Heart failure in low-income and middle-income countries

Irina Mbanze,[1,2] Timothy F Spracklen,[2,3] Neusa Jessen,[4] Albertino Damasceno ,[4] Karen Sliwa [2,5]

[1]Division of Cardiology, Department of Medicine, Maputo Central Hospital, Maputo, Mozambique
[2]Cape Heart Institute, University of Cape Town, Cape Town, South Africa
[3]Department of Paediatrics and Child Health, University of Cape Town, Cape Town, South Africa
[4]The Faculty of Medicine, Eduardo Mondlane University, Maputo, Mozambique
[5]Department of Medicine, University of Cape Town, Cape Town, South Africa

Correspondence to
Professor Karen Sliwa;
Karen.Sliwa-Hahnle@uct.ac.za

Received 29 July 2024
Accepted 27 October 2024

To cite: Mbanze I, Spracklen TF, Jessen N, *et al*. *Heart* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/heartjnl-2024-324176

ABSTRACT

Heart failure (HF) is a complex syndrome which leads to significant morbidity and mortality, poor quality of life and extremely high costs to healthcare systems worldwide. Although progress in the management of HF in high-income countries is leading to an overall reduction in the incidence and mortality of HF, there is a starkly different scenario in low- and middle-income countries (LMICs). There is a substantial lack of data on HF in LMICs, as well as a scarcity of diagnostic tools, limited availability and affordability of healthcare and high burdens of cardiovascular risk factors and communicable diseases. Patients in this setting present with more advanced HF at much younger ages and are, more often, women. In this review, we aim to comprehensively describe the burden of HF from an LMIC perspective, based on the more recent available data. We summarise the major causes of HF that are endemic in these regions, including hypertension, cardiomyopathy, rheumatic heart disease, HIV-associated heart disease and endomyocardial fibrosis. Finally, we discuss the challenges faced by the least developed health systems and highlight interventions that may prove to be more efficient in changing the paradigm of HF of the more vulnerable populations.

EPIDEMIOLOGY AND PARTICULARITIES OF HEART FAILURE IN LOW- AND MIDDLE-INCOME COUNTRIES: CURRENT KNOWLEDGE

Heart failure (HF) was traditionally defined as a state in which the heart fails to maintain an adequate circulation to meet the body's needs, despite having a normal venous filling pressure.[1] Although the definition of HF has been changing over the years (see definitions of HF in table 1), some definitions focused on the clinical syndrome, whereas others focused on haemodynamic and physiological aspects.[2] The definition of HF was only standardised in 2021 when a universal definition and classification of HF was proposed by American, European and other worldwide HF associations. The aim of a standardised HF classification was to improve diagnostic accuracy, facilitate better communication and understanding of HF between patients and healthcare professionals and increase the recognition of standard diagnoses and end points in research, clinical trials and registries.[2] In this universal classification, HF is defined as a clinical syndrome with current or prior symptoms and/or signs of HF caused by structural and/or functional cardiac abnormality, corroborated by elevated natriuretic peptide levels or objective evidence of cardiogenic pulmonary or systemic congestion.[2] This universal classification is recent and posterior to the data that is shared in this document and this should be taken into account.

HF is a global pandemic, affecting ~64.3 million people worldwide.[3] Recently, data from high-income countries (HICs) have shown a substantial decrease in the incidence of HF, with a prevalence that ranges between 1% and 3% in general adult populations, which is projected to increase due to the ageing of these populations and the availability of life-saving evidence-based treatments that have increased survival.[4] In contrast, there is not a single population-based epidemiological study of prevalence or incidence of HF in Africa, and very few in South America.[3] Most of the available data comes from hospital-based studies, which are subject to known bias implications. Figure 1 illustrates the global prevalence of HF.

Described as a disease of the elderly and of men in HICs, globally HF occurs in all ages and equally in both genders.[5] With a notable myriad of risk factors and complex pathways that may lead to HF occurrence, the epidemiological picture of the disease in LMICs is not solely due to ischaemic heart disease.[1] High levels of poverty and malnutrition, high rates of communicable diseases, air pollution (including exposure to indoor pollutants) as well as suboptimal access to healthcare systems due to socioeconomic inequities modulate this picture.[1 5 6] For all these reasons, the pattern of HF in more vulnerable communities in an LMIC is diverse, with more women affected than men, and patients presenting at much younger ages and with more advanced heart disease.[5]

The recently published Global Congestive HF (G-CHF) registry was an important paper that included 23 341 patients, followed for 2 years and represented 40 countries, with a large percentage of participants from LMICs.[7] In this paper, the mean age at presentation was 10 years lower in low-income countries (LICs), compared with HICs, and the percentage of women was a little more than 50% in LICs and less than a third in HICs. The prevalence of ischaemic heart disease increased with the increase of wealth, and the opposite happened with rheumatic heart disease (RHD) that accounted for 11% of prevalence in LICs, and was <1% in HICs. Mortality, even adjusted for the most important variables was more than twice the one registered in HICs, in contrast with the rate of hospitalisation that was almost three times more frequent in wealthy countries than in the poor ones.

Another large registry, the prospective international REgistry to assess medical Practice with lOngitudinal obseRvation for Treatment of HF

Table 1 Heart failure definitions

ACC/AHA Heart Failure Guidelines 2005	Heart failure is a complex clinical syndrome that occurs as a result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or to eject blood.
ESC Heart Failure Guidelines 2012	Heart failure is a syndrome in which patients present with typical symptoms (e.g., breathlessness, ankle swelling and fatigue) and signs (e.g., elevated jugular venous pressure, pulmonary crackles and displaced apex beat) as a result of either an abnormality of cardiac structure or function.
JCS/JHFS 2017	Heart failure is a clinical syndrome composed by dyspnoea, malaise, swelling and/or reduced exercise capacity resulting from the loss of compensation for cardiac pumping function as consequence of structural and/or functional abnormalities of the heart.
ESC Guidelines 2021	Heart failure is a clinical syndrome, which consists of cardinal symptoms (e.g., breathlessness, ankle, swelling and fatigue) that might be associated with signs (e.g., elevated jugular venous pressure, pulmonary crackles and peripheral oedema), caused by a structural and/or functional abnormality of the heart, resulting in elevated intracardiac pressures and/or inadequate cardiac output at rest and/or during exercise.
Universal definition	Heart failure is a clinical syndrome characterised by current or prior symptoms or signs caused by a structured and/or a functional abnormality, corroborated by elevated natriuretic peptide levels and/or objective evidence of cardiogenic pulmonary or systemic congestion in diagnostic image modalities or haemodynamic measurement either at rest or during exercise.

Adapted from Sliwa and Stewart,[1] Bozkurt *et al*[2] and McDonagh *et al*.[67]
ACC, American College of Cardiology; AHA, American Heart Association; ESC, European Society of Cardiology; JCS, Japanese Circulation Society; JHFS, Japanese Heart Failure Society.

(REPORT-HF), that included 18 102 patients from 42 countries, but very few from sub-Saharan Africa (SSA), showed that ischaemic heart disease (40%) was the most prevalent aetiology in all regions followed by hypertension (19%), cardiomyopathy (19%) and valvular heart disease (16%). In this study, ischaemic heart disease was significantly more prevalent in LMICs (40%) than in the upper middle-income countries (37%) or HICs (28%).[8]

A previous study, the International Congestive HF registry (INTER-CHF), a prospective cohort study conducted in 108 centres, in 16 LMICs, from Africa, China, India, Middle East, Southeast Asia and South America, reported an overall mortality of 16.5% in patients with HF.[9] Numbers were highest in Africa (34%) and India (23%), intermediate in Southeast Asia (15%) and lowest in China (7%), South America (9%) and the Middle East (9%). Additionally, when compared with other regions, patients from Africa and India were much younger, more symptomatic at presentation, had little education, low rates of health insurance, were more often from a rural area and had little access to recommended treatment according to European and American HF guidelines.

According to The Sub-Saharan Africa Survey of HF (THESUS-HF), the largest African multicentre observational survey of acute HF in Africa, HF is mainly due to non-ischaemic causes, such as hypertension, idiopathic dilated cardiomyopathy (DCM) and RHD.[10] This was also replicated in several national registries in other African countries.[11 12]

Some aetiologies are particularly more common in some parts of the world, for example, the peripartum cardiomyopathy (PPCM) that is predominantly found in SSA or the Chagas disease almost exclusively found in South America.[5]

In summary, the aetiology of HF varies significantly between countries and regions. Table 2 illustrates the diversity of causes of HF in LMICs based on the available data.

HYPERTENSION

It has been reported that hypertension is the leading attributable risk factor for death globally, accounting for 10.8 million deaths in 2019.[13] In the past four decades, the number of people with hypertension has increased by 90%, mainly in LMICs.[14]

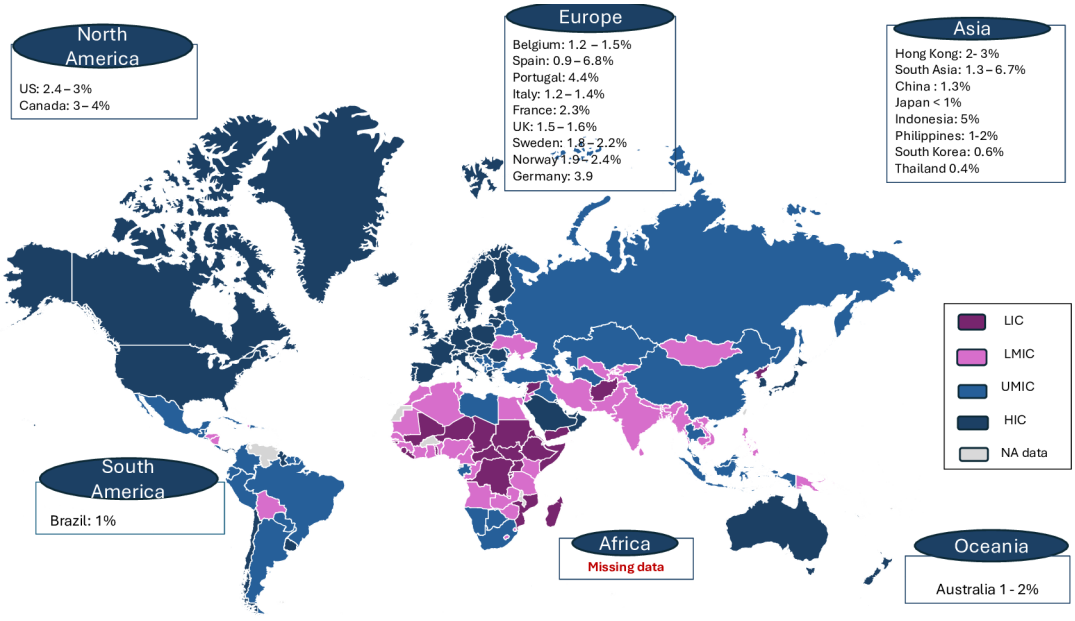

Figure 1 Global prevalence of heart failure worldwide. HIC, high-income country; LIC, low-income country; LMIC, low- and middle-income country; UMIC, upper middle-income country; NA data, not available data on income. Adapted from Savarese *et al*,[4] Groenewegen *et al*[3] and The World Bank 2024.[68]

Table 2 Aetiology of HF in low- and middle-income countries

Evidence	Region	Countries	Period	Population	Causes of HF
THESUS-HF study	Sub-Saharan Africa	Sudan, Ethiopia, Uganda, Kenya Nigeria, Senegal, Cameroon, Mozambique and South Africa	2007–2010	N=1006	Hypertension 45.4% Idiopathic dilated cardiomyopathy 18.8% Rheumatic heart disease 14.3%
INTER-CHF study	South America	Argentina, Chile, Columbia and Ecuador	2012–2014	N=869	Ischaemic heart disease 22% Hypertensive heart disease 21% Idiopathic dilated cardiomyopathy 15% Rheumatic heart disease 6%
INTER-CHF study	Middle East	Saudi Arabia, Egypt and Qatar	2012–2014	N=1000	Ischaemic heart disease 50% Idiopathic dilated cardiomyopathy 19% Hypertensive heart disease 10% Valvular heart disease 6%
INTER-CHF study	Asia	China, India, Malaysia and The Philippines	2012–2014	N=2661	Ischaemic heart disease 48% Hypertensive heart disease 14% Idiopathic dilated cardiomyopathy 10% Rheumatic heart disease 9%
INTER-CHF study	Africa	Nigeria, Sudan, Uganda, South Africa and Mozambique	2012–2014	N=1294	Hypertensive heart disease 35% Ischaemic heart disease 20% Idiopathic dilated cardiomyopathy 15% Rheumatic heart disease 7%

Adapted from Dokainish *et al*,[9] Damasceno *et al*.[10]
HF, heart failure; INTER-CHF, International Congestive Heart Failure; THESUS-HF, The Sub-Saharan Africa Survey of Heart Failure.

HF secondary to hypertension is the result of long periods of untreated and/or uncontrolled blood pressure.[13] This can result in both HF with preserved ejection fraction (HFpEF) and HF with reduced ejection fraction (HFrEF). Of concern, high blood pressure is more prevalent and more frequently uncontrolled in LMICs, compared with HICs.[14] In black African populations, hypertension is considered to be a distinct biologic entity, being more severe, more prone to end organ damage - particularly the heart - and more resistant to treatment, often leading to HF.[1]

Ojji *et al*[15] reported on a carefully characterised, prospective registry of patients with HF residing in Abuja, Nigeria (n=1 515), and compared them with 4 626 patients from the Heart of Soweto project, South Africa. This study showed that hypertension, although the leading cause of HF in both populations, was much more common in Abuja, contributing to 60% of all cases, compared with 33% in Soweto. Schutte *et al*[14] have demonstrated that in LMICs, only one in three patients is aware of their hypertension status and approximately 8% have their blood pressure controlled.

The established risk factors for hypertension include unhealthy diet (high in salt and low in fruit and vegetables), physical inactivity, tobacco and alcohol use and obesity.[16] However, emerging risk factors include air, water, noise and light pollution, urbanisation and loss of green spaces; many of these risk factors are increasing in LMICs.[14] Schutte *et al* highlighted that additional risk factors may include low birth weight and social and commercial determinants of health, although the role of these in hypertension requires further investigation.[14]

Studies related to other pathophysiological mechanisms of hypertension are not yet conclusive, particularly regarding gender-based heterogeneity.[1] In the Heart of Soweto registry, detailed information was captured on >6 000 *de novo* presentations, presenting to the Cardiology unit of the Baragwanath Hospital, in South Africa. Women were the single biggest contributors to case presentations (2 863 or 54%) with 575 (20%) presenting with a primary diagnosis of hypertension.[1]

During the last few decades, SSA has shown a constant increase in the prevalence of hypertension, without any significant improvement in the levels of awareness, treatment or control.[14] The May Measurement Month (MMM) global blood pressure awareness campaign of 2018 and 2019 demonstrated that, when compared with other regions in the world, SSA had lower levels of awareness, treatment and control of hypertension: 40.5%, 32.1% and 15.4%, respectively. Unfortunately, MMM may not represent the underlying population because sampling was by convenience.[13]

DILATED CARDIOMYOPATHY

Cardiomyopathies are a group of morpho-functional cardiac disorders and are the leading cause of sudden cardiac death (SCD) and HF in childhood and early adulthood.[17] It has been reported that in Africa, cardiomyopathies account for 20% to 30% of cases of HF, with important causes including both genetic and idiopathic forms of cardiomyopathy: DCM, PPCM, endomyocardial fibrosis (EMF) and HIV-related cardiomyopathy.[1] DCM and PPCM will be expanded on below, while EMF-related and HIV-related cardiovascular disease will be discussed in the next sections.

DCM is a heterogenous group of heart muscle diseases of diverse causes.[18] It is characterised by a dilated left ventricle with systolic dysfunction that is not caused by ischaemic, valvular heart disease or hypertension.[17 18] It can be classified into familial (or genetic) and non-familial that can be either acquired (secondary to a specific cause, e.g., infections, autoimmunity, toxins and others) or idiopathic.[19] In some patients, it results from the combination of these two conditions.[20]

Although studies from Europe and North America have indicated that 20% to 50% of patients with DCM might have familial disease, little is known about the frequency and clinical genetics of this disease in Africa.[1] Ntusi *et al* have shown that familial DCM is present in at least a quarter of African patients with DCM and that these patients presented 10 years younger compared with their peers with idiopathic DCM.[21] Approximately 60 different genes have been implicated, among them, involvement of the sarcomeric gene *TTN* is most prevalent (40%), followed by the nuclear laminin gene *LMNA* (10%).[17] In a cohort of 402 patients from Tanzania, n=220 (54.7%) were males with a median (IQR) age of 55.0 (41.0, 66.0) years. The causes of DCM were hypertensive n=218 (54.2%), idiopathic

n=116 (28.9%), PPCM n=45 (11.2%), alcoholic n=10 (2.5%) and other causes n=13 (3.2%). The authors reported suboptimal use of novel guideline-recommended medications, with angiotensin receptor/neprilysin inhibitors (ARNIs) prescribed to 10 patients (2.5%) and sodium-glucose cotransporter-2 (SGLT-2) inhibitors prescribed to two patients (0.5%).[22]

Other cardiomyopathies also occur in Africa, but they are less common, including hypertrophic cardiomyopathy, restrictive cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy and non-compactation of the left ventricle.[23] There are several conditions that impose this lower frequency like the limited number of specialists and trained technicians, lack of infrastructure, scarcity of cardiovascular imaging diagnostic tools, including echocardiography, cardiac magnetic resonance, CT and single-photon emission CT-myocardial perfusion imaging. In many African countries, the diagnosis of these conditions is often based only on echocardiography and there are regions where it is not available.[24]

Limited availability of intracardiac device implantation and other invasive treatment ultimately have influenced the poor patients' outcomes in Africa.[23]

PPCM is defined as an idiopathic form of cardiomyopathy, presenting with HF secondary to left ventricular (LV) systolic dysfunction towards the end of pregnancy, or in the months following delivery, where no other cause of HF is identified.[25] The incidence of PPCM varies markedly around the globe. The highest incidence of one in 102 deliveries was found in Nigeria, followed by one in about 300 births in Haiti and the lowest incidence was one in about 15 000 births in Japan.[26] Data have also suggested that there is a high risk for PPCM in black women.[26] According to the PPCM EURObservational Research Programme (EORP) registry, this condition occurs in women from different ethnic groups globally with largely similar presentations.[25] Studies using plasma of African patients newly diagnosed with PPCM have found elevated pro-inflammatory serum markers, such as sFas/Apo1, C-reactive protein, interferon-gamma and interleukin-6, suggesting that pro-inflammatory processes may also be involved in the induction and progression of PPCM, and possibly influence survival rates.[1]

Experimental research by Sliwa and Stewart,[1] Sliwa *et al*[25] and Goli *et al*[27] has indicated that multiple factors can induce PPCM. However, they merge on a common downstream mechanism of enhanced oxidative stress, cleavage of prolactin into an angiostatic N-terminal 16 kDa prolactin fragment (16 kDa Prl) and impaired VEGF signalling because of upregulated sFlt-1.[25] Massive endothelial damage and myocardial dysfunction is caused by 16 kDa prolactin and sFlt-1, supporting the idea that angiogenic imbalance could play a role in PPCM.[25] Additionally, two Western studies and one South African case series have suggested that a subset of patients with PPCM may be part of the spectrum of familial DCM.[22] Haghikia *et al* reported on a positive family history of cardiomyopathy in 16.5% (19/115) of PPCM cases of a German PPCM cohort, supporting the idea that genetic factors may be involved in some patients with PPCM.[28]

A genome-wide association was discovered and replicated for rs258415 at chromosome 12p11.22 near *PTHLH* with PPCM.[25] Recently, Arany *et al* identified truncating variations in genes *TTN*, *DSP*, *FLNC* and *BAG3* in patients with PPCM, which was nearly identical to the prevalence in cohorts with DCM. This supports the idea of a high degree of genetic similarity between these entities.[27]

Between 2012 and 2018, 739 women with suspected PPCM from 49 countries (33% from Europe, 29% from Africa, 15% from Asia-Pacific and 22% from the Middle East) were included in a prospective, global, observational registry to investigate PPCM around the world.[29] Women with PPCM in Europe were older and were more likely to be smokers than in other regions and worst outcome was found in women from the Middle East. Furthermore, pre-eclampsia was much more common in Asia-Pacific (46%) than in Europe (24%), Africa (21%) and the Middle East (19%) (p<0.001). The delay between symptom-onset and diagnosis was greatest in Africa (median 23 days (IQR 5–61)) and shortest in Europe (median 6 days (IQR 1–20)).

Bromocriptine is a prolactin-blocker that has emerged as a very promising therapeutic approach for the treatment of patients with PPCM.[1] In a proof-of-concept randomised South African pilot study, mortality was reduced and cardiac function improved in patients treated with bromocriptine 2.5 mg/day for 8 weeks in addition to standard HF therapy.[30] Later, in a multicentre trial in Germany, 63 patients with PPCM were randomly assigned to either short-term (1 week: bromocriptine, 2.5 mg, 7 days) or long-term bromocriptine treatment (8 weeks: 5 mg for 2 weeks, followed by 2.5 mg for 6 weeks) in addition to standard HF therapy. Bromocriptine treatment was associated with a higher rate of full LV recovery and lower morbidity and mortality in patients with PPCM, compared with other PPCM cohorts not treated with bromocriptine.[31 32]

More recently, in a subanalysis of the EORP registry, among women with PPCM, bromocriptine treatment was associated with better maternal outcomes after 6 months and no increased risk of thromboembolic events.[33] This therapeutic option has been highlighted in the current European Society of Cardiology Guidelines on cardiac disease in pregnancy.[34]

RHEUMATIC HEART DISEASE

RHD is a chronic autoimmune disease that occurs as a consequence of poor treatment of beta-haemolytic streptococcal (Group A *Streptococcus*) infection of the throat or skin that can affect the heart, leading to scarring, fibrosis and calcification of heart valves.[5 35] See the pathogenesis of RHD in figure 2.

Nearly a century after the eradication of rheumatic fever (RF) and RHD in HICs, the disease remains endemic in many LMICs, with grim health and socioeconomic impacts.[36] Figure 3 illustrates the advances in RF and RHD.

In LMICs of the Southern Hemisphere, and in some areas of Asia, RHD is the most common cause of HF in children, after congenital heart disease, and the third most common cause of HF in adolescents and young adults.[37 38] Figure 4A illustrates the world regions where RHD is prevalent.

Although less is known about mortality from RHD in the general population,[39] in the Global Rheumatic Heart Disease Registry (the REMEDY study), the largest international multicentre, hospital-based prospective registry of patients with RHD conducted in 12 African countries, Yemen and India, patients with RHD were young (with a median age of 28 years), mainly female (66.2%) and largely unemployed (75.3%).[40] The majority had moderate-to-severe valvular heart disease, associated with pulmonary hypertension (PH), LV dysfunction, atrial fibrillation and thromboembolic events. Inadequate use of secondary antibiotic prophylaxis was also reported in the REMEDY study, with lack of preventive treatment in nearly half of patients, as well as poor access to surgical interventions.[40]

Ensuring timely access to surgical care is a key aspect of addressing the current burden of RHD in LMICs. Unfortunately, many individuals present too late to benefit from surgery, so early detection efforts, accompanied by priority-based follow-up

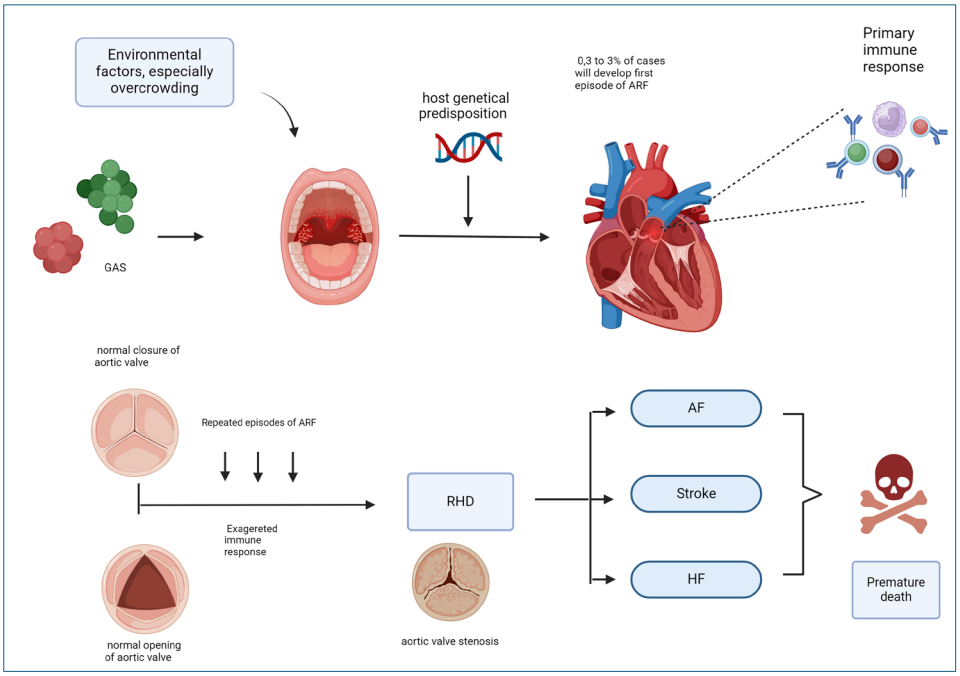

Figure 2 Pathogenesis of RHD. AF, atrial fibrillation; GAS, Group A *Streptococcus*; HF, heart failure; RHD, rheumatic heart disease. Adapted from Sliwa[5] and Mayosi.[69]

are required to ensure that surgical programmes have maximal impact.[40]

The concept of screening for subclinical disease and provision of antibiotic prophylaxis to slow disease progression deserves further efforts and attention in LMICs. The World Heart Federation (WHF) 2023 guidelines for the echocardiographic diagnosis of RHD is a contemporary resource for researchers and healthcare practitioners in RHD-endemic regions around the world.[41] It provides an updated, evidence-based set of criteria for diagnosing RHD, which empowers clinicians to make management decisions on the basis of the risk of an individual of disease progression. The authors also highlighted the recommendations for at-risk populations, equipment use and task sharing for RHD screening that might be very helpful in this part of the world.[41]

The Cape Town Declaration on Access to Cardiac Surgery in the Developing World was published in August 2018, as a sign of commitment of the global cardiac surgery and cardiology communities to improve care for patients with RHD.[35] Following that, in 2019, the Cardiothoracic Surgery Intersociety Alliance was established to focus on supporting two pilot surgical centres in LMICs (from a list of 11 applications from SSA and Asian

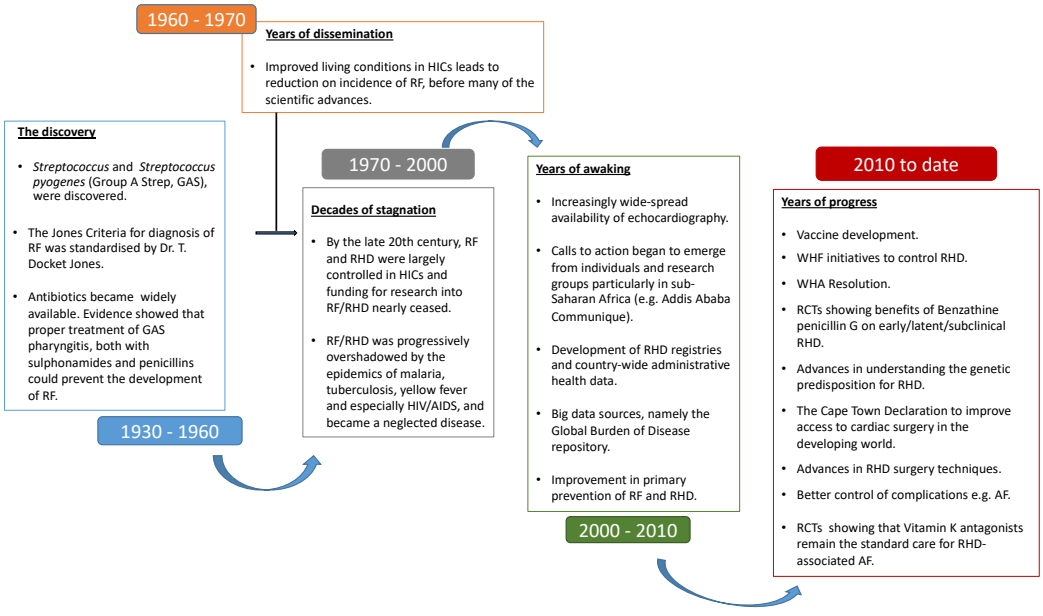

Figure 3 Advances in RF and RHD. AF, atrial fibrillation; GAS, Group A Streptococcus; HICs, high-income countries; RCTs, randomised controlled trials; RF, rheumatic fever; RHD, rheumatic heart disease; WHF, World Heart Federation; WHA, World Heart Assembly. Adapted from Sliwa,[5] Zilla *et al*[35] and Rwebemera *et al*.[36]

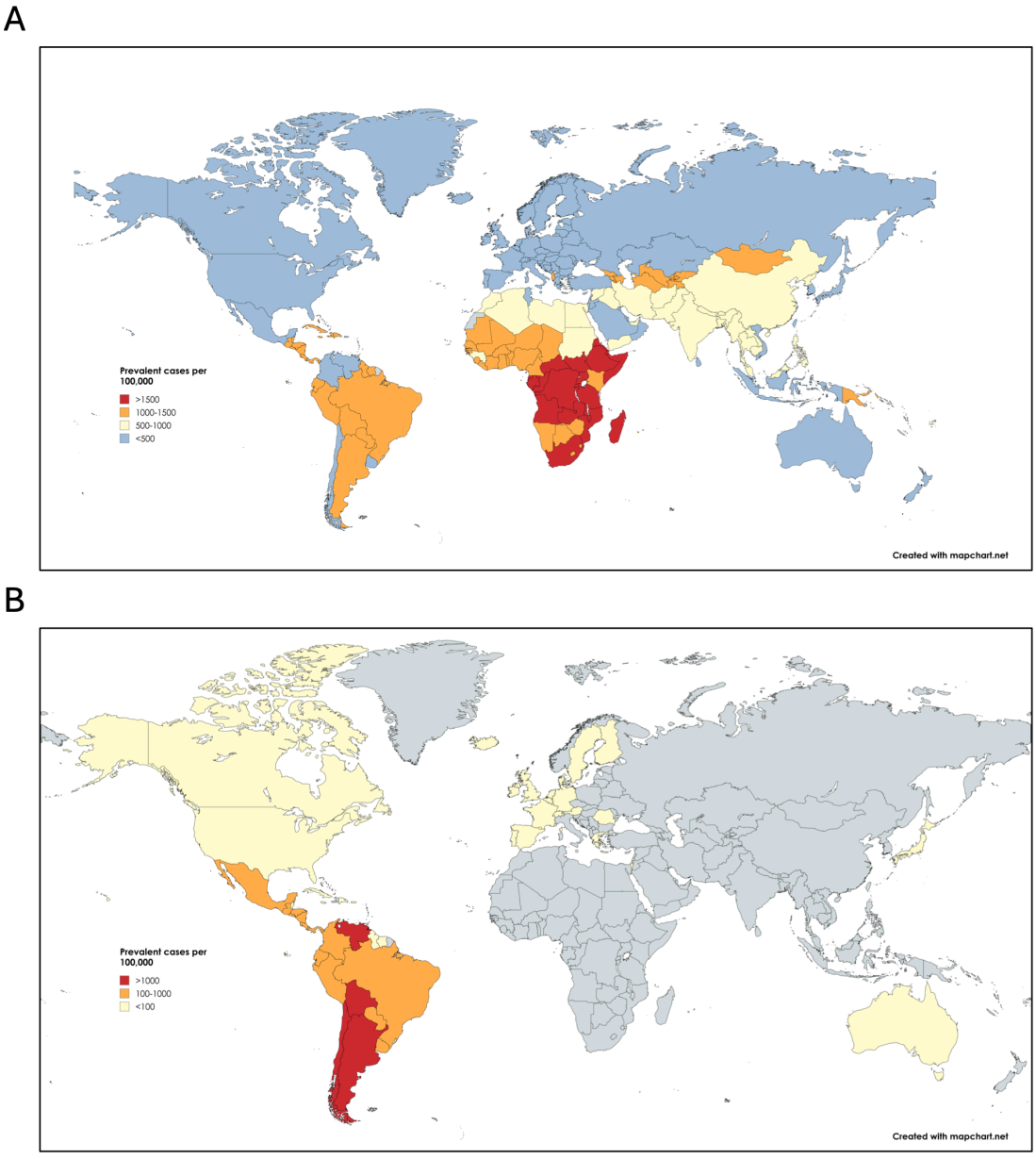

Figure 4 World regions where (A) rheumatic heart disease and (B) Chagas disease are prevalent. Based on 2021 Global Burden of Disease data.[70]

countries, Mozambique and Rwanda were selected), especially to build local capacity to address the need of RHD surgery.[42]

Recently, 13 696 patients with RHD from 24 LMICs were included in the INVestIgation of rheumatiC AF Treatment Using Vitamin K Antagonists (INVICTUS) trial.[43] The mean (SD) age of patients was 43.2 (16.9) years overall, with 72% being women. Nearly 15% of patients died at 3 years, mostly due to HF or sudden death. The investigators also emphasised that, although early surgical intervention in these patients has been shown to reduce mortality rates, it is important to note that mechanical valve replacement in young patients may, in some ways, constitute a disease in itself. This is due to the need for lifelong warfarin use, regular monitoring and the potential complications of bleeding and thrombosis, which are particularly problematic for women of reproductive age, especially in countries with limited capacity to control anticoagulant treatment.[43]

Percutaneous balloon mitral valvuloplasty is an alternative treatment option for patients with mitral stenosis and favourable valve anatomy. In LMICs, it offers significant benefits for young patients of reproductive age, as it allows them to postpone valve replacement and the complications associated with lifelong oral anticoagulation.[44] It is also recommended for pregnant women with symptomatic mitral stenosis and favourable anatomy.[45]

HIV-RELATED CARDIOVASCULAR DISEASE

Although the epidemiology of HIV infection has changed over the years, the timely use of antiretroviral therapy (ART) has led to an increase in the life expectancy of people with HIV (PWH).[46]

Of concern is that it has been reported that the prevalence of HIV-associated cardiovascular disease has tripled globally in the past 20 years, accounting for over 2.6 million annual disability-adjusted life-years, particularly in SSA and the Asian Pacific regions.[46] Furthermore, some antiretroviral agents may also contribute to this increased rate of cardiovascular disease in HIV, so their selection should carefully take the underlying cardiovascular risk factors into account.[47]

According to Thienemann *et al*, the most common cardiac manifestations in PWH are pericardial disease (often related to tuberculosis (TB)), cardiomyopathy and PH.[47] In a recent meta-analysis of over 125 000 PWH, the pooled prevalence of LV systolic dysfunction was 12.3%, compared with 29.3% for grades I to III diastolic dysfunction, 11.7% for grades II to III diastolic dysfunction, 11.5% for PH and 8% for right ventricular dysfunction.[46]

Pericarditis is common in PWH and can be caused by a myriad of opportunistic agents, such as bacteria, mycobacteria, viruses and fungi and protozoa, or can be associated with malignancies and immune reconstitution inflammatory syndrome. The aetiology largely depends on the degree of immunosuppression and exposure to infection.[47] Although it has been reported that PWH with pericardial effusion have a significantly shorter survival rate compared with patients with HIV without pericardial effusion, data have shown a significant reduction in the incidence of pericardial effusion in patients with HIV receiving combination ART (cART).[47]

Cardiomyopathy in PWH is significantly associated with longer duration of HIV infection, lower CD4 count and higher viral load.[1] Previous data from a cohort of South African patients from the Heart of Soweto study have shown that 24% of patients with HIV-associated cardiomyopathy had LV systolic dysfunction without symptoms.[1] According to more recent data, the aetiology of HIV-related cardiomyopathy is multifactorial. The implicated mechanisms include direct viral-induced myocardial damage, with or without myocarditis, immune dysregulation, systemic and local inflammation, PH, newer highly active ART toxicity, ischaemic heart disease and mental health disorders.[46] In HICs, the prevalence of HIV-associated DCM (HIV-DCM) dropped by ∼30% after the introduction of cART, while in LMICs the cART implementation is still delayed, with minimal penetration, particularly in rural areas, so HIV-DCM remains common, possibly with a multifactorial pattern.[46]

PH is a serious and life-threatening disease which is highly prevalent in patients with HIV.[48] Previously, it has been estimated that 0.5% of PWH had HIV-associated pulmonary arterial hypertension (HIV-PAH).[49] Despite the differences between studies, in a recent meta-analysis of 42 642 PWH, PH was prevalent in 8.3% of adults and 14.0% of adolescents.[33] Of note, most patients with PWH live in Africa (70%), particularly in sub-Saharan regions, followed by Southeast Asia and former Soviet Republic countries.[47] PH is classified into five groups: first, PAH; second, due to left-sided heart disease; third, associated with lung diseases or hypoxia; fourth, due to pulmonary artery obstruction and, fifth, of unclear and/or multifactorial mechanisms. HIV-associated PH is part of the first group.[50] HIV-PAH can develop at any stage of the disease, regardless of the degree of immunosuppression. HIV infection per se increases the risk for several lung infections, including bacterial pneumonia, TB and Pneumocystis pneumonia, all of which can lead to the development of PH.[49] The mechanism of HIV-causing PAH therefore remains unclear.[48] The HIV viral proteins may play a key role in PAH-associated vascular remodelling by causing endothelial cell proliferation, inflammation, oxidative stress and deregulation of apoptosis.[46] Furthermore, there are mechanisms related to ART that are emerging, which may also lead to vasculopathy and hypercoagulability, leading to potential life-threatening thromboembolic events.[49] To the best of our knowledge, Pan African Pulmonary hypertension Cohort (PAPUCO) is the only PH registry in Africa to date, the findings of which have been previously published.[51] In a subanalysis focused on HIV-associated PH, patients presented with PH at younger ages compared with HIV-negative participants.[49] PAH was found in 36% of the participants with PWH, compared with in 15% of HIV-negative participants. PH due to lung diseases and hypoxia was also frequent in patients with PWH compared with HIV-uninfected patients, as well as chronic embolism.[49]

ENDOMYOCARDIAL FIBROSIS

EMF is an important cause of HF in some parts of the LMICs, accounting for up to 20% of the cases in endemic areas of Africa (such as Mozambique and Uganda), India (province of Kerala) and China (province of Guangxi).[6] In the past, it also has been reported in South America (Colombia and Brazil).[5] In this condition, an extensive fibrosis of the ventricular endocardium and myocardium occurs with consequent architectural distortion that results in restrictive ventricular filling.[52] Although diverse factors have been implicated in the pathogenesis of EMF, it remains poorly understood.[53] Figure 5 summarises the pathogenesis of EMF.

According to Mocumbi *et al*, biventricular involvement is the most common form of presentation (55.5%), followed by isolated right-sided EMF (29%).[54]

Although the first description was by Davies in Uganda in 1948 and the aetiology and natural history of EMF has recently been reviewed, its aetiology remains poorly understood.[52] The clinical presentation depends on the chambers and/or valves affected and, therefore, patients can present in right, left or global ventricular failure. The typical clinical presentation is gross hepatomegaly and congestive splenomegaly, with no limber oedema, associated with atrial fibrillation and thromboembolism.[54] Studies have shown that EMF affects predominantly young adults, living in very poor conditions, with a bimodal distribution peaking at 10 and 30 years of age with sex predominance that differs from region to region, for example, in Uganda a female predominance was reported, while in Mozambique and Nigeria, a male preponderance was reported.[52]

Echocardiography is fundamental in the EMF investigation and cardiovascular MRI provides precise morphological evaluation including early detection of thrombi.[5] The prognostic outlook of EMF is very poor, as currently there is no effective medical treatment.[54] Although surgery is technically challenging, it can improve the prognosis.[54]

CHAGAS DISEASE

Chagas disease is typically acquired during childhood through infection with *Trypanosoma cruzi*, and it remains common in South America, with an estimated prevalence ranging from 10% to 28%.[6] Figure 4B illustrates the world regions where Chagas disease is prevalent. Disease control programmes have shown a significant reduction in the number of infected individuals—from 16 to 18 million in the early 1990s, compared with 10 to 12 million in the early 2000s.[5] The acute phase can present as a non-specific febrile illness lasting several weeks, it clinically manifests in <1% of infected subjects, but the chronic Chagas cardiomyopathy evolves over several decades after infection.[1] More than half of chronic Chagas cardiomyopathy subjects remain asymptomatic. However, echocardiographic findings include early Doppler abnormalities such as prolongation of isovolumic contraction and relaxation times.[1] Systolic function is initially normal, but stress testing can provoke dysfunction.[5] More than half of the symptomatic patients have LV apical aneurysm and contractile abnormalities. Other forms of presentation include DCM arrhythmias, embolic events and SCD.[6] Overall,

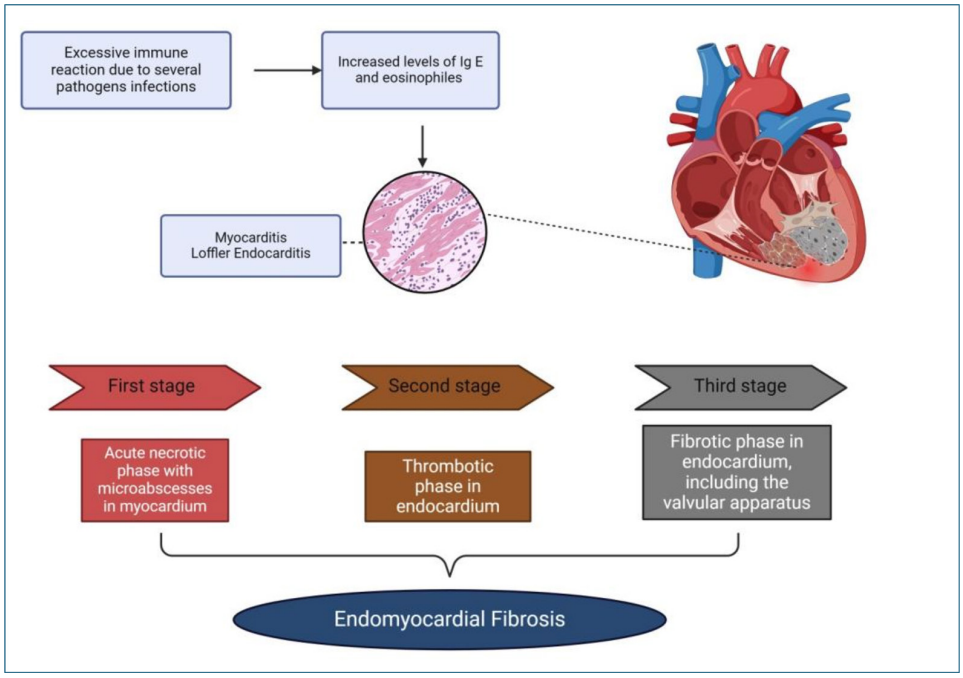

Figure 5 Pathogenesis of endomyocardial fibrosis. Adapted from de Carvalho and Azevedo.[53]

the prognosis of patients with Chagas heart disease is worse in comparison with other causes.[5]

Figure 6 shows echocardiographic images of three patients with HF with different aetiologies.

DIAGNOSIS AND MANAGEMENT OF HF: CHALLENGES AND OPPORTUNITIES IN LMICS

Although above 85% of the world population live in LMICs, advances in our understanding of HF, the clinical diagnosis criteria and the introduction of new treatment modalities are still largely framed by studies conducted in HICs.[1] Despite all progress and irrespective of the aetiology, HF remains a progressive syndrome and in most cases, an irreversible condition.[55]

Based on LV ejection fraction (LVEF), patients with HF are most often categorised as having HF with reduced (LVEF <40%), mid-range (LVEF 40%–49%) or preserved ejection fraction (LVEF ≥50%). Recently, a new entity, called HF with improved EF, was introduced and defined as HF with a baseline

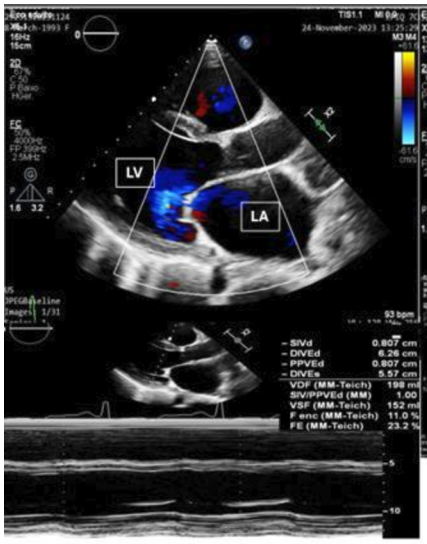

Figure 6a.A 30 years old female admitted with congestive heart failure 3 months after delivery. Diagnosed with **peripartum cardiomyopathy**. Echocardiographic images showing dilated left atrium (LA) and ventricle (LV) with severe LV dysfunction (Ejection fraction estimated in 23%).

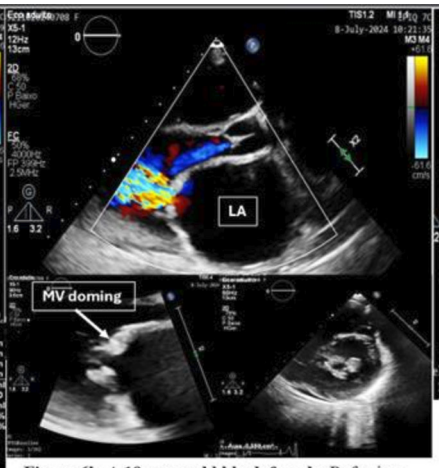

Figure 6b. A 19 years old black female. Referring 2 years of evolution with dyspnea, cough and hemoptysis, treated as tuberculosis in a primary health center with progression of symptoms. Admitted in Maputo Central Hospital and diagnosed with **rheumatic heart disease**. Echocardiographic images showing severe mitral stenosis (severe thickening of leaflets, commissural fusion and "doming of the anterior mitral valve leaflet", valve area of 0.5 cm²). Thickening of aortic valve with mild regurgitation. Dilated left atrium.

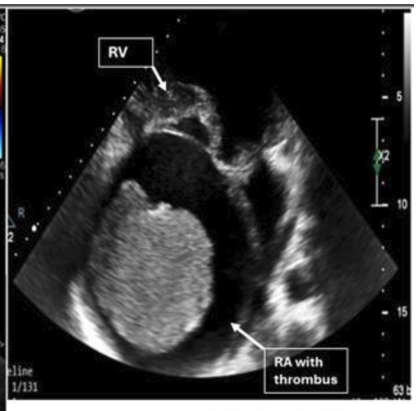

Figure 6c. A 25 years old black male, followed in outpatient clinic of Maputo Central Hospital for 15 years now with diagnosis of **endomyocardial fibrosis** of the right-side and atrial fibrillation. Echocardiographic image showing calcification with retraction of right ventricle (RV) apex and aneurismatic dilatation of the right atrium (RA) with a gigantic thrombus.

Figure 6 Echocardiographic images of three patients with heart failure with different aetiologies: (a) peripartum cardiomyopathy; (b) rheumatic heart disease; (c) endomyocardial fibrosis.

Table 3 Challenges faced in controlling HF in LMICs and possible strategies to overcome[57]

Challenges	Possible consequences	Strategies for improvement
Lack of trained human resources ► Shortage of faculty ► Poor quality of training ► Poor remuneration and 'brain drain'	► Late diagnosis and treatment ► Inadequate treatments ► Poor outcomes	► Establish cardiology training centres in-country ► Improve training at all levels of care ► Incentives for health professionals ► Fostering collaboration with strong external cardiology training institutions ► Develop local guidelines based on available consensus-based and evidence-based guidelines
Inadequate facilities for imaging and procedures	► Under-reporting of aetiologies ► Uncomplete diagnosis ► Poor prognosis	► Investment in high standard diagnostic and treatment facilities
System and individual financial constraints ► Low family monthly income ► Low health budget allocation ► Insufficient health financing systems	► High out-of-pocket expenditures	► Effective policies and government commitment ► Creation of health insurance plans
Low access to evidenced-based HF medications	► Non-adherence to treatment plan ► Poor outcomes	► Availability of effective drugs should be prioritised ► Provision of guideline-directed treatment as essential medicines ► Strengthening and integration of treatment at primary care setting (task sharing)
Low education and health literacy levels	► Poor health choices ► Reduced health-seeking behaviour ► Late presentation and diagnosis	► Investment in education ► Advocacy at community level
Lack of preventive efforts	► Presentation in advanced clinical status	► Design a government preventive programme for HF ► Identify and implement cost-effective, preventive strategies (targeting high-risk and general population)
Lack of research infrastructure ► Inadequate research productivity ► Lack of systematic surveillance data (vital statistics)	► Poor application of resources and undesired health outcomes ► Precludes disease burden estimates ► Difficult monitoring and evaluation of interventions	► Increase research capacity ► Investments to strengthening vital statistic data and systematic surveillance
Poverty, corruption and economic instability ► Low financial investment in health ► Dependence on external donors funding	► Limited access to healthcare ► Limited scope of health problems can be addressed ► Limited translation of research findings to develop cost-effective health programmes	► Commitment of the government and better planning, investment and accountability for improvement in all health-related sectors that influence the social determinants of health

HF, heart failure; LMICs, low- and middle-income countries.

EF ≤40% with a ≥10 point EF increase from baseline and a second measurement of EF >40%.[2] Nonetheless, the use of LVEF, which is based on arbitrary cut-off values, to categorise a dynamic entity such as HF has been criticised.[56] In fact, such values differ across guidelines. Furthermore, as recently reported by the G-CHF study, conducted across 257 centres in 40 HICs, middle-income countries and low-income countries, the causes of HF, the EF phenotypes and the severity of symptoms differ between women and men.[7] Compared with men, women reported more symptoms and signs of HF, lower quality of life and more often presented with HFpEF.

Currently, advances in methods and modalities of imaging allow for earlier diagnosis, personalised management and prognostic evaluation of HF. Although echocardiography continues to be the main evaluation and monitoring method for patients with HF, cardiac CT, single-nuclear imaging and cardiac MRI may be fundamental for aetiological diagnosis, design of the management plan and stratification of risk of patients presenting with specific phenotypes of HF.

Among LMICs, financial constraints of the health systems limit availability of adequate technical infrastructure and equipment, and human expertise to allow for the use of advanced imaging modalities.[24] The availability of echocardiograms, the most affordable among the recommended heart imaging modalities, can be as low as 35%, as observed in a study conducted in Maputo city, the capital of Mozambique.[57] As such, compliance to the recommended categorisations and the reporting of specific aetiologies of HF is difficult.

Besides imaging, blood biomarkers, particularly B-type natriuretic peptide/N-terminal pro B-type natriuretic peptide, are well-established diagnostic components for HF, but they are also usually unavailable or inaccessible in most of LMICs.[58] Similarly, genetic testing is recommended for DCM in HICs, where results can inform prognosis and recurrence risk of HF in families; such genetic testing is not routine in LMICs.[59]

Another important consideration in LMICs is the potential impact of comorbidities (such as chronic kidney disease) on the ability to make a timely and accurate diagnosis of HF. It is not uncommon for patients with cardiovascular diseases who present with a bloody cough to receive TB treatment at primary healthcare level units in low-income countries were TB is endemic.

Besides the evolution of diagnostic capacity in HICs, the choice of medications and other treatment modalities for HF have been increasing rapidly. Among others, the SGLT-2 inhibitor has been shown to reduce progression of HFrEF and improve quality of life.[60] Unfortunately, access to HF treatment (medicines, interventions and rehabilitation programmes) is very low in LMICs.[57 61] The Safety, Tolerability and Efficacy of Up-Titration of Guideline-Directed Medical Therapies for Acute HF (STRONG-HF) study has shown that an intensive treatment strategy of rapid up-titration of guideline-directed medication and close follow-up after an acute HF admission improved quality of life, and reduced the risk of 180-day all-cause death or HF readmission compared with usual care.[62] However, the cost of HF treatment is tremendous for the average of patients living in SSA.[63] Compared with reports from Asia, Middle East and South America, Africa has the highest proportion of patients with HF who are illiterate (42.7%) and have poor access to health (65.8%) and medication (67.3%) insurance.[63] Although the benefits of implantable devices in the treatment of HF are well documented, their high cost is prohibitive.[64] Thus, due to

financial constraints, most patients with HF in LMICs cannot afford the essential treatment.[63]

In fact, several factors contribute to making the diagnosis and management of HF so challenging in LMICs. These challenges, which lead to poorer outcomes in these countries, are summarised in table 3, along with possible strategies for improvement.

A 'Roadmap for Heart Failure' was designed by the WHF[65] and can be used by governments in LMICs to help identify and overcome barriers to prevention and management of HF. Implementation of preventive measures for already known risk factors for HF should be a priority and primary care settings should be the centre for initial diagnosis, identification of risk factors and treatment. Proven effective interventions, such as treatment of streptococcal pharyngitis to prevent RF and antibiotic prophylaxis for patients with RHD, should be implemented.[66] Some strategies that are already available and being used for different programmes, such as task sharing with nurses and community health workers, could be used. Non-governmental organisations working with different sectors of the government should be involved to improve access to healthcare and influence industry to reduce exposure to known risk factors for HF.

There is an urgent need for appropriate data from LMICs to guide the design of context-specific potentially effective interventions to prevent and control HF. Hospital records do not portray the true picture of HF in a population. Random samples from the population and validated criteria should be used for correct estimations of the prevalence and incidence of HF and related aetiologies. Several features of HF, including its outcomes, call for more research. However, particular attention should be given to aspects that make conducting high-quality research in African settings challenging: losses to follow-up are frequent, as observed in THESUS-HF study,[10] and special precautions should be taken, such as obtaining multiple contact details from patients when possible. Local culture may influence adoption of some recommendations, and the role of important stakeholders, such as traditional healers, is also important and should not be disregarded.

CONCLUSIONS

HF is a serious, life-threatening and multifaceted syndrome, which has contributed to premature death in LMICs. Considering the available scientific data of the burden of HF in LMICs, as well as its risk factors, urgent efforts are needed to develop preventative strategies, based on each disease group (hypertension, cardiomyopathy, EMF, RHD, HIV-associated HF), as many cardiovascular deaths are due to preventable causes. Much more funds should be allocated to upscale existing heathcare services, rather than build more infrastructures without equipment or trained professionals. Massive investment must be done in high-quality education programmes for the healthcare professionals to allow them to effectively improve the outcomes of patients with HF. More research is needed to better understand the epidemiology and spectrum of HF in this part of the globe.

X Karen Sliwa @CHI_UCT

Acknowledgements We would like to thank Sylvia Dennis for tremendous support preparing the manuscript. We would also like to thank the Hippocrate Foundation for a donation allowing us to purchase the institutional BioRender licence for drawing the figures. IM is funded by Schlumberger Foundation.

Contributors IM and KS conceptualised the review. All authors contributed to the literature review, manuscript drafting and revisions. IM, TFS and NJ created the figures and tables. All authors approved the final version of the manuscript. KS acts as the guarantor.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Commissioned; externally peer reviewed.

ORCID iDs
Albertino Damasceno http://orcid.org/0000-0003-0925-494X
Karen Sliwa http://orcid.org/0000-0002-8272-0911

REFERENCES

1 Sliwa K, Stewart S. Heart failure in the developing world. In: Mann D, FelkerG, eds. *Heart Failure: A Companion to Braunwald's Heart Disease*. Philadelphia: Elsevier, 2015: 410–9.
2 Bozkurt B, Coats AJS, Tsutsui H, *et al*. Universal definition and classification of heart failure: a report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure: Endorsed by the Canadian Heart Failure Society, Heart Failure Association of India, Cardiac Society of Australia and New Zealand, and Chinese Heart Failure Association. *Eur J Heart Fail* 2021;23:352–80.
3 Groenewegen A, Rutten FH, Mosterd A, *et al*. Epidemiology of heart failure. *Eur J Heart Fail* 2020;22:1342–56.
4 Savarese G, Becher PM, Lund LH, *et al*. Global burden of heart failure: a comprehensive and updated review of epidemiology. *Cardiovasc Res* 2023;118:3272–87.
5 Sliwa K. Heart failure can affect everyone: the ESC Geoffrey Rose lecture. *Eur Heart J* 2020;41:1298–306.
6 Sliwa K, Viljoen CA, Hasan B, *et al*. Nutritional heart disease and cardiomyopathies: JACC focus seminar 4/4. *J Am Coll Cardiol* 2023;81:187–202.
7 Walli-Attaei M, Joseph P, Johansson I, *et al*. Characteristics, management, and outcomes in women and men with congestive heart failure in 40 countries at different economic levels: an analysis from the Global Congestive Heart Failure (G-CHF) registry. *Lancet Glob Health* 2024;12:e396–405.
8 Tromp J, Bamadhaj S, Cleland JGF, *et al*. Post-discharge prognosis of patients admitted to hospital for heart failure by world region, and national level of income and income disparity (REPORT-HF): a cohort study. *Lancet Glob Health* 2020;8:e411–22.
9 Dokainish H, Teo K, Zhu J, *et al*. Global mortality variations in patients with heart failure: results from the International Congestive Heart Failure (INTER-CHF) prospective cohort study. *Lancet Glob Health* 2017;5:e665–72.
10 Damasceno A, Mayosi BM, Sani M, *et al*. The causes, treatment, and outcome of acute heart failure in 1006 Africans from 9 countries. *Arch Intern Med* 2012;172:1386–94.
11 Ogah OS, Sliwa K, Akinyemi JO, *et al*. Hypertensive Heart Failure in Nigerian Africans: Insights from the Abeokuta Heart Failure Registry. *J of Clinical Hypertension* 2015;17:263–72.
12 Stewart S, Wilkinson D, Hansen C, *et al*. Predominance of heart failure in the Heart of Soweto Study cohort: emerging challenges for urban African communities. *Circulation* 2008;118:2360–7.
13 Schutte AE, Jafar TH, Poulter NR, *et al*. Addressing global disparities in blood pressure control: perspectives of the International Society of Hypertension. *Cardiovasc Res* 2023;119:381–409.
14 Schutte AE, Srinivasapura Venkateshmurthy N, Mohan S, *et al*. Hypertension in Low- and Middle-Income Countries. *Circ Res* 2021;128:808–26.
15 Ojji D, Stewart S, Ajayi S, *et al*. A predominance of hypertensive heart failure in the Abuja Heart Study cohort of urban Nigerians: a prospective clinical registry of 1515 de novo cases. *Eur J Heart Fail* 2013;15:835–42.
16 McCarthyCP, Bruno RM, BrouwersS, *et al*. 2024 ESC Guidelines for the management of elevated blood pressure and hypertension. *Eur Heart J* 2024;45:3912–4018.
17 Shaboodien G, Spracklen TF, Kamuli S, *et al*. Genetics of inherited cardiomyopathies in Africa. *Cardiovasc Diagn Ther* 2020;10:262–78.
18 Falk R, Hershberger R, *et al*. The dilated, restrictive, and infiltrative cardiomyopathies. In: Mann D, Zipes D, Libby P, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 10th edn. Ellsevieer. 2014: 1551–72.
19 Fundikira LS, Julius J, Chillo P, *et al*. Yield of family screening in dilated cardiomyopathy within low-income setting: Tanzanian experience. *Cardiovasc J Afr* 2023;34:1–6.
20 Heymans S, Lakdawala NK, Tschöpe C, *et al*. Dilated cardiomyopathy: causes, mechanisms, and current and future treatment approaches. *Lancet* 2023;402:998–1011.

21 Ntusi NBA, Badri M, Gumedze F, *et al*. Clinical characteristics and outcomes of familial and idiopathic dilated cardiomyopathy in Cape Town: a comparative study of 120 cases followed up over 14 years. *S Afr Med J* 2011;101:399–404.
22 Fundikira LS, Chillo P, Alimohamed MZ, *et al*. Characterization of Non-Ischemic Dilated Cardiomyopathy in a Native Tanzanian Cohort: MOYO Study. *Glob Heart* 2024;19:26.
23 Minja NW, Nakagaayi D, Aliku T, *et al*. Cardiovascular diseases in Africa in the twenty-first century: Gaps and priorities going forward. *Front Cardiovasc Med* 2022;9:1008335.
24 Lakshmanan S, Mbanze I. A comparison of cardiovascular imaging practices in Africa, North America, and Europe: two faces of the same coin. *Eur Heart J Imaging Methods Pract* 2023;1:qyad005.
25 Sliwa K, Hilfiker-Kleiner D, Mebazaa A, *et al*. EURObservational Research Programme: a worldwide registry on peripartum cardiomyopathy (PPCM) in conjunction with the Heart Failure Association of the European Society of Cardiology Working Group on PPCM. *Eur J Heart Fail* 2014;16:583–91.
26 Isogai T, Kamiya CA. Worldwide Incidence of Peripartum Cardiomyopathy and Overall Maternal Mortality. *Int Heart J* 2019;60:503–11.
27 Goli R, Li J, Brandimarto J, *et al*. Genetic and Phenotypic Landscape of Peripartum Cardiomyopathy. *Circulation* 2021;143:1852–62.
28 Haghikia A, Podewski E, Libhaber E, *et al*. Phenotyping and outcome on contemporary management in a German cohort of patients with peripartum cardiomyopathy. *Basic Res Cardiol* 2013;108:366.
29 Sliwa K, Petrie MC, van der Meer P, *et al*. Clinical presentation, management, and 6-month outcomes in women with peripartum cardiomyopathy: an ESC EORP registry. *Eur Heart J* 2020;41:3787–97.
30 Sliwa K, Blauwet L, Tibazarwa K, *et al*. Evaluation of bromocriptine in the treatment of acute severe peripartum cardiomyopathy: a proof-of-concept pilot study. *Circulation* 2010;121:1465–73.
31 Haghikia A, Podewski E, Berliner D, *et al*. Rationale and design of a randomized, controlled multicentre clinical trial to evaluate the effect of bromocriptine on left ventricular function in women with peripartum cardiomyopathy. *Clin Res Cardiol* 2015;104:911–7.
32 Hilfiker-Kleiner D, Haghikia A, Berliner D, *et al*. Bromocriptine for the treatment of peripartum cardiomyopathy: a multicentre randomized study. *Eur Heart J* 2017;38:2671–9.
33 van der Meer P, van Essen B, Viljoen C, *et al*. Bromocriptine treatment and outcomes in peripartum cardiomyopathy: the EORP PPCM registry. *Eur Heart J* 2024.:ehae559.
34 Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, *et al*. ESC guidelines for the management of cardiovascular diseases during pregnancy: the task force for the management of cardiovascular diseases during pregnancy of the European Society of Cardiology (ESC). *Eur Heart J* 2018;39:3165–241.
35 Zilla P, Bolman RM, Yacoub MH, *et al*. The Cape Town declaration on access to cardiac surgery in the developing world. *Eur J Cardiothorac Surg* 2018;54:407–10.
36 Rwebembera J, Nascimento BR, Minja NW, *et al*. Recent Advances in the Rheumatic Fever and Rheumatic Heart Disease Continuum. *Pathogens* 2022;11:179.
37 Yuyun MF, Sliwa K, Kengne AP, *et al*. Cardiovascular Diseases in Sub-Saharan Africa Compared to High-Income Countries: An Epidemiological Perspective. *Glob Heart* 2020;15:15.
38 Antunes MJ. The Global Burden of Rheumatic Heart Disease: Population-Related Differences (It is Not All the Same!). *Braz J Cardiovasc Surg* 2020;35:958–63.
39 Watkins DA, Beaton AZ, Carapetis JR, *et al*. Rheumatic Heart Disease Worldwide: JACC Scientific Expert Panel. *J Am Coll Cardiol* 2018;72:1397–416.
40 Zühlke L, Engel ME, Karthikeyan G, *et al*. Characteristics, complications, and gaps in evidence-based interventions in rheumatic heart disease: the Global Rheumatic Heart Disease Registry (the REMEDY study). *Eur Heart J* 2015;36:1115–22a.
41 Rwebembera J, Marangou J, Mwita JC, *et al*. 2023 World Heart Federation guidelines for the echocardiographic diagnosis of rheumatic heart disease. *Nat Rev Cardiol* 2024;21:250–63.
42 Enumah ZO, Bolman RM, Zilla P, *et al*. United in earnest: First pilot sites for increased surgical capacity for rheumatic heart disease announced by Cardiac Surgery Intersociety Alliance. *J Thorac Cardiovasc Surg* 2021;161:2108–13.
43 Narayanan K, Marijon E. Rheumatic Heart Disease-A Neglected Tragedy in Young Patients. *JAMA Cardiol* 2024;9:597–8.
44 Mutagaywa RK, Cramer MJ, Chillo P, *et al*. Characteristics and immediate outcomes of patients who underwent percutaneous balloon mitral valvuloplasty at the Jakaya Kikwete Cardiac Institute, Tanzania. *Cardiovasc J Afr* 2024;35:16–26.
45 Sliwa K, Johnson MR, Zilla P, *et al*. Management of valvular disease in pregnancy: a global perspective. *Eur Heart J* 2015;36:1078–89.
46 Papamanoli A, Muncan B, Yoo J, *et al*. Human Immunodeficiency Virus Infection-Associated Cardiomyopathy and Heart Failure. *J Pers Med* 2022;12:1760.
47 Thienemann F, Sliwa K, Rockstroh JK. HIV and the heart: the impact of antiretroviral therapy: a global perspective. *Eur Heart J* 2013;34:3538–46.
48 Dai H-L, Zhang M, Xiao Z-C, *et al*. Pulmonary Arterial Hypertension in HIV Infection: A Concise Review. *Heart, Lung and Circulation* 2014;23:299–302.
49 Thienemann F, Katoto PDMC, Azibani F, *et al*. Long-Term Follow-up of Human Immunodeficiency Virus-Associated Pulmonary Hypertension: Clinical Features and Survival Outcomes of the Pan Africa Pulmonary Hypertension Cohort (PAPUCO). *Open Forum Infect Dis* 2022;9:ofac604.
50 Humbert M, Kovacs G, Hoeper MM, *et al*. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J* 2022;43:3618–731.
51 Thienemann F, Dzudie A, Mocumbi AO, *et al*. Rationale and design of the Pan African Pulmonary hypertension Cohort (PAPUCO) study: implementing a contemporary registry on pulmonary hypertension in Africa. *BMJ Open* 2014;4:e005950.
52 Grimaldi A, Mocumbi AO, Freers J, *et al*. Tropical Endomyocardial Fibrosis: Natural History, Challenges, and Perspectives. *Circulation* 2016;133:2503–15.
53 de Carvalho FP, Azevedo CF. Comprehensive Assessment of Endomyocardial Fibrosis with Cardiac MRI: Morphology, Function, and Tissue Characterization. *Radiographics* 2020;40:336–53.
54 Mocumbi AO, Stothard JR, Correia-de-Sá P, *et al*. Endomyocardial Fibrosis: an Update After 70 Years. *Curr Cardiol Rep* 2019;21.
55 Sullivan RD, Gladysheva IP. Advances and Challenges in Diagnosis and Management of Heart Failure. *Diagnostics (Basel)* 2022;12:1103.
56 Triposkiadis F, Butler J, Abboud FM, *et al*. The continuous heart failure spectrum: moving beyond an ejection fraction classification. *Eur Heart J* 2019;40:2155–63.
57 Jessen N, Mocumbi AO, Sliwa K. *Heart Failure in Africa: Challenges of Dealing with a Heterogeneous Syndrome in a Heterogeneous Continent*. Oxford University Press US, 2023.
58 Jessen N, Sharma A, Jones J, *et al*. Access to Essential Medicines and Diagnostic Tests for Cardiovascular Diseases in Maputo City, Mozambique. *Glob Heart* 2023;18:8.
59 Bozkurt B, Colvin M, Cook J, *et al*. Current Diagnostic and Treatment Strategies for Specific Dilated Cardiomyopathies: A Scientific Statement From the American Heart Association. *Circulation* 2016;134:e579–646.
60 Hernandez M, Sullivan RD, McCune ME, *et al*. Sodium-Glucose Cotransporter-2 Inhibitors Improve Heart Failure with Reduced Ejection Fraction Outcomes by Reducing Edema and Congestion. *Diagnostics (Basel)* 2022;12:989.
61 Chow CK, Nguyen TN, Marschner S, *et al*. Availability and affordability of medicines and cardiovascular outcomes in 21 high-income, middle-income and low-income countries. *BMJ Glob Health* 2020;5:e002640.
62 Mebazaa A, Davison B, Chioncel O, *et al*. Safety, tolerability and efficacy of up-titration of guideline-directed medical therapies for acute heart failure (STRONG-HF): a multinational, open-label, randomised, trial. *Lancet* 2022;400:1938–52.
63 Agbor VN, Essouma M, Ntusi NAB, *et al*. Heart failure in sub-Saharan Africa: A contemporaneous systematic review and meta-analysis. *Int J Cardiol* 2018;257:207–15.
64 Rohde LE, Bertoldi EG, Goldraich L, *et al*. Cost-effectiveness of heart failure therapies. *Nat Rev Cardiol* 2013;10:338–54.
65 Ferreira JP, Kraus S, Mitchell S, *et al*. World Heart Federation Roadmap for Heart Failure. *Glob Heart* 2019;14:197–214.
66 Remenyi B, Carapetis J, Wyber R, *et al*. Position statement of the World Heart Federation on the prevention and control of rheumatic heart disease. *Nat Rev Cardiol* 2013;10:284–92.
67 McDonagh TA, Metra M, Adamo M, *et al*. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J* 2021;42:3599–726.
68 World Bank Country and Lending Groups - World Bank Data Helpdesk. The World Bank, Available: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups [Accessed 2024].
69 Mayosi B. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 10th edn. Beaverton: Ringgold, Inc, 2015.
70 Network GBoDC. Global burden of disease study 2021 (GBD 2021) covariates 1980–2021. Seattle Institute for Health Metrics and Evaluation (IHME); 2024.