Position statement of the World Heart Federation on the prevention and control of rheumatic heart disease

Bo Remenyi, Jonathan Carapetis, Rosemary Wyber, Kathryn Taubert and Bongani M. Mayosi

Abstract | In the 21st century, rheumatic fever (RF) and rheumatic heart disease (RHD) are neglected diseases of marginalized communities. Globally, RHD remains the most-common cardiovascular disease in young people aged <25 years. Although RF and RHD have been almost eradicated in areas with established economies, migration from low-income to high-income settings might be responsible for a new burden of RHD in high-income countries. The World Heart Federation (WHF) and its Working Group on RF and RHD unites global experts, combines their experience and enthusiasm, and provides a platform for RHD control. This paper is a declaration of the WHF institutional strategic goal—a 25% reduction in premature deaths from RF and RHD among individuals aged <25 years by the year 2025. The position statement affirms WHF commitments to five key strategic targets: comprehensive register-based control programmes, global access to benzathine penicillin G, identification and development of public figures as 'RHD champions', expansion of RHD training hubs, and support for vaccine development. In this paper, we also review existing barriers to RF and RHD control and identify the actions required to change the trajectory of control for these diseases. This approach provides the foundation for governments, civil society, patient advocates, clinicians, researchers, and funding agencies to develop partnerships and unify global efforts to control RF and RHD. The WHF plans to expand this position statement to an operational plan that will be founded on science, research, and quantifiable progress indicators to impact positively on the millions of people who are affected by RHD and its long-term sequelae.

Introduction

Rheumatic fever (RF) is an autoimmune disease that follows a group A β-haemolytic streptococcal (GAS) infection of the throat (streptococcal pharyngitis).[1] Streptococcal skin infection has also been implicated in the disease process.[2,3] After recovery from the initial episode of RF, 60–65% of patients develop valvular heart disease.[4,5] RF recurrences can lead to progressive valve damage (rheumatic heart disease; RHD), which in turn can cause atrial fibrillation and heart failure. As the disease progresses, lifesaving cardiac surgery often becomes necessary, and patients who do not have access to such treatment often die prematurely from RHD and its complications;[6,7] in some studies the mean age of death was <25 years.[7–9]

In the mid-20th century, economic and sociopolitical change coincided with a surge of activity in research and control of RF and RHD, which resulted in the virtual elimination of RF in high-income regions of North America and Europe by the 1980s.[10,11] A substantial proportion of this early work can be credited to the AHA and the WHO. However, the human, social, and economic costs of RF and RHD continue to burden many low-income and middle-income countries, and some indigenous populations of higher-income countries.[6] Anecdotal reports suggest that demographic shifts over the past 10 years, with immigration from low-income countries, where RF and RHD are endemic, to high-income countries, have resulted in a rise in RHD prevalence in some regions where the disease was previously thought to have been eliminated.

The conservative estimate of the global burden of RHD in 2005 was 15.6–19.6 million existing cases, and an approximate global incidence of 282,000 new cases per year.[6] Although questions remain about the importance of subclinical RHD—the rate of progression to clinical RHD and whether early treatment with secondary prophylaxis is justified to improve patient outcomes—emerging echocardiographic data suggest that the true prevalence of RHD might be several-fold higher than the 2005 global estimate.[12–18] An estimated 233,000–468,164 individuals die from RHD each year, and hundreds of thousands of people are disabled by this disease and its long-term complications, which include heart failure, atrial fibrillation, stroke, infective endocarditis, and pregnancy-related complications.[6] In the late 1990s, RHD was the most-common cardiovascular disease among individuals aged <25 years worldwide.[19] Despite the paucity of epidemiological data from countries where RF and RHD are endemic, the 2010 Global Burden of

World Heart Federation, 7 rue des Battoirs, Case Postale 155, 1211 Geneva 4, Switzerland (**B. Remenyi**, **R. Wyber**, **K. Taubert**). Telethon Institute for Child Health Research, Centre for Child Health Research, University of Western Australia, 100 Roberts Road, Subiaco, Perth, WA 6008, Australia (**J. Carapetis**). Department of Medicine, Groote Schuur Hospital and University of Cape Town, Main Road, Observatory, Cape Town 7935, South Africa (**B. M. Mayosi**).

Correspondence to:
K. Taubert
kathryn.taubert@worldheart.org

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Disease study demonstrated that RHD remains one of the leading cardiovascular causes of disability-adjusted life years lost in those aged <25 years.[20] Expanded statistics on RF and RHD from the 2010 Global Burden of Disease study are due for publication in 2013.

The WHO Expert Report on RHD identifies that the prevention of RF and RHD can be undertaken at a number of levels.[21] 'Primordial prevention' refers to the improvement of environmental, social, and economic conditions of populations at risk of RF and RHD.[22] In the absence of an effective vaccine, 'primary prevention' refers to treatment of acute streptococcal pharyngitis with antibiotics to reduce the incidence of RF. 'Secondary prevention' is the use of antibiotic prophylaxis to reduce the recurrence of RF in people with a history of RF or RHD[21–24] and, therefore, limit disease progression and allow disease resolution.[25–27] Finally, 'tertiary prevention' refers to medical and surgical treatment of the complications of RF and RHD.[21,22]

Role of the WHF in RF and RHD control

The World Heart Federation (WHF) is a collaboration between heart foundations and medical societies worldwide,[28] and is recognized by the WHO as its leading nongovernmental organization partner in cardiovascular disease prevention.[28] The WHF focuses on three strategic priorities to achieve its goals: global leadership and advocacy, risk factors, and treatment and care. In turn, three 'building blocks' provide tactics for these priorities: building evidence, building capacity, and building support. The WHF generates revenue from organizational memberships, scientific meetings, corporate partnerships, and donations.

The collaboration between the WHF and other international bodies is exemplified by 'The Global Programme on RF and RHD', which was jointly administered by the United Nations Educational, Scientific and Cultural Organization, the WHO, and the International Society and Federation of Cardiology (the predecessor to WHF) from 1996 to 2001. After the programme was disbanded in 2001 owing to competing global health priorities,[29,30] the WHF and other international organizations continued their activities for the control of RF and RHD. In July 2011, the WHF Working Group on RF and RHD was formally established to address the strategic goal of minimizing RHD burden and eliminating RF (Box 1).[31] The Working Group on RF and RHD is comprised of experts from regions where RHD is endemic and global partners.

Opportunities for RF and RHD control

In the 20th century, RF prevention by treatment of streptococcal pharyngitis and control of RHD using antibiotic prophylaxis became possible.[23,32,33] The challenge that remains is how best to apply this knowledge to low-income and middle-income countries where RF and RHD are still endemic. In such nations, estimates of disease burden are often inadequate or inaccurate, primary health care is not universally available, and disease control or elimination is not on government

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Box 1 | The role of the WHF in the control of RF and RHD

- Coordination: the WHF seeks to lead and to coordinate global partnerships in efforts to control RF and RHD
- Integration: the WHF seeks to align its specific goals for RF and RHD into global health priorities, and integrate its control programme activities with the wider health system, including the WHO-aligned target of a 25% reduction in premature deaths from RF and RHD by 2025
- Networking and collaboration: the WHF, in partnership with its member organizations, seeks to partner communities, private sectors, primary health-care and other service providers, policy-makers, researchers, and patients
- Education: the WHF seeks to provide leading educational materials and training opportunities for the global RHD community
- Advocacy: the WHF seeks to provide compassionate global, regional, and national advocacy and give voice to a silent disease

Abbreviations: RF, rheumatic fever; RHD, rheumatic heart disease; WHF, World Heart Federation.

Box 2 | WHF mission, goals, and targets for control of RF and RHD

Mission
- Minimize the burden of RHD and eliminate RF

Goal
- Achieve a 25% reduction in premature deaths from RF and RHD among individuals aged <25 years by 2025

Targets
- Ensure that 90% of countries with endemic RHD have integrated and comprehensive control programmes by 2025
- Ensure the availability of high-quality benzathine penicillin G for 90% of patients with RHD in 90% of countries with a high burden of this disease within 10 years
- Foster at least one prominent public figure as an 'RHD champion' in every country where RHD is endemic
- Establish at least one hub of training, research, and advocacy for RF and RHD in each WHO-defined geographic region by 2025
- Test a group A β-haemolytic streptococcal vaccine in phase III clinical trials in RHD-endemic countries within 10 years

Abbreviations: RF, rheumatic fever; RHD, rheumatic heart disease; WHF, World Heart Federation.

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agendas. We are, however, witnessing a new surge of research and advocacy in low-income and middle-income countries.[34] The WHF Working Group on RF and RHD now has the opportunity to foster a strategic approach to minimizing the burden of RHD and eliminating RF worldwide.

Aims and development of position paper

The primary aim of this position paper is to serve as a guide on how to achieve the objective of controlling RHD and eliminating RF in our generation. The paper also includes descriptions of existing barriers that limit disease control efforts and a discussion of the actions required to change the trajectory of RF and RHD control. This paper will provide a foundation for a WHF operational plan to achieve specific targets, over a set period of time, for control of RF and RHD (Box 2). Like other organizations, the WHF intends to make the activities and strategic targets of the organization widely accessible and open to scrutiny. This position paper includes an outline of priorities for policy makers, clinicians, researchers, and donors, and aims to engender a collaborative approach.

In April 2012 at the World Congress of Cardiology in Dubai, United Arab Emirates, the WHF Working Group on RF and RHD met to develop a position statement on RHD control to pave the way for an operational

Advocacy

- Advocate control of RF and RHD on the global stage as part of a noncommunicable diseases programme, with a focus on major international organizations and meetings including the World Health Assembly
- Develop partnerships with relevant industry bodies, corporations, and nongovernment organizations interested in RF and RHD control, research, and advocacy
- Develop a network of national level prominent public figures as 'champions' or ambassadors to address domestic and international political will for control of RF and RHD and to promote regional approaches to the control of RF and RHD
- Develop a 'toolkit' for RF and RHD advocacy for use at country level, outlining the evidence base for disease control activities and a structured guide to programme development

Funding

- Develop a robust economic argument for disease control on the basis of ongoing, up-to-date analysis of economic and disability adjusted life year burden
- Analyze the cost benefit and cost-effectiveness of specific components of a comprehensive primary, secondary, and tertiary prevention programme
- Develop and implement a comprehensive fundraising strategy for RF and RHD control and advocacy activities led by the World Heart Federation
- Advocate core government funding for research and comprehensive control programmes for RF and RHD

Abbreviations: RF, rheumatic fever; RHD, rheumatic heart disease.

plan. Targets for disease control were developed in consultation with attendees from 20 countries affected by RF and RHD. The WHF Working Group aligned itself with the 65th United Nations General Assembly resolution (A/RES/66/2),[35] and subsequently adopted the voluntary targets and language of the WHO 65th World Health Assembly, which include a reduction in premature deaths from noncommunicable diseases (NCDs) by 25% by the year 2025.[36]

Barriers to the control of RF and RHD
Neglect of RF and RHD

RF and RHD cause disproportionate burdens of disease between populations within nations and between different countries, affecting the most-vulnerable communities. Yet these diseases have largely been eliminated in high-resource settings.[37,38] Therefore, in many respects, RF and RHD meet the WHO requirements of 'common features of neglected tropical diseases'.[39,40] Neglect is manifested in the relative lack of engagement in disease control by governments, civil society, patient advocates, and funding agencies (Box 3).[30,41] The interest in controlling RF and RHD fluctuated during the 20th century, and activities declined after the dissolution of The Global Programme on RF and RHD in 2001. RHD-related academic publications between 1996 and 2006 were 66% fewer than between 1966 and 1976.[42]

Although RHD is the most-common cardiovascular disease among young people (age <25 years) worldwide,[19] just 0.1% of global health research funding for neglected diseases was targeted towards RF between 2007 and 2010, which equated to US$1,736,877 in 2010.[43] This figure represents a 42.3% decrease compared with 2009.[43] The G-Finder report on research and development for neglected diseases identified only four organizations that invested in RF and RHD research in 2010.[43] The US NIH and Australian National Health and Medical Research Committee have been the only consistent funders of RF research and development over the past 4 years. Philanthropic funding is disproportionately low compared with that for other neglected diseases. Public health research institutes provided 91.4% of total funding for RHD research, with philanthropic organizations contributing only 8.6%.[43] Industry provided negligible funding in 2010, after investing US$1.4 million in 2009.[43] This decrease in funding was attributed to the effect of the global financial crisis, the impact of which on neglected disease research and development first became evident in 2010.[43]

Control of RF and RHD will require a substantial increase in funding. Increasingly, access to funding is predicated on evidence of affordable and cost-effective interventions.[44,45] Treatment of pharyngitis with antibiotics for the primary prevention of RF has been deemed to be cost-effective by some investigators in South Africa and India.[32,46,47] Historical analysis has shown that secondary prevention with benzathine penicillin G (BPG) is the most cost-effective measure for RHD control (Table 1).[48] However, a need exists for contemporary cost-effectiveness analyses of primary and secondary prevention in multiple settings to galvanize support for disease control. Investigating the affordability of specific components of a comprehensive programme is urgent. The cost-effectiveness of large-scale

Table 1 | Cost for each case of RHD prevented in regions where RHD is highly endemic

Population/ outcome	n	Intervention	Unit cost (US$)	Total cost (US$)	DALY averted (US$; calculation‡)	Cost per DALY averted (US$)
Healthy children*	10,000	Vaccine	3–10	30,000–100,000	218 (287.4×0.8×0.95)	137–458
Cases of pharyngitis	100,000	Primary prevention	10–15	1.0–1.5 million	45 (287.4×0.8×0.25)	22,075–33,113
Cases of RF	39	Secondary prevention	5,890–6,620	229,710–258,180	230 (287.4×0.8)	999–1,123
Deaths§	13.65	Surgery	13,949	320,966	172 (287.4×0.6)	1,861

*Hypothetical cohort of children aged 5–14 years observed for 10 years. ‡Calculations are based on the following assumptions: for vaccination, 80% efficacy with coverage of 95%. For primary prevention, 90% efficacy, 70% of patients being symptomatic, approximately 25% of whom might seek a medical consultation. For successful secondary prevention programmes, 100% coverage by the health sector, 100% provider performance, and 80% patient compliance. For surgery (valve replacement or repair), efficacy is assumed to be 60% after 10 years. These assumptions were used to calculate DALYs averted. §Hypothetical number of deaths extrapolated from speculative RF mortality of 35% over 10 years. Figure 29-8 from Michaud, C., Rammohan, R. & Narula, J. Cost-effectiveness analysis of intervention strategies for reduction of the burden of rheumatic heart disease. Rheumatic Fever (eds Narula, J., Virmani, R., Reddy, K. & Tandon, R), © American Registry of Pathology, 1999). Abbreviations: DALY, disability-adjusted life year; RF, rheumatic fever; RHD, rheumatic heart disease.

echocardiographic screening and primary prevention programmes should be among the highest priorities.[17,29] Building a strong economic case for disease control is central to securing government and nongovernmental funds. Programme success will be dependent on sustained core government funding and political will.

Paucity of data and scientific knowledge
Epidemiology

To achieve the global targets set in the 65th World Health Assembly[36] by 2025, the burden of cardiovascular disease (particularly RHD) must be reduced. Global prioritizing of NCDs provides an unprecedented opportunity for the international RHD community to align itself with these WHO targets. Descriptive and prognostic epidemiological data outlining disease prevalence, mortality, and morbidity are critical for developing realistic targets and key performance indicators towards disease control (Box 4). The current global figure for RHD mortality is speculative and likely to be a gross underestimate.[6] Calculations assumed mortality of 1.5% of all patients with RHD per year, extrapolated from data from the USA and Japan.[6] In resource-poor settings, where RHD is most prevalent, mortality has been estimated to be between 3.0% and 12.5% per year.[7–9] Updated estimates of RHD prevalence and RHD-related mortality and morbidity are expected in the next 12 months from the Global Burden of Disease, Injury and Risk Factors study[49] and from the Global Rheumatic Heart Disease Registry.[50] Contemporary mortality data from resource-poor settings, however, remain scarce. Nevertheless, such data are vital to achievement of the overarching goal of reducing mortality from RF and RHD by 25% and for the development of quantifiable progress indicators.

Since the 2005 global disease estimate, a small number of countries have conducted population-based echocardiographic screening surveys for RHD allowing more-comprehensive estimates of disease burden.[17] However, most countries have no epidemiological data to inform the development of national RHD programmes. The development of standardized guidelines on how to perform and conduct systematic echocardiographic screening to estimate disease prevalence would facilitate such epidemiological data collection. Currently, no internationally endorsed definition of a country where RHD is endemic exists. Classification of countries (or regions) as 'nonendemic', 'endemic', or 'hyperendemic' by the WHF would allow for objective and tangible target setting, and co-ordination of global resources and advocacy activities.

Research priorities

Elimination (incidence reduced to below a given threshold) or total eradication (0 deaths per 100,000 of the population per year) of RF and RHD have been cited as the ultimate goals of control activities for these diseases. However, this aspiration has not been clearly defined, nor its feasibility robustly investigated despite frequent references to 'virtual elimination'.[10,51,52] Although total eradication of RF is a noble goal, this target has only

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Box 4 | Improving scientific knowledge of RF and RHD

Descriptive epidemiology
- Define 'endemic' and 'hyperendemic' categories for RF and RHD
- Periodically produce updated estimates of RF and RHD burden
- Develop an atlas of RF and RHD endemic regions
- Support the systematic collation of epidemiological data to inform development of national programmes for RF and RHD control, setting of realistic targets, and appropriate allocation of resources
- Promote a series of carefully selected field sites for intensive epidemiological data collection
- Develop a rapid assessment tool for RF and RHD burden for low-resource settings

Prognostic epidemiology
- Support the development of local, national, and international RHD registers to monitor longitudinal disease outcomes

Basic science
- Improve understanding of RF and RHD pathogenesis (immunology and genetics), with a view to improving diagnosis and treatment
- Define and investigate the feasibility of elimination of RF below a certain threshold as the 'end game' of disease control

Implementation science
- Support the development of regional hubs to address key research questions
- Promote early identification of RHD
- Continue to clarify the role of echocardiographic screening for RHD, and support and promote its use according to World Heart Federation guidelines
- Find effective approaches to primary prevention of RF

Effective vaccine
- Become a lead partner with the Global GAS Vaccine Group with the aim of making a vaccine against RF available by 2025

Abbreviations: GAS, group A β-haemolytic streptococcal; RF, rheumatic fever; RHD, rheumatic heart disease.

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ever been achieved for one human disease—smallpox.[53] For other diseases, such as malaria, elimination has been the target.[54] Clearly elucidating the 'end game' of RF and RHD control will help to define development of research priorities in the field (Box 4).

Global research priorities for RF and RHD were identified in 2011 by Carapetis and Zühlke.[29] First, translating existing knowledge into practical RHD control. Second, early identification of RHD so that preventative measures have an increased chance of success. Third, enhancing our understanding of RF and RHD pathogenesis with a view to improving diagnosis and treatment. Fourth, finding effective approaches to primary prevention of RF and RHD.[29] Addressing these challenges is fundamental to the success of programmes for the control of RF and RHD and for resource allocation. In addition, existing and emerging programmes must be robustly monitored and continuously evaluated to inform best practice. Qualitative and quantitative evaluation of disease control programmes will allow for meaningful dissemination of data, and for implementation strategies to be adapted as required.

Research, implementation of trials of components of RHD control programmes, capacity building to increase quantity and quality of community health workers, specialized training, and sharing of information should be coordinated from regional hubs with a dual focus on research and clinical service delivery. This approach would facilitate knowledge exchange between comparable geographical settings, peer-review

Box 5 | Improving access to health care for RF and RHD

Medication
- Establish a reliable supply of high-quality BPG
- Develop international manufacturing guidelines and methods to monitor the quality of BPG
- Establish a reliable and affordable supply of WHO-listed essential cardiac medication for tertiary prevention
- Develop innovative methods of BPG delivery, such as implants
- Support clinical trials and licensure of anticoagulant medications that do not require therapeutic monitoring for valvular heart disease, for example dabigatran

Technology
- Ensure that community-based anticoagulation monitoring is available and affordable
- Ensure that portable echocardiography is available and affordable to promote early detection of RHD in communities and support clinical management of patients

Surgical capacity
- Increase the capacity for cardiac surgery in countries where RHD is endemic
- Establish links with surgical colleges to support the training of surgeons from countries where RHD is endemic
- Support the practice of rheumatic valve repair in countries where RHD is endemic

Clinical care
- Translate into various languages and disseminate international best-practice guidelines for medical and surgical management of RF and RHD and early echocardiographic diagnosis of RHD
- Promote the uptake of coordinated, register-based control programmes for RF and RHD to improve medical and surgical care and secondary prevention
- Trial new strategies to improve adherence to BPG injection schedules

Abbreviations: BPG, benzathine penicillin G; RF, rheumatic fever; RHD, rheumatic heart disease.

of activities, and professional collegiality. Facilitation, coordination and communication between regional hubs within the domain of the WHF should be administered by the WHF and its members.

Vaccines
A GAS vaccine is required for effective population-level primary prevention of RF (Box 4).[55] GAS vaccine development and human testing has been underway for nearly a century with fluctuating enthusiasm.[55] Involvement of the pharmaceutical industry in the development process has been sporadic and transient. Although a number of major companies retain an interest in GAS vaccine development, few have active internal programmes. The global interest in vaccine development has been renewed over the past decade, with a number of publically funded agencies engaged in the field. Through the National Institute of Allergy and Infectious Diseases, the NIH has provided support and strategic grants that have aided the development of the two main vaccine candidates: multivalent M protein and J8-DT. To reach the goal of successful global licensure of an effective GAS vaccine, a number of elements are necessary: advocacy for vaccine development, involvement of pharmaceutical companies, completion of a plan for vaccine development, and funding. The position statement by the Decade of Vaccine Collaboration on this subject is due for publication in 2013.[56]

Access to health care
A number of consensus-based and evidence-based guidelines exist on how best to prevent, diagnose, and treat RF and RHD.[21,22,57–60] However, these efforts have not translated into improved medical and surgical care worldwide. Barriers to optimal primary and secondary prevention, and medical and surgical care (tertiary prevention), are outlined below (Box 5).

Primary prevention
In the absence of an effective GAS vaccine, definitive control of RF and RHD must incorporate alternative measures of primary prevention of RF. Primary prevention, by treatment of GAS pharyngitis with antibiotics, is effective in preventing RF. However, the cost-effectiveness of sore throat screening programmes and how they should be incorporated into an overall control strategy for RF and RHD requires further clinical and economic evaluation.[29,61] In addition, the role of skin infections in the pathogenesis of RF requires further investigation.[3,29] In some tropical regions with a high incidence of RF, GAS pyoderma is endemic yet rates of GAS pharyngeal carriage and symptomatic pharyngitis are low.[2,3,5,62] Should GAS skin infection be implicated in RF pathogenesis, a new approach to primary prevention would potentially be opened.

Secondary prevention
Intramuscular injection of BPG every 3–4 weeks is required to prevent recurrence of RF and development or progression of RHD.[21,23,61,63] BPG is on the WHO list of essential medicines, but the global supply and quality of this drug has been inconsistent.[64–68] The manufacturing process for the powdered form of BPG, effective dose, and quality parameters are largely undocumented, and the drug is produced by an unknown number of generic manufacturers. A branded, premixed liquid formulation of BPG (Bicillin®, King Pharmaceuticals, Inc., Bristol, TN, USA) is manufactured by Pfizer and is the predominantly used formulation in high-resource settings. The product is expensive and requires a cold supply chain, limiting feasibility in countries where RF and RHD are endemic. Developing ways to monitor quality of BPG, and working with manufacturers to guarantee supply of the powdered form of the drug is a high priority.[29] In addition to inconsistent quality and supply of BPG, low patient compliance with 3–4 weekly BPG injections limits the efficacy of secondary prophylaxis programmes. The determinants of BPG compliance are incompletely understood;[29] however, pain related to injections does not seem to be the predominant factor.[69] Access to health care and providing culturally appropriate health education to patients and their families might be the most important factors.[69] Implantable or nanocarrier-based delivery of BPG would be a potential alternative to monthly injection, but innovation has been limited in this field.[29,70] Approaches to optimize compliance with secondary prophylaxis remain important research questions. For example, a community randomized trial in the Aboriginal population in Australia is currently being conducted to evaluate a health service intervention aimed at improving adherence rates to secondary prophylaxis.[71]

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Box 6 | Improving health education and training

Skilled health workers
- Develop regional training hubs to systematically increase global capacity to control RHD via primary, secondary, and tertiary prevention
- Explore e-learning opportunities for all aspects of control programmes for RF and RHD
- Improve education of clinicians, community health workers, database managers, and allied health staff
- Investigate the role of community health workers in the early echocardiographic diagnosis of RHD

Applied technology
- Identify technology-based solutions to RHD control, for example portable echocardiography, web-based RHD registers, portable anticoagulation monitoring

Cultural and language barriers
- Support the systematic development and dissemination of community educational materials for the public in regions where RF and RHD are endemic
- Support the modification and translation of existing health-care literature (posters, brochures, and online materials) into key languages and dialects
- Improve public access to Internet-based resources on RF and RHD

Clinical training
- Advocate a greater focus on RF and RHD in the training curriculum of doctors and other health professionals worldwide

Abbreviations: RF, rheumatic fever; RHD, rheumatic heart disease.

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Box 7 | Improving health systems

Government engagement
- Advocate the uptake of national register-based comprehensive RF and RHD control programmes to government ministries of health and education

Clinical integration
- Identify how best to integrate activities for RF and RHD control into routine health-service delivery

Partnerships
- Establish partnerships with other global health movements, such as those for maternal and child health and neglected tropical diseases and the NCD Alliance
- Establish formal partnerships with the WHO and other international bodies

National programmes
- Develop a rapid assessment tool to gauge existing national infrastructure for services related to RF and RHD
- Implement such a tool for evaluation of existing programmes for RF and RHD control and to guide programme development and allocation of funds

Abbreviations: NCD, noncommunicable diseases; RF, rheumatic fever; RHD, rheumatic heart disease.

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Tertiary prevention: medical care

Optimal medical care is critical to minimize morbidity and mortality related to RHD. Sequelae of RHD include heart failure, atrial fibrillation, stroke, infective endocarditis, and pregnancy-related complications. The availability of WHO-listed essential cardiac medications, including diuretics, angiotensin-converting-enzyme inhibitors, and β-blockers, has been identified as a modifiable barrier to effective clinical care in many regions where RHD is endemic.[68] Similarly, access to anticoagulant drugs that are required in the setting of arrhythmias and after mechanical valve replacement is often limited. Optimal medical care also requires access to basic diagnostic modalities, including electrocardiographic and echocardiographic monitoring, as well as regular biochemical, microbiological, and anticoagulant blood tests. Of concern, warfarin is the only oral anticoagulant licensed for use in the setting of valvular heart disease and requires regular therapeutic monitoring. Point-of-care portable monitoring of anticoagulant status is feasible and has been shown to improve clinical care.[72] However, the majority of low-income countries, many with geographically dispersed populations, rely on centralized laboratories and are stymied by transport, procurement, and communication issues. The result is often suboptimal therapeutic monitoring of anticoagulation with catastrophic outcomes, particularly embolic and haemorrhagic stroke.[73]

Challenges in the medical care of patients with RHD are epitomized by poor maternal, foetal, and neonatal outcomes in the perinatal period.[74] Late diagnosis of RHD, suboptimal care, and insufficient anticoagulation have been highlighted as key contributing factors.[75] Antenatal screening for RHD and timely referral to tertiary care medical facilities could improve outcomes and warrants investigation.[76]

Tertiary prevention: surgical care

The majority of individuals with RHD do not have access to expensive lifesaving cardiac surgery, as few low-income countries where RHD is endemic have cardiosurgical facilities.[77] For example, access to open heart surgery in Africa is poor; 18 such procedures per million of the population are performed in Africa compared with 1,222 per million in the USA.[14,77] Travelling abroad for cardiac surgery is expensive and often unsustainable on a national level.[78] Increasingly, charities provide funding for individuals from low-income countries to have cardiac surgery abroad, or for overseas surgical teams to visit developing countries. These services are not always accompanied by adequate long-term post-operative care, and rarely take place in countries with coordinated secondary prophylaxis programmes.[29] Embedding surgical services within sustainable health-care systems should be a priority.

Over the past decade, increasing numbers of cardiosurgical centres, predominantly in high-income countries, have developed expertise in valve repair to avoid the need for long-term anticoagulation and therapeutic monitoring. However, in resource-poor settings, where RF and RHD are most prevalent, access to valve repair is minimal and complications related to mechanical valves are unacceptably high.[79,80] For example, some organizations are able to offer only mechanical valve replacement, and not valve repair, to individuals with RHD from low-income environments, presumably due to technical limitations of surgeons attending cardiosurgical missions.

Box 8 | Components of register-based programmes for RF and RHD

- Conducting surveys to determine the burden of disease, community participation, and capacity of primary health-care centres
- Identifying cases of known or suspected RF and RHD
- Promoting the appropriate treatment of streptococcal pharyngitis
- Maintaining a centralized register of all known cases of RF and RHD
- Employing motivated staff to compile data, generate reports, and support health-care staff in the management of patients with RF or RHD
- Standardizing guidelines for monitoring and improving delivery of secondary prophylaxis and medical management
- Engaging a committee to oversee the programme
- Training key health workers and maintaining a skilled health workforce
- Educating patients with RF or RHD and their families
- Promoting awareness of RF and RHD in the community
- Evaluating and reporting the effectiveness of control activities for RF and RHD
- Reporting epidemiological data

Abbreviations: RF, rheumatic fever; RHD, rheumatic heart disease.

Health education and training

With advances in community-based diagnostics and treatment modalities, such as portable echocardiography and anticoagulation monitoring, prevention and medical care for RF and RHD are now within reach even in the most-marginalized communities.[12,13,15,18,81] However, the global shortage of skilled community health workers, nurses, and doctors limits the extent to which established cost-effective methods of RHD control can be delivered (Box 6). This issue is not unique to RF and RHD; an estimated 1 million community health workers are needed in Africa alone to meet the health-related targets of the Millennium Developmental Goals.[82]

Successful national control programmes for RF and RHD have invested heavily in the education of clinicians and in community awareness programmes to promote the importance of primary and secondary prevention.[83] WHF workshops and scientific meetings are avenues for clinical training and education, but only a privileged few from resource-poor regions have the opportunity to attend such meetings, which are often held in well-resourced settings. The establishment of regional hubs for RF and RHD would expand the scope and volume of long-term training and minimize the cost and time required for centralized international meetings.[84]

The WHF RHDnet website[31] hosts up-to-date clinical guidelines and educational materials in a number of languages. Improved access to the Internet in developing countries offers an opportunity for education and training to be delivered from a distance. Cardiologists, sonographers, echocardiographers, and nurses are scarce in resource-poor settings.[14] To make progress, community health-workers must be recruited, trained, and empowered to take a leading role in the control of RF and RHD.

Health systems

Successful prevention of RF and control of RHD requires education, treatment of streptococcal infection (primary prevention), register-based secondary prevention interventions, and the medical and surgical treatment of patients with complications of RHD (Box 7).[51,82,85,86] The successful examples of such comprehensive programmes highlight the need to strengthen primary health care to combat the disease.[52,83] Despite the recommendations of the WHO and the WHF, only a handful of regions within countries such as Australia, Brazil, India, New Zealand, and Tonga have adopted comprehensive register-based control programmes, which are universally accepted to be the most cost-effective method of RF and RHD control.[21] Key components of such programmes are outlined in Box 8.

Integration of RF and RHD control programmes into wider health systems is a high priority to avoid the development of 'unsustainable monolithic programmes'.[21,29] This risk of isolated, disease-specific programmes contributing to inefficient or narrow-spectrum care has been identified over a number of decades.[21,87] Some degree of centralization is necessary for effective delivery of services, given that RHD occurs in mobile and vulnerable populations with the need for long-term follow up and timely delivery of secondary prophylaxis. Centralized registries also enable descriptive and prognostic epidemiological data to be collected, and enable research to be conducted to improve our understanding of the disease.[88] However, this approach must be combined with improved delivery of primary health care.[89]

Mapping the intersections between initiatives for RF and RHD control could identify synergies for programmatic integration and complementary policy agendas. For example, collaboration with other programmes that are also dependent on BPG, such as the control of syphilis and yaws, both of which are caused by the bacterium *Treponema*, could ensure a secure supply of high-quality BPG. Partnering with other health-care specialties, such as obstetrics and emergency medicine, that utilize ultrasonography could allow widespread incorporation of portable ultrasonography equipment that is economically justifiable even in resource-poor settings. At a local level, operational partnerships could enhance service delivery, for example, combining RHD screening with antenatal visits in areas where the disease is endemic.[76] Strengthening partnerships with established groups, such as those focused on maternal and child health, NCDs, and neglected tropical diseases, could support sustainable integration of control programmes for RF and RHD into the wider health system and advance the advocacy agenda on a global scale.

Conclusions

This paper is a declaration of commitment from the WHF Working Group on RF and RHD to fight these diseases, and will form the platform for a detailed operational plan to address the barriers to RF and RHD control. The operational plan will be founded on science, research, and quantifiable progress indicators to impact positively on millions of individuals with RHD and its long-term sequelae. Actions must be prioritized, acknowledging capacity and resource limitations. Priorities include clearly identifying regions where RF and RHD are endemic, securing supplies of high-quality BPG, and developing training hubs to build local capacity. Clinicians, researchers, governments, civil societies, patient advocates, and funding agencies will need to unite to achieve success.

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