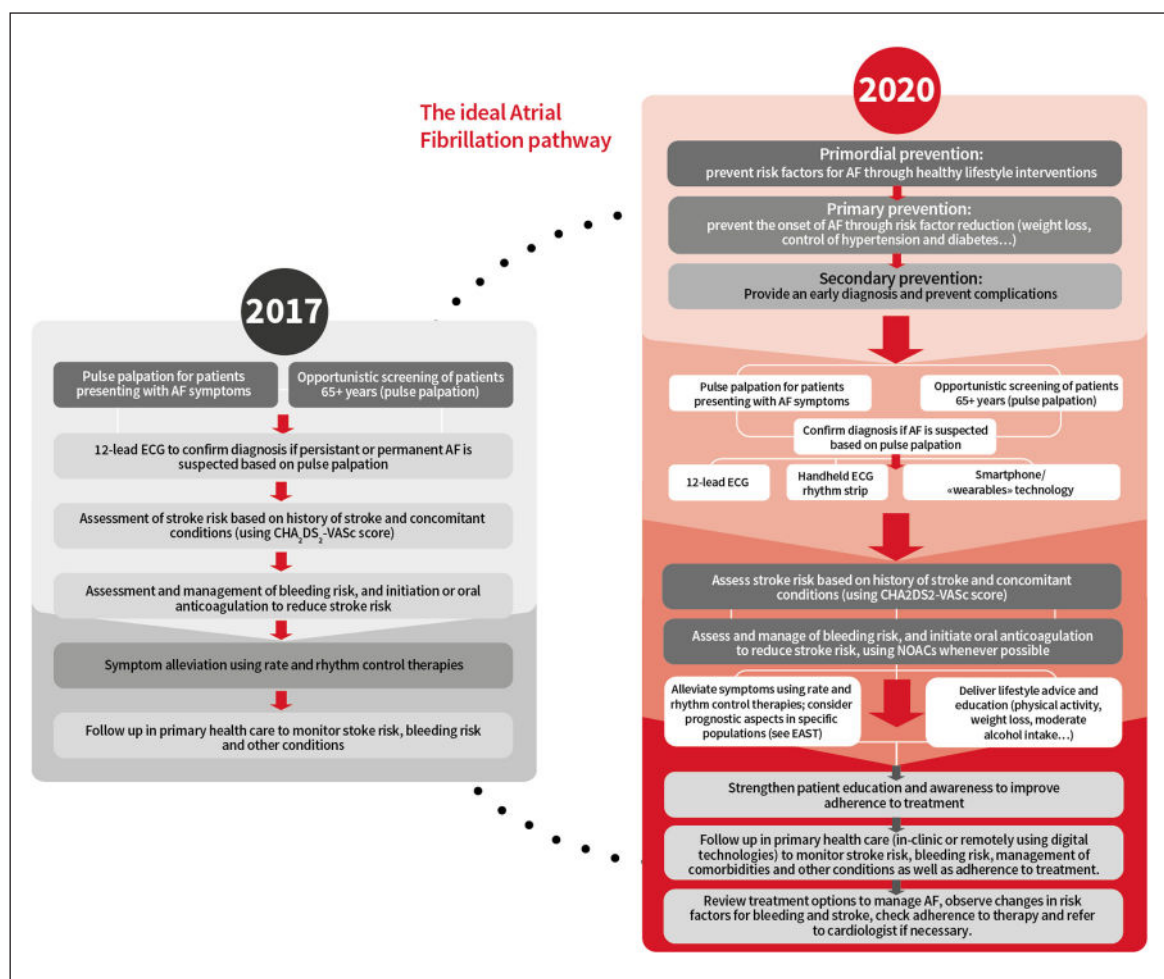


Figure 1: Ideal AF pathway © World Heart Federation.

3. Identifying Roadblocks and Strategies to Overcome Them

The following sections focus on a series of new opportunities to overcome roadblocks in the detection and management of AF. An updated overview of roadblocks and possible solutions based on the 2017 WHF Roadmap, WHF members' feedback, and a review of the literature by the expert writing group is shown in **Table 3**.

Table 3: Roadblocks, strategies, and potential solutions.

Dimension	Roadblock	Strategy	Potential solutions
Geographic accessibility	Long distances to clinics result in low numbers of rural patients presenting to clinics for screening and follow-up appointments.	<ol style="list-style-type: none"> 1. Improve accessibility of screening for rural populations. 2. Strengthen capacity for ECG testing in remote areas. 3. Promote the use of digital technology to improve screening and diagnosis of AF. 	<ol style="list-style-type: none"> 1. Train community health workers or pharmacists to screen for possible AF with pulse-checking in non-clinic settings. Educate in schools about checking pulse and relationship of AF with stroke. 2. Educate at-risk populations (e.g., those 65+ years of age) to self-screen with pulse checks. 3. Implement novel telemedicine technologies (e.g., transmission of ECG results from rural areas to urban facilities) including handheld digital rhythm strips (accepted by ESC for AF diagnosis). 4. Use digital technology or 'wearables' to conduct non-invasive screening (e.g., PPG readings generated from smartphones, though ECG still required for diagnosis). 5. Use digital technology for remote patient follow up (e.g., phone or video calls).
Availability	Shortage of health care professionals with training in AF, including interpretation of ECG, initiation of and monitoring of anticoagulation therapy. Absence of rhythm-control strategies Lack of integration of AF management services with other cardiology and medical care.	<ol style="list-style-type: none"> 1. Raise awareness of AF among health care professionals. 2. Reduce dependence on highly trained medical staff for AF screening and management. 3. Implement coherent rhythm control strategies. 4. Better integration with other cardiology and medical services. 	<ol style="list-style-type: none"> 1. Conduct awareness campaigns through healthcare professional networks. 2. Improve postgraduate training and CME. 3. Develop simple and locally applicable AF guidelines. 4. Implement non-physician healthcare workers (NPHW)-managed anticoagulation program. 5. Increase governmental funding. 6. Progress towards Universal Health Coverage (UHC). 7. Train human resources. 8. Set up AF research and registries in LMICs to ascertain the disease patterns specific to these countries. 9. Involve allied health professionals for monitoring and follow-up purposes. 10. Rely on electronic solutions (e.g., smartphones and apps) to provide patients with regular guidance. 11. Promote awareness of AF management in related medical services (hypertension, heart failure, coronary artery disease, medical). 12. Treat and prevent contributory factors (e.g., hypertension, heart failure, coronary artery disease).

(Contd.)

Dimension	Roadblock	Strategy	Potential solutions
Affordability	OACs potentially unaffordable for patient households, resulting in nonadherence to treatment regime. Pharmaceutical poverty. Access to non-pharmacological rhythm control strategies, i.e., catheter ablation, LAAO.	<ol style="list-style-type: none"> 1. Improve affordability of OACs and other essential medicines so that every patient can access them. 2. Design novel treatment environments such as office-based labs. 	<ol style="list-style-type: none"> 1. Provide universal health care coverage for essential medicines, or provide similar support via a not-for-profit organisation). 2. Implement internationally recognized policies for the reduction of essential medicine costs. 3. Ensure that national essential medicines lists include NOACs. 4. Promote the availability of NOACs as generics. 5. Office-based labs provide safe and affordable spaces for interventions in AF patients.
Acceptability	Reluctance of physicians and patients to initiate anticoagulation therapy. Lack of awareness of importance of persistent adherence to OAC therapy.	<ol style="list-style-type: none"> 1. Improve awareness of and capacity for managing OAC therapy among physicians. 2. Improve patient understanding of importance of OAC therapy and capacity to adhere to therapy. 	<ol style="list-style-type: none"> 1. Conduct country-specific training on OAC therapy management and support programmes for non-cardiologist health care professionals with the support of professional patient organisations when available. 2. Develop and implement country-specific patient education, health literacy, and support programmes for diagnosed AF patients on OAC therapy and foster the dissemination of existing resources across countries. 3. Support the development of structured patient organisations. 4. Foster patient-centred approaches to support medication adherence and effective lifestyle risk reduction. 5. Foster patient self-management and adherence to medication through digital technology and connected devices. 6. Conduct research into feasibility of self-monitoring programmes for patients on OAC therapy in LMICs.
Quality	Unavailability of standards or norms to ascertain the quality of certain new devices, services, and treatments. Lack of patient-reported outcomes. Lack of a clear definition of quality indicators and markers, including specificities per regions.	<p>Implement robust mechanisms for the accreditation/certification of new devices, services, and treatments.</p> <p>Rely on a set of standardised patient report outcomes.</p> <p>Adopt a globally acceptable definition of quality indicators and markers.</p>	<ol style="list-style-type: none"> 1. Create a list of certified devices, apps, etc. 2. Ensure that technology is supported by a clear pathway to treatment. 3. Foster implementation research. 4. Promote the use of a standard set of patient-reported outcomes among health practitioners (195). 5. Use a common definition of quality indicators and markers.

4. Opportunities for New Digital Technologies to Overcome Barriers in Screening, Diagnosis, and Monitoring for AF

a. *Mobile technology*

AF is often paroxysmal [71–74] and frequently asymptomatic [75–77], as noted when implanted devices are interrogated [72]. Therefore, detection that relies on reported symptoms, intermittent pulse checks, or 12-lead ECGs will miss a sizable number of cases. Given the substantial thrombo-embolic risk of asymptomatic and/or paroxysmal AF [74, 78, 79], long-term monitoring with ambulatory ECG recordings or implanted loop recorders has been increasingly deployed to improve detection, particularly in high-risk clinical settings such as after cryptogenic stroke [80, 81]. Digital technology in smart phones or ‘wearables’; however, it might allow long-term, non-invasive screening to improve AF diagnosis in broad populations across the globe.

Multiple investigators [82–84] have evaluated the use of photoplethysmography (PPG), a low-cost transdermal optical technique available on most fitness trackers, smartwatches, and smartphones that detects blood volume changes in the microvascular tissue bed, indirectly measuring heart rate and regularity of rhythm [85]. A prospective evaluation [86] of a PPG-based smartwatch algorithm in hospitalized patients confirmed a sensitivity of 93.7% and specificity of 98.2% for AF detection, though performance in real-world settings as opposed to research study environments are significantly worse. In asymptomatic younger people (mean age 35 and 40), two very large prospective trials in China [84] and USA [87] screened 187,912 and 419,297 people using Huawei and Apple PPG-enabled devices respectively, detecting ‘suspected AF’ in 424, and 2,161, but with confirmation of diagnosis in only a limited proportion through follow-up. While these studies suggest that the technology may develop into an effective tool, multiple barriers remain to be resolved: inadequate quality recordings in up to 22% of subjects, [84, 86, 88] lower reliability of PPG at higher heart rates, [85, 88] cost/affordability for LMICs, and lower penetration of digital technology in older populations amongst whom AF is more prevalent [88, 89]. Other technologies that support early AF diagnosis also rely on detection of regularity of the pulse wave using oscillometry in blood pressure sphygmomanometry [90] and even phasic changes in facial colour using a video camera [91]. Sphygmomanometers have been used in LMICs, but all of these pulse-based technologies suffer from the problem of requiring an ECG to make the diagnosis, which leads to delays or loss of follow-up through requirement for distant referral, as in a recent community study in Thailand [92]. In the end, a 12-lead ECG or 30-second ECG rhythm strip is required to make the diagnosis of AF [73].

Proprietary technologies already allow direct recording and interpretation of an ECG tracing from a smartwatch [93]. For example, the Kardia Band used an Apple smartwatch to detect possible AF from intermittent PPG registrations, with user wrist haptic/buzz notification to record an ECG from the band, followed by an automated ECG interpretation [94], but this device is no longer available. The same principle is now inbuilt in the Apple smartwatch (but not enabled in all countries outside USA) and is being used in the large prospective Heartline screening study (NCT04276441). Many more of these smartwatch PPG/ECG systems are now available in HICs, though not yet in most LMICs. While promising, the cost and technical issues listed above could limit global generalisability as scalable screening tools.

A number of stand-alone handheld or chest-applied ECG devices, or small inexpensive devices attached to a smartphone, are available and commonly used as event recorders providing an ECG rhythm strip for AF diagnosis when symptoms are suggestive or to estimate AF burden in known AF. These devices can also be used to screen for AF by either health professionals or personnel with minimal training in LMICs [25, 95] or by individuals themselves [96, 97], with single or multiple intermittent ECG 30-second snapshots [50]. As a 30-second rhythm strip is considered sufficient for AF diagnosis, this may be the preferred technology for making an AF diagnosis after non-ECG devices or pulse-based screening.

Although adoption of smart watch technology in LMICs is very low, surveys conducted in 11 LMICs in four global regions found that 53% of adults have access to a smartphone capable of accessing the internet and running apps [98]. Data from UNESCO suggests that one third of adults in developing countries already use smart phones, and the Global System for Mobile Communications (GMSA) predicts that largest growth in smartphone use by 2025 will be in sub-Saharan Africa [99]. Prospective data of self-recording fingertip PPG intermittently from a standard smartphone shows promise for detecting AF [83]. However, a 2020 survey of 588 healthcare professionals showed almost 70% believe we are not yet ready for mass consumer-initiated AF screening using wearables/apps [100]. This suggests that smartphones/PPGs may allow more effective global screening and diagnosis of AF at some stage in the future (possibly within the next decade), provided that the technology matures adequately, the burden of data analysis and follow-up can be managed, and issues of privacy are adequately anticipated.

b. Artificial intelligence (AI) to predict AF

A potential alternative or addition to using wearables/apps and devices utilizes modern computing technology to examine existing clinical specimens, samples, or data (including ECG data) to identify patients at high risk of actionable AF, or even cardiovascular disease [101]. Such technologies could provide a means to identify patients at high risk of impending or undiagnosed paroxysmal AF or AF-related stroke, and thus might serve to identify those who could benefit from AF screening or potentially even anticoagulation, such as in the setting of stroke of uncertain source (ESUS) [81]. These technologies may also be essential to facilitating interpretation and integration of the massive amount of data collected using mobile and consumer-centered technologies.

A recent study showed that an AI-ECG algorithm trained using over 500,000 normal sinus rhythm ECGs from over 180,000 patients, had favorable performance characteristics for the identification of concomitant paroxysmal AF (area under the receiver operator curve [AUC] of 0.87, sensitivity of 79%, specificity of 79.5%) [102]. While still investigational and requiring validation in additional prospective cohorts that do not include cardioversion, the promise of this technology is as a low-cost and easily scalable intervention to identify patients with increased likelihood of paroxysmal or future AF from a single 12-lead ECG in sinus rhythm. Clinicians could even apply this technology retrospectively to existing ECG databases to segment a population by levels of risk for more intensive screening. A provocative case study recently described a patient with recurrent cryptogenic stroke in whom the AI-ECG identified a signal of AF risk many years before the onset of clinically recognized AF [103]. While studies examining empiric anticoagulation in patients with ESUS have not demonstrated a benefit of anticoagulation in the absence of documented AF [104, 105], perhaps an AI-ECG could be used to identify patients in whom the risk-benefit balance would favor earlier anticoagulation.

Before such approaches can be implemented, considerable work is needed to externally validate these algorithms in diverse populations [106] and to test them prospectively with other monitoring approaches (clinicaltrials.gov NCT04208971). Furthermore, the lack of 'explainability' of current convolutional neural networks leaves many clinicians reluctant to accept the predictions that emerge from a 'black box'. While the potential implications of AI-ECG in AF screening and treatment is only beginning to emerge, it is clear that significant questions remain.

c. Wearable or implantable ECG monitors

Wearable ECG monitors are noninvasive, easy to use, and readily available compared to other medical devices [107] but may be relatively expensive for scaled use in LMICs. Currently, wearable continuous ECG monitors built into a belt, vest, or adhesive patch are available. Many are designed to measure heart or pulse rate for fitness rather than rhythm and are not appropriate for medical use. Some products, particularly adhesive patch ECG recorders (some waterproof allowing showering), have the capability to record and store continuous ECG recordings for up to two weeks, and have regulatory approval for detecting rhythms such as AF. The mStoPS trial revealed that use of a home-based self-applied 14-day patch ECG monitor improved AF diagnosis [108]. A wearable dry-electrode belt monitor worn around the chest for 30 days significantly improved AF detection in cryptogenic stroke [109]. There are a number of other wearable external devices and patches that permit continuous telemetry, but availability is variable. Implantable loop recorders have much higher detection rates of undiagnosed AF than these noninvasive ECG monitors [110] but at present are too expensive for AF screening at scale. A recent study simulating various AF screenings using implantable loop recorder as gold standard demonstrated that intermittent AF screening using three 24-hour monitoring periods are superior to one 72-hour monitoring: even with 30-day monitoring, 40% of AF will go undetected [111]. However, the AF missed by two-week intermittent recordings compared to continuous recordings has a lower AF burden, which may have lesser prognostic significance.

d. Overcoming roadblocks

Developments in technology certainly show promise for increasing detection and diagnosis of AF that may lead to stroke and other complications, which could be prevented by interventions such as OAC therapy. PPG on smartphones seems the most scalable option, but the diagnosis still requires an ECG for confirmation – that is, another test – which poses challenges. Smartphone ECG devices can provide an AF diagnosis without another test and have been used successfully for screening in many countries, including LMICs [25, 28, 112–114] (**Figure 2**). However, many LMICs do not have a ready access to expert ECG readers required to confirm the rhythm, or even 12-lead digital ECG recorders with a valid automated algorithm. This might be facilitated by a global or country-specific ECG consultative service for digitally acquired ECGs as in Brazil



Figure 2: Recording of ECG rhythm strip by a woman instructed by a village health worker using a mobile hand-held smartphone ECG device. Reprinted from International Journal of Cardiology, 280, Soni A, Karna S, Fahey N, Sanghai S, Patel H, Raithatha S, et al., Age-and-sex Stratified Prevalence of Atrial Fibrillation in Rural Western India: Results of SMARTIndia, a population-based screening study, pp. 84–88, 2019, with permission from Elsevier.

[115]. We must also keep in sight that pulse palpation has sufficient sensitivity and specificity to be still recommended as a screening tool. It is readily available and certainly scalable in all countries: skills can be acquired by training health workers or by raising public awareness through organisations such as the Atrial Fibrillation Association (AFA). Whichever approach to screening is taken, there must be a system-wide mechanism in place to link diagnosis of new or actionable AF with an evidence-based management pathway including OAC thrombo-prophylaxis to prevent complications, and rate and rhythm control where required.

5. Rate-Control and Rhythm-Control Strategies – Perspective and Challenges

a. Rate-control vs. rhythm-control strategy

The decision for rate or rhythm control strategy in patients with AF is one of the key elements in the patient treatment pathway. Major AF guidelines, including the new 2020 ESC guideline, have defined the patient's symptoms as leading criterion for rate- or rhythm-control therapy selection [73]. This recommendation is based on a number of clinical trials showing no difference in major outcome measures including stroke and mortality between these treatment strategies [116]. Although one very recent clinical trial comparing early rhythm-control intervention with usual care (rate-control) suggests advantages for an early rhythm-control strategy (in a selected subgroup of 'early' AF) [117], the main decision pathway for the majority of AF patients will remain based on symptoms in the foreseeable future. Importantly, the indications for long-term anticoagulation to reduce risk of thromboembolism, particularly stroke, in patients with AF stroke risk factors, are identical for both treatment strategies [118, 119].

b. Methods for rate- or rhythm-control

Rate-control is achieved by pharmacologic slowing of atrio-ventricular conduction mainly with beta-blockers, calcium antagonists, and digitalis [120–122]. These drugs are usually well tolerated and globally available at relatively low cost [123]. Rate-control therapy can be applied in ambulatory settings, but may necessitate 24-hour ECG monitoring, not readily available in LMICs [124]. Rhythm-control is medically more complex as it may involve initial interventions such as pharmacological or electrical cardioversion that require a medical center/hospital setting and prescription of antiarrhythmic drugs for maintenance of

sinus rhythm [125]. Lifestyle modifications, especially weight control, are also important for symptom control and reducing symptoms [126, 127]. Compared to rate-control drugs, antiarrhythmic drugs for rhythm-control carry a higher risk of significant cardiac and extracardiac side effects so therapy requires closer medical monitoring and follow-up [125]. Moreover, as most membrane-active antiarrhythmic drugs are contraindicated in patients with structural heart disease (particularly ischemic heart disease and advanced heart failure), exclusion of such disease (including ECG, cardiac imaging, and in selected cases cardiac catheterization) is often necessary before therapy initiation [128–134]. Thus, in geographies without such diagnostic and monitoring facilities it is difficult and potentially risky to promote rhythm control with antiarrhythmic drugs. For selected patients with symptomatic AF, catheter ablation has evolved as an alternative rhythm-control strategy [135–138]: it is more effective than antiarrhythmic drugs and proven relatively safe [139]. Application of catheter ablation is highest in HICs in Europe and North America. It is also increasingly used in many Asian countries and South America [140, 141], but is available in only seven African countries (Algeria, Egypt, Kenya, Libya, Morocco, South Africa, Tunisia) [142, 143], mostly with low caseloads. In general, catheter ablation rates will be higher in the private than public health sectors, and this differential may be greater in LMICs.

c. Challenges and roadblocks for rhythm-control strategies in LMICs

The field of arrhythmia management has evolved in a disconnected way across LMICs with significant variation in local expertise, cost, and uptake of management strategies. Recent surveys across LMICs found wide and glaring gaps in availability of and access to catheter ablation and antiarrhythmic drugs and services [142, 144]. AF rhythm-control is generally rarely employed in many LMICs [145]. The same roadblocks highlighted in the original WHF Roadmap [1] as contributing factors to the care gaps in rate management and anticoagulation of patients with AF apply to rhythm management, with some additional ones. These numerous challenges include:

- i) Limited antiarrhythmic drug availability:* Amiodarone is the only AF cardioverting agent available in >60% of the countries surveyed; other drugs are largely unavailable. No AF-cardioverting antiarrhythmic drugs are on the essential medicines lists of surveyed countries [142, 144].
- ii) Workforce shortage:* There are few trained cardiologists and electrophysiology physicians in many LMICs. Interventional treatment of complex arrhythmias, such as AF ablation, requires highly skilled personnel. In the PASCAR surveys, 15% of countries in Africa did not have a single general cardiologist let alone a specialist electrophysiologist. There is a critical lack of specialty training programs in LMICs [142, 144].
- iii) Lack of specialized facilities:* including cardiac catheterization laboratories and electrophysiology equipment. For example, 55% of African countries have no electrophysiology laboratory; only six countries reported cardiac catheterization laboratories with 3D mapping systems required for complex ablation procedures like AF.
- iv) Lack of political will:* Many LMIC governments do not see establishment and support of hospitals, specialist training, and specialized EP equipment purchase and maintenance as a priority [142, 144].
- v) High cost of AF interventional infrastructure relative to the overall public health budgets [1].*
- vi) Low level of clinical research and international collaboration [146].*
- vii) No local AF clinical practice guidelines or prospective registries.*
- viii) Lack of or inadequate public health policies or healthcare system:* Few LMICs provide universal health coverage to their populations [147–149], resulting in heterogeneous access to healthcare infrastructure. Public health orientation and patient education may not be priorities and will adversely affect adherence to rhythm-control drugs.

6. Interventional Prevention of Cardioembolism by Left Atrial Appendage Occlusion (LAAO)

Percutaneous LAAO and surgical LAAO/exclusion are non-pharmacologic strategies for stroke prevention [150–152], as the LAA is the main source of cardiac thrombi leading to arterial embolization and stroke. In two relatively small clinical trials LAAO has been shown to be non-inferior to OAC with warfarin for a composite endpoint including stroke [153]. Multiple registries and observational studies indicated safety and efficacy for stroke prevention; however, efficacy compared to NOAC therapy (current standard of care for stroke prevention) has not yet been evaluated in a randomized trial. The most frequent accepted

indications for LAAO are high stroke risk with contraindications to NOAC/OAC treatment (mainly severe bleeding risk/complications) or AF-related stroke despite effective anticoagulation, but LAAO needs further validation before it can be widely recommended. In experienced hands LAAO is effective and relatively safe [154], though serious complications may be more common in practice than in trials, and device thrombosis may not be benign [127]. Additionally, the same human and equipment resource limitations as for catheter ablation, including onsite cardio-thoracic surgical back-up for complications, largely limit LAAO to HICs. LAAO is unlikely to play a major role for stroke prevention in LMICs using a 10-year perspective.

7. Anticoagulant Therapy to Prevent AF-Related Stroke

Appropriate initiation of anticoagulant therapy is the key intervention for AF-related stroke reduction in patients with stroke risk factors [127]. Benefits of oral anticoagulation with VKA and NOACs have been clearly demonstrated in multiple large-scale trials. However, NOACs have distinct advantages over VKA as they do not require monitoring and have fewer drug and diet interactions. In addition, they reduce stroke, intracranial hemorrhage, and mortality [155]. Thus, recent guidelines clearly recommend preferred use of NOACs over VKA [127].

a. Addition of NOACs to WHO Essential Medicines List (EML)

Despite guideline recommendations, NOACs are infrequently used in low-resource settings due to barriers of cost and accessibility. In 1977 the WHO EML was established to address inaccessibility of many medications to certain populations [156]. Medicines added to the EML must be available in the correct dosage, with quality assurance and in adequate amounts for population needs and should reflect population health priorities [156]. They are intended to guide development of national EMLs adopted in national policy and practice.

In 2019, the EML panel reviewed efficacy, safety, and cost-effectiveness of NOACs following a submission by members of the WHF Emerging Leaders Programme, concluding that current evidence supported global use. Consequently, NOACs were added to the WHO EML, an important first step in global prevention of AF-related stroke, especially in LMICs, where OAC therapy uptake is low. The next step requires advocacy to ensure national EMLs include NOACs, other steps to increase affordability [157] followed by action to include implementation into local policy and practice.

b. Implementation of OAC therapy for non-valvular and valvular AF in HICs and LMICs

In HICs, OAC use seems to be increasing in the past 10 years. For example, between 2006 to 2016, OAC use in the UK increased from <50% to almost 80%, mostly in the latter five years after NOACs were available [158], and similar HIC increases have been shown in the Garfield Registry [39]. A more than two-fold increase (to 35.6% in 2015) in OAC prescription rates (73% NOACs) was observed in Taiwan [159], while in Korea, OAC use rose from 34.7% to 50.6% during 2008–2015 (almost half NOACs) [160]. Modelling indicated that increasing OAC use was associated with declining stroke rates in both UK and Taiwan [158, 159], a strong indicator of the value of achieving a global increase in OAC uptake for AF.

Despite these improvements, OAC use is not consistent at a global, country, or even regional levels. Many LMICs lack data on AF management, even though the population in these countries may be at higher AF-related stroke risk. Contemporary registry studies and trials [39, 161] from various geographical regions have consistently shown widespread but extremely variable OAC underuse for AF, more severe for LMICs [29, 40–43, 162]. Prevalence of stroke among AF patients in LMICs range from 10.7% to 27% [29], compared with 5% in HICs [41]. OAC use was as low as 2.2% in patients with AF and a history of stroke in China, according to the community-based National Stroke Screening Survey conducted during 2013–2014 [163]. In contrast, OAC use increased to 36.5% during the same time period among hospital-based patients in the capital city of Beijing [164]. These differences highlighted that OAC use may be influenced by factors such as physician specialization, patient medical literacy, and population subgroup economic status.

AF and stroke related to rheumatic valvular heart disease (RVHD) remains a significant problem [27, 43]. The current recommendation of VKA for AF with RVHD produces continuing need for international normalized ratio (INR) testing, which can be problematic. There is a need for research on use of NOACs versus VKA in RVHD [165], given their non-inferiority in bioprosthetic valves [166]. Inclusion of point-of-care INR testing in OAC programs would avoid travel costs [27, 167, 168]. This is also important for NVAF when NOACs are not available, as time in therapeutic range (TTR) is lower in LMICs even in clinical trials [169]. To maximize INR TTR and ensure drug adherence, incorporating smartphone-based apps guiding VKA dose

will be helpful. Use of NOACs over VKA should be encouraged in all NVAF at risk of stroke. This could be implemented by use of generic NOACs and national government-funded programs to reduce stroke as previously outlined.

Even within HICs, pockets of social deprivation and poverty can produce disparities in OAC usage that may require a different approach. High AF risk at a younger age and low OAC utilization are seen in first nation peoples and minorities [170–172].

c. Strategies to increase OAC uptake and promote adherence and persistence, such as physician education, patient education, and enhanced health literacy

Many of the strategies described in *i* to *vii* are equally applicable to risk-factor management and rate and rhythm control.

i. Issues for LMICs

To improve OAC use in LMICs calls for a team approach. Delivery of anticoagulation services can be expanded to a large geographical area through a hub-and-spoke model (**Figure 3**), applicable particularly for rural and semi-urban areas. In this model, a specialist physician trained in anticoagulation therapy serves as the expert at the hub, while general practitioners (GP), and community health workers, including trained nurses, operate the spokes at two levels. Case detection and patient follow-up can be carried out at the periphery by health workers, while initiation of OAC therapy, patient evaluation, and complex issues around anticoagulation or choice of rhythm- or rate-control strategy are carried out in consultation between the GPs and the specialist physician (in person or by tele-consultation). Standard anticoagulation services including point-of-care INR testing can be carried out in the periphery close to the patient. Setting-specific apps can facilitate OAC and other management, but patient involvement with apps will depend on educational and economic status. Workflow can be integrated through telemedicine, which acts as the bridge between spoke and the hub.

LMICs face a number of challenges in providing cost-effective antithrombotic therapy in AF patients. Monitoring quality of anticoagulation for VKA to achieve the minimum TTR threshold is required for optimal results [161]. Robust cost-effectiveness analyses, taking into account short-term budget impact and longer-term economic impact of strokes prevented, are important for LMIC decision makers to consider switching from VKA to NOACs: in Brazil NOAC use may even lower total healthcare costs [173]. Anticoagulation for

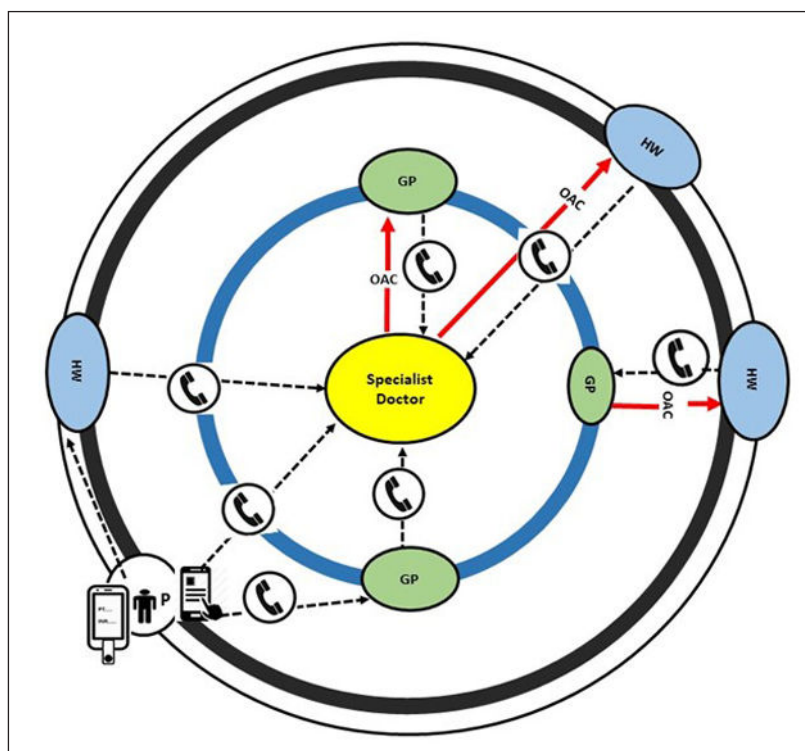


Figure 3: Proposed hub-and-spoke model of oral anticoagulant therapy in patients with atrial fibrillation in low- and middle-income countries. Specialist doctor at hub – If no specialist is available, the hub may be a GP. GP – general practitioner, HW – health worker at spoke. P – the depicted Patient (P) here has point-of-care INR monitoring facility and dosage adjustment and data sharing app.

AF is suboptimal in LMICs: improving physician awareness is crucial, as nearly half of patients not receiving OACs result from physician choice [39]. Periodic healthcare provider education and 24/7 hub backup helpline will ensure accessibility of safe and effective OAC therapy. Hub back-up for ECG rhythm diagnosis is another potential advantage of this model.

ii. Medication adherence

Medication adherence to durable anticoagulation therapy is essential for reducing AF-related stroke and thrombotic events, health-care related cost, and rate of hospitalizations [174]. Although long-term treatment with OACs is emphasized in different guidelines, both adherence and persistence with treatment is suboptimal and variable in real-world studies from 23% to 53–95% [174–181]. Multiple possible factors are associated with higher medication adherence: female gender, older age, lower body weight, anticoagulation-naïve user, lower medication dose, and electronic transmission of prescriptions [177, 180, 182–185]. Non-adherence increases with polypharmacy, particularly pertinent in AF patients typically on five medications daily [186]. Some non-adherence is unintentional and relates to forgetfulness: memory aids and establishing routines can improve adherence, particularly for the elderly or cognitively impaired. Health care providers managing AF patients should not only estimate the risk of non-adherence, but also provide solutions including improving patient's knowledge or using shared decision-making tools to increase medication adherence and persistence [187, 188]. Some medication non-adherence, particularly non-persistence, is intentional and influenced by beliefs about medications, a component of health literacy. OAC non-persistence is associated with a continuing risk of avoidable stroke [189, 190].

iii. Health literacy

Health literacy refers to the appropriate skills and knowledge needed to understand, and the confidence to access, evaluate, utilise, and navigate health care [191]. It has been demonstrated that higher levels of AF-related knowledge not only improve therapy uptake and adherence but also reduce AF-related complications such as stroke, thrombotic events, as well as health-care related costs and rate of hospitalizations [73].

Two multinational surveys showed that more than half of the patients with AF had low levels of knowledge about the increased risk of stroke related to AF or did not even know the name of their condition [192, 193]. A recent European Heart Rhythm Association (EHRA) survey showed there is still room for improvement in education of patients taking OACs, mainly for NOACs [194]. Therefore tailored, context-specific strategies to increase medication adherence and persistence are essential.

iv. Patient knowledge gaps

Identification of deficiencies of patients' knowledge plays a substantial role in designing and conducting evaluation of effective patient education platforms [195, 196]. The following items have been identified as the most common knowledge gaps: recognizing AF presentations, AF risk factors, awareness about their diagnosis, drug and food interactions of OACs, dietary vitamin K food content and intake, meaning of INR and its interpretation, how to handle missed OAC doses, and OAC side effects [197]. Little or no data about patient knowledge of rate and rhythm medications are available. Patient support groups like the AF Association and Arrhythmia Alliance could play an important role both in assessing knowledge in different countries or regions and in filling the gaps.

v. Educational interventions

Educational intervention programs to improve patient knowledge, particularly about therapy, could significantly impact therapeutic adherence, persistence, and therefore efficacy [198]. An easy to use online tailored-education platform improved AF- and procedure-related knowledge in patients, with a durable effect for at least 12 weeks post-ablation [199]. Another simple educational intervention improved therapeutic adherence 15–25%, and reduced stroke [200, 201]. More recently the IMPACT-AF study, including education of patients, their families, and health care providers, led to a significant increase in OAC treatment and significantly fewer strokes. This suggests that education needs to be extended to health care professionals and patient families to achieve increased prescription and appropriate advice for patients [201]. In another trial, 3324 patients with AF were randomized to receive usual care or integrated care with a mobile AF application (mAFA) [202]. The integrated care arm provided clinical support tools for doctors and an educational programme combined with dynamic risk monitoring. The composite outcome of 'ischemic stroke/systemic thromboembolism, death, and rehospitalization' was significantly lower with mAFA compared to usual care [202]. Although the influence of educational interventions on quality of AF management are not definitive,

studies highlight the importance of such interventions in increasing patients' satisfaction with clinical decisions, establishing a therapeutic alliance with the care team to decrease decisional conflicts, and increase therapeutic adherence [201, 203–205].

vi. Patient educational resources

Most physicians (80–95%) deliver patient information themselves, 30% recommend information brochures, and around 25% refer patients to other clinics specialized in OAC management for further education [206]. Only 9–15% of physicians refer patients to educational websites, a lost opportunity, while more than 60% of patients search for their disease and diagnostic or therapeutic-related information in the internet pages [199]. Among available AF patient education resources, the EHRA NOAC anticoagulation card is one of the most reliable, containing the critical educational issues in easy to understand points for patients to be delivered by healthcare practitioners (**Table 4, Figure 4**) [207]. This card is available for download in various languages at www.NOACforAF.eu. Patient-led organisa-

Table 4: Educational items for anticoagulant medication adherence to be delivered by physicians or other health professionals to patients with atrial fibrillation.

Important patient instructions

- A non-vitamin K antagonist anticoagulant (NOAC) thins the blood and reduces the risk of getting dangerous blood clots, in the same way as vitamin K antagonists (VKA, e.g., warfarin).
- Not taking the drug means no protection!
- Take your drug exactly as prescribed (once or twice daily for NOAC, once a day with the correct dose for VKA).
- Do not skip a prescribed dose to ensure optimal protection from blood clots and stroke!
- Do not stop your medication without consulting your physician.

For NOACs, you may need occasional creatinine blood tests to check kidney function

For VKA, ensure a stable diet of vitamin K containing foods, and have your INR checked regularly to make sure you have optimal anticoagulation protection against clots without increasing bleeding risk.

- After a trauma or bleeding event, consult with your physician regarding further management
- Do not add any other medication without consulting your physician, not even short-term painkillers that you can get without a prescription. You may need INR testing after starting any new medication if you are taking VKA
- Alert your dentist, surgeon, or another physician before an intervention.

What to do in certain occasions

When should I contact a healthcare provider?

Bleeding is the most common side effect of an anticoagulant. However, the reduction in the risk for stroke outweighs the bleeding risk. Contact your healthcare provider if you have any signs or symptoms of bleeding such as:

- Unusual bruising, nosebleeds, bleeding of gums, bleeding from cuts that take a long time to stop
- Menstrual flow or vaginal bleeding that is heavier than normal
- Blood in urine, red or black stools
- Coughing up blood or vomiting blood
- Dizziness, paleness, or weakness

What should I do if I missed a dose of NOAC?

You should still take that dose unless the time until your next dose is less than the time after your missed dose.

What if I accidentally took two doses of NOAC?

- Twice daily NOAC: you can opt to forgo the next planned dose and restart after 24 h.
- Once daily NOAC: you can continue the normal regimen without skipping a dose.

What if I missed a dose of VKA or accidentally took an extra dose?

Continue your normal dosing if you missed a dose. Omit one dose and have an INR check if you took a double dose

* This table is adapted from the 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation [264].

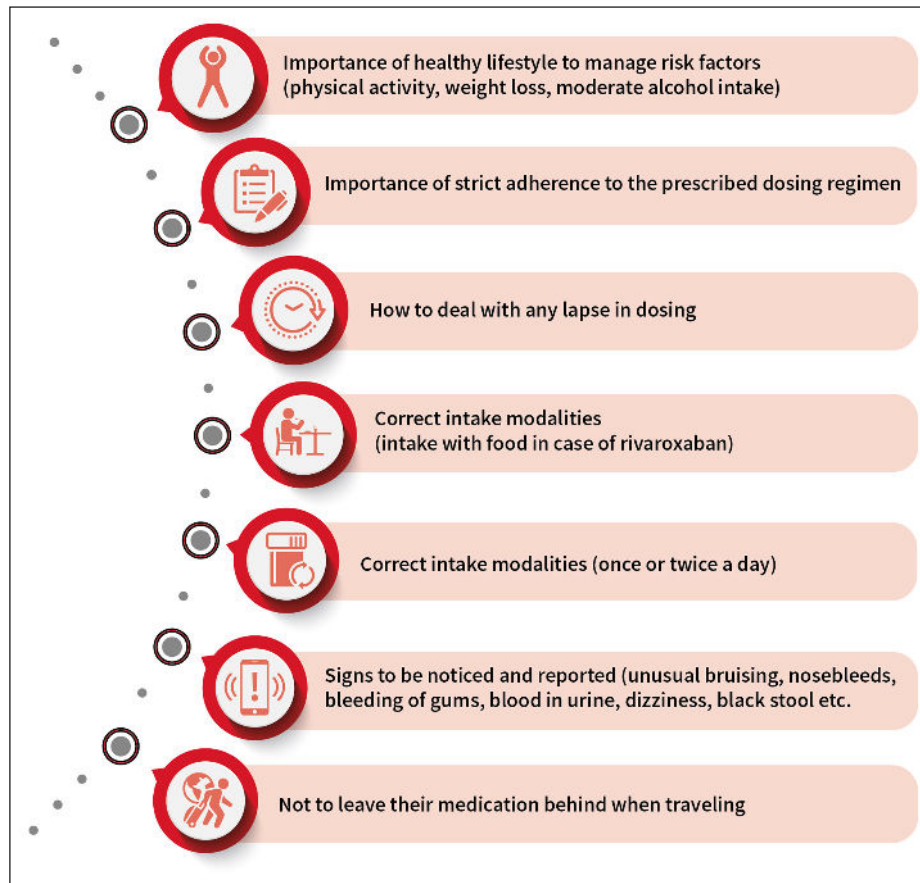


Figure 4: Key educational points to convey to the patients with atrial fibrillation at each visit by physicians. © World Heart Federation. Adapted based on the 2018 European Heart Rhythm Association Practical Guide recommendations [264].

tions such as the Arrhythmia Alliance and the AF Association also provide valuable information, awareness, education, and support but are not active in many LMICs. Establishing such networks would be valuable.

Technology effectively supports patient self-management and can facilitate medication adherence. Connected devices provide information about wider health and well-being issues related to AF, quite apart from ability to monitor for AF as previously discussed. It is essential that diagnostic technology is supported by a clear treatment pathway to ensure anxiety is not heightened by an abnormal result [208]. Paradoxically, patients who understand more about their AF may have greater anxiety than those who don't, but are also more likely to adhere to guideline-based therapy [209]. Therefore, a careful balance is necessary to ensure people understand but are not distressed by potential risk. Mobile Health applications (mHealth) also have a substantial role in supporting patients to self-manage, both alone and in consultation with health care professionals (eg **Figure 3**). mHealth apps can provide updated, clinically relevant, and personalised information to individuals, offering far-reaching support for individuals, because they are capable of delivering targeted and tailored evidence-based educational content alongside tracking functions designed to enhance self-management.

vii. Role of nurse-based support, physician assistants, non-physician staff

In the context of shared decision, nursing and allied professionals have an important role to play in supporting patients through detection, management, and treatment of AF. Successful community AF screening programs (such as the Arrhythmia Alliance Know Your Pulse campaign) have been led across the globe by patient organisations, pharmacists, and nurses, with high levels of participant satisfaction. Management of AF requires a patient-centered approach to support medication adherence and effective lifestyle risk reduction. Guidelines now recommend an 'integrated-care' approach, involving primary care physician, exercise specialists, dietitians, pharmacists, specialist nurses, psychologists, podiatrists, sleep physicians, as well as electrophysiologists, and cardiologists [73, 210], which could be implemented in the hub-and-spoke model as previously described (**Figure 3**). A systematic review and

meta-analysis of integrated care in AF demonstrated reductions in all-cause mortality and cardiovascular hospitalisations.

Access to a range of specialists including professional patient organisations can support people with AF to self-manage. Management of AF requires a collaborative approach with the patient and family at the centre of all decisions [211]. In AF, the majority of patients will need to take lifelong medication, especially OAC, to reduce their risk of AF-related stroke. Unless the patient is highly symptomatic, medication is usually given for the purpose of risk reduction, such as antihypertensives or OACs. These medications treat largely 'silent' risks, have no short-term benefit for the patient, and may cause side effects – which makes adherence and persistence challenging. Furthermore, lifestyle risk reduction is important, as studies have shown that weight loss, being physically active, and reducing alcohol consumption reduce occurrence and symptoms of AF, and non-physician support can be vital [127]. Because AF is multi-factorial, a team approach is beneficial to address the complex nature of the condition. Use of the ABC pathway (Atrial fibrillation Better Care pathway, including A = avoid stroke, B = better symptom control, C = cardiovascular risk factors and comorbidities management [212]), as advocated in ESC guidelines [127], could assist team management of all aspects of AF. In low-resource or remote settings, access to a specialist cardiologist may not be possible, but other members of the interdisciplinary team may be able to facilitate specialist support through access to videoconferencing, decision support aids, and mobile app-based support (**Figure 1, Figure 3**).

8. Additional considerations: Role of AF in heart failure and dementia/cognitive decline

While stroke prevention has been the primary focus of therapy for AF, heart failure is the most common cause of death among individuals with atrial fibrillation, and one of the leading causes of hospitalization [213–215]. The risk factors for AF and heart failure vary across the world. Hypertension is prevalent in all regions, but older age, obesity, and ischemic heart disease are more common in HICs, while rheumatic and valvular heart disease are more prevalent in LMICs [43]. Many of these risk factors are possible targets for both primary prevention of AF and prevention of its complications, including stroke and heart failure [216]. There is also evidence that an increased burden of AF is associated with worsening of heart failure symptoms [217]. There is a need for greater focus on heart failure prevention strategies which might parallel the success of stroke prevention in AF. Although randomized trials of anti-arrhythmic drug therapy failed to show a reduction in cardiovascular outcomes [218], catheter ablation of AF shows promise for patients with AF and heart failure [219].

In addition to stroke, patients with AF are at increased risk of silent cerebral thromboembolic lesions [220, 221], and of worsening cognitive function over time [222]. It has been hypothesized that AF may lead to cognitive decline via repeated, small cerebral thromboembolic events, and that these might be preventable by OACs. Research is ongoing to determine if NOACs can prevent cognitive decline in AF, including patients with only subclinical AF [223], and those with clinical AF but no additional stroke risk factors [224]. Given the global burden of cognitive impairment and the morbidity and costs associated with dementia, there is an urgent need to determine whether OAC will reduce progression of cognitive impairment, even in those without a current definite indication for OAC thromboprophylaxis for stroke.

9. Prioritization

The global impact of AF is evident from current epidemiological data and projections. Aside from the impact of AF on quality of life, the deleterious effects of AF on stroke and heart failure on healthcare costs including hospital admissions will only increase the economic burden of the condition. As a result of the COVID-19 pandemic, there has been an understandable concentration of the health care sector on this infectious disease. This has had an adverse and hopefully transient impact on non-committable diseases such as AF.

The focus of this Roadmap update was to identify what has changed in the recognition and management of AF, particularly the emerging role of mobile technology and mHealth, and to consider the advances described in recent publications, many summarized in the 2020 ESC guideline on AF [127]. Most of the identified barriers and priorities in the 2017 WHF Roadmap for AF are still valid in 2020, as evident from the survey of its members that the WHF conducted alongside this update. This update has therefore redefined the global priorities for AF management and emphasized those especially important for LMICs.

- a. **Advocacy:** Dissemination of knowledge on the importance of AF as one of the leading issues of cardiovascular disease must be improved. Too many decision makers in the health care sector do not know the threats of AF precisely and intensely enough. The campaign to change this should be led by the continental cardiac societies (AHA, ASC, ESC, ACC, HRS, EHRA, APHRS, SOLEACE, PASCAR, and

others), national heart societies and foundations, patient organisations such as the Arrhythmia Alliance and AF Association, and civil organisations, supported and united by the World Heart Federation.

- b. **Implementation:** There are still gaps in implementation of guidelines for management of AF, particularly in LMICs. Although patient education is important, improving healthcare provider awareness and education updates is crucial. Periodic educational courses and 24/7 hub backup helpline are examples of effective methods to increase adherence to guideline-based therapeutic approaches.
- c. **Access:** Aside from knowledge dissemination and implementation, global access to cost-effective health care resources must be achieved. Priorities are precise diagnosis and access to pharmacologic treatment, preferentially to modern oral anticoagulation using NOACs [157], and also to rate control medications.
- d. **Literacy:** Improving health literacy among patients and using shared decision-making tools by improving adherence to and long-term persistence with therapy will reduce AF-related complications and health-care related costs. Therefore, promotion of tailored, context-specific strategies to increase medication adherence and persistence should be considered as one of the priorities for all health-care units.
- e. **Integrated Care:** In the context of shared decision-making, use of an 'integrated-care' approach for AF management to further improve the structured management of patients, promote patient values, and finally improve patient outcomes should be prioritized in all countries, irrespective of income status.
- f. **Digital Transformation of Care:** Use of mHealth technologies to educate patients, provide patient support in areas with less health care facilities, increase adherence to lifestyle and pharmacological therapeutic approaches, and facilitate AF screening should be considered as one of the priorities in the next years. At the same time, finding practical solutions for the previously mentioned potential barriers for using these technologies, mainly for AF screening using wearables/apps, should be kept in focus. Moreover, digital technologies will enable the systemic implementation of quality indicators for several domains in the AF management pathway.
- g. **Prevention and Screening:** Much more attention should be paid to AF preventive strategies including development of new strategies. Both physicians and patients need to be better informed about the important role of risk factors and lifestyle in AF development and recurrence after a successful ablation or other rhythm control strategy. Identification of unrecognized AF using technological advances is another important priority for prevention of complications, especially stroke.
- h. **Overcoming Barriers:** Local stakeholders at the national level should hold roundtables to improve understanding of local barriers and develop practical solutions to identified local barriers, thus contextualizing and adapting the AF roadmaps. Publishing the result of such interventions is encouraged to increase understanding of remaining problems and to generate solutions from other experts.

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Competing Interests

Ben Freedman reports prior fees and advisory board honoraria from Bayer Pharma AG, Boehringer Ingelheim, Daiichi-Sankyo, Omron and Pfizer/BMS, loan devices from Alivecor, and grants to the institution for investigator-initiated studies from BMS/Pfizer, unrelated to the current work. Jeff Healey has held research grants and received speaking fees from BMS/Pfizer, Bayer, Servier, Medtronic, Boston Scientific, Abbott, ARCA biopharma, Cipher pharma, and Myokardia. Lis Neubeck has received honoraria from Pfizer BMS and Daiichi Sankyo (<£2000). Renate Schnabel has received lecture fees from BMS/Pfizer outside this work. Jesper Hastrup Svendsen reports grants, personal fees, and other from Medtronic and grants from Gilead. Isabel Arbelo has received speaker fees from Biosense Webster. FD Richard Hobbs has received occasional fees and or travel expenses reimbursed in the past five years for consultancy, speaking, or advisory meetings from BI and Bayer. Janina Stepinska has received research grants from Bayer and Sanofi; consulting or lecture fees from AstraZeneca, Bayer, Boehringer Ingelheim, Novartis, Pfizer, Sanofi, and Servier. Antoni Martínez-Rubio has participated in scientific advisory boards or research projects financed by Bayer, Boehringer Ingelheim, Daiichi-Sankyo, and Pfizer.

Author Contributions

Ben Freedman and Gerhard Hindricks are co-chairs of the Roadmap update and contributed equally to this manuscript.

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