

# Prevention and control of rheumatic heart disease: Overcoming core challenges in resource-poor environments

Scott Dougherty, Andrea Beaton<sup>1</sup>, Bruno R Nascimento<sup>2</sup>, Liesl J Zühlke<sup>3</sup>, Maziar Khorsandi<sup>4</sup>, Nigel Wilson<sup>5,6</sup>

Department of Internal Medicine, Ministry of Health, Belau National Hospital, Koror, Republic of Palau, <sup>1</sup>Children's National Medical Center, Cardiology, Washington DC, USA, <sup>2</sup>Telehealth Center, School of Medicine, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil, <sup>3</sup>Divisions of Paediatric Cardiology and Cardiology, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa, <sup>4</sup>Department of Cardiothoracic Surgery, Royal Infirmary of Edinburgh, Edinburgh, United Kingdom, <sup>5</sup>Green Lane Paediatric and Congenital Cardiology Department, Starship Children's Hospital, <sup>6</sup>Department of Paediatrics, University of Auckland, Auckland, New Zealand

## ABSTRACT

Rheumatic heart disease (RHD) has long receded as a significant threat to public health in high-income countries. In low-resource settings, however, the specter of RHD remains unabated, as exemplified by recent data from the Global Burden of Diseases Study. There are many complex reasons for this ongoing global disparity, including inadequate data on disease burden, challenges in effective advocacy, ongoing poverty and inequality, and weak health systems, most of which predominantly affect developing nations. In this review, we discuss how each of these acts as a core challenge in RHD prevention and control. We then examine key lessons learnt from successful control programs in the past and highlight resources that have been developed to help create strong national RHD control programs.

**Keywords:** Control, developing countries, prevention, rheumatic heart disease

## INTRODUCTION

As recently as the mid-20<sup>th</sup> century, both acute rheumatic fever (ARF) and rheumatic heart disease (RHD) were commonly encountered by physicians worldwide. However, the epidemiological trends of these diseases are emblematic of socioeconomic inequality and failing health systems. Recent data from the Global Burden of Diseases (GBD) Study estimates that in 2015, RHD may have affected 31.4 million individuals worldwide.<sup>[1]</sup> Among these cases, 99% were attributable to endemic areas, mainly low- and middle-income countries (LMICs), with an age-standardized prevalence of 444/100,000 population, compared with 3.4/100,000 population in nonendemic countries, the majority of which were high income.

The GBD study also suggests that there was an 8.1% decline in worldwide deaths (347,500 deaths in

1990 decreasing to 319,400 deaths in 2015) and a 47.8% reduction in global age-standardized mortality (9.2 deaths/100,000 population in 1990 decreasing to 4.8 deaths/100,000 population in 2015) from RHD. Again, endemic areas were the worst affected given that these gains were not seen in most LMICs, which have seen a rise in their shared proportion of the RHD burden (from 77% in 1990 to 82% in 2015).<sup>[1]</sup> This is a concerning trend, as within resource-constrained settings RHD not only poses substantial challenges to severely strained healthcare resources<sup>[2]</sup> but also cripples economic and social development, predominantly affecting those in the prime of life.<sup>[3]</sup>

Despite this significant ongoing global burden, RHD has been relatively ignored in the last half-century,

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

**For reprints contact:** reprints@medknow.com

**How to cite this article:** Dougherty S, Beaton A, Nascimento BR, Zühlke LJ, Khorsandi M, Wilson N. Prevention and control of rheumatic heart disease: Overcoming core challenges in resource-poor environments. *Ann Pediatr Card* 2018;11:68-78.

### Access this article online

Quick Response Code:



Website:

www.annalspc.com

DOI:

10.4103/apc.APC\_135\_17

**Address for correspondence:** Dr. Scott Dougherty, Department of Internal Medicine, Ministry of Health, Belau National Hospital, 40461 Main Street, Koror 96940, Republic of Palau. E-mail: s.dougherty\_imca@yahoo.com

receiving little attention, advocacy, or research funding. One crucial reason, as Bongani Mayosi states, is that “it (RHD) is a disease of the bottom billion of the poorest people in the world – one of the most neglected of the neglected diseases”.<sup>[4]</sup> Moreover, as more countries undergo the epidemiological transition from communicable to noncommunicable diseases (NCDs),<sup>[5]</sup> RHD continues to struggle for a home, lost between yet within both of these two disease paradigms. Indeed, it has been labeled an “orphan disease,” impossible to be neatly categorized within current global health priorities.

However, dovetailing with the United Nations’ sustainable development goal to eliminate poverty and inequality and the World Health Organization (WHO) renewed focus on NCDs, there is a rising tide of action and advocacy focused on the prevention and control of RHD. The WHO plan, endorsed by all 193 WHO member countries, is targeting an ambitious 25% reduction in premature mortality from NCDs by 2025 – the “25 × 25” goal.<sup>[6]</sup> The World Heart Federation (WHF) bolstered this goal, aligning itself with the voluntary targets and language set forth by the WHO Global Action Plan. The plan was extended to include a 25% reduction in premature deaths from ARF and RHD among individuals aged <25 years by 2025 – the “25 × 25 <25” goal.<sup>[7]</sup>

Although RHD is eminently preventable achieving the 25 × 25 <25 goal is not simple. High-resource settings ultimately succeeded in virtually eliminating ARF and RHD [Box 1] through a combination of improved quality of housing and a reduction in overcrowding, with a supplementary effect through improved access to and availability of high-standard healthcare and medicines, in particular penicillin.<sup>[8]</sup> While each of these remains a significant challenge in LMICs, concerted public health efforts have led to a few stories of success.

This review article will examine the core challenges LMICs face in the prevention and control of RHD, discuss key lessons learnt from successful control programs, and

### Box 1: Epidemiological definitions

Endemic: Usual prevalence of a disease in a population within a geographic area

Hyperendemic: Constantly high incidence or prevalence of disease rate in a population within a geographic area

Importantly, there is no current consensus definition for endemic or hyperendemic incidence or prevalence of ARF or RHD

Control: A reduction in the incidence, prevalence, morbidity, or mortality of a disease to a locally acceptable level. Continual interventions required

Elimination: Reduction to zero (or very low target rate) the incidence of a disease within a defined geographical area. Continual interventions required

Eradication: Permanent reduction to zero of the worldwide incidence of the disease. Control interventions no longer required<sup>[23]</sup>

ARF: Acute rheumatic fever, RHD: rheumatic heart disease

highlight the resources and roadmap that have been developed to help others replicate these successes.

## IDENTIFYING CORE CHALLENGES IN THE PREVENTION AND CONTROL OF RHEUMATIC HEART DISEASE

Despite a large number of reviews, profile articles, and calls to action,<sup>[4,7,9-18]</sup> including four key statements from Africa (under the auspices of the pan-African society of cardiology [PASCAR]) in little over a decade [Table 1], there remain significant fundamental issues preventing global RHD prevention and control. Here, we will discuss some of these outstanding challenges that include an incomplete understanding of the true burden of disease, ineffective advocacy and prioritizing RHD on the global stage, persistent poverty and inequality, and a pervasively inadequate global health workforce.

### Incomplete understanding of the true burden of disease

Establishing the true burden of RHD is a fundamental prerequisite for developing an objective, quantified argument for policy change, and prioritization of RHD in limited-resource environments.<sup>[19]</sup> However, the best current global estimates, GBD 2015, rely heavily on modeling to overcome the lack of data.<sup>[1]</sup> This is particularly true in RHD-endemic areas, where scarce primary data result in wide uncertainty intervals. For example, only 15 of 53 countries in Africa had any primary data on either fatal or nonfatal RHD cases, highlighting the need for more accurate primary source data.<sup>[20]</sup>

Establishment of high quality, regularly maintained ARF/RHD registries are a vital component of primary data collection.<sup>[19,21]</sup> Making ARF and RHD notifiable diseases seems to help increase case detection and establish disease burden. This has occurred in New Zealand and Australia, in many Pacific Islands, South Africa, and Tunisia.<sup>[7,21-23]</sup> However, maintaining physicians’ awareness of their legal obligation to notify and correctly implement the notification can be significant barriers.<sup>[22]</sup>

It is important also that physicians remain up to date with the latest iteration of the Jones criteria (last revised in 2015),<sup>[24]</sup> which, among several significant changes, accepts subclinical carditis (diagnosed by echocardiography) as a major manifestation. Decentralizing diagnostic services through point-of-care technologies, such as portable echocardiography and rapid antigen detection test kits are therefore needed to further maximize case detection although most LMICs do not possess the technology or requisite skilled workers. Task-shifting/sharing and telemedicine<sup>[25]</sup> may play an important role in bridging these gaps.

**Table 1: Summary of recommendations for acute rheumatic fever and rheumatic heart disease control from Africa**

<b>The Drakensberg Declaration (2005)<sup>[10]</sup></b>	<b>The Mosi-o-Tunya Call to Action (2014)<sup>[11]</sup></b>	<b>The Addis Ababa communiqué (2016)<sup>[12]</sup></b>	<b>The Cairo Accord on RHD (2017)<sup>[18]</sup></b>
Raising public and healthcare worker's awareness of ARF and RHD	Reduce poverty and overcrowding Develop integrated national programs for the prevention and control of ARF and RHD that incorporates raising awareness, surveillance, advocacy, and prevention	Establish prospective RHD registries	Strengthen existing databases (e.g., PASCAR e-register) for better understanding of the epidemiology and natural history of RHD Limit echocardiographic screening programs to research until further evidence on its impact on prognosis and cost-effectiveness is available
Improving epidemiological surveillance regarding incidence, prevalence, and burden of ARF and RHD	Lead collaborative efforts: Enlist the help of healthcare workers, educators, and international/ community-based organizations in the implementation of national ARF and RHD programs Build health capacity at all levels of healthcare (primary, secondary, tertiary)	Ensure adequate supply and quality of benzathine penicillin G	Study the genetics of rheumatogenic streptococcal strains and susceptible individuals Enhance and coordinate global efforts to develop a GAS vaccine
Greater advocacy as a means of changing public policy to improve healthcare facilities needed to treat and prevent ARF and RHD	Create centers of excellence for surveillance, research, treatment, and training etc. Declare national awareness events	Guaranteed universal access to reproductive health for women with RHD	Search for biomarkers for early diagnosis and follow-up of disease Provide high-quality penicillin to endemic areas for both primary and secondary prevention
Establishment of national primary and secondary prevention programs for ARF and RHD	Educate teachers at primary and secondary schools and ARF/RHD should be included in school health programs Utilize champions, such as celebrities and other high-profile individuals to raise awareness for ARF/RHD and advocate for patients  Implement surveillance through regional and national ARF/RHD registries Support research that improves our understanding of ARF/RHD Ensure appropriate treatment guidelines for children presenting with a sore throat (primary prevention) Ensure appropriate treatment guidelines for patients with ARF/RHD (secondary prevention) Ensure high-quality diagnostic tools, medicines, and laboratory services, including the availability of high-quality benzathine penicillin Support development of a GAS vaccine	Decentralize appropriate technical expertise to the primary and district levels to ensure adequate diagnosis and treatment of ARF and RHD. This expertise includes echocardiography, anticoagulation testing, and rapid antigen tests for GAS pharyngitis Establish centers of excellence for cardiothoracic surgery  Facilitate multisectorial and integrated national RHD control programs led by ministries of health  Cultivate a strong communication framework and partnerships between government, industry, academia, civil society, and other stakeholders to monitor and evaluate the progress of the proposed actions	Study the potential role of anti-inflammatory or immunosuppressive therapy after ARF as well as optimize therapy against cardiac thromboembolism and for heart failure management Accelerate the development of regional centers of excellence equipped with adequate human and physical resources  Use dedicated training programs and the exchange of expertise to maximize the use of valve repair procedures Accelerate efforts to develop tissue-engineered valve substitutes and affordable transcatheter valves that are easy to implant

ARF: Acute rheumatic fever, RHD: Rheumatic heart disease, GAS: Group A *Streptococcus*, PASCAR: Pan-African society of cardiology

Finally, understanding the clinical significance of asymptomatic RHD detected through echocardiographic screening (subclinical RHD) needs further clarification.<sup>[26]</sup> Although there is a paucity of data regarding outcomes of these patients, recent evidence suggests that screening-detected RHD can progress significantly within 4–5 years with clinically-diagnosed RHD progressing

the most rapidly.<sup>[27-29]</sup> Some screening-detected RHD cases have progressed to require valve surgery,<sup>[28]</sup> yet other studies have demonstrated a more stable course with over 90% of patients remaining only mildly affected.<sup>[29,30]</sup> Given that subclinical RHD was excluded from the GBD estimates, it is likely, therefore, that the study underestimates the true burden of disease, at least

to some degree. Funding for more prospective studies is needed to help understand the natural history of subclinical RHD and by extension, the true burden of disease.

### **Ineffective advocacy and prioritizing rheumatic heart disease on the global stage**

There has been a vigorous and enthusiastic renaissance in RHD advocacy and research over the last 10–15 years. This has not, unfortunately, been matched by action and funding from governments and large funding agencies, such as the World Bank or the Global Fund. This raises the question as to why RHD has failed to gain traction, compared to issues such as malaria and HIV, for which there are widespread action and support.<sup>[31]</sup>

One of the most critical barriers to galvanizing RHD support and action has been the difficulty in presenting a simple and unified explanation of RHD. Evidence suggests that the clarity and cohesion of ideas used to define and describe a disease impact the attention, funding, and action generated.<sup>[32]</sup> RHD presents a challenge here, as the pathogenesis is complex and multifactorial and so does not lend itself to quick solutions and marketable messages.

A streptococcal infection in childhood may or may not, depending on host and pathogenic properties, lead to ARF which may or may not acutely affect the heart and which may or may not lead to chronic RHD. Moreover, the complex interplay of variables that can influence these outcomes may depend not only on socioeconomic factors but also geographic considerations.<sup>[33]</sup> Projects like “Take Heart” can help bring clarity to the RHD narrative. This award-winning, film-based advocacy campaign was designed to put the stark reality of the disease on everyone’s table, from the global media to public health agendas (available from: [www.takeheart.tv](http://www.takeheart.tv)).

A second challenge in advocacy for ARF/RHD is the difficulty in framing the disease within established funding priorities in global health. The political climate where a health issue is presented may be a key determinate in the decision for funding and action.<sup>[32]</sup> Historically, the international health community has focused on infectious diseases, in particular, those that cause high mortality in the first 5 years of life as well as the “big three” infectious diseases (HIV/AIDS, tuberculosis, and malaria).<sup>[34–37]</sup> Comparing the global death rates from each of these three diseases with ARF, which are around 3–5 times greater,<sup>[38]</sup> with development funding in 2013, which was a massive 500–1000 times greater,<sup>[39]</sup> exemplifies the ongoing neglect suffered by ARF.

Although RHD is at its roots an infectious disease of childhood, the majority of the morbidity and mortality attributable to ARF is apparent in later decades, and only

rarely affects those <5.<sup>[8]</sup> It is noteworthy that 3 of the most important players in global health (The Bill and Melinda Gates Foundation, the Global Alliance for Vaccines and Immunizations, and the Global Fund) focus almost entirely on infectious diseases<sup>[40]</sup> but exclude Group A streptococcal disease and their sequelae from funding priorities.

Finding synergy between RHD and established high-priority targets in global health could help RHD gain a stronger foothold. For example, the sustainable development agenda and the recent global focus on NCD prevention have both provided a new platform for RHD advocacy. Moreover, in June 2017, the Executive Board of the WHO recommended a resolution (expected to be adopted at the 71<sup>st</sup> World Health Assembly (WHA) in 2018) on “rheumatic fever and RHD”.<sup>[41]</sup>

This significant high-level policy recognizes for the first time that RHD is a global health priority on the world stage. Lobbying (e.g., by clinicians, researchers, and advocates) at local and national government level for increased RHD recognition and funding (e.g., for control programs) will now have added weight and visibility. This should also help ensure that the WHO’s own agenda and funding priorities more accurately reflect the international burden of disease, something it has not always gotten right.<sup>[34,42]</sup> Other strategies too, such as framing heart health as a fundamental human right and asserting that population health is the responsibility of governments can continue with a greater and more powerful impetus.

Another, mostly untapped resource is the intersection of maternal/fetal health and RHD, which is known to be a high-risk condition of pregnancy. Ongoing research in Uganda and in high-risk Australian populations, to name a few, aims to clarify this contribution – which may broaden resources available for RHD research and clinical care.

Finally, while clinical and epidemiological RHD research has grown quickly over the past decade, there remains incomplete data to support the investment case against RHD, especially subclinical disease. Understanding and packaging the most cost-effective strategy for RHD control are of utmost importance for engendering support of low-resource health ministries faced with a myriad of healthcare challenges. Cross-disciplinary, community-engaged, and multisector research are needed to fill this gap and should be prioritized.

### **Persistent poverty and inequality**

Although “we have in our hands one of the oldest antibiotics (penicillin) that still works against one of the oldest heart diseases,” RHD continues unabated for the majority of the world’s population. The medical approach alone is unable to eradicate RHD because poverty is the

underlying problem,<sup>[4]</sup> a fact that is underscored by its virtual elimination in high-resource populations.<sup>[1,43]</sup>

Poor health and premature death significantly impair a nation's ability to prosper and eradicate poverty.<sup>[44]</sup> Many LMICs have been trapped in a cycle that has circled around for decades: poverty drives poor health, and poor health maintains poverty.<sup>[45]</sup> Globally, RHD is the fifth leading cause of cardiovascular-related mortality and sixth leading cause of cardiovascular-related disability.<sup>[1]</sup> The combination of years of life lost (premature deaths) and years lived with disability, expressed as disability-adjusted life years, is 10.5 million/year.<sup>[1,46]</sup> It goes without saying that RHD is an important cause and consequence of poverty in those countries.

Yet, although LMICs are becoming wealthier (e.g., low-income countries (LIC) now make up only 12% of all nations, whereas that figure was 58% in 1990),<sup>[47]</sup> economic development is not always associated with a reduction in poverty for all. In India, for example, where the economy is booming, there has been a huge reduction in the burden of ARF and RHD mostly in the southwestern states and some northern states, but little improvement in central India and the Northeast, where poverty rates are 3–4 times higher.<sup>[23]</sup>

Two-year results from the REMEDY study, a prospective registry of 12 countries from sub-Saharan Africa, Yemen, and India, further exemplify the effects of income inequality, where the highest RHD mortality rates were in LICs (20.8%), followed by LMICs (16.8%), and then lowest in the upper middle-income countries (MICs) (12.5%).<sup>[48,49]</sup>

Some of the reasons for these disparities include geographic accessibility (there is an inverse relationship between distance to health clinics and the use of these facilities<sup>[50]</sup>), healthcare availability (universal health coverage is uncommon in LMICs), financial accessibility (physicians in LMICs are often concentrated within expensive private hospitals in large cities<sup>[51]</sup>), and quality of care (there is often a two-tiered health system, with weak, underfunded public systems struggling in stark contrast to private hospitals that provide high-quality care to the wealthy few<sup>[52]</sup>).

The consequences are that in most LMICs, health inequality is widening, and healthcare is becoming less affordable.<sup>[53]</sup> Without tackling these critical issues,<sup>[49]</sup> RHD will continue to exert a large global toll.

### **Pervasively inadequate global health workforce**

RHD is a chronic condition that requires a strong health system, adequate infrastructure, and a complex and multitiered workforce. Primary, secondary, and tertiary services need to respond to the acute and chronic needs of patients with ARF and RHD and also help deliver

prevention and control strategies at each stage of the RHD disease continuum.

Providing good quality healthcare is expensive and requires a robust commitment from national governments. However, government healthcare spending in LMICs is inadequate: in LICs, it is only around 2% of GDP; in MICs, it is about 3%–5% whereas in high-income countries, it is as high as 12%.<sup>[54]</sup>

Integration of RHD programs within existing health systems, especially when primary care services are available, may be a key strategy in low-resource settings. Delivering adequate primary care is particularly important given that primary and secondary prophylaxis of ARF can be delivered at this level. The WHO estimates that to achieve adequate primary healthcare outcomes, countries need >23 healthcare workers (midwives, nurses, and physicians)/10,000 individuals.<sup>[55]</sup> Yet, there is a chronic shortage of well-trained healthcare workers in LMICs.

In Kenya and India, for example, the healthcare worker national averages are 1.8 and 6.5/10,000 people, respectively,<sup>[55]</sup> and globally, the worst-off fifth are served by only 2% of the world's physicians.<sup>[56]</sup> Some also claim that in sub-Saharan Africa, where there is a deficit of 2.4 million doctors and nurses, this health worker deficit is the greatest barrier to healthcare.<sup>[57]</sup> Compounding the issue is that most LMICs are currently unable to train sufficient numbers of healthcare workers to meet their population needs<sup>[58]</sup> and if we continue as things stand, the UN has warned that by 2030 there will be a shortfall of 18 million healthcare workers, mostly in LMICs.<sup>[59]</sup>

Task shifting or sharing (the delegation of skills and responsibilities traditionally held by professional workers to those with shorter training or less rigorous qualifications such as medical officers or community health workers) is an approach that has been recognized as a way of increasing access to healthcare and improving outcomes for over 50 years.<sup>[60]</sup> It is a concept that has been embraced by the WHO<sup>[61]</sup> and in addition to addressing health worker shortages, it also has the potential to reduce the cost of training and help shift care to cadres of healthcare workers that are more easily retained in rural or isolated areas.<sup>[61,62]</sup>

Task shifting has already been successfully employed within the RHD arena, most notably within echocardiographic RHD screening programs where mid-level providers (such as nurses or medical students) assume echocardiography responsibilities, a role previously fulfilled by cardiologists or expert sonographers.<sup>[63–66]</sup> There is potential too for further progress, for example, by integrating sore throat treatment into other programs or utilizing community health workers in the education and treatment of ARF and RHD.<sup>[67]</sup> However, education

would be needed to dispel healthcare workers and community fears of intramuscular penicillin, another barrier to RHD prevention.

Additional strategies could also be employed to increase the effectiveness of task-shifting including telemedicine resources for improving education, training, community awareness, and even screening tasks. Telemedicine may also help improve the generalizability of RHD control programs and facilitate global collaborations for disease control.<sup>[25]</sup>

Nevertheless, it is important to remember that unless developing countries invest in building and strengthening their workforce and health systems, task shifting is unlikely to succeed in covering these cracks: it is not a panacea for all the systemic shortcomings within a healthcare system, but only part of an overall healthcare improvement strategy.<sup>[68-70]</sup> The reason: evidence suggests that delegation of tasks from one part of a weak healthcare system to another, in the absence of adequate numbers of either, is no more likely to be successful than the status quo.<sup>[68,69]</sup>

## SUCCESSSES IN RHEUMATIC HEART DISEASE PREVENTION AND CONTROL: LESSONS FROM THE PAST

For inspiration, we can look to historical evidence that confirms concerted public health efforts can dramatically reduce the burden of ARF and RHD. Here, we discuss successes from register-based control programs and how RHD programs have been integrated into low-resource health systems.

### Register-based control programs

More than 30 years ago the WHO, in close collaboration with what is now the WHF, established a global program for control of ARF and RHD in 16 countries from Africa,

South America, the Eastern Mediterranean, Southeast Asia, and the Western Pacific.<sup>[71]</sup> By the 1980s, this program had expanded to 22 countries. The program identified 3,135 cases of ARF and RHD, with 63.2% of these completing secondary prophylaxis. The rates of adverse events (0.3%) and ARF recurrences (0.4%), the best measure of success of an ARF/RHD control program, were low. Unfortunately, emerging issues, such as HIV, began to dominate the global healthcare agenda, and the RHD program was abandoned in 2002. One notable success of the program, however, was that it was the first to give rise to the concept of register-based control programs for RHD.

Some of the pilot programs from the global program managed to persist and produce some dramatic results, such as those seen in Cuba.<sup>[72]</sup> Other nations too have seen remarkable reductions in the incidence of ARF through control programs, including the French Caribbean islands of Martinique and Guadeloupe,<sup>[73]</sup> Costa Rica,<sup>[74]</sup> and Tunisia<sup>[23]</sup> [Table 2]. More recently, in New Zealand, the recurrence rate of ARF is <10%<sup>[75]</sup> and in the Australian northern territories, the recurrence rate dropped from 45% in 1997<sup>[76]</sup> to 26% by 2015.<sup>[77]</sup>

Most of these programs employed a register-based approach to ARF and RHD control with a combination of primary, secondary, and tertiary care (i.e., “comprehensive RHD control programs”). It is difficult to determine which elements were critical to the success of each program in each country, but it is likely that it was a combination of approaches, but particularly primary and secondary care.<sup>[78]</sup> Indeed, both primary prophylaxis and register-based ARF/RHD control programs have been identified as 2 of the 10 “best buys” for combating heart disease in Africa.<sup>[79]</sup>

### Integrating rheumatic heart disease programs into health systems

In addition to setting the precedent for RHD control programs, the WHO global program also led to the

**Table 2: Summary of the key features and outcomes of successful acute rheumatic fever/rheumatic heart disease control programs in low-resource countries**

Country	Standardized treatment for sore throat with penicillin	ARF/RHD registry and secondary prophylaxis	Educational programs	ARF incidence per 100,000*		Other key features
				START	END	
Costa Rica <sup>[74]</sup> 1970-1990	Yes	Yes	Healthcare workers only	90	1.9	GAS pharyngitis diagnosed clinically without the need for a positive throat culture
Martinique <sup>[73]</sup> 1982-1992	Not stated	Yes	Healthcare workers and public	19.6	4.3	Martinique and Guadeloupe: large number of physicians (>2/1000); free access to drugs and medical care; cost of medical expenses related to ARF declined by 86% (a saving higher than the cost of the program)
Guadeloupe <sup>[73]</sup> 1982-1992	Not stated	Yes	Healthcare workers and public	17.4	4.5	
Cuba <sup>[72]</sup> 1986-1996	Yes	Yes	Healthcare workers and public	18.6	2.5	RHD incidence (/1000) reduced from 2.27 to 0.24; undertook screening for RHD
Tunisia <sup>[23]</sup> 1978-2015	Yes	Yes	Healthcare workers and public	8.7	0.08	ARF made a notifiable disease; undertook screening for RHD

\*Given as two figures: “START” is data at the beginning of the control program and “END” is data when the program finished. ARF: Acute rheumatic fever, GAS: Group A *Streptococcus*, RHD rheumatic heart disease

integration of RHD into the WHO's 2001 NCD initiative. This helped enhance disease control efforts by integrating RHD with primary healthcare NCD interventions.<sup>[4]</sup>

However, perhaps the most effective method of integrating RHD into healthcare systems is through a “diagonal” approach, which best accommodates the complex nature of RHD as it intersects numerous different specialities, domains, and levels of care.<sup>[80]</sup> A diagonal approach encompasses a combination of both “vertical” programs (which address specific diseases, such as RHD or HIV), and “horizontal” programs (which involve health systems strengthening interventions, such as improving primary care).<sup>[81]</sup>

We have already seen examples of such an approach. In Tunisia, their national control program included making ARF a notifiable disease and screening for RHD (vertical components), as well as improving access to primary care and referral pathways, and standardizing the treatment of sore throats<sup>[23]</sup> (horizontal components). This helped to produce a remarkable 100-fold reduction in ARF incidence in the country, from 8.7/100,000 in 1980 to 0.08/100,000 in 2015 [Table 2].<sup>[23]</sup> An ongoing project in Brazil (PROVAR+) is also testing the integration of screening for RHD-related valve disease in the primary care system, with active education of the public by community health agents and screening for valve disease during scheduled visits.

There is further evidence that integrating vertical components of an RHD control program into existing horizontal components from another disease is feasible. Leveraging existing HIV/AIDS infrastructure is one particularly attractive approach given the degree of investment over the last 10 years (particularly in sub-Saharan Africa). This has been successfully implemented in Uganda where clinicians created a joint RHD treatment registry for disease monitoring and adherence to treatment, and hundreds of HIV-infected children that were receiving routine care were also screened for RHD.<sup>[82]</sup>

## RESOURCES AND ROADMAP

Unfortunately, sustained effective implementation, scale-up, and spread of the innovative strategies employed by the WHO in Cuba, Costa Rica, and other countries have not been replicated in most LMICs. Moreover, the African and WHF calls to action have failed to bear fruit on a global scale, as evidenced by the paucity of successful control programs in existence today.

Realizing the need for tools to help put existing knowledge into practice and bridge the gap to implementation – the so-called “knowledge-practice” gap – the WHF and RhEACH (Rheumatic Heart Disease Evidence Advocacy

Communication Hope) have recently released practical guidance documents that can be used at the global, national, or regional level.<sup>[17,81]</sup>

### The World Heart Federation rheumatic heart disease roadmap

The WHF RHD roadmap is a tool that is designed to help reduce cardiovascular morbidity and mortality through improved prevention and control of RHD.<sup>[17]</sup> The roadmap can be used as both a general guide and framework in the examination of key barriers and potential solutions at the policy and health systems levels. The barriers and solutions are examined in four domains: primary prevention, secondary prevention, tertiary care, and health system limitations.<sup>[83]</sup>

In line with the WHO recommendations,<sup>[84]</sup> the solutions generated from the RHD roadmap promote comprehensive control programs and are intended to integrate into healthcare systems. Solutions should also be responsive to local needs and challenges because RHD control cannot follow a one-size-fits-all approach<sup>[85]</sup> as there are often unique socioeconomic and cultural barriers to implementation. The WHF RHD roadmap involves four main steps:

1. Develop and convene a multisectorial coalition: This might include various stakeholders (such as government, civil society, and private sector) and sectors (such as providers from primary and specialized care, public health, and environment)
2. Conduct a situational analysis: This involves an assessment of the country's epidemiological profile, healthcare system, and policy environment to identify targeted interventions in ARF and RHD control and prevention at the local and national level. To facilitate this, RhEACH has developed a Needs Assessment Tool (NAT) that makes use of scientifically validated methods and charts the patient journey through the health system to determine and quantify barriers and enablers to care<sup>[86]</sup>
3. Conduct policy dialogs with multiple local stakeholders: Data acquired through the NAT process can then be used in discussions with multiple stakeholders to help identify and discuss specific barriers and local problems and plan relevant strategies that are appropriate to the given context<sup>[17,83]</sup>
4. Develop a plan to evaluate implementation of the selected strategies.

### The TIPS handbook

Developed by the WHF and RhEACH, the TIPS handbook (Tools for Implementing RHD Control Programs)<sup>[81]</sup> is designed to support the description, development, and delivery of RHD control programs at the national level. It is based on a priority-based framework for program delivery.

The framework emphasizes the need to tackle components of a comprehensive RHD control program in approximate order of priority. Hence, for example, burden of disease data and funding should be addressed before more complex interventions such as health worker training and cardiac surgery.

## CONCLUSION

The political agenda is beginning to align with the burden of RHD. The initial steps taken by the UN and WHO in setting goals to tackle poverty, inequality, and cardiovascular disease have helped crystalize the calls to action by the WHF and PASCAR. The subsequent WHA Resolution has placed RHD back on the global stage as an important NCD.

By building on this common vision and aligned goals, and utilizing tools summarized in this review, efforts to reduce the burden of RHD will be enhanced. Governments must take primary responsibility for tackling this disease by prioritizing sustainable public health approaches (such as the RHD best buys). As governments work toward meeting these goals, RHD advocates can capitalize on the political windows opened up by these coordinated efforts.

We are on a precipice of change and now is the time to act because the elimination of ARF and RHD “in our lifetime,” as many leading authors and organizations propose,<sup>[7,11,87]</sup> demands that we find a resonance that stretches beyond the medical and scientific community: in advocacy, awareness, and political will. This is where RHD rests in the 21<sup>st</sup> century.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

## REFERENCES

1. Watkins DA, Johnson CO, Colquhoun SM, Karthikeyan G, Beaton A, Bukhman G, *et al.* Global, regional, and national burden of rheumatic heart disease, 1990-2015. *N Engl J Med* 2017;377:713-22.
2. Seckeler MD, Hoke TR. The worldwide epidemiology of acute rheumatic fever and rheumatic heart disease. *Clin Epidemiol* 2011;3:67-84.
3. Robertson KA, Mayosi BM. Rheumatic heart disease: Social and economic dimensions. *S Afr Med J* 2008;98:780-1.
4. Maurice J. Rheumatic heart disease back in the limelight. *Lancet* 2013;382:1085-6.
5. Omran AR. The epidemiologic transition. A theory of the epidemiology of population change. *Milbank Mem Fund Q* 1971;49:509-38.
6. WHO. Global Action Plan for the Prevention and Control of Noncommunicable Diseases 2013-2020. Geneva: World Health Organization; 2013.
7. Remenyi B, Carapetis J, Wyber R, Taubert K, Mayosi BM; World Heart Federation, *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.
8. Carapetis JR, Beaton A, Cunningham MW, Guilherme L, Karthikeyan G, Mayosi BM, *et al.* Acute rheumatic fever and rheumatic heart disease. *Nat Rev Dis Primers* 2016;2:15084.
9. Carapetis JR, Zühlke LJ. Global research priorities in rheumatic fever and rheumatic heart disease. *Ann Pediatr Cardiol* 2011;4:4-12.
10. Mayosi B, Robertson K, Volmink J, Adebo W, Akinyore K, Amoah A, *et al.* The drakensberg declaration on the control of rheumatic fever and rheumatic heart disease in Africa. *S Afr Med J* 2006;96:246.
11. Mayosi BM, Gamra H, Dangou JM, Kasonde J 2<sup>nd</sup>; All-Africa Workshop on Rheumatic Fever and Rheumatic Heart Disease Participants. Rheumatic heart disease in Africa: The Mosi-o-Tunya call to action. *Lancet Glob Health* 2014;2:e438-9.
12. Watkins D, Zühlke L, Engel M, Daniels R, Francis V, Shaboodien G, *et al.* Seven key actions to eradicate rheumatic heart disease in Africa: The addis ababa communiqué. *Cardiovasc J Afr* 2016;27:184-7.
13. Moloi AH, Mall S, Engel ME, Stafford R, Zhu ZW, Zühlke LJ, *et al.* The health systems barriers and facilitators for RHD prevalence: An epidemiological meta-analysis from Uganda and Tanzania. *Glob Heart* 2017;12:5-15000.
14. Kheir SM, Ali SK. The control of rheumatic fever and rheumatic heart disease: A call to raise the awareness. *Sudan J Paediatr* 2014;14:21-4.
15. Bhaumik S. Doctors call for countries to step up the fight against rheumatic heart disease. *BMJ* 2013;346:f3504.
16. Beaton A, Sable C. Health policy: Reducing rheumatic heart disease in Africa – Time for action. *Nat Rev Cardiol* 2016;13:190-1.
17. Palafox B, Mocumbi AO, Kumar RK, Ali SKM, Kennedy E, Haileamlak A, *et al.* The WHF roadmap for reducing CV morbidity and mortality through prevention and control of RHD. *Glob Heart* 2017;12:47-62.
18. The Cairo Accord on Rheumatic Heart Disease – 2017. Available from: <http://www.ahc-scienceandpractice.com/rhd/>. [Last accessed on 2017 Aug 12].
19. Zühlke LJ, Engel ME. The importance of awareness and education in prevention and control of RHD. *Glob Heart* 2013;8:235-9.
20. Marijon E, Celermajer DS, Jouven X. Rheumatic heart disease – An iceberg in tropical waters. *N Engl J Med* 2017;377:780-1.
21. McDonald M, Brown A, Noonan S, Carapetis JR. Preventing recurrent rheumatic fever: The role of register based programmes. *Heart* 2005;91:1131-3.
22. Nkgudi B, Robertson KA, Volmink J, Mayosi BM.



- Notification of rheumatic fever in South Africa – Evidence for underreporting by health care professionals and administrators. *S Afr Med J* 2006;96:206-8.
23. Yusuf S, Narula J, Gamra H. Can we eliminate rheumatic fever and premature deaths from RHD? *Glob Heart* 2017;12:3-4.
  24. Gewitz MH, Baltimore RS, Tani LY, Sable CA, Shulman ST, Carapetis J, *et al.* Revision of the Jones criteria for the diagnosis of acute rheumatic fever in the era of doppler echocardiography: A scientific statement from the American Heart Association. *Circulation* 2015;131:1806-18.
  25. Lopes EL, Beaton AZ, Nascimento BR, Tompsett A, Dos Santos JP, Perlman L, *et al.* Telehealth solutions to enable global collaboration in rheumatic heart disease screening. *J Telemed Telecare* 2016. pii: 1357633X16677902.
  26. Dougherty S, Khorsandi M, Herbst P. Rheumatic heart disease screening: Current concepts and challenges. *Ann Pediatr Cardiol* 2017;10:39-49.
  27. Engelman D, Mataika RL, Ah Kee M, Donath S, Parks T, Colquhoun SM, *et al.* Clinical outcomes for young people with screening-detected and clinically-diagnosed rheumatic heart disease in Fiji. *Int J Cardiol* 2017;240:422-7.
  28. Engelman D, Wheaton GR, Mataika RL, Kado JH, Colquhoun SM, Remenyi B, *et al.* Screening-detected rheumatic heart disease can progress to severe disease. *Heart Asia* 2016;8:67-73.
  29. Zühlke L, Engel ME, Lemmer CE, van de Wall M, Nkepu S, Meiring A, *et al.* The natural history of latent rheumatic heart disease in a 5 year follow-up study: A prospective observational study. *BMC Cardiovasc Disord* 2016;16:46.
  30. Beaton A, Okello E, Aliku T, Lubega S, Lwabi P, Mondo C, *et al.* Latent rheumatic heart disease: Outcomes 2 years after echocardiographic detection. *Pediatr Cardiol* 2014;35:1259-67.
  31. Palma AM, Rabkin M, Nuwagaba-Biribonwoha H, Bongomin P, Lukhele N, Dlamini X, *et al.* Can the success of HIV scale-up advance the global chronic NCD agenda? *Glob Heart* 2016;11:403-8.
  32. Shiffman J. A social explanation for the rise and fall of global health issues. *Bull World Health Organ* 2009;87:608-13.
  33. Shulman ST, Tanz RR, Dale JB, Steer AC, Smeesters PR. Added value of the emm-cluster typing system to analyze Group A *Streptococcus* epidemiology in high-income settings. *Clin Infect Dis* 2014;59:1651-2.
  34. Stuckler D, King L, Robinson H, McKee M. WHO's budgetary allocations and burden of disease: A comparative analysis. *Lancet* 2008;372:1563-9.
  35. Nozaki I. WHO's budgetary allocation and disease burden. *Lancet* 2013;382:937-8.
  36. Ralston J, Reddy KS, Fuster V, Narula J. Cardiovascular diseases on the global agenda: The United Nations high level meeting, sustainable development goals, and the way forward. *Glob Heart* 2016;11:375-9.
  37. Moran M, Guzman J, Ropars AL, McDonald A, Jameson N, Omune B, *et al.* Neglected disease research and development: How much are we really spending? *PLoS Med* 2009;6:e30.
  38. GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: A systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015;385:117-71.
  39. Chapman N, Abela-Oversteegen L, Doubell A, Chowdhary V, Gurjav U, Ong M. Neglected Disease Research and Development: A Pivotal Moment for Global Health. Surry Hills, NSW, Australia: Policy Cures Research; 2016. Available from: <http://www.policycuresresearch.org/downloads/Y9%20GFINDER%20full%20report%20web.pdf>. [Last accessed on 2017 Aug 03].
  40. Allen L. Why is there no funding for non-communicable diseases? *J Glob Health Perspect* 2016; 1<sup>st</sup> ed. Available from: <http://www.jglobalhealth.org/article/why-is-there-no-funding-for-non-communicable-diseases/>. [Last Modified on 2016 Oct 16].
  41. WHO. Rheumatic Heart Disease: Draft Resolution Proposed by Australia, Brazil, Canada, Cook Islands, Ecuador, Fiji, Japan, Namibia, New Zealand, Pakistan, Samoa, Tonga and Tuvalu. Geneva, Switzerland: World Health Organization; 2017. p. 1-3.
  42. Kitamura T, Obara H, Takashima Y, Takahashi K, Inaoka K, Nagai M, *et al.* World Health Assembly agendas and trends of international health issues for the last 43 years: Analysis of World Health Assembly agendas between 1970 and 2012. *Health Policy* 2013;110:198-206.
  43. Gordis L. The virtual disappearance of rheumatic fever in the United States: Lessons in the rise and fall of disease. T. Duckett Jones memorial lecture. *Circulation* 1985;72:1155-62.
  44. G8 Communiqué. Okinawa 2000. Available from: <http://www.g8.utoronto.ca/summit/2000okinawa/finalcom.htm>. [Last accessed on 2017 Aug 19].
  45. Wagstaff A. Poverty and health sector inequalities. *Bull World Health Organ* 2002;80:97-105.
  46. Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, *et al.* Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: A systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;380:2197-223.
  47. Jamison DT, Summers LH, Alleyne G, Arrow KJ, Berkley S, Binagwaho A, *et al.* Global health 2035: A world converging within a generation. *Lancet* 2013;382:1898-955.
  48. Zühlke L, Karthikeyan G, Engel ME, Rangarajan S, Mackie P, Cupido-Katya Mauff B, *et al.* Clinical outcomes in 3343 children and adults with rheumatic heart disease from 14 low- and middle-income countries: Two-year follow-up of the global rheumatic heart disease registry (the REMEDY study). *Circulation* 2016;134:1456-66.
  49. Peters DH, Garg A, Bloom G, Walker DG, Brieger WR, Rahman MH, *et al.* Poverty and access to health care in developing countries. *Ann N Y Acad Sci* 2008;1136:161-71.

50. Hjortsberg C. Why do the sick not utilise health care? The case of Zambia. *Health Econ* 2003;12:755-70.
51. WHO. World Health Statistics 2014. Geneva: World Health Organization; 2014.
52. Yusuf S, Wood D, Ralston J, Reddy KS. The World Heart Federation's vision for worldwide cardiovascular disease prevention. *Lancet* 2015;386:399-402.
53. Heller RF, Chongsuvivatwong V, Hailegeorgios S, Dada J, Torun P, Madhok R, et al. Capacity-building for public health: <http://peoples-uni.org>. *Bull World Health Organ* 2007;85:930-4.
54. World Development Indicators: Health Systems. The World Bank; 2014. Available from: <http://www.wdi.worldbank.org/table/2.15>. [Last accessed on 2017 Aug 19].
55. WHO. A Universal Truth, No Health Care Without a Workforce. Available from: [http://www.who.int/workforcealliance/knowledge/resources/GHWA-a\\_universal\\_truth\\_report.pdf?ua%41](http://www.who.int/workforcealliance/knowledge/resources/GHWA-a_universal_truth_report.pdf?ua%41). [Last accessed on 2017 Aug 19].
56. WHO. Working Together For Health. The World Health Report 2006. Geneva, Switzerland: World Health Organization; 2006.
57. Anyangwe SC, Mtonga C. Inequities in the global health workforce: The greatest impediment to health in sub-Saharan Africa. *Int J Environ Res Public Health* 2007;4:93-100.
58. Kinfu Y, Dal Poz MR, Mercer H, Evans DB. The health worker shortage in Africa: Are enough physicians and nurses being trained? *Bull World Health Organ* 2009;87:225-30.
59. WHO. Working for Health and Growth: Investing in the Health Workforce - Report of the High-Level Commission on Health Employment and Economic Growth; 2016. Available from: <http://www.apps.who.int/iris/bits/tream10665/250047/1/9789241511308-eng.pdf>. [Last accessed on 2017 Aug 21].
60. Jarvis JD, Kataria I, Murgor M, Mbau L. Community health workers: An underappreciated asset to tackle NCD. *Glob Heart* 2016;11:455-7.
61. WHO. WHO Recommendations: Optimizing Health Worker Roles to Improve Access to Key Maternal and Newborn Health Interventions through Task Shifting. Geneva: World Health Organization; 2012.
62. Schneeberger C, Mathai M. Emergency obstetric care: Making the impossible possible through task shifting. *Int J Gynaecol Obstet* 2015;131 Suppl 1:S6-9.
63. Beaton A, Nascimento BR, Diamantino AC, Pereira GT, Lopes EL, Miri CO, et al. Efficacy of a standardized computer-based training curriculum to teach echocardiographic identification of rheumatic heart disease to nonexpert users. *Am J Cardiol* 2016;117:1783-9.
64. Sims Sanyahumbi A, Sable CA, Karlsten M, Hosseinipour MC, Kazembe PN, Minard CG, et al. Task shifting to clinical officer-led echocardiography screening for detecting rheumatic heart disease in Malawi, Africa. *Cardiol Young* 2017;27:1133-9.
65. Saxena A. Task shifting rheumatic heart disease screening to non-experts. *Lancet Glob Health* 2016;4:e349-50.
66. Shmueli H, Burstein Y, Sagy I, Perry ZH, Ilia R, Henkin Y, et al. Briefly trained medical students can effectively identify rheumatic mitral valve injury using a hand-carried ultrasound. *Echocardiography* 2013;30:621-6.
67. Zühlke LJ, Karthikeyan G. Primary prevention for rheumatic fever: Progress, obstacles, and opportunities. *Glob Heart* 2013;8:221-6.
68. Philips M, Zachariah R, Venis S. Task shifting for antiretroviral treatment delivery in sub-Saharan Africa: Not a panacea. *Lancet* 2008;371:682-4.
69. Berer M. Task-shifting: Exposing the cracks in public health systems. *Reprod Health Matters* 2009;17:4-8.
70. Mumtaz Z, Patterson P. Does task shifting among parts of a weak health system help? *Lancet Glob Health* 2017;5:e734-5.
71. WHO. The WHO Global Programme for the Prevention of Rheumatic Fever and Rheumatic Heart Disease: Report of a Consultation to Review Progress and Develop Future Activities. Geneva, Switzerland: World Health Organization; 1999.
72. Nordet P, Lopez R, Dueñas A, Sarmiento L. Prevention and control of rheumatic fever and rheumatic heart disease: The Cuban experience (1986-1996-2002). *Cardiovasc J Afr* 2008;19:135-40.
73. Bach JF, Chalons S, Forier E, Elana G, Jouanelle J, Kayemba S, et al. 10-year educational programme aimed at rheumatic fever in two French Caribbean Islands. *Lancet* 1996;347:644-8.
74. Arguedas A, Mohs E. Prevention of rheumatic fever in Costa Rica. *J Pediatr* 1992;121:569-72.
75. Thornley C, McNicholas A, Baker M, Lennon D. Rheumatic fever registers in New Zealand. *N Z Public Health Rep* 2001;8:41-4.
76. Carapetis JR, Wolff DR, Currie BJ. Acute rheumatic fever and rheumatic heart disease in the top end of Australia's Northern Territory. *Med J Aust* 1996;164:146-9.
77. Zühlke LJ, Beaton A, Engel ME, Hugo-Hamman CT, Karthikeyan G, Katzenellenbogen JM, et al. Group A *Streptococcus*, acute rheumatic fever and rheumatic heart disease: Epidemiology and clinical considerations. *Curr Treat Options Cardiovasc Med* 2017;19:15.
78. Watkins DA, Mvundura M, Nordet P, Mayosi BM. A cost-effectiveness analysis of a program to control rheumatic fever and rheumatic heart disease in Pinar Del Rio, Cuba. *PLoS One* 2015;10:e0121363.
79. Mayosi BM. The 10 'best buys' to combat heart disease, diabetes and stroke in Africa. *Heart* 2013;99:973-4.
80. Wyber R, Zühlke L, Carapetis J. The case for global investment in rheumatic heart-disease control. *Bull World Health Organ* 2014;92:768-70.
81. Wyber R, Grainger Gasser A, Thompson D, Kennedy D, Johnson T, Taubert K, et al. Tools for Implementing RHD Control Programmes (TIPS) Handbook. Perth, Australia: World Heart Federation and RheACH; 2014.
82. Longenecker CT, Okello E, Lwabi P, Costa MA, Simon DI, Salata RA, et al. Management of rheumatic heart

- disease in Uganda: The emerging epidemic of non-AIDS comorbidity in resource-limited settings. *J Acquir Immune Defic Syndr* 2014;65:e79-80.
83. Perel P, Bianco E, Poulter N, Prabhakaran D, Pais P, Ralston J, *et al.* Adapting the World Heart Federation roadmaps at the national level: Next steps and conclusions. *Glob Heart* 2015;10:135-6.
84. WHO. Rheumatic Fever and Rheumatic Heart Disease: Report of a WHO Expert Consultation, Geneva, 29 October, 1 November, 2001. Geneva, Switzerland: World Health Organization; 2004.
85. Watkins DA, Zühlke LJ, Narula J. Moving forward the RHD agenda at global and national levels. *Glob Heart* 2017;12:1-2.
86. Zühlke LJ, Watkins DA, Perkins S, Wyber R, Mwangi J, Markbreiter J, *et al.* A comprehensive needs assessment tool for planning RHD control programs in limited resource settings. *Glob Heart* 2017;12:25-31.
87. Mayosi BM. The challenge of silent rheumatic heart disease. *Lancet Glob Health* 2014;2:e677-8.