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RHEUMATIC HEART DISEASE: CURRENT STATUS OF DIAGNOSIS AND THERAPY

Riya Negi, Medical Student, Samarkand state medical university, Uzbekistan
negiriya836@gmail.com
Akhila Shaji, Medical Student , Samarkand state medical university, Uzbekistan
akhilashaji3103@gmail.com
Fathima Hanna, Medical Student, Samarkand state medical university, Uzbekistan , fthhanna123@gmail.com
Savitha Sreenivasan, Medical Student , Samarkand state medical university, Uzbekistan, savitha1482006@gmail.com

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INTRODUCTION

Rheumatic heart disease (RHD) represents one of the most significant yet preventable causes of cardiovascular morbidity and mortality worldwide. It develops as a chronic sequela of acute rheumatic fever (ARF), an autoimmune inflammatory reaction triggered by infection with Group A beta-hemolytic *Streptococcus* (GAS). Despite being virtually eliminated from high-income nations through improved living conditions and access to healthcare, RHD continues to afflict an estimated **38 to 40.8 million people globally** , with the highest burden concentrated in low- and middle-income countries, particularly in sub-Saharan Africa, South Asia, and the Pacific Islands. The disease predominantly affects children and young adults, with a median age at diagnosis of approximately **28 years**, and disproportionately impacts females, who account for roughly **two-thirds of cases** in endemic regions .

The pathophysiology of RHD begins with an untreated or inadequately treated GAS pharyngitis or skin infection. The host immune response generates cross-reactive antibodies that target cardiac tissues, particularly the valvular endothelium. Over time, repeated episodes of ARF produce progressive structural damage to the heart valves,

most commonly the mitral valve, followed by the aortic valve. This cascade results in valvular stenosis, regurgitation, or a combination of both, ultimately leading to heart failure, atrial fibrillation, stroke, and premature death. The World Health Organization estimates that RHD causes between **260,000 and 300,000 deaths annually** , a figure that underscores the urgent need for strengthened prevention, early diagnosis, and effective therapeutic strategies.

In **2024**, the World Health Organization released landmark guidelines on the prevention and diagnosis of rheumatic fever and rheumatic heart disease , providing the first globally standardized, evidence-based framework for addressing this neglected tropical disease. These guidelines, alongside updated criteria from the World Heart Federation and the American Heart Association, represent a pivotal moment in the global fight against RHD. This review examines the current landscape of RHD diagnosis and therapy, synthesizing recent evidence and guideline recommendations to provide a comprehensive overview for clinicians, policymakers, and public health practitioners.

EPIDEMIOLOGY AND GLOBAL BURDEN

The global distribution of RHD reflects a stark health inequity. Prevalence rates range from fewer than 100 cases per 100,000 population in non-endemic regions such as North America and Western Europe, to over **1,300 per 100,000** in the most affected areas of sub-Saharan Africa and Oceania . A global registry encompassing more than 3,300 RHD cases from 14 lower- to middle-income countries revealed that the majority of patients present with moderate to severe multivalvular disease, complicated by congestive heart failure in **33%** of cases, pulmonary hypertension in **29%**, atrial fibrillation in **22%**, and stroke in **7%** .

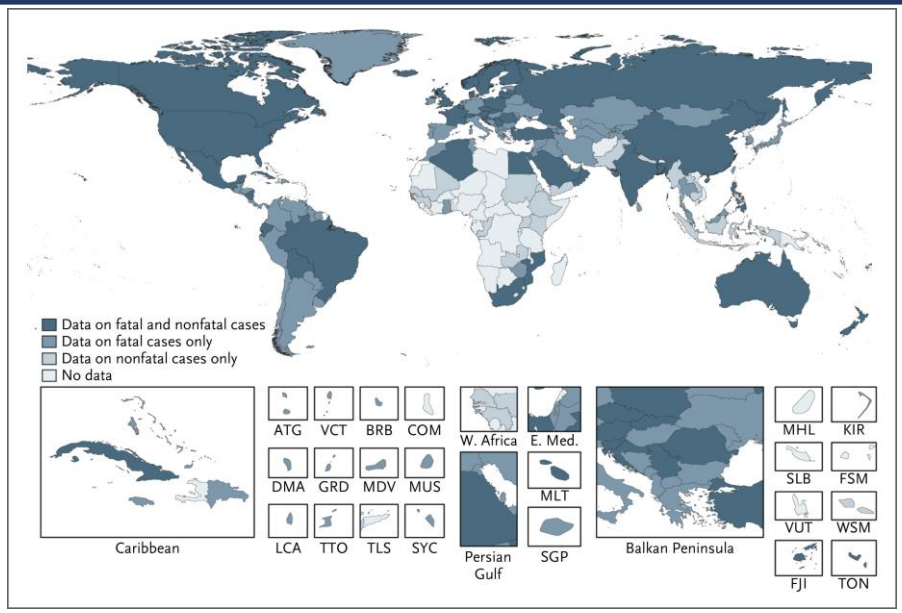

Figure 1. Global distribution of rheumatic heart disease prevalence. Darker shading indicates higher burden, concentrated in sub-Saharan Africa, South Asia, and Oceania. (Source: NEJM Global Burden Study)

The demographic profile of RHD is particularly concerning. The disease strikes during the most productive years of life, with peak incidence occurring between ages **5 and 14** for initial ARF episodes, and diagnostic peaks for chronic RHD in young adults aged **20 to 39 years** . This age distribution has profound socioeconomic consequences, as affected individuals face reduced educational attainment, diminished workforce participation, and substantial out-of-pocket healthcare expenditures. The World Heart Federation has established an ambitious target to reduce the burden of RHD by **25% by 2025** , a goal that requires coordinated multisectoral action spanning healthcare, education, and socioeconomic development.

Several factors contribute to the persistence of RHD in endemic regions. Overcrowding, poor housing conditions, limited access to clean water and sanitation, and inadequate primary healthcare infrastructure facilitate the transmission of GAS. Furthermore, the nonspecific nature of streptococcal pharyngitis symptoms, combined with limited diagnostic capacity at the primary care level, results in high rates of untreated infections. In many endemic settings, up to **one-third of patients with ARF report no history of sore throat** , further complicating early recognition and intervention.

Table 1. Global Burden of Rheumatic Heart Disease by Region (2024–2025 Estimates)

Region	Estimated Cases (millions)	Prevalence per 100,000	Annual Deaths
Sub-Saharan Africa	15.6	1,200–1,400	120,000
South Asia	12.4	800–1,100	85,000
Oceania/Pacific	0.8	900–1,300	8,000
Middle East & North Africa	2.1	400–700	18,000
Latin America	1.9	200–500	12,000
East Asia & Pacific	3.2	150–400	22,000
Europe & North America	0.5	<100	3,000
Global Total	**~38–40.8**	**Variable**	**~260,000–300,000**

Table 1 - Global Burden *Table 1. Global Burden of Rheumatic Heart Disease by Region (2024–2025 Estimates)*

PATHOPHYSIOLOGY AND NATURAL HISTORY

The transition from ARF to chronic RHD follows a well-characterized pathological sequence. During the acute phase, rheumatic carditis manifests as pericarditis or valvulitis, with the mitral valve affected in the vast majority of cases. Isolated aortic valve involvement or right-sided valve disease is relatively uncommon. Acute mitral valvulitis produces characteristic changes including anterior leaflet prolapse, annular dilation, chordal elongation, and varying degrees of mitral regurgitation . These acute lesions are potentially reversible with appropriate anti-inflammatory therapy and antibiotic prophylaxis.

However, when recurrent episodes occur, chronic inflammation leads to irreversible structural remodeling. The valve cusps become rigid and deformed, commissures fuse, and chordae tendineae shorten and thicken. This process transforms the initially regurgitant valve into a stenotic one, or produces combined stenosis-regurgitation lesions. Histopathologically, **Aschoff nodules**—focal collections of lymphocytes and large mononuclear cells within the myocardium—represent the hallmark of rheumatic inflammation and demonstrate the cellular immune basis of the disease .

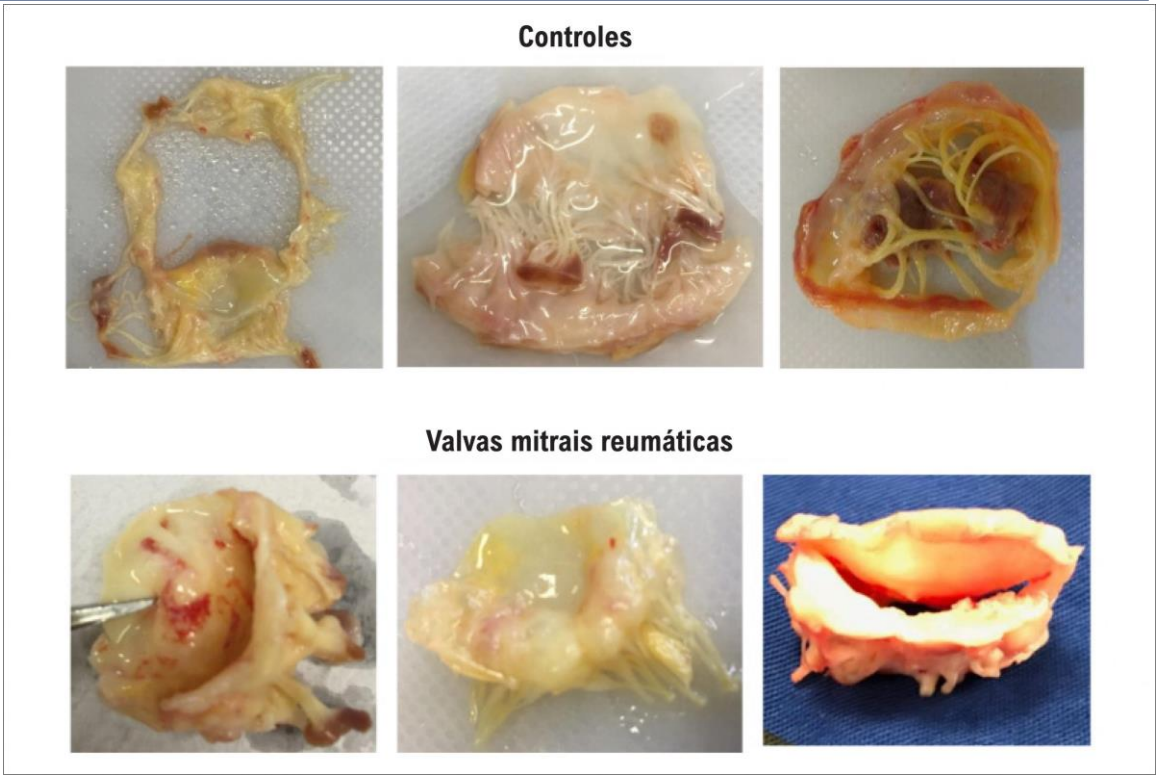

Figure 2. Gross pathology of rheumatic mitral valves (bottom row) compared to normal controls (top row), demonstrating commissural fusion, leaflet thickening, and chordal shortening. (Source: Arquivos Brasileiros de Cardiologia)

The natural history of untreated RHD is one of inexorable progression. Studies from endemic regions indicate that up to **70% of patients with rheumatic carditis during ARF** will eventually develop chronic RHD if not enrolled in secondary prophylaxis programs . The interval between the initial ARF episode and the development of clinically significant valvular disease can range from months to decades, providing a critical window for preventive intervention. Unfortunately, in many resource-limited settings, this window is missed due to delayed diagnosis, poor healthcare-seeking behavior, and fragmented care coordination.

CURRENT DIAGNOSTIC APPROACHES

The diagnosis of ARF and RHD remains challenging, particularly in primary healthcare settings where the disease first manifests. In the absence of a definitive pathognomonic test, clinicians must rely on a combination of clinical criteria, laboratory evidence of GAS infection, and cardiac imaging.

The Modified Jones Criteria

The **Modified Jones Criteria**, originally established in 1944 and most recently revised in **2015** by the American Heart Association, remain the gold standard for ARF diagnosis . These criteria comprise five major manifestations—carditis, polyarthritis, chorea, erythema marginatum, and subcutaneous nodules—and four minor features, including fever, arthralgia, elevated inflammatory markers, and prolonged PR interval on electrocardiography. A diagnosis requires evidence of preceding GAS infection plus either two major criteria or one major and two minor criteria. The 2015 revision notably introduced **subclinical carditis**, defined by abnormal echocardiographic findings in the absence of clinically detectable murmurs, thereby enhancing sensitivity for cardiac involvement .

Despite their widespread acceptance, the Jones Criteria have significant limitations in endemic settings. They miss approximately **10% of true ARF cases** , require laboratory facilities that are often unavailable in rural primary care centers, and can be confounded by endemic diseases such as malaria and viral infections that produce similar clinical features. The transient nature of migratory polyarthritis means that many patients present to secondary care after the arthritis has resolved, further complicating diagnosis.

Echocardiography: The Diagnostic Cornerstone

Echocardiography has emerged as the cornerstone of RHD diagnosis and has substantially improved detection rates compared to clinical auscultation alone. The **World Heart Federation published updated echocardiographic criteria in 2023** , providing well-defined minimal criteria for definite and borderline RHD. These criteria assess leaflet mobility, thickening, subvalvular apparatus changes, valvular calcification, commissural morphology, and leaflet displacement. Color Doppler and spectral Doppler imaging allow quantification of regurgitation severity and transvalvular gradients, essential for therapeutic decision-making.

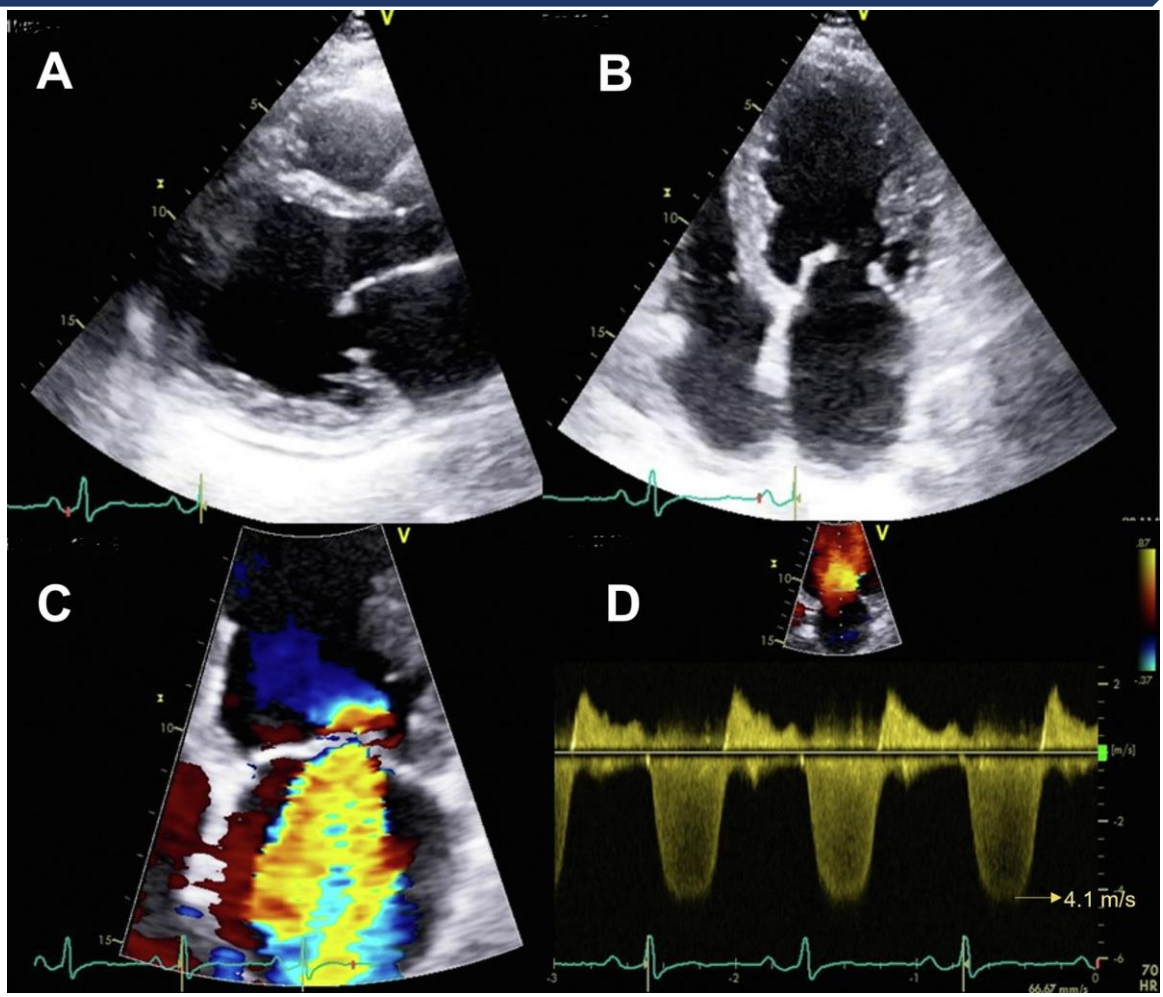

Figure 3. Echocardiographic assessment of rheumatic heart disease. (A) Parasternal long-axis view showing thickened mitral leaflets; (B) Apical four-chamber view; (C) Color Doppler demonstrating severe mitral regurgitation; (D) Continuous-wave Doppler across the mitral valve. (Source: American Society of Echocardiography)

Handheld and Point-of-Care Ultrasound

A particularly promising development is the deployment of **handheld point-of-care echocardiography** for RHD screening. The WHO 2024 guidelines explicitly recommend the use of portable ultrasound devices when standard echocardiography is unavailable . Studies have demonstrated that handheld echo performed by non-expert operators, with remote expert verification, achieves diagnostic accuracy comparable to standard laboratory-based echocardiography . This innovation holds transformative potential for endemic regions, enabling community-based screening of school-aged children and pregnant women—the two populations with the greatest potential to benefit from early detection and secondary prophylaxis.

Simplified Clinical Algorithms

Recognizing the impracticality of applying full Jones Criteria in resource-constrained primary care settings, several endemic countries have developed **simplified clinical algorithms** . These pragmatic approaches emphasize the recognition of acute migratory polyarthritis, new cardiac murmurs, and chorea as sufficient indicators to initiate empiric antibiotic prophylaxis while awaiting specialist evaluation. Although sensitivity is lower than the full Jones Criteria, these algorithms improve detection in settings where delayed diagnosis is the norm and where the consequences of missed ARF are devastating.

THERAPEUTIC STRATEGIES

Primary Prevention

Primary prevention of RHD hinges on the prompt identification and eradication of GAS pharyngitis. The WHO recommends that all suspected cases of GAS pharyngitis be evaluated using either rapid antigen detection testing or throat culture, with treatment initiated within **nine days of symptom onset** to prevent ARF . First-line antibiotic regimens include oral penicillin V or amoxicillin for ten days, or a single intramuscular dose of benzathine penicillin G. For patients with documented penicillin allergy, macrolides such as erythromycin or azithromycin serve as acceptable alternatives, though local resistance patterns must be considered.

The effectiveness of primary prevention is limited by several barriers. In endemic regions, healthcare access is often delayed, with patients presenting weeks after symptom onset. Additionally, the nonspecific nature of pharyngitis leads to widespread empiric antibiotic use, contributing to antimicrobial resistance. Improved community awareness, training of community health workers, and deployment of rapid diagnostic tests at the primary care level are essential strategies to strengthen primary prevention.

Secondary Prophylaxis

Secondary prophylaxis with long-term antibiotics represents the **single most effective intervention** to prevent recurrent ARF and halt progression to severe RHD. **Benzathine penicillin G** administered intramuscularly every three to four weeks remains the cornerstone of secondary prophylaxis, offering superior protection compared to oral penicillin regimens due to guaranteed adherence with each injection

. The WHO 2024 guidelines recommend this approach for all patients with ARF or RHD, including those with minimal echocardiographic criteria detected through screening programs .

The recommended duration of secondary prophylaxis varies according to disease severity and patient age : - **ARF without carditis:** 5 years or until age 21 (whichever is longer) - **ARF with carditis but no residual valvular disease:** 10 years or until age 21 - **Mild RHD:** 10 years or until age 35 - **Moderate to severe valvular disease:** Lifelong, even following surgical valve intervention

Table 3. Secondary Prophylaxis Regimens for Rheumatic Fever and Rheumatic Heart Disease (WHO 2024)

Patient Category	Preferred Regimen	Alternative Regimen	Recommended Duration
ARF without carditis	Benzathine penicillin G 1.2 MU IM every 3–4 weeks	Penicillin V 250 mg PO twice daily	5 years or until age 21 (whichever is longer)
ARF with carditis but no residual valvular disease	Benzathine penicillin G 1.2 MU IM every 3–4 weeks	Penicillin V 250 mg PO twice daily	10 years or until age 21 (whichever is longer)
RHD with mild valvular disease	Benzathine penicillin G 1.2 MU IM every 3–4 weeks	Penicillin V 250 mg PO twice daily	10 years or until age 35 (whichever is longer)
RHD with moderate/severe valvular disease	Benzathine penicillin G 1.2 MU IM every 3–4 weeks	Penicillin V 250 mg PO twice daily (if IM contraindicated)	Lifelong, even after valve surgery
Penicillin-allergic patients	Erythromycin 250 mg PO twice daily	Azithromycin 5 mg/kg (max 250 mg) PO twice weekly	Same as above based on disease severity

Table 3 - Prophylaxis *Table 3. Secondary Prophylaxis Regimens for Rheumatic Fever and Rheumatic Heart Disease (WHO 2024)*

Despite its proven efficacy, secondary prophylaxis faces formidable implementation challenges. Global supply chains for benzathine penicillin have been disrupted in multiple countries, leading to stockouts that directly threaten patient outcomes . The intramuscular injection is painful and requires regular healthcare visits, which poses logistical barriers for rural populations. Adherence rates are suboptimal, with studies indicating that fewer than **40% of patients** in some settings receive more than 80% of prescribed doses . Furthermore, rare but serious adverse reactions—including sudden death attributed to arrhythmic or vasovagal events in patients with severe valvular disease—have generated anxiety among families and healthcare workers, occasionally disrupting control programs .

Medical Management of Heart Failure and Complications

For patients who develop symptomatic RHD, medical therapy focuses on heart failure management and prevention of complications. Loop diuretics such as furosemide form the mainstay of decongestive therapy, often supplemented with spironolactone for

additional diuresis and neurohormonal blockade . Afterload reduction with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers improves cardiac output, particularly in mitral and aortic regurgitation, though these agents must be initiated cautiously in hemodynamically fragile patients. Beta-blockers provide rate control and neurohormonal modulation in appropriate candidates.

Atrial fibrillation and flutter are common complications of advanced RHD, occurring in up to **22% of patients** in endemic registries . Anticoagulation is mandatory for stroke prevention, with vitamin K antagonists historically serving as the standard of care. The ongoing **INVICTUS-VKA trial** is evaluating the noninferiority of direct oral anticoagulants such as rivaroxaban compared to warfarin in RHD-associated atrial fibrillation, with results anticipated to inform future guidelines .

Interventional and Surgical Management

When medical therapy proves insufficient, interventional and surgical options become necessary. **Percutaneous balloon mitral valvuloplasty (PBMV)** is the preferred treatment for symptomatic mitral stenosis with favorable valve anatomy—defined as pliable, non-calcified leaflets without significant regurgitation . PBMV offers lower cost, rapid recovery, and preservation of the native valve compared to surgery. Long-term benefit is observed in approximately **75%** of appropriately selected patients. However, complications including cardiac tamponade and leaflet rupture occur in **2% to 5%** of procedures, necessitating on-site surgical backup.

Surgical mitral valve repair, when performed by experienced surgeons, is feasible in more than **75% of RHD cases** and offers the advantage of avoiding lifelong anticoagulation . However, in RHD-endemic regions where surgical expertise is scarce—sub-Saharan Africa has approximately **one cardiothoracic surgeon per 3.3 million people** —valve replacement remains the more common practice. Mechanical prostheses require lifelong anticoagulation, while bioprosthetic valves carry a higher risk of structural deterioration necessitating reoperation. For patients requiring double-valve surgery, mechanical replacement is typically favored to minimize the risk of redo operations, given the limited surgical capacity in endemic areas.

Access to cardiac surgery represents the most critical gap in RHD care. International declarations and global alliances are working to expand surgical capacity through structured training programs, twinning partnerships between high-volume and low-resource centers, and mobile surgical missions. These efforts, while commendable, remain insufficient to meet the overwhelming need.

EMERGING DEVELOPMENTS AND FUTURE DIRECTIONS

Several promising developments may reshape the RHD landscape in the coming years. **Biomarker discovery research**, including the START study in Australia and New Zealand and the multinational ARF Diagnostic Collaborative Network, aims to identify serological signatures that distinguish ARF from other febrile illnesses . A reliable biomarker would revolutionize diagnosis, particularly in primary care settings where current criteria perform poorly.

Vaccine development against GAS represents the ultimate primary prevention strategy. Multiple vaccine candidates targeting conserved M protein epitopes or other streptococcal antigens are in various stages of preclinical and clinical development . A safe, effective, and affordable GAS vaccine could potentially eliminate RHD at its source, though significant scientific, regulatory, and manufacturing hurdles remain.

Technological innovations in ultrasound are rapidly expanding the reach of echocardiographic screening. Low-cost handheld devices with artificial intelligence-assisted image interpretation are being evaluated for deployment by minimally trained operators in community settings . If validated, these tools could enable population-wide screening at a fraction of the cost of conventional echocardiography.

Finally, **health systems strengthening** remains fundamental to RHD control. The integration of RHD services into existing primary healthcare platforms, such as the WHO Package of Essential Non-Communicable Disease Interventions and its PEN-PLUS extension in the African Region, offers a sustainable pathway to improve access to prevention, diagnosis, and chronic disease management .

CONCLUSION

Rheumatic heart disease persists as a devastating, yet entirely preventable, cause of cardiovascular death and disability among the world's most vulnerable populations. The release of the **WHO 2024 guidelines** marks a watershed moment, providing the first globally endorsed framework for RHD prevention and management. However, translating these guidelines into measurable health outcomes requires addressing the deep structural inequities that sustain the disease.

The diagnostic paradigm is evolving from reliance on clinical criteria alone toward integration of portable echocardiography, simplified algorithms, and future biomarkers. Therapeutically, secondary prophylaxis with benzathine penicillin remains the bedrock of disease control, though supply chain vulnerabilities and adherence

challenges demand innovative solutions. For those who progress to severe valvular disease, balloon valvuloplasty and surgical intervention offer life-saving options, but the profound shortage of cardiac surgical capacity in endemic regions represents a critical unmet need.

Eliminating RHD as a public health problem is an achievable goal, as demonstrated by the historical experience of high-income countries. Achievement of this goal in the 21st century will require sustained political commitment, substantial investment in primary healthcare infrastructure, expansion of surgical and interventional capacity, accelerated research into vaccines and diagnostics, and above all, a steadfast commitment to health equity. The global cardiovascular community must seize the momentum generated by the WHO guidelines to ensure that no child dies from a disease that should have been prevented decades ago.

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