The World Heart Federation Roadmap for Nonvalvular Atrial Fibrillation

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ABSTRACT

Background: The World Heart Federation has undertaken an initiative to develop a series of Roadmaps to promote development of national policies and health systems approaches, and to identify potential roadblocks on the road to effective prevention, detection, and management of cardiovascular disease in low-and middle-income countries (LMICs) and develop strategies for overcoming these. This Roadmap focuses on atrial fibrillation (AF). AF is the most common, clinically significant arrhythmia and, among other clinical outcomes, is associated with increased risk of stroke.

Methods: Development of this Roadmap included a review of published guidelines and research papers, and consultation with an expert committee comprising experts in clinical management of AF and health systems research in LMICs. The Roadmap identifies 1) key interventions for detection, diagnosis, and management of AF; 2) gaps in implementation of these interventions (knowledge-practice gaps); 3) health system roadblocks to implementation of AF interventions in LMICs; and 4) potential strategies for overcoming these.

Results: More research is needed on determinants and primary prevention of AF. Knowledge-practice gaps for detection, diagnosis, and management of AF are present worldwide, but may be more prominent in LMICs. Potential barriers to implementation of AF interventions include long distances to health facilities, shortage of health care professionals with training in AF, including interpretation of ECG, unaffordability of oral anticoagulants for patient households, reluctance on the part of physicians to initiate oral anticoagulant (OAC) therapy, and lack of awareness of the importance of persistent adherence to OAC therapy. Potential solutions include training of nonphysician health workers and pharmacists in pulse-taking, use of telemedicine technologies to transmit electrocardiogram results, engagement of nonphysician health workers in OAC therapy adherence support, and country-specific support and education programs for noncardiologist health care professionals.

Conclusions: AF affects millions of people worldwide and, left untreated, increases the risk and severity of stroke and heart failure. Although guidelines for the detection, diagnosis, and management of AF exist, there are gaps in implementation of these guidelines globally, and in particular in LMICs. This Roadmap identifies some potential solutions that may improve AF outcomes in LMICs but require further evaluation in these settings.

1. BACKGROUND AND AIM

It is now well known that the number of deaths from noncommunicable diseases (NCDs) is increasing globally, particularly in low- and middle-income countries (LMICs) [1,2]. Many NCDs, including cardiovascular diseases (CVDs) and related conditions, can be detected early and treated with cost-effective interventions, thus preventing costly hospitalizations and death. However, this requires coordinated health system responses built around evidence-based strategies. In many LMICs, health resources are scarce, and identifying priority, cost-effective interventions for CVD and related conditions is vital for planning effective health system responses to these diseases.

The aim of the World Heart Federation (WHF) Roadmap Initiative is to provide guidance on priority interventions on a global level that can be adapted to regional and national contexts. The initiative does so by focusing on a few priority interventions for CVD and related conditions that are: 1) supported by high-quality evidence of a measurable reduction in CVD; 2) feasible in various

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TABLE 1. Global burden of AF in 1990 and 2013

	Cases* (All Ages)		Rate per 100,000 (Age Standardized)	
	Mean	95% UI	Mean	95% UI
Global prevalence				
Year				
1990	6,841,147	6,602,764–7,114,686	213.7	205.9–222.6
2013	11,178,627	10,655,102–11,683,727	191.3	182.1–200.1
Global DALYs				
Year	Mean	95% UI	Mean	95% UI
1990	854,714	693,332–1,049,075	26.7	21.7–32.7
2013	1,888,690	1,590,032–2,224,863	32.5	27.5–38.2

Data from GBD (Global Burden of Disease) 2013 study [4].
AF, atrial fibrillation; DALYs, disability-adjusted life years; UI, uncertainty interval.
*Cases rounded to the nearest whole number.

country contexts; and 3) affordable and cost effective. The WHF Roadmaps not only identify key interventions, but also aim to document barriers to implementing these interventions and to identify potential strategies for overcoming them. Roadmaps for addressing gaps in secondary prevention of CVD, tobacco control, and hypertension have already been published and are in the implementation phase. The focus of this WHF Roadmap is nonvalvular atrial fibrillation (AF), in particular the detection and management of AF in LMICs using evidence-based drug therapy to prevent stroke. Valvular AF is also an important public health problem in LMICs, but is not addressed in detail here. Although AF is the main focus of this Roadmap, much of the recommendations on treatment and health system roadblocks can be applied to atrial flutter as well.

2. AF: EPIDEMIOLOGY AND BURDEN OF DISEASE

AF is the commonest clinically significant arrhythmia [3]. A Roadmap that promotes national policies and health systems approaches to the management of AF and provides tools and solutions for adaptation at a regional and national level is particularly timely. Between 1990 and 2013, although the global prevalence rate of AF decreased slightly, the overall number of AF cases increased, according to the GBD (Global Burden of Disease) 2013 study (Table 1) [4]. The morbidity burden associated with AF, as measured by disability-adjusted life years (DALYs), also increased. Estimates of the prevalence of AF, and DALYs associated with AF, are likely to underestimate true burden due to the high prevalence of asymptomatic AF [3]. AF is also associated with high costs incurred by individuals, health care systems, and economies [3,5–8]. Common clinical outcomes associated with AF are outlined in Box 1 [9]. Among other clinical outcomes, AF is associated with increased risk of stroke and is found in one-third of all ischemic strokes [10].

Past GBD studies have also suggested that the burden of AF varies among regions, with high-income countries experiencing higher prevalence, incidence, DALYs, and mortality associated with AF than do LMICs [3]. However, estimates of the extent of this difference should be interpreted with caution, as the lower rates of AF documented in developing countries may be related to weaker surveillance systems and geographical disparity in published data [3]. Moreover, in countries at all levels of development, a substantial proportion of AF cases are asymptomatic [11], making them more difficult to detect without advanced medical technology. Research from the RE-LY (Randomized Evaluation of Long-Term Anticoagulation Therapy) registry also suggests that patients with AF in LMICs tend to be younger, more likely to experience heart failure, and less likely to be managed according to published AF guidelines (i.e., patients with AF in LMICs show lower use of oral anticoagulants [OACs] and lower time in therapeutic range) [12].

Estimated differences in AF burden between developed and developing countries should also be interpreted in light of the risk factor profile of this condition. Although European ancestry has been identified as one risk factor for AF (compared to African and Asian ancestry) [13,14], the risk of AF mainly increases with age [15] and is higher among those with CVD such as myocardial infarction and CVD risk factors such as hypertension, diabetes mellitus, obesity, smoking, and alcohol use [13,16–22]. As these

Box 1. Common clinical outcomes as a consequence of AF [9]

- Increased mortality
- Increased risk and severity of stroke
- Increased risk of hospitalization
- Reduction in quality of life
- Reduction of exercise capacity
- Increased risk of heart failure

AF, atrial fibrillation.

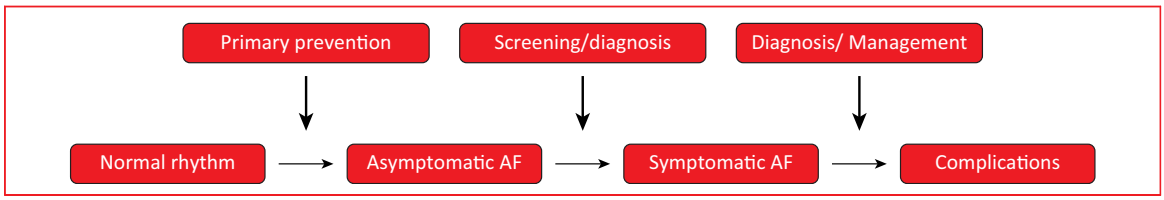

FIGURE 1. Stages of AF and intervention strategies. AF, atrial fibrillation.

risk factors continue to increase in developing countries, so likely will the burden of morbidity and mortality from AF. This burden may be further compounded by the shortage of health care resources in many developing countries, as successful management of AF requires consistent and long-term interaction between the patient and health care system.

3. KEY INTERVENTIONS FOR DETECTION, DIAGNOSIS AND MANAGEMENT OF AF

3.1. Primary prevention

As with all health conditions, primary prevention of AF (i.e., reducing the risk of first onset by targeting modifiable risk factors) (Fig. 1) is the ultimate goal of the medical and public health community, but is made challenging by persistent gaps in knowledge regarding determinants of AF. Models such as CHARGE-AF (Cohorts for Heart and Aging Research in Genomic Epidemiology AF consortium) score [23] have been developed to predict risk of AF, and to identify patients who may benefit from preventative interventions, based on age, race, height, weight, blood pressure, smoking, use of antihypertensive medication, diabetes, and history of myocardial infarction and heart failure. However, this model has only been validated for populations in the United States and Western Europe [23]. Moreover, although the benefits of interventions to manage risk factors such as weight, blood pressure, smoking, and diabetes for health outcomes generally are well established and relevant to populations globally, primary prevention trials for AF have yet to establish a role for interventions for specific risk factors. There is an urgent need for research that can inform primary prevention efforts for AF in more geographically and racially diverse populations, while also evaluating the effectiveness of preventative strategies aimed at reducing the risk of AF globally [24].

3.2. Screening

Although a shortage of evidence of AF determinants and prevention strategies restricts primary prevention efforts, there is stronger evidence that early detection and treatment can reduce morbidity and mortality due to AF. Guidelines recommend that all patients who present with symptoms of AF—breathlessness, palpitations, syncope, chest discomfort, or stroke—should have their pulse checked for irregularities as well as 12-lead electrocardiogram (ECG) [25]. Prolonged ECG monitoring may be especially useful in patients with heart failure and post-stroke, to enhance detection and reduce health resource utilization and costs, depending on local resource and expertise. This strategy should be complemented by screening for asymptomatic AF. In a large randomized trial comparing routine practice versus targeted population-based screening and opportunistic screening, opportunistic palpation (pulse taking) of patients 65 years of age and older, with or without known AF risk factors (with follow-up ECG for those with an irregular pulse), was found to be the cheapest and most effective method of screening for AF (opportunistic screening was found to detect similar numbers of new cases compared with systematic screening [1.64% vs. 1.62%], and requires fewer resources) [26]. One limitation of opportunistic pulse palpation is the high number of false positives that can result in unnecessary ECGs (although unnecessary ECGs are not harmful per se, accurate interpretation of ECGs can only be done by specifically trained staff, of which there may be few in low-resource settings). A recent meta-analysis has suggested that newer technologies such as modified blood pressure monitors and single-lead ECGs may be more accurate in detecting AF [27], and at-home blood pressure monitors have been estimated to reduce strokes and save costs by the UK National Institute of Clinical Evaluation [28]. However, these technologies are not widely available and therefore their use for large-scale screening initiatives is not yet feasible.

3.3. Diagnosis

Although an irregular pulse may point to AF, an ECG is still required to confirm the diagnosis. A negative ECG does not exclude the diagnosis of AF by pulse taking because AF may be paroxysmal (transient). In patients with suspected AF, diagnosis should be confirmed using a single-lead rhythm strip or 12-lead ECG documenting $\geq$30 seconds of AF [29,30]. A 12-lead ECG can detect other abnormalities such as left ventricular hypertrophy, ischemia, and other clinical features. At first diagnosis, AF can be classified as 1 of 4 types: paroxysmal (self-terminating, usually within 48 hours), persistent (lasts longer than 7 days), long-standing persistent (has lasted 1 year or more), or permanent (when presence of arrhythmia is accepted and no rhythm control [i.e., stabilizing sinus rhythm] is attempted). Although paroxysmal AF is associated with somewhat lesser risk of thromboembolism than

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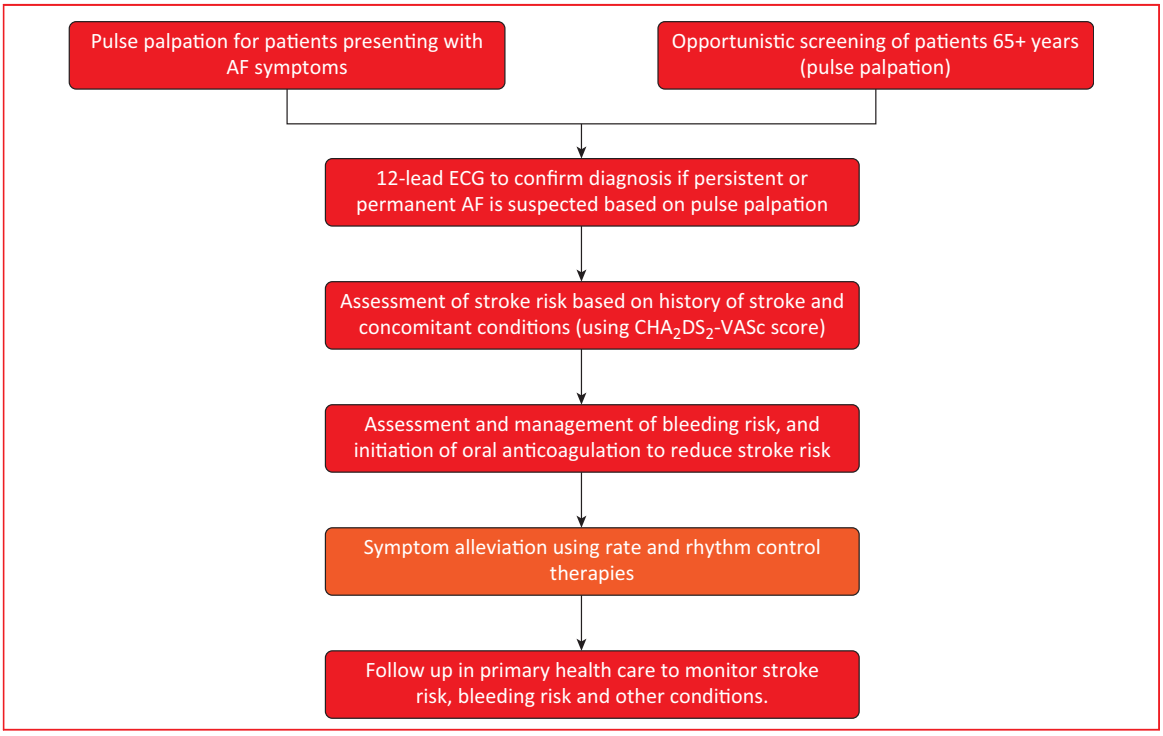

FIGURE 2. The ideal patient care pathway for AF patients. AF, atrial fibrillation; CHA_2DS_2-VASc, congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke, transient ischemic attack, or thromboembolism, vascular disease, age 65 to 74 years, sex category (female); ECG, electrocardiogram.

nonparoxysmal AF [31], all types of AF are associated with sufficiently increased risk of thromboembolism, especially stroke [32], making detection of even paroxysmal AF critical (for any pattern of AF, a prime determinant of risk of thromboembolism and prognosis is the presence of CVD comorbidities such as hypertension or diabetes [see following paragraph]). If AF is not detected with single-lead rhythm strip or 12-lead ECG, a 24-hour ambulatory monitor (Holter) or other long-term ECG monitoring may be necessary. Only a few studies exist comparing methods and duration of ECG monitoring but prolonged monitoring has been recommended for highly symptomatic patients, and those with cryptogenic stroke [9,33–36]. Inexpensive smartphone-based rhythm monitoring equipment has potential applications in LMICs, but systems for deployment and validation require further development and investigation.

Presence of CVD and other risk factors affects the risk of stroke and prognosis in patients with AF. Patients with confirmed AF should undergo a thorough clinical assessment including an analysis of family history, risk factors and concomitant disease, to assess stroke risk. The risk factors for stroke among AF patients for which there is an evidence base include prior stroke, transient ischemic attack, thromboembolism, age, hypertension, diabetes and structural heart disease [9,37,38]. One tool for evaluating stroke risk among AF patients is the CHA_2DS_2-VASc score [39]. The CHA_2DS_2-VASc is a point-based risk stratification system that assigns 2 points to a history of stroke, transient ischemic attack, or thromboembolism and ≥75 years of age, and 1 point each to a history of congestive heart failure, hypertension, diabetes, or vascular disease; 65 to 74 years of age; or female sex. OAC therapy is recommended for those with a CHA_2DS_2-VASc score of 2 or above [29]. In East Asian people, there is evidence that the risk benefit balance of anticoagulation may justify use of a lower cutoff (e.g., CHA_2DS_2-VASc score of 1, younger age) [40]. In addition to a thorough clinical examination, all patients with AF should also undergo an echocardiogram to assess for underlying heart disease that requires treatment [9,25]. Heart failure was more common among individuals with AF in Africa than in other regions of the world [12]. The absence of symptoms among patients presenting with AF does not suggest lower risk of stroke and these asymptomatic patients should also undergo thorough clinical assessment [11,41,42].

3.4. Management

After clinical assessment of confirmed AF cases and based on stroke risk, anticoagulant therapy should be initiated to reduce risk of stroke and systemic thromboembolism, while also taking into account the risk of major bleeding (discussed subsequently). Anticoagulation for medium-

and high-risk nonvalvular AF is identified as a recommended policy option by the World Health Organization (WHO) in the WHO Global Action Plan for the Prevention and Control of NCDs 2013 to 2020 [43]. Until recently, warfarin and other vitamin K antagonists were the only class of OACs available, but since 2009 non—vitamin K anticoagulants (NOACs) have been introduced that reduce the need for frequent monitoring, and the side effects associated with vitamin K antagonists are as effective as warfarin in reducing stroke and may be associated with a lower risk of bleeding [44]. Evidence suggests that NOACs may be cost-effective options for stroke prevention in AF patients [45], although possibly more so in settings with poor warfarin management [46]. Nevertheless, warfarin remains the most widely available anticoagulant and is the only anticoagulant on the World Health Organization's Essential Medicines list [47]. Aspirin, which is widely used as an antithrombotic therapy for AF is neither effective nor safe and has been written out of most published guidelines [48]. The combination of aspirin plus clopidogrel is more effective than aspirin alone but less effective than warfarin when the time in therapeutic range is reasonably well managed, and has no advantage over warfarin in terms of major bleeding [49,50].

The decision to initiate anticoagulant therapy to reduce risk of stroke must be weighed against the risk of major bleeding complications associated with anticoagulant therapy, the most dangerous of which is intracerebral hemorrhage [29,51]. Prior to initiating anticoagulant use, risk of bleeding should be assessed. Assessment tools for identifying risk factors for bleeding have been recommended by some national guidelines in high-income countries, including risk factors such as hypertension, abnormal renal function, abnormal liver function, prior stroke, prior major bleeding or predisposition to bleeding, labile international normalized ratio (INR), ≥65 years of age, prior alcohol or drug usage, and medication usage predisposing to bleeding (e.g., antiplatelet agents, nonsteroidal anti-inflammatory drugs) [29,52,53], but these tools have not been validated in LMICs. Some research suggests that those of Chinese ethnicity are more susceptible to intracerebral hemorrhage than are those of European

TABLE 2. Roadblocks, strategies, and potential solutions for achieving effective AF management

Dimension	Roadblock	Strategy	Potential Solutions
Geographic accessibility	Long distances to clinics result in low numbers of rural patients presenting to clinics for screening.	1. Improve accessibility of screening for rural populations. 2. Strengthen capacity for ECG testing in remote areas.	1. Train community health workers or pharmacists to screen for possible AF with pulse-checking in nonclinic settings. Educate at risk-populations (e.g., those 65+ years of age) to self-screen with pulse checks. 2. Implement novel telemedicine technologies (e.g., transmission of ECG results from rural areas to urban facilities).
Availability	**Shortage of health care professionals with training in AF, including interpretation of ECG, initiation of and monitoring of anticoagulation therapy.**	**1. Raise awareness of AF among health care professionals.** **2. Reduce dependence on highly trained medical staff for AF screening and management.**	**1. Conduct awareness campaigns through health care professional networks.** **Improve postgraduate training and CME.** **Develop simple and locally applicable AF guidelines.** **2. Implement NPHW-managed anticoagulation program.**
Affordability	OACs potentially unaffordable for patient households, resulting in nonadherence to treatment regime.	1. Improve affordability of OACs.	1. Provide universal health care coverage for essential medicines. 2. Implement internationally recognized policies for the reduction of essential medicine costs (Box 2).
Acceptability	**Reluctance of physicians and patients to initiate anticoagulation therapy.** **Lack of awareness of importance of persistent adherence to OAC therapy.**	**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.**	**1. Conduct country-specific training on OAC therapy management and support programs for noncardiologist health care professionals.** **2. Develop and implement country-specific patient education, medical literacy, and support programs for diagnosed AF patients on OAC therapy.** **3. Conduct research into feasibility of self-monitoring programs for patients on OAC therapy in LMICs.**

AF, atrial fibrillation; CME, continuous medical education; ECG, electrocardiogram; LMICs, low- and middle-income countries; NPHW, nonphysician health worker; OAC, oral anticoagulant.

descent [54]. If bleeding risk factors are present with increased bleeding risk, in general, anticoagulant therapy should not be withheld, but regular review and attempts to address bleeding risk factors are recommended [29]. Control of hypertension and avoidance of concomitant antiplatelet therapy are among the more important strategies to reduce the risk of major bleeding in anticoagulated patients with AF.

Although anticoagulant therapy is the only proven way to reduce stroke or systemic embolism among patients with AF, arrhythmia management therapies may reduce AF symptoms and improve patient quality of life [55]. The first aim of arrhythmia management is to slow the ventricular rate to a resting rate of <100 beats/min. Initiation of drug therapy to stabilize sinus rhythm (rhythm control) is based on extent of symptoms and patient and physician values and preferences, as currently there is no evidence that rhythm control therapies reduce the risk of stroke [55].

After diagnosis and a treatment plan are established, most patients with AF can be followed in primary health care (PHC) to monitor heart rate and rhythm and to reassess risk stratification [25]. Monitoring of AF patients in PHC also provides the opportunity to monitor and treat comorbid cardiovascular conditions [56,57], in particular hypertension, heart failure, diabetes, and valvular abnormalities. Conversely, in PHC, individuals presenting with these conditions have a high prevalence of AF, which should be borne in mind during their assessment. Although valvular AF is not the focus of this Roadmap, management of AF should include consideration of the management of rheumatic heart disease (RHD) and valvular heart disease, as these diseases are common in LMICs and a large proportion of those suffering from them (30% to 40%) develop AF [58]. Further guidance on management of and health system responses to RHD is included in the WHF RHD Roadmap.

3.5. The "ideal" patient care pathway for AF patients

Based on the evidence cited previously, Figure 2 outlines key recommendations for detection, diagnosis and management of AF, or the "ideal patient pathway" for AF patients. This includes: 1) screening of individuals with known AF risk factors and opportunistic screening of patients 65 years of age or older coming in for review; 2) 12-lead ECG to confirm suspected persistent or permanent AF; 3) assessment of stroke risk; and 4) initiation of anticoagulant therapy, combined with lifestyle modification advice if appropriate (e.g., weight reduction, smoking cessation). Although rate and rhythm control are important steps for management of symptoms, they are included in a different color, as this pathway is intended to outline only the bare minimum evidence-based interventions for reducing mortality associated with AF. However, it should be noted that several other opportunities to change prognosis in AF exist (e.g., prevention and management of tachycardiomyopathy).

4. KNOWLEDGE-PRACTICE GAPS

Despite evidence supporting opportunistic pulse palpation of patients 65 years of age and older, with confirmatory diagnosis using 12-lead ECG [26], the pulse is not routinely palpated in individuals older than 65 years of age. It should be noted that the basis of this pragmatic recommendation is a single randomized controlled trial in a high-income country where cardiology review was widely available, and therefore more context-specific research from LMICs is needed. Also despite guideline-recommended prevention of stroke with anticoagulant therapy [29], large gaps in implementation of this therapy remain [10]. These knowledge-practice gaps are present worldwide. The GARFIELD (Global anticoagulant registry in the field) registry, a study of 19 countries in 2009 to 2011, revealed that 38.0% of patients with high risk of stroke had not received anticoagulant therapy, whereas 42.5% of those at low risk (score 0) did [59]. The PINNACLE (Practice Innovation and Clinical Excellence) study in the United States found that less than half of high-risk patients were receiving OAC therapy [60]. In the EORP-AF (EURObservational Research Programme-Atrial Fibrillation) general registry of 9 European countries, while use of OACs was higher (approximately 81% to 81% of high stroke risk patients), persistence of therapy was still not optimal (84% of those prescribed with vitamin K antagonist remained on therapy 1 year later), and despite guidelines, antiplatelet therapy (commonly aspirin) was used in 15% of low risk patients and in 31% of high-risk patients [61].

Although present worldwide [61,62], these gaps vary in degree across countries, appearing to be most prominent in LMICs. Data from LMICs are scarce but what does exist points to very low rates of oral anticoagulation therapy among AF patients [12,24,63]. A review of existing literature [63] found that estimated rates of anticoagulant use range from only 2.7% to 50% in China [63–65], 26% to 44% in Pakistan [66], 16% in Malaysia [67], from 46.7% to 57.8% in Brazil [68], 36.8% in Mexico [69], 72.7% in Argentina [70], 33% in South Africa [71], 34.2% in Cameroon [72], from 11.5% (rural) to 26.5% (urban) in Zimbabwe [73], 62% in Senegal [74], from 30.1% to 67.3% in Turkey [75,76], 13% to 53.9% in Serbia [77], 27% in Kosovo [78], and 7.1% in Moldova [79]. The Gulf SAFE (Gulf Survey of Atrial Fibrillation Events) registry revealed similarly low rates of anticoagulation use (49% of patients) in 6 Gulf countries (Bahrain, Kuwait, Oman, Qatar, United Arab Emirates, and Yemen) [80].

Most evidence on AF knowledge-practice gaps in LMICs focuses on gaps in management of stroke risk among AF patients with OACs. However, there is evidence of gaps across the continuum of care for AF globally, which are likely to apply in LMICs. For example, research in Canada suggested that noncardiologist physicians lack

sufficient knowledge, skills and confidence to diagnose AF, with diagnosis of paroxysmal or asymptomatic AF being particularly challenging, and that continuous professional education and development is necessary to strengthen the capacity of physicians to navigate AF screening and diagnosis guidelines [81].

5. ROADBLOCKS AND SOLUTIONS

Table 2 identifies potential roadblocks along the ideal patient pathway for AF screening, diagnosis, and management. Potential roadblocks and solutions were identified through a review of published literature as well as through consultation with an expert committee, comprised of experts in AF clinical management and health systems research in LMICs. These roadblocks are presented in terms of barriers to geographical accessibility, availability, affordability and acceptability of AF health care, drawing on existing frameworks for identifying health systems barriers in LMICs [82–84]. Also outlined are strategies for addressing these roadblocks and specific potential solutions for executing these strategies.

Box 2. Strategies for improving the affordability of CVD medications [102]

1. Provide free essential drugs through universal health coverage.
2. Increase the efficiency of the medication supply chain to promote access to medicines within existing health budgets (through more efficient selection, quantification and forecasting, procurement, storage, and distribution of medications).
3. Promote the use of high-quality, safe, and efficacious generic medications by overcoming legal barriers relating to patents and licenses in LMICs.
4. Develop policies to reduce end-user prices, including regulating retail mark-ups and eliminating tariffs on medicines.
5. Engage the pharmaceutical industry to price CVD medicines at affordable levels in LMICs.

CVD, cardiovascular disease; LMICs, low- and middle-income countries.

Box 3. The IMPACT-AF trial in India

The IMPACT-AF trial is testing the effectiveness of a comprehensive customized intervention for increasing the rate and persistence of use of OACs in patients with AF in 5 LMICs. In India the intervention will involve training nonphysician health workers to educate patients in: 1) AF, stroke, and recognizing the symptoms of a stroke; 2) the importance of OACs to prevent stroke, and precautions to be taken while on warfarin therapy (as most Indian AF patients are on warfarin); and 3) the importance of medication adherence, identifying barriers in nonadherent patients, and providing strategies to overcome those barriers. Diaries are given to patients to allow them to record days when they take medications, and included educational content. NPHWs are trained to follow-up patients, monitor international normalized ratio, identify nonadherent patients and barriers to treatment adherence, and support the patient toward getting back on treatment. The intervention also includes an educational intervention for physicians hosted at Duke University, consisting of webinars and access to guidelines on the use of OACs in AF.

AF, atrial fibrillation; IMPACT-AF, Integrated Management Program Advancing Community Treatment of Atrial Fibrillation; LMICs, low- and middle-income countries; OACs, oral anticoagulants.

5.1. Improving accessibility and availability of screening for rural populations

This Roadmap recommends that screening for AF is best conducted via opportunistic palpation (pulse taking) of patients 65 years of age and older, with or without known AF risk factors, with follow-up ECG for those with an irregular pulse. Following this recommendation may be challenging, however, in remote settings in LMICs. In these settings, when at-risk individuals present at clinics, health professionals who are trained in interpretation of ECGs may not always be available. This may make the diagnosis of paroxysmal AF particularly difficult as it would require multiple ECG measurements to detect. Novel technologies that allow for cardiac rhythm assessment by nonspecialist health care workers may reduce the dependence on specialists for AF screening [85]. These include approaches for measuring pulse irregularity with inexpensive tools such as oscillometric blood pressure devices [86], smartphones [87,88], or handheld ECG devices that facilitate multiple ECG measurements [87,88]. As mentioned previously, however, these technologies are not yet readily available in LMICs; they have not been tested in these settings and the training and support required to implement them effectively must be considered [85]. New research on the feasibility of a nonphysician health worker (NPHW)–led screening AF program in community health centers in China is planned and will offer valuable evidence of the effectiveness of such programs. In the meantime, experiences in successful training of NPHWs to screen for CVD [89,90] and cancer

[91] in LMICs may provide useful insights for implementation of nonspecialist screening programs for AF.

The field of telemedicine may also provide opportunities for addressing trained health care professional shortages in LMICs [92,93], with some findings suggesting that transmission of ECG results from remote, rural areas to urban facilities may improve detection of CVD generally [94]. However, the effectiveness and cost effectiveness of telemedicine in LMICs generally [93–95], and specifically for detection of AF, has not been sufficiently evaluated and requires further research. Any strategies that make use of novel technologies for detection of AF will only be effective in reducing mortality associated with AF if OAC treatment is also available and affordable to those with diagnosed AF, and if structures are in place for the successful management of OAC therapy.

5.2. Improving the affordability of OACs

Any effort to reduce mortality associated with AF will only succeed if drug treatment, whether warfarin or NOACs, is readily available to those who need it, without causing undue financial hardship [43]. The affordability of warfarin specifically has not been studied, but evidence of a link between poor adherence to OACs and poverty [96,97], of the unaffordability of other CVD medications in LMICs [98] and the of catastrophic impact of health care costs for CVD generally [99,100] may provide some indication of the likely burden that most chronic CVD medication costs impose on patient households. Currently, the affordability of NOACs in LMICs in uncertain [101], and research on the cost effectiveness of these drugs in these settings is needed. The WHF Roadmap for secondary prevention of CVD [57] identified strategies that have been previously recommended to increase the affordability of CVD medications [102] and NCD medications generally [103]. These strategies are relevant to OAC drug therapies (Box 2).

Box 4. Examples of international AF registries [12,59,61,80,112]

- **RE-LY registry: 47 countries across all world regions**
- **Garfield-AF registry: 19 countries worldwide with 34 total planned**
- **EORP-AF European registry: 9 European Society of Cardiology member countries**
- **Gulf SAFE registry: 6 Middle Eastern Gulf countries**
- **J-TRACE: Japan Thrombosis Registry for atrial fibrillation, coronary, or cerebrovascular events**

AF, atrial fibrillation.

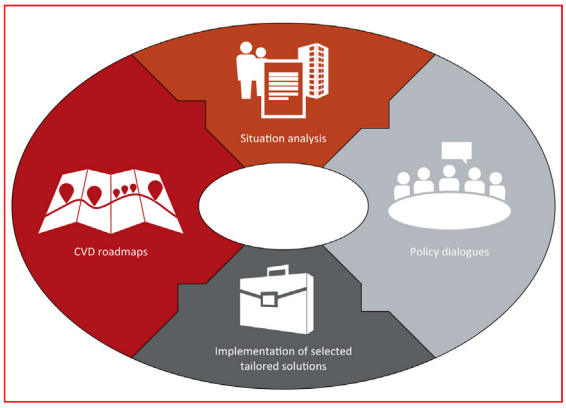

FIGURE 3. Adapting the WHF Roadmaps at the national level. Reproduced with permission from Perel et al. [113]. CVD, cardiovascular disease; WHF, World Heart Federation.

5.3. Reducing dependence on highly trained medical staff for AF management

Dependence on medical specialists for AF treatment management can be challenging in LMIC settings that suffer from a shortage of highly trained medical professionals. Research from the United Kingdom and the Netherlands has suggested that nurse-led management of AF treatment, with the use of computerized decision support systems and near-patient testing in a primary-care setting, can be an effective [104] and cost-effective [105] alternative to hospital-based management. Novel interventions for improving management of AF by family physicians in LMICs supported by NPHWs are currently being studied (Box 3) and the results will provide valuable insights for how to increase the role of family physicians and NPHWs across the AF patient treatment pathway.

5.4. Improving capacity for management of OAC therapy among patients

Successful management of stroke risk with OAC therapy among AF patients requires maintenance of INR within a target therapeutic range through regular monitoring and dose adjustments. Over- or undercoagulation can result in thrombotic or hemorrhagic events [106]. The risks associated with OAC therapy are an important factor in physician and patient preferences regarding initiation of OAC [107], and perhaps even more likely so in LMIC contexts where regular visits to a physician may be difficult due to travel distances, long wait times, or high out-of-pocket costs [43,84,108]. Research from high-income countries has suggested that self-management of OAC therapy among AF patients, with appropriate support and education, may be at least as effective as physician monitoring in reducing risk of thromboembolism [109], and possibly more cost effective [110]. Self-monitoring requires the patient measure the INR using a point-of-care device

and self-adjust, if necessary, their dose of warfarin using a nomogram (dose prediction chart) [110,111]. However, evidence surrounding self-monitoring of OAC among AF patients and the necessary elements for success of such interventions remains limited, and what exists has focused on high-income countries alone. Further research is required on the potential for patient self-monitoring of OAC therapy as a means of reducing risk of thrombotic or hemorrhagic events in LMICs. Such research should be interpreted in light of different contextual factors, in particular that of the likely increase of the availability and affordability of NOACs in LMICs, which reduce the need for improved INR monitoring.

5.5. Strengthening health information systems

As noted previously, there is a paucity of data on the incidence and quality of care of individuals with AF globally, and in particular in LMICs. Without this information, resource allocation for the solutions proposed here or other strategies to improve AF detection, diagnosis, and treatment in any country is unlikely to be evidence-based and efficient. In order to support the planning and monitoring of AF interventions, health information systems must be developed. These should be simple, representative, context appropriate, and timely, and be established as part of a larger NCD surveillance strategy. Some existing AF registries are identified in Box 4. Further guidance on the development of health information systems for high- and middle-income countries (e.g., national or regional registries and electronic health records) as well as low-income countries (e.g., periodic representative surveys), is provided in the WHF Roadmap on secondary prevention of CVD [57].

6. ADAPTING THE AF ROADMAP TO REGIONAL AND NATIONAL CONTEXTS

The AF and other WHF Roadmaps provide general guidance on screening, diagnosis, and management of AF; identify roadblocks to implementing evidence-based approaches in LMICs; and suggest potential strategies to overcoming these. The application of these strategies to specific contexts must be considered further to adapt region- or country-specific Roadmaps. The WHF has described the process of producing region- and country-specific Roadmaps [113].

National roadmaps should be developed within multisectoral partnerships, including intergovernmental organizations, heart health advocacy foundations, cardiovascular scientific organizations, healthcare leaders, providers from primary and specialized care, private-sector stakeholders, and people affected by CVD (including patients and caregivers). To be successful, they will also require effective advocacy toward policy makers and politicians in national governments.

The necessary steps for adapting the WHF AF Roadmap at the national level include (Fig. 3):

1. Develop and convene a multisectoral coalition to adapt the global Roadmap to local circumstances.
2. Conduct a situation analysis of the health system for AF, including epidemiologic profiling, relevant policies, and assets.
3. Conduct policy dialogues with multiple local stakeholders. Local problems, specific barriers, and potential solutions should be discussed and appropriate strategies selected according to context.
4. Develop a plan to evaluate the implementation of the selected strategies.

7. CONCLUSIONS

AF affects millions of people worldwide and, left untreated, increases the risk and severity of stroke and heart failure. Although guidelines for the screening, diagnosis, and management of AF exist, there are gaps in implementation of these guidelines globally, and in particular in LMICs. Long distances to health facilities, a shortage of trained health professionals, and low awareness of and adherence to OAC treatment among health professionals and patients may all serve as roadblocks to guideline adherence. This Roadmap identifies some potential solutions, such as NPHW-led AF screening programs, the use of novel telemedicine technologies and OAC education interventions, all of which may be feasible strategies for improving AF outcomes in low-resource settings. It also highlights areas where more research is needed, for example on determinants and primary prevention of AF, the cost effectiveness of novel technologies and telemedicine for screening and diagnosis of AF in LMICs, gaps in management of AF in LMICs and the feasibility of NPHW-led interventions to improve AF management in these contexts. Although this Roadmap can serve as guidance on potential strategies for improved AF screening, diagnosis, and management in LMICs, the applicability of these strategies to specific LMIC settings must be considered further.

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