

# Global disparities in arrhythmia care: Mind the gap



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Delivery of comprehensive arrhythmia care requires the simultaneous presence of many resources. These include complex hospital infrastructure, expensive implantable equipment, and expert personnel. In many low- and middle-income countries (LMICs), at least 1 of these components is often missing, resulting in a gap between the demand for arrhythmia care and the capacity to supply care. In addition to this treatment gap, there exists a training gap, as many clinicians in LMICs have limited access to formal training in cardiac electrophysiology. Given the progressive increase in the burden of cardiovascular diseases in LMICs, these patient care and clinical training gaps will widen unless further actions are taken to build capacity. Several strategies for building arrhythmia care capacity in LMICs have been described. Medical missions can provide donations of both equipment and clinical expertise but are only intermittently present and therefore are not optimized to provide the longitudinal support needed to create self-sustaining infrastructure. Use of

donated or reprocessed equipment (eg, cardiac implantable electronic devices) can reduce procedural costs but does not address the need for infrastructure, including diagnostics and expert personnel. Collaborative efforts involving multiple stakeholders (eg, professional organizations, government agencies, hospitals, and educational institutions) have the potential to provide longitudinal support of both patient care and clinician education in LMICs.

**KEYWORDS** Global health; Health disparities; Social determinants of health; Health policy; Cardiac electrophysiology

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## Introduction

The impact of noncommunicable diseases, including cardiac arrhythmias, is growing fastest in low- and middle-income countries (LMICs). Diagnostic and therapeutic interventions for cardiac arrhythmias are among the most resource-intensive within cardiology and can be particularly difficult to provide in environments where resources are constrained. Failure to address the unmet need for arrhythmia care in these resource-constrained environments could have severe public health consequences on a global scale.

In addition to the gap between supply and demand for arrhythmia care in LMICs, there exists a training gap, as many clinicians working in resource-constrained environments have decreased access to training in cardiac electrophysiology (EP). In this review, we describe the challenges that limit the provision of cardiac arrhythmia care in resource-constrained environments. We also discuss strategies that could address some of the challenges responsible for identified gaps in arrhythmia care delivery.<sup>1</sup>

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## Epidemiology of cardiac arrhythmias in resource-constrained environments

Inability to address the increasing burden of noncommunicable diseases, notably cardiovascular diseases, in LMICs could result in avoidable human suffering and economic destabilization.<sup>2</sup> The most recent Global Burden of Disease Study revealed that among noncommunicable diseases, cardiovascular disease is the leading cause of mortality worldwide.<sup>3</sup> Cardiovascular disease carries twice the mortality rate of HIV/AIDS, malaria, and TB combined.<sup>4</sup> Data from the 2019 Global Burden of Cardiovascular Diseases and Risk Factors report revealed regional disparities in disability-adjusted life years (DALYs) associated with cardiovascular disease. The greatest impact on DALYs was present in Africa, Eastern Europe, Central Asia, the Middle East, and Oceania.<sup>2</sup> This study also revealed that women were disproportionately affected by cardiovascular diseases in these regions.

Cardiac arrhythmias are thought to contribute to a significant proportion of cardiovascular disease burden in LMICs, but data pertaining to the incidence of cardiac arrhythmias are lacking in many regions.<sup>5</sup> There are few studies describing the incidence of heart block, sudden cardiac death, or tachyarrhythmia in large parts of Africa, Eastern Europe, and Central Asia. It is possible that reduced access to diagnostic studies and treatment in some of these regions may lead to

## KEY FINDINGS

- Delivery of comprehensive arrhythmia care, which is typically resource-intensive, is challenging in resource-constrained environments.
- Several strategies that address challenges associated with arrhythmia care delivery in low- and middle-income countries have been described. These include medical missions, utilization of donated/reprocessed devices/catheters, and cardiac electrophysiology training programs involving cooperation between multiple stakeholders.
- The unique features of each resource-constrained setting must be understood in detail if attempts to build arrhythmia treatment capacity are to be successful.
- Building locally sustainable infrastructure is key to achieving durable increase in arrhythmia treatment capacity.

underreporting of the true burden of cardiac arrhythmias.<sup>4,5</sup> There are no studies indicating that the burden of cardiac arrhythmias is clearly different in high-income countries (HICs) and LMICs.

### Current state of cardiac arrhythmia care in resource-constrained environments Incidence of heart block vs pacemaker availability in resource-constrained environments

The worldwide prevalence of third-degree heart block is estimated to be 0.04%.<sup>6</sup> It is estimated that 2.5 million people die annually due to lack of access to pacemaker implantation.<sup>7</sup> In the United States, the permanent pacemaker (PPM) implantation rate is approximately 62 per 100,000 people, and the implantable cardioverter-defibrillator (ICD) implantation rate is approximately 46 per 100,000 people (based on data from 2006).<sup>8,9</sup> The PPM implantation rate in Western Europe was estimated to be 103 per 100,000 people in 2014.<sup>10</sup> Calculation of PPM and ICD implantation rates in many LMICs is limited by the absence of cardiac implantable electronic device (CIED) registries. Available data indicate that CIED implantation rates are considerably higher in HICs than in LMICs (Table 1).

A recent Pan-Africa Society of Cardiology (PASCAR) survey stated that PPMs are not implanted in 18% of African countries for which data are available.<sup>11,12</sup> In this survey, the median PPM implantation rate in Africa was approximately 0.3 per 100,000 people, which is more than 200-fold lower than the implantation rate in Western Europe.<sup>5,10–12</sup> The 11th World Survey of Cardiac Pacing and Implantable Cardioverter-Defibrillators, published in 2011, demonstrates that CIED implantation rates in many LMICs (predominantly in Asia and Africa) are <1 per 100,000 people.<sup>13</sup>

This care gap has been shown to result in worse patient outcomes. In a recent analysis of the Africa-Pace program, approximately 50% of 1077 patients for whom PPM was recommended (the predominant indication was complete heart block) died while waiting for the arrival of international medical missions.<sup>1</sup> The median waiting time between diagnosis and intervention was 18.4 months. Even higher mortality rates are suspected in areas where device implantation is not available.<sup>1</sup> The lack of CIED availability in LMICs will become a more pressing concern as the global population ages.<sup>14</sup>

### Impact of atrial fibrillation in resource-constrained environments

Atrial fibrillation (AF) prevalence in the United States is approximately 1%, and the prevalence of AF in Caucasians is >2-fold higher than in other racial groups.<sup>15,16</sup> While genetic and cardiac structural variation have been postulated as reasons for racial differences in AF incidence, heterogeneous access to health care leading to AF underdetection is likely a significant contributor.<sup>17–19</sup> AF prevalence in East Asian countries is between 0.3% and 1.6%.<sup>20–22</sup> Based on regional projections of growth in AF prevalence, it is estimated that by 2050 twice as many people in Asia will have AF than in North America and Europe combined.<sup>23–25</sup>

The global prospective RE-LY (Randomized Evaluation of Long-Term Anticoagulation Therapy) AF registry, which enrolled approximately 15,000 patients from 46 countries, demonstrated regional disparities in AF care. For example, patients from India, China, and Africa who were treated with oral anticoagulants (OACs) were found to spend a sub-optimal amount of time in therapeutic range (32%–40%).<sup>26</sup> More recent data from the Global Registry on Long-Term Oral Anti-Thrombotic Treatment in Patients with Atrial Fibrillation (GLORIA-AF) demonstrated a lower rate of direct OAC (DOAC) utilization in Latin America and Asia than in Europe and North America. This registry data also revealed geographic disparities in time to treatment.<sup>27</sup> Regional disparities in the delivery of OAC therapy are particularly concerning given the higher risk of stroke and cardiovascular mortality among patients not receiving optimal anticoagulation reported in Global Anticoagulant Registry in the Field-Atrial Fibrillation (GARFIELD-AF).<sup>28</sup>

A 2018 publication from PASCAR reported that pharmacological and interventional therapies for cardiac arrhythmias are not available in most of Africa.<sup>5</sup> This survey includes data for 33 of 55 countries in Africa.<sup>5</sup> Of the 33 countries for which data was available, 14 reported that DOACs were available to them. Warfarin was available in the majority of countries surveyed. Digoxin and amiodarone were the most common drugs used for rhythm control in sub-Saharan Africa.<sup>5</sup> Of the countries surveyed in this PASCAR study, 5 of 33 utilized catheter ablation and 16 of 33 had capacity for electrical cardioversion.<sup>5</sup> Intravenous formulations of antiarrhythmic drugs medications were not readily available, further compounding the challenges of AF management.

**Table 1** Geographical disparities in CIED implantation

| Region/country           | PPM implantation rate per 100,000 | ICD implantation rate per 100,000 |
|--------------------------|-----------------------------------|-----------------------------------|
| <b>Americas</b>          |                                   |                                   |
| United States            | 61.6                              | 46.2                              |
| Uruguay                  | 32.4                              | 3.9                               |
| Argentina                | 28.7                              | 5.6                               |
| Chile                    | 21.6                              | 1.4                               |
| Brazil                   | 13.6                              | 1.5                               |
| Trinidad/Tobago          | 12.7                              | 1.8                               |
| Bolivia                  | 6.5                               | n/a                               |
| Peru                     | 3.0                               | 0.1                               |
| <b>Europe</b>            |                                   |                                   |
| Western Europe           | 102.6                             | 25.2                              |
| Germany                  | 115.2                             | 29.5                              |
| Sweden                   | 96.9                              | 21.6                              |
| Lithuania                | 78.9                              | 3.8                               |
| Poland                   | 74.2                              | 21.9                              |
| United Kingdom           | 70.8                              | 10.2                              |
| Croatia                  | 58.2                              | 3.9                               |
| Serbia                   | 50.7                              | 6.3                               |
| Romania                  | 19.6                              | 1.5                               |
| <b>Africa</b>            |                                   |                                   |
| African Continent        | 0.2                               | <0.1                              |
| Tunisia                  | 14.9                              | 1.3                               |
| Mauritius                | 12.0                              | n/a                               |
| South Africa             | 10.5                              | 1.2                               |
| Algeria                  | 6.0                               | 0.2                               |
| Morocco                  | 2.8                               | 0.08                              |
| Sudan                    | 0.7                               | n/a                               |
| Kenya                    | 0.4                               | n/a                               |
| Cameroon                 | 0.3                               | n/a                               |
| Uganda                   | 0.06                              | n/a                               |
| Nigeria                  | 0.01                              | n/a                               |
| Chad                     | 0                                 | n/a                               |
| Central African Republic | 0                                 | n/a                               |
| <b>Asia and Oceania</b>  |                                   |                                   |
| Australia                | 56.5                              | 16.0                              |
| New Zealand              | 54.2                              | 9.3                               |
| Japan                    | 50.8                              | 4.6                               |
| Taiwan                   | 29.6                              | 3.7                               |
| Hong Kong                | 22.1                              | 3.1                               |
| Singapore                | 16.1                              | 7.3                               |
| South Korea              | 8.4                               | 2.2                               |
| Sri Lanka                | 7.8                               | n/a                               |
| Thailand                 | 6.6                               | 1.6                               |
| China                    | 6.2                               | 0.3                               |
| India                    | 3.3                               | 0.3                               |
| Malaysia                 | 2.7                               | 0.6                               |
| Vietnam                  | 2.1                               | 0.3                               |
| Pakistan                 | 1.9                               | 0.1                               |
| Philippines              | 0.8                               | 0.1                               |
| Indonesia                | 0.7                               | 0.02                              |
| <b>Middle East</b>       |                                   |                                   |
| Israel                   | 42.9                              | 16.7                              |
| Bahrain                  | 4.8                               | 1.1                               |
| Iran                     | 4.7                               | 1.8                               |
| Qatar                    | 3.6                               | 0.9                               |
| Oman                     | 3.1                               | 0.5                               |

U.S. data pertaining to pacemaker implantation<sup>8</sup> and defibrillator implantation<sup>9</sup> were obtained from 2 separate studies. European CIED implantation data were procured from a single study.<sup>10</sup> Data pertaining to pacemaker<sup>11</sup> and defibrillator<sup>12</sup> implantation in Africa were taken from 2 separate studies. For pacemaker implantation in Africa, reported values represent the mean implantation rates for all years in which data were avail-

able.<sup>11</sup> CIED implantation data for the Middle East, Central and South America, and Australia were obtained from a single study.<sup>13</sup> Data pertaining to CIED implantation in Asia and Oceania (except for Australia) were taken from the Asia Pacific Heart Rhythm Society registry.<sup>9,2</sup> Data for cardiac resynchronization therapy systems were not listed in a separate category.

CIED = cardiac implantable electronic device; ICD = implantable cardioverter-defibrillator; n/a = not available; PPM = permanent pacemaker.

Consequently, a rhythm control strategy for AF was not used frequently in this region.<sup>29</sup>

Rheumatic heart disease predominantly afflicts resource-constrained regions, with the highest rates reported in South Asia and Oceania.<sup>3,29,30</sup> The burden of rheumatic heart disease further compounds the burden of AF, embolic stroke, and heart failure within these regions. The RE-LY study demonstrated coexistent rheumatic heart disease and AF in 31.5% of Indian and 21.5% of African patients compared with 2.2% North American patients.<sup>26</sup>

### Impact of sudden cardiac death in resource-constrained environments

Sudden cardiac death (SCD) is responsible for over half of deaths from cardiovascular disease.<sup>31</sup> The rate of SCD is unknown or inaccurate in many resource-constrained environments due to several factors, including lack of case capture, lack of accurate prospective ascertainment of cause of death, and disparities in cardiac arrest registry coverage.<sup>32</sup> There are no cardiac arrest or SCD registries in Russia, India, China, or Africa (except for Egypt). In addition, there are no out-of-hospital cardiac arrest or SCD registries in South America. There is 1 in-hospital cardiopulmonary resuscitation (CPR) registry in Brazil.

Autopsy data indicate that a substantial proportion of SCD events in LMICs are attributable to coronary artery disease.<sup>33</sup> An inverse relationship between socioeconomic status and burden of cardiovascular risk factors has been observed.<sup>34</sup> The suspected etiology of SCD does vary by region. Data from Latin America implicated Chagas disease in a substantial proportion of SCD cases, with autopsy data from Nigeria demonstrating hypertensive cardiomyopathy in a significant proportion of SCD cases.<sup>35,36</sup> Studies of hereditary syndromes (eg, cardiomyopathies and channelopathies) in resource-constrained environments are ongoing. Variability in the prevalence of Brugada syndrome among ethnic and racial groups has also been described.<sup>37</sup>

The Douala study was the first population-based cohort survey of SCD in sub-Saharan Africa.<sup>38</sup> This study, which described a small cohort, demonstrated many challenges associated with SCD management in sub-Saharan Africa. The observed incidence of SCD was 34 per 100,000 person-years. In this study, out-of-hospital cardiac arrest (OHCA) carried a 100% mortality rate with no CPR attempted out of hospital. The main transport to a hospital for patients with witnessed OHCA was a taxi, with the remainder of patients brought directly to a mortuary after being presumed dead without attempted resuscitation.<sup>38</sup> Several Asian

registries have been established to measure the rate of survival after OHCA.<sup>39–41</sup> Available data from the Taichung Sudden Unexpected Death Registry (THUNDER) in Taiwan reveal lower rates of a shockable rhythm (ventricular tachycardia or ventricular fibrillation) as a presenting rhythm in OHCA (19%) than in studies of Western populations.<sup>40</sup> For patients in the THUNDER registry, survival to hospital discharge was lower than described in other regions, possibly driven by the lower incidence of ventricular tachycardia or ventricular fibrillation in OHCA.

These studies highlight several areas of unmet need in LMICs, including early activation of medical services, access to ambulance services, education in bystander CPR, and access to automated external defibrillators. CIED implantation is also an unmet need: rates of ICD implantation for primary or secondary prevention of SCD are lower in resource-constrained environments (Table 1).

### Importance of local infrastructure and local training programs to the delivery of effective arrhythmia care

The provision of arrhythmia care in resource-constrained environments is limited by a lack of clinicians available to provide care and the absence of clinical infrastructure required to deliver care effectively (eg, procedural suites, inpatient cardiac telemetry units, outpatient device clinics). Access to consumable equipment (eg, CIEDs, ablation catheters) is also limited. The PASCAR survey of 2018 revealed that 18% of responding countries in sub-Saharan Africa did not have a cardiologist in 2018, with 0.1 CIED implanters per 1 million people. The number of implanting centers was also approximately 0.1 per 1 million people.<sup>5</sup> Training is hampered by the rarity of dedicated fellowship programs and by the limited retention of senior physicians, who frequently choose to work in areas with more resources.

The first Latin American catheter ablation registry demonstrated <50% of countries surveyed had access to a dedicated EP lab. This registry revealed that a limited number of centers in Argentina and Brazil were responsible for 80% of ablation procedures performed in Latin America as a whole.<sup>42</sup> Less than half of African countries have a functioning cardiac catheterization laboratory.<sup>5</sup> South Africa is the only country in sub-Saharan Africa with the capacity to provide comprehensive arrhythmia care, including catheter ablation.<sup>5</sup> North African countries are generally better equipped to provide EP studies and catheter ablation than those in sub-Saharan Africa.<sup>5</sup> Other hurdles that limit the provision of invasive EP procedures in LMICs include the lack of sterilization facilities, imaging facilities, and the staff required for the efficient functioning of such facilities.

### Opportunities to build arrhythmia treatment capacity in resource-constrained environments

Not all resource-constrained environments have the same needs (Figure 1). Therefore, attempts to build arrhythmia treatment capacity should start with a sensitive assessment

of local, unmet needs (eg, diagnostics, devices, physical plant, human resources). This appraisal should also incorporate all health needs of the population, including resources needed for emergency relief management, primary care, maternal-fetal medicine, and vaccination programs. Capacity is dynamic and interval reappraisal is required to address the observed rise in the prevalence of noncommunicable diseases and decline in prevalence of certain communicable diseases in LMICs.<sup>43–45</sup> This section focuses on some of the resources required to help local clinicians create self-sustaining infrastructure for arrhythmia management.

### Improving access to diagnostics in resource-constrained environments

The electrocardiogram (ECG) is a noninvasive and inexpensive tool to assess cardiac arrhythmia. It is recommended that an ECG be performed for patients with a history of syncope, lightheadedness, chest pain, palpitations, or family history of sudden death. Availability of facilities that provide surface ECG recording and interpretation varies as a function of resources available in individual regions.<sup>46</sup> Several factors limit ECG use in resource-constrained environments. These include availability of necessary equipment, reliable electrical power, and consumables such as electrode stickers. Availability of specialists trained to interpret ECGs is also limited in rural areas, where a higher proportion of care is provided by primary care physicians.<sup>47,48</sup>

Several strategies that address lack of ECG availability have been described. In India, where 80% of the population is rural and 30% of physicians are rurally located, mobile vans equipped with satellite terminals (supported by the Indian Space Research Organization) facilitate transmission of ECGs from rural areas to central urban hospitals, where rapid physician interpretation can be performed.<sup>49</sup> Telehealth initiatives, including transmission of the results of noninvasive studies (eg, ECGs) from rural clinics to tertiary hospitals for interpretation can enhance the identification of patients in need of care. Early involvement of cardiac electrophysiologists could also facilitate rapid identification of patients whose management requires resources present at tertiary care centers (eg, facilities with capabilities for invasive EP testing, CIED implantation, and ablation).<sup>50</sup> These transmissions can be supplemented by virtual or in-person patient visits as needed.<sup>51</sup> Additional measures that could help identify patients who would benefit from transport to tertiary care centers include: remote proctoring of ECG interpretation, creation of low-cost ECG devices, and interpretation assistance from artificial intelligence software. Further study will be required to assess the efficacy and cost-effectiveness of handling ECGs and other diagnostic studies in this manner.

### Identifying patients who would benefit most from CIED implantation

In environments in which the demand for CIEDs is greater than the available supply of devices and implanting facilities

| CHALLENGES  | OPPORTUNITIES  |
|---|--|
| <p><b>Devices used in EP procedures are expensive</b></p> <ul style="list-style-type: none"> <li>Ablation/mapping catheters</li> <li>Cardiac implantable electronic devices (CIEDs)</li> </ul>  | <p><b>Reduce costs by utilizing alternative sources of devices</b></p> <ul style="list-style-type: none"> <li>Reprocessed catheters</li> <li>Re-used CIEDs</li> <li>Philanthropic support for new equipment</li> </ul>   |
| <p><b>Experts capable of CIED implantation and catheter ablation are rare because few clinicians have access to training in cardiac electrophysiology</b></p>   | <p><b>Create in-person and virtual educational activities to improve access to training</b></p> <ul style="list-style-type: none"> <li>Proctorship-based missions</li> <li>EP fellowship programs and nurse/technician certificate programs (longitudinal presence is required)</li> </ul> |
| <p><b>Physical infrastructure necessary for cardiac arrhythmia care is absent</b></p> <ul style="list-style-type: none"> <li>EP laboratories / operating rooms</li> <li>Inpatient cardiac telemetry units</li> <li>Outpatient device clinics</li> </ul> | <p><b>Build infrastructure through cooperative efforts involving multiple stakeholders</b></p> <ul style="list-style-type: none"> <li>Government agencies</li> <li>Professional organizations</li> <li>Hospitals and medical schools</li> </ul>  |

**Figure 1** Opportunities to address the challenges associated with the delivery of cardiac arrhythmia care in resource-constrained environments. Challenges associated with delivery of comprehensive arrhythmia care in resource-constrained environments are described. For each challenge, corresponding opportunities to build capacity are listed. CIED = cardiac implantable electronic device; EP = electrophysiology.

and physicians, allocation of CIEDs to patients with the most immediate need is indicated. For example, patients with complete heart block and a slow ventricular escape rhythm would typically have a more immediate indication for pacing than patients with symptomatic sinus node dysfunction. As resources become more available, extension of pacing provision to incrementally less dangerous arrhythmias could ensue.

In the 11th World Survey of Cardiac Pacing and Implantable Cardioverter-Defibrillators, at least 70% of PPM implantation procedures in Pakistan, Bangladesh, Nepal, Bahrain, and Sudan were performed for patients with high-degree atrioventricular block.<sup>13</sup> Approximately 95% of CIED implantations in Sudan were performed for the same indication, likely reflecting prioritization of CIED implantation for those with the most immediate need.<sup>13</sup> Mismatch between supply and demand for CIEDs will inevitably vary between regions and over time. Therefore, selection of the most appropriate patients for CIED implantation is a point-of-care decision made by the implanting physician.

### Availability of pharmacotherapy in resource-constrained environments

Access to pharmacotherapy is limited for a third of the world's population.<sup>52</sup> The factors that limit availability include drug pricing and access to providers. Product development

partnerships have been developed by stakeholders such as pharmaceutical companies, governments, and philanthropic organizations to improve access to essential medications in developing countries.<sup>53</sup> Differential or tiered pricing in which essential medications are sold at lower prices in LMICs than in HICs is another solution used to reduce costs; however, this strategy is not immune to competition-related price increase.<sup>54</sup> Although generic drugs usually provide a lower-cost alternative, lack of regulatory requirements for generic quality in LMICs can create uncertainty for consumers. Placing a limited number of carefully selected medications on an essential medical list is one way for LMICs to prioritize the purchase of specific medications.<sup>55</sup>

Underutilization of OACs is due to several factors that disproportionately impact resource-constrained environments. These include cost of the medications and the absence of dedicated anticoagulation clinics (important given the predominance of warfarin use). Preferential use of DOACs (when appropriate) may be the most practical strategy to improve anticoagulation adoption, reduce long term costs of international normalized ratio testing, and reduce need for ongoing physician consultation for dose-adjustment.<sup>56,57</sup> Licensing agreements between pharmaceutical companies and LMICs have reduced cost of DOACs, but they remain more expensive than warfarin.<sup>58</sup> Safety of DOAC in rheumatic heart disease, particularly mitral stenosis, is the subject

of ongoing study.<sup>59</sup> The higher prevalence of rheumatic heart disease in LMICs may reduce the number of patients in whom DOAC therapy is appropriate.

Availability of drug therapy for medical issues that impact cardiac risk factors (eg, hypertension, diabetes, dyslipidemia) could also forestall development of ischemic heart disease, heart failure, and associated arrhythmias. Hypertension in particular is responsible for 55% of deaths caused by ischemic heart disease. There are opportunities to improve hypertension management in LMICs, as 30% of people with hypertension who live in LMICs receive treatment and only 10% achieve control.<sup>60,61</sup> Improving access to medications could improve population-wide management of hypertension and other medical conditions that impact cardiac risk. The World Health Organization describes a 4-part framework intended to maintain access to medications. This framework is based on rational use, affordable pricing, sustainable financing, and reliable supply systems. Components of this framework could help maintain access to essential cardiovascular medications.<sup>62</sup> Further study will be required to determine the relative impact of such a system on arrhythmia management. In addition, the relative impact of direct pharmacotherapy for arrhythmias (OAC for AF) vs pharmacotherapy of medical conditions that increase cardiac risk in resource-constrained environments has not yet been determined.

## Reutilization of expensive equipment involved in arrhythmia management, such as CIEDs and mapping or ablation catheters

### *CIED reuse*

Reimplantation of previously explanted CIEDs with a significant amount of battery life remaining may expand access to CIEDs. This strategy has been used not only in resource-constrained environments but also in parts of Europe for some time. One source of such devices is patients who have died with a CIED in place for whom cremation is planned, as CIEDs need to be removed prior to cremation to avoid explosion. Recently reported cremation rates in the United States and United Kingdom were 58% and 77%, respectively.<sup>63–65</sup> A Heart Rhythm Society (HRS) Task Force on Device Performance Policies and Guidelines recommended that funeral directors notify physicians of patients with CIEDs in place and to routinely return the device to the manufacturer after consent is obtained from the family.<sup>66</sup> Despite this, a recent study demonstrated that a majority of CIEDs explanted after death are discarded as medical waste or stored with no intended purpose.<sup>67,68</sup> It could be that patient preference is not the limiting factor in CIED reuse. In one study, 91% of patients undergoing CIED implantation were willing to sign an advanced directive donating their device to a medically underserved nation at the time of death.<sup>68</sup>

Observational studies of recycled PPMs reveal infection rates that are comparable to those of new implants.<sup>69–73</sup> A

comprehensive sterilization protocol can result in sterility assurance levels meeting biocompatibility standard, with effective removal of protein, hemoglobin, and organic carbon residuals.<sup>74</sup> No CIED-related prion transmission has been reported to date, with all documented cases of Creutzfeldt-Jakob disease resulting from exposure to elements of the central nervous system or eye tissue.<sup>75</sup> Although the rate of recycled PPM malfunction is several-fold higher than for new PPMs, the overall malfunction rate is quite low.<sup>76</sup> Recycled, dual-chamber pulse generators have also been used with a single pacing lead to maximize the number of patients who can be helped with a limited supply of equipment.<sup>77</sup> A recent international survey of patients and family members in LMIC countries demonstrated 79% were willing to accept a reused device when unable to afford a new device.<sup>78</sup>

Collaborative initiatives that include patients, physicians, funeral directors, and nonprofit charitable organizations can enable CIED reuse.<sup>79–82</sup> The My Heart Your Heart Pacemaker Reutilization Initiative is an example of this type of collaboration (<https://clinicaltrials.gov/ct2/show/NCT04016870>).<sup>80</sup> This initiative includes a clinical trial in which patients are randomized to receive reconditioned or new devices. Heartbeat International, Pace4Life (United Kingdom), and STIM Développement (France) are other examples of organizations that facilitate reuse of pacing equipment.<sup>83</sup> Data describing reuse of ICD and cardiac resynchronization therapy systems are promising but limited. Available studies describing ICD and cardiac resynchronization therapy reuse are mostly observational, with little prospectively collected data.<sup>81,82</sup> Mission-based programs such as the Africa-Pace program have also distributed CIEDs close to expiry (provided by manufacturers free of charge) to patients.

### *Reuse of EP catheters*

The use of reconditioned EP catheters has been in practice for decades. This sustainable cost-reduction strategy could help enable development of arrhythmia services in LMICs.<sup>84–89</sup> Limited studies demonstrate safety of ablation and mapping catheters, with the Food and Drug Administration determining no increased risk to health from use of remanufacturing.<sup>88</sup> No incidents of prion transmission attributed to use of a reconditioned EP catheter has been identified to date, with the caveat that prion infection may remain indolent for decades. A recent European survey of over 200 electrophysiologists demonstrated that over two-thirds have used reprocessed EP materials, including catheters. Of these physicians, 65% reported a reduction in equipment costs.<sup>89</sup>

Legislation pertaining to catheter reprocessing is variable and the practice is illegal in some European Union (EU) countries such as Spain, Italy, and France. Use of reprocessed catheters in those EU countries where it is legal (Belgium, Portugal, Sweden, and Germany) is regulated according to established guidelines.<sup>90</sup> There are challenges associated with the reprocessing of catheters, including the validation and monitoring of reprocessed single-use devices. Most

recent EU legislation states that the legal entity that reprocesses the single-use device is considered the manufacturer of the device and assumes obligations incumbent on the manufacturer within the legislation. This creates possible legal implications for the entity responsible for the reprocessing. Additional investigation, including prospective research and internal auditing, will be necessary to determine the appropriateness and safety of reconditioned catheter use in resource-constrained environments. Further study will also be required to compare the public health impact of CIED and catheter reutilization with other medical interventions (eg, pharmacotherapy) in resource-constrained environments.

### **Existing initiatives that address the training gap in resource-constrained environments**

The Africa-Pace program has successfully empowered clinicians in sub-Saharan Africa to manage arrhythmias in their local environments.<sup>1</sup> This proctorship-based program, which includes delivery of technology and training to clinicians in their home environments, was established to foster self-sustaining growth in arrhythmia treatment capacity. Through this program, the proportion of implantations that were performed solely by local teams increased from 3% in 1996 to 98% in 2018, with 542 PPM implanted in 14 countries over this time period. Initial, on-site support was provided by missions from abroad followed by support from countries in the region to ensure longevity of the program.

Selected hospitals participating in the Africa-Pace program were designated as centers of excellence and functioned as clinical training sites. Most operators who are based in Africa received their training within Europe. Smaller numbers of operators were trained in Africa, Asia, or North America. The University of Cape Town has provided pacing fellowship training via PASCAR for fellows from Tanzania, Sierra Leone, and Kenya. A similar training program has also been launched in Senegal.<sup>5</sup> Institutes participating in such programs may also collaborate with (or obtain assistance from) the World Society of Arrhythmia or regional EP or cardiology societies.<sup>91</sup> For example, the Asia Pacific Heart Rhythm Society provides financial support for a 1-year overseas fellowship training program within the Asia-Pacific region, with the stipulation that participating fellows return to work in their countries of origin upon completion of their training.<sup>92</sup>

### **Collaboration between national and multinational cardiology organizations and policymakers in resource-constrained regions**

Several professional organizations, including the HRS and the European Heart Rhythm Association, have supported the development of EP services in affiliated nations. International collaborations of this type could also help the creation of registries and white book surveys, which can in turn be used to measure the burden of disease and guide future resource allocation.<sup>5,91,92</sup> Creation of professional networks

via these societies can coordinate efforts with other stakeholders, including government agencies and nongovernmental organizations. Coordinated activities could also support further development of resource level-specific patient care guidelines and referral patterns.

Standardized educational programs overseen by cardiac EP or cardiology societies could support the development of local leaders who would then oversee arrhythmia care provision. Ongoing collaboration between the African Heart Rhythm Association (AFHRA) and PASCAR to create educational programs is an example of this model for professional development. The AFHRA contains an educational group that has developed a cardiac EP training course, a 30-week online course covering basic of arrhythmia care, and an invasive EP course overseen by regional and international faculty followed by a final exam. This course is run annually and includes additional educational content, including presentation of live cases. There exist plans for African EP accreditation as well as AFHRA support for accessing EP fellowships and creation of EP hubs.<sup>91</sup>

### **Use of telemedicine and digital health tools in resource-constrained environments**

Virtual care has become an integral part of arrhythmia management. According to the HRS guidelines, remote monitoring of CIEDs is supported by a class 1 indication. Many digital applications designed to collect health information (eg, vital signs, medication administration history) from patients have been developed and are in common use.<sup>93–96</sup> Survey data from HRS and European Heart Rhythm Association demonstrate a significant increase in the use of telemedicine after the start of the COVID pandemic.<sup>93–96</sup>

Utilization of digital health tools in LMICs is constrained by limited internet access.<sup>95,97,98</sup> Data from the World Bank indicates that 35% of people in developing countries have access to the internet.<sup>97</sup> In the least developed countries, the percentage of the population using the Internet is <10%.<sup>98</sup> Smartphone ownership is increasing in many LMICs.<sup>99–101</sup> Almost half of adults in LMICs now report owning a smartphone, albeit with skewed ownership favoring the wealthy and young.<sup>99</sup>

Growth of digital infrastructure in LMICs, including robust Internet connections and readily available smartphones, could help clinicians gather data and communicate with patients. The potential power of telehealth to improve arrhythmia care provides yet another motivator to expand internet access and mobile phone access for people living in LMICs.

### **Conclusion**

The burden of cardiovascular diseases, including cardiac arrhythmias, is growing in LMICs. The demand for arrhythmia treatment in these resource-constrained environments has not yet been matched by growth in treatment capacity. Alongside this treatment gap, there frequently exists a training gap, as many clinicians working in resource-

constrained environments have limited access to formal training in cardiac EP. Several strategies for closing such gaps have been described. These strategies include medical missions, utilization of reprocessed CIEDs and catheters, and collaborative efforts between multiple stakeholders (eg, professional organizations, government agencies, hospitals/educational institutions). Although these strategies have succeeded in addressing gaps in patient care and clinician training, global disparities in arrhythmia care persist. Larger-scale efforts will be necessary to prevent worsening of global disparities in the treatment of cardiac arrhythmias.

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