



OPEN ACCESS

EDITED BY

Fidelia Bode-Thomas,
University of Jos, Nigeria

REVIEWED BY

Susy Kotit,
Aswan Heart Center, Egypt
Brian Mendel,
National Cardiovascular Center Harapan Kita,
Indonesia

*CORRESPONDENCE

Maria C. P. Nunes
✉ mcarmo@waymail.com.br

[†]These authors share first authorship

RECEIVED 20 April 2025

ACCEPTED 24 October 2025

PUBLISHED 06 November 2025

CITATION

Mutarelli A, Pantaleao AN, Melo PHC, Nogueira W, Nogueira A, Felix N, Generoso G, Cardoso R, Lupieri A, Aikawa E, Levine RA and Nunes MCP (2025) Global prevalence and sex differences in rheumatic heart disease: a systematic review and updated meta-analysis. *Front. Cardiovasc. Med.* 12:1615158. doi: 10.3389/fcvm.2025.1615158

COPYRIGHT

© 2025 Mutarelli, Pantaleao, Melo, Nogueira, Nogueira, Felix, Generoso, Cardoso, Lupieri, Aikawa, Levine and Nunes. This is an open-access article distributed under the terms of the [Creative Commons Attribution License \(CC BY\)](#). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Global prevalence and sex differences in rheumatic heart disease: a systematic review and updated meta-analysis

Antonio Mutarelli^{1,2†}, Alexandre N. Pantaleao^{1,2†}, Pedro H. C. Melo³, Wilson Nogueira⁴, Alleh Nogueira⁵, Nicole Felix⁶, Giuliano Generoso^{7,8}, Rhanderson Cardoso⁹, Adrien Lupieri¹⁰, Elena Aikawa^{10,11}, Robert A. Levine² and Maria C. P. Nunes^{1*}  on behalf of PRIMA Network

¹School of Medicine, Federal University of Minas Gerais, Belo Horizonte, Brazil, ²Cardiac Ultrasound Lab, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States, ³The Cardiovascular Research Foundation, New York, NY, United States, ⁴School of Medicine, State University of Piauí, Teresina, Brazil, ⁵Medical and Public Health School of Bahia, Salvador, Brazil, ⁶School of Medicine, Federal University of Campina Grande, Campina Grande, Brazil, ⁷Division of Cardiology, Sirio-Libanes Hospital, São Paulo, Brazil, ⁸Center for Clinical and Epidemiological Research, Medical School, São Paulo University, São Paulo, Brazil, ⁹Heart and Vascular Center, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, United States, ¹⁰The Center for Excellence in Vascular Biology, Cardiovascular Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, United States, ¹¹The Center of Interdisciplinary Cardiovascular Sciences, Cardiovascular Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, United States

Background: Rheumatic heart disease (RHD), a sequela of acute rheumatic fever (ARF), remains as the leading cause of acquired cardiac disease in children, posing a significant burden to health systems, especially in low-to-middle-income countries. While ARF shows equal prevalence among sexes in children, clinically manifest RHD in adulthood is strikingly more prevalent in females, with at least a 2:1 ratio. We conducted a meta-analysis to evaluate the global prevalence of RHD and sex disparities alongside risk factors.

Methods: PubMed, Embase, Cochrane, and Lilacs were searched for cross-sectional studies on RHD prevalence in individuals aged 5–20, evaluated through echocardiogram-based screening in endemic areas. Studies relying on auscultation were excluded. RHD was defined as borderline/definite by 2012 WHF criteria or possible/probable/definite by WHO criteria.

Results: Fifty-eight studies with 215,552 subjects were included. Echo-detected RHD prevalence was 24/1,000 (95%-CI: 20–30) globally. Subgroup analyses showed consistently lower RHD prevalence in males (RR: 0.70; 95%-CI: 0.61–0.80; $p < 0.01$). Definite RHD prevalence was 9/1,000 (95%-CI: 7–12), with lower rates among males (RR: 0.71; 95%-CI: 0.59–0.86; $p < 0.01$). Children in private schools (RR: 0.68; 95%-CI: 0.48–0.97; $p = 0.03$), medium-high-income families (RR: 0.57; 95%-CI: 0.41–0.81; $p < 0.01$), and urban areas (RR: 0.49; 95%-CI: 0.26–0.93; $p = 0.03$) exhibited reduced RHD prevalence.

Conclusion: This meta-analysis highlights early gender disparities in RHD, with female predominance preceding established valve lesions. Prevalence remains higher in rural areas, public schools, and low-income families, with global prevalence in endemic regions at 24/1,000.

Systematic Review Registration: <https://www.crd.york.ac.uk/PROSPERO/view/CRD42023491941>, PROSPERO CRD42023491941.

KEYWORDS

rheumatic heart disease, prevalence, sex disparity, meta-analysis, latent RHD

Introduction

Rheumatic heart disease (RHD) disproportionately affects developing countries and remains the predominant acquired heart disease among the young in these regions (1). According to the most recent Global Burden of Disease estimates, RHD prevalence has decreased in high-income countries (2); however, it has increased in low-to-middle-income countries, affecting nowadays over 40 million patients worldwide (2). RHD also accounts for more than 300,000 annual deaths and nine million disability-adjusted life years lost (3).

RHD development involves complex interactions among host susceptibility factors, with sex predisposition playing a crucial role (4, 5). The prevalence ratio of acute rheumatic fever (ARF) between males and females is unclear, but most evidence supports equal prevalence (4, 6, 7). Despite that, the risk of heart valve damage from RHD significantly rises in adult females, especially between the ages of 25 and 45 (8, 9). Chronic RHD has a clear female predominance, with ratios ranging from 2:1 to 4:1 in different studies (9, 10). Nonetheless, the precise age when these sex differences become evident is still a gap in the literature. This epidemiological data is crucial to stimulate further research in sex predisposition in RHD, increasing our understanding of RHD pathophysiology and potentially improving disease management through new therapeutic targets.

Early identification of RHD, prior to established valvular dysfunction, and the prompt initiation of penicillin prophylaxis may prevent disease progression and reduce RHD burden worldwide (1). Moreover, a double-blind placebo-controlled trial indicated that regular use of penicillin G benzathine every four weeks can significantly reduce the risk of progression of echocardiographically detected RHD (11). RHD burden tends to be highest in resource-limited countries owing to social disparities and lack of access to adequate diagnostic tools and therapies. Echocardiographic screening for RHD allows early detection, supporting timely decision-making for initiating antibiotic prophylaxis. (12, 13).

Our study aims to provide current insights into the prevalence of RHD across continents, ages, and risk factors, with a particular focus on sex disparities. Aligned with research priorities set by both the American Heart Association and World Heart Federation (WHF), we conducted a systematic review and updated meta-analysis of the prevalence, severity, and variations of RHD across clinical and socioeconomic subgroups (1, 14). This is a summary of the literature prior to the application of 2023 WHF diagnostic criteria for RHD screening (15).

Methods

This systematic review and meta-analysis were conducted in line with Cochrane recommendations and Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement guidelines (16, 17). Accordingly, it was prospectively

registered with the International Prospective Register of Systematic Reviews (PROSPERO number CRD42023491941).

Eligibility criteria

We restricted inclusion in this meta-analysis to: (i) population-based studies published in English; (ii) that analyzed individuals aged 5–20 years; (iii) from areas with a high burden of RHD; (iv) with a sample size of at least 500 subjects; and (v) reported the prevalence of echocardiogram-assessed latent RHD. We excluded conference abstracts, studies with overlapping populations, retrospective studies, prospective studies not primarily focused on screening of latent RHD, or studies including specific subgroups such as individuals with symptoms of RHD, abnormal cardiac auscultation, or family history of RHD. Studies published in languages other than English were excluded.

RHD was identified through echocardiographic screening in asymptomatic individuals (18). We considered RHD as borderline or definite by the 2012 WHF diagnostic criteria and possible, probable, or definite by the World Health Organization (WHO) diagnostic criteria (WHO criteria were defined by an expert panel under WHO and National Institutes of Health supervision in 2005) (19). Additional information on the diagnostic criteria is available in the supplement.

Search strategy and data extraction

We systematically searched four databases (PubMed, Excerpta Medica Database [Embase], Latin American and Caribbean Center on Health Sciences Information [LILACS], and the Cochrane Central Register of Controlled Trials) from inception to November 2024 using combined subject headings including rheumatic, heart, cardiopathy, valvular, prevalence, screening, surveillance, epidemiology, child, teenager, adolescent, and school. The full search string applied to each database is available in [Supplementary Table S1](#).

To avoid missing data, we proactively requested pertinent information from the authors of the selected articles. Two investigators (AM and ANP) independently assessed search results according to predefined criteria to identify eligible studies. Four investigators (AM, ANP, PHCM, and WN) worked in pairs to extract key study characteristics and endpoints. In both instances, any disagreements were resolved through consensus.

Endpoint definition and subgroups

The study endpoint was the echocardiographic prevalence of RHD in endemic areas. Secondary endpoints encompassed prevalence (i) by continent; (ii) of borderline RHD and definite RHD by 2012 WHF criteria; (iii) by age; (iv) by disease severity; and (v) of the echocardiographic findings.

We also performed the first meta-analysis directly comparing RHD prevalence between different subgroups: (i) males and females; (ii) population from rural and urban areas; (iii) children from private and public schools; and (iv) individuals from low- and medium-to-high income families.

Quality assessment

Two investigators (AM and ANP) independently evaluated the quality of each included article using the risk of bias assessment tool for prevalence studies established by Hoy et al (20). Any discrepancies in the quality assessment were resolved through consensus. The assessment by Hoy et al. comprises ten items categorized into two groups: external validity and internal validity (20).

Each item is given a score of 1 (indicating yes) or 0 (indicating no). The aggregate scores yield an overall quality assessment that categorizes the study as having either a low, moderate, or high risk of bias. A score of 7 or higher indicates a study with a low risk of bias, while 4–6 signifies moderate risk and 3 or lower indicates high risk.

We investigated the potential for small study effects that might be associated with publication bias by closely evaluating funnel plots and assessing the distribution of point estimates against their standard errors. Furthermore, when the number of studies exceeded ten, we conducted Egger's regression analysis as a formal statistical test to detect funnel plot asymmetry (21).

Statistical analysis

To accommodate the anticipated between-study heterogeneity stemming from differences in study populations, assessments, and settings, we calculated binary event prevalence with 95% confidence intervals (CI) using random-effects generalized linear mixed models (GLMM). We applied the Mantel-Hazel random-effects model to pool prevalence ratios (RR) with 95% CI for secondary analyses directly comparing the incidence of events in specific subgroups. *P*-values less than 0.05 were deemed statistically significant.

Estimates from individual studies were pooled using generalized inverse variance weighting. We examined the influence of continuous and categorical covariates on the prevalence or RR of binary events through meta-regressions. The impact of between-study heterogeneity on the estimates was assessed using Cochran's *Q* test and the I^2 statistic. In accordance with Cochrane guidelines, we regarded a *p*-value of less than 0.10 or an I^2 greater than 40% as indicating substantial heterogeneity affecting the estimates (17).

As part of sensitivity analyses, we conducted meta-regressions and leave-one-out analyses to identify sources of heterogeneity and potential effect modifications in the estimated outcomes. All statistical analyses were independently performed by two authors (AM and AN) using R version 4.3.0 (R Foundation for Statistical Computing, Vienna, Austria) (22).

Results

Study selection and characteristics

The initial search yielded 12,871 articles and conference abstracts. Following the removal of 2,588 duplicates, we screened 10,283 articles, of which 10,199 were excluded based on title and abstract screening. Subsequently, we evaluated 84 full-text manuscripts for eligibility, ultimately including 58 that met our criteria, and provided data on latent RHD prevalence (Figure 1) (12, 13, 23–78). This analysis encompassed a total of 215,552 screened children and adolescents. The diagnostic criteria used included WHF criteria in 46 studies, WHO criteria in eight, and other criteria (criteria based on the WHF with only one echocardiographic view) in four.

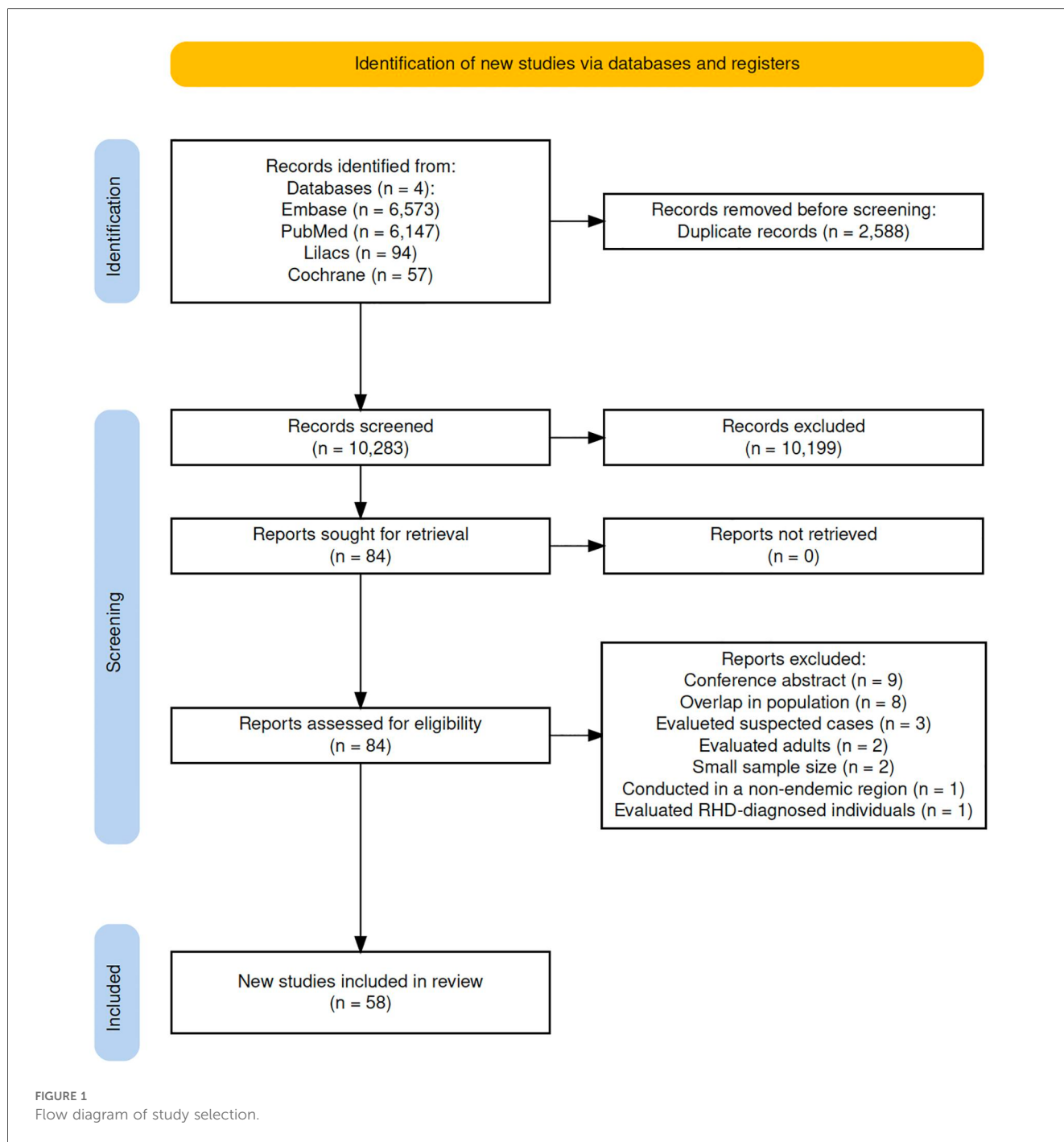
Additional information regarding the excluded studies is available in the supplement (Supplementary Table S2). Seven studies investigated the difference in RHD prevalence among children enrolled in public vs. private schools. Ten studies directly compared RHD prevalence between rural and urban populations, while 38 studies furnished data on RHD prevalence among both male and female participants. The supplement depicts the methodological and baseline clinical characteristics of the included studies (Supplementary Table S3).

Briefly, participant recruitment spanned from 2001 to 2022, with individual study sample sizes varying between 522 and 16,294. Most of the studies [48 (83%)] were conducted within school settings. Africa was the most frequently represented region in terms of study count, with 27 studies, and in terms of the highest number of children and adolescents screened, totaling 73,304 (34%). In contrast, Latin America was least represented, featuring three studies and 16,221 (7.5%) screened children and adolescents.

Prevalence of RHD

The overall prevalence of echo-detected RHD was 24 per 1000 individuals (95% CI 20–30; $I^2 = 98\%$; Figure 2), with similar findings across the continents (Figure 3). When evaluating prevalence using the criteria outlined by both the WHO and the WHF, the definite RHD prevalence rate was 9 per 1,000 individuals (95% CI 7–12; $I^2 = 97\%$; Supplementary Figure S1).

Six studies investigated the prevalence and severity of valvular lesions at the time of diagnosis in definite RHD, revealing moderate-to-severe lesions in 41% (95% CI 28–55; $I^2 = 74\%$; Figure 4). In a more detailed analysis focusing on the 2012 WHF criteria, we scrutinized each diagnostic criterion for both definite RHD (19). The prevalence of criteria A, B, C, and D for definite RHD is illustrated in the supplement (Supplementary Figure S7), with criterion A (mitral regurgitation accompanied by two or more morphological features of RHD) demonstrating the highest prevalence, at 82% (95% CI 75–87; $I^2 = 50\%$; Supplement Figure S7). Complete echocardiographic diagnostic criteria for RHD, as specified by the WHF, are illustrated in the supplement (Supplementary Figure S7).



Among the 28 studies that reported latent RHD prevalence data across sex, there was a lower prevalence in males (RR 0.70; 95% CI 0.61–0.70; $p < 0.01$; $I^2 = 50\%$; **Figure 5A**). Within this set of 28 studies, 15 provided figures for definite RHD, corroborating a lower prevalence among males (RR 0.71; 95% CI 0.59–0.86; $p < 0.01$; $I^2 = 0\%$; **Supplementary Figure S5**).

Ten studies directly compared RHD prevalence between rural and urban populations, uncovering a lower urban prevalence (RR 0.49; 95% CI 0.26–0.93; $p = 0.03$; $I^2 = 88\%$; **Figure 5B**). Seven studies assessed RHD prevalence among children attending public and private schools, demonstrating a lower prevalence among children in private schools (RR 0.68; 95% CI 0.48–0.97;

$p = 0.03$; $I^2 = 73\%$; **Figure 5C**). Five studies compared RHD prevalence between low- and medium-to-high income families, with a lower prevalence in medium-to-high income families (RR 0.57; 95% CI 0.41–0.81; $p < 0.01$; $I^2 = 13\%$; **Figure 5D**).

Oceania had the highest prevalence rate among all continents, 33 per 1,000 individuals (95% CI 22–50; $I^2 = 98\%$; **Figure 3** and **Supplementary Figure S4**), followed by Africa (25 per 1,000, 95% CI 17–35; $I^2 = 98\%$), Latin America (22 per 1,000, 95% CI 6–76; $I^2 = 92\%$), and Asia (20 per 1,000, 95% CI 14–28; $I^2 = 98\%$).

When analyzing the prevalence of echo-detected RHD by WHO regions, the Western Pacific revealed the highest rate, with a prevalence of 31 per 1,000 individuals (95% CI 21–47;

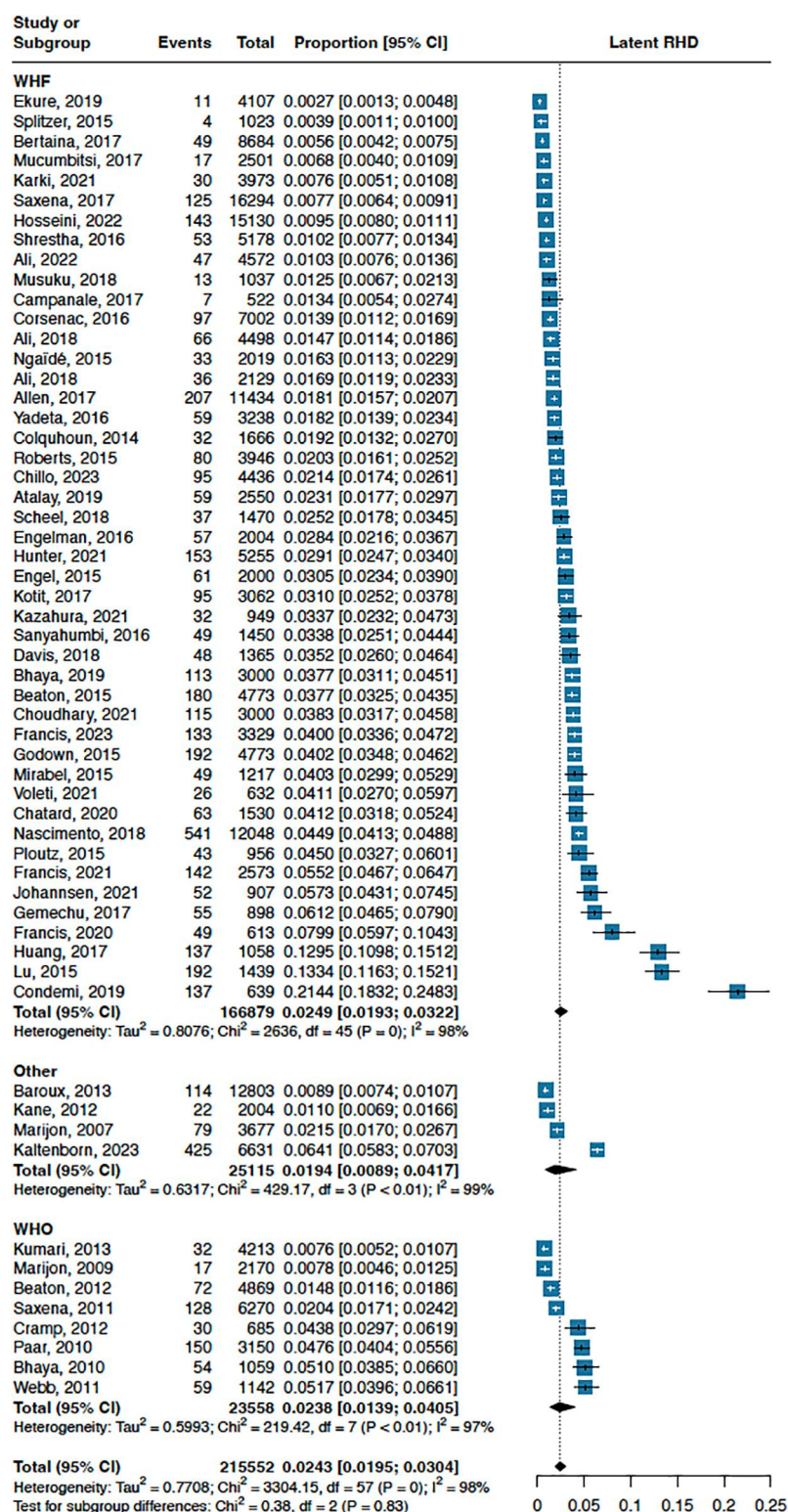


FIGURE 2

Prevalence of latent RHD with different diagnostic criteria (WHF criteria and WHO criteria).

$I^2 = 98\%$; Supplementary Figure S5). African region had a prevalence of 24 per 1,000 (95% CI 17–34; $I^2 = 98\%$), while the Americas presented a prevalence rate of 22 per 1,000 (95% CI 6–76; $I^2 = 92\%$), Eastern Mediterranean of 15 per 1,000 (95% CI

10–22; $I^2 = 95\%$), and the South East Asian of 21 per 1,000 (95% CI 13–32; $I^2 = 98\%$). The European region, represented only by the study of Atalay et al. (30) performed in Turkey, had a prevalence of 23 per 1,000 individuals (95% CI 18–30).

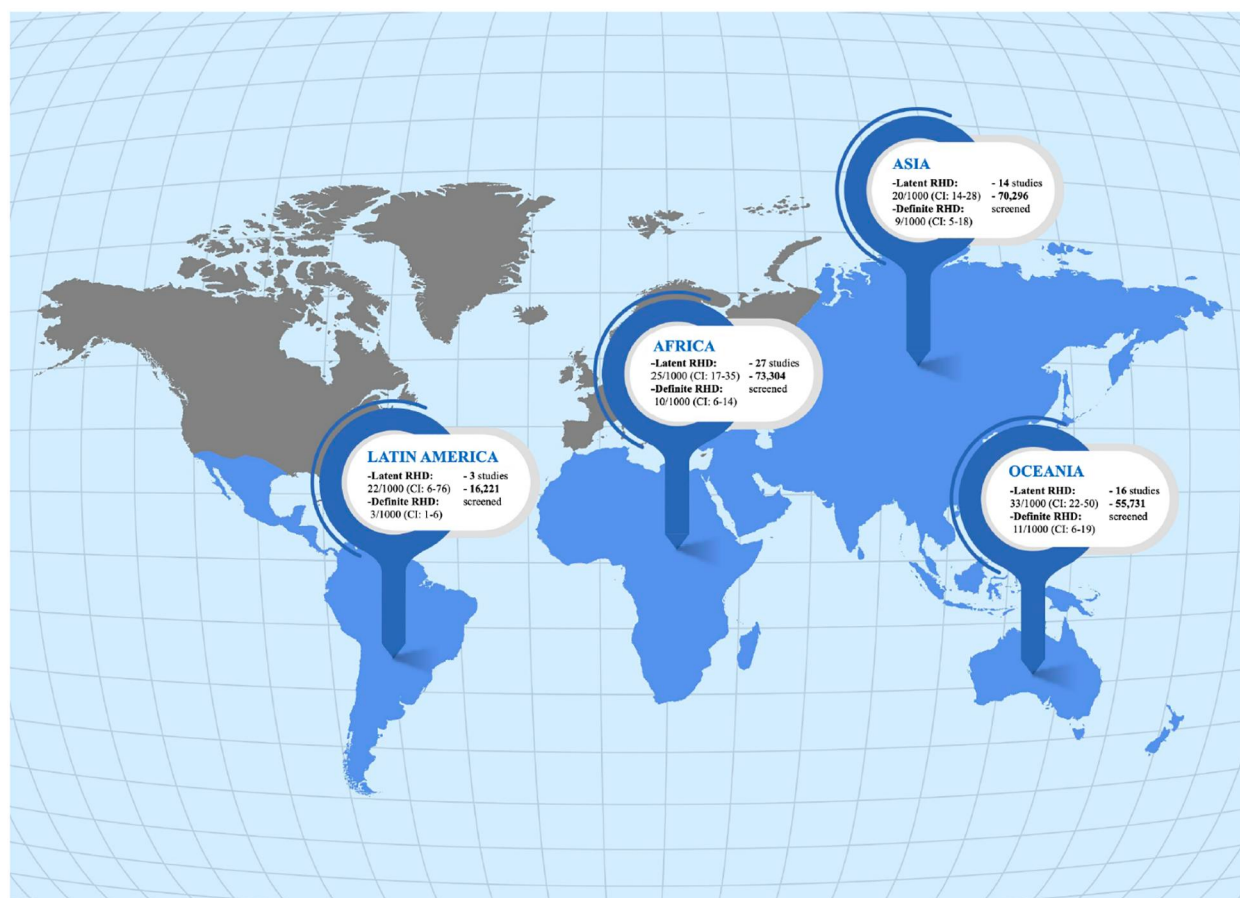


FIGURE 3
Consistent prevalence of latent RHD globally across endemic areas.

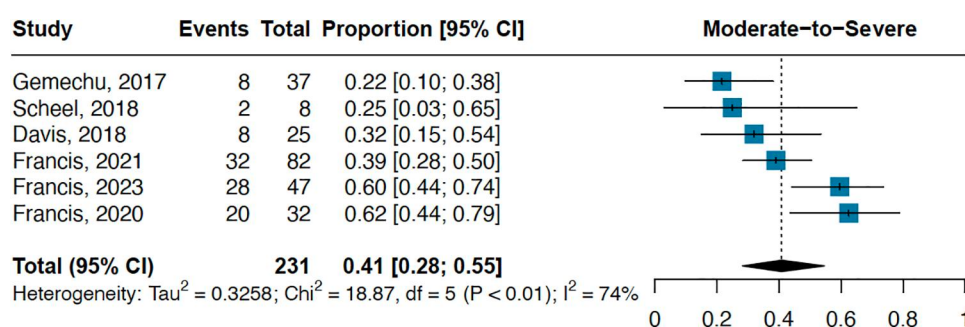
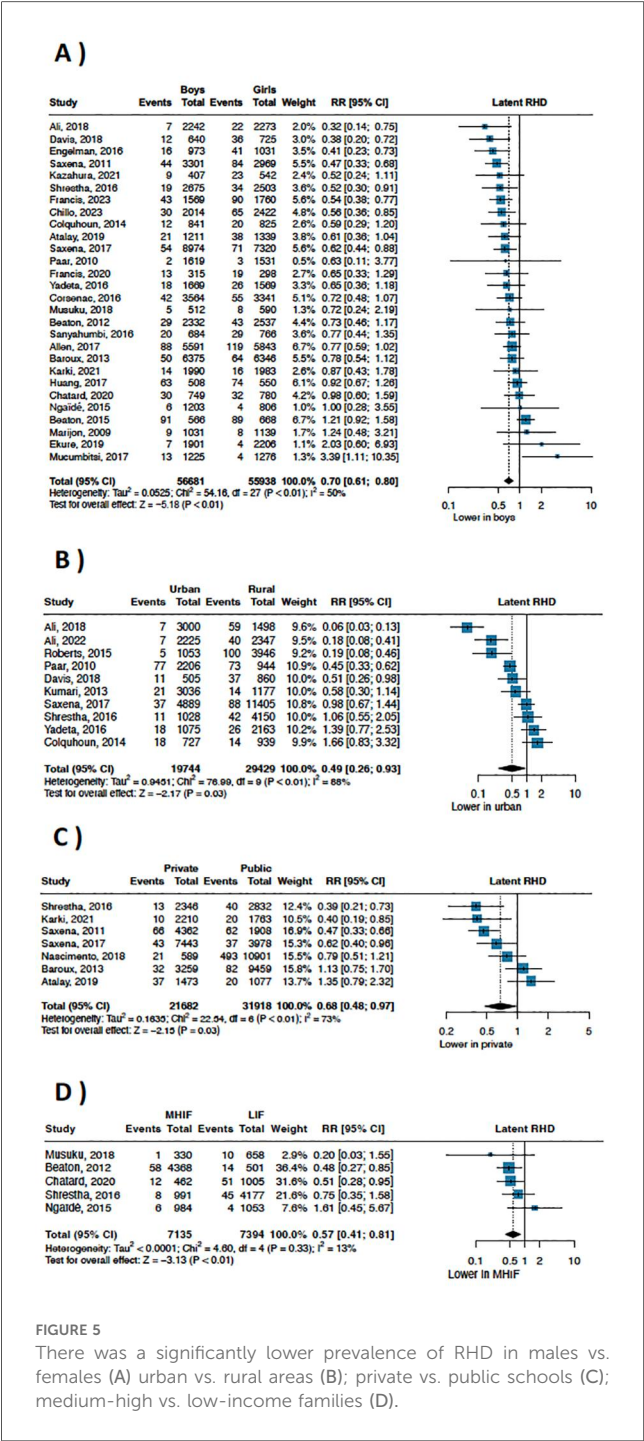


FIGURE 4
Prevalence of 41% of moderate-to-severe definite RHD.

Sensitivity analyses

Meta-regression analyses explored potential sources of heterogeneity and effect-modifications influencing the prevalence of RHD, covering both the overall prevalence and prevalence specific to continents and countries ([Supplementary Table S5](#)).

The initial and final screening years did not yield statistically significant variations in prevalence. In contrast, age and GNI per capita exhibited a positive association with latent RHD prevalence. The supplement presents results for both the leave-one-out sensitivity analysis, which evaluates the influence of individual studies on the pooled estimated prevalence, and the



funnel plots, which indicated asymmetry, possibly due to high study heterogeneity (Supplementary Figure S8, S9). The leave-one-out sensitivity analysis confirms the consistency of our results.

Quality assessment

Out of the 58 studies reviewed, two were found to exhibit a moderate risk of bias, while the remaining 56 studies were deemed to have a low risk of bias. All 58 studies collected data

directly from the participants, and the instruments employed to assess the variables of interest were considered suitable. Given that most of the screenings took place in school settings, non-response bias was minimal. Among the 58 studies, only 14 incorporated a form of randomization in sample selection, by randomizing the schools where the screening occurred. For more detailed information on the ten risks of bias criteria across all studies, refer to the supplement (Supplementary Table S4).

Discussion

We conducted a comprehensive systematic review and meta-analysis to determine the prevalence of RHD, analyzing data from 58 studies encompassing a total of 215,552 children and adolescents. The overarching prevalence of RHD was found to be 24 per 1,000 individuals, and we identified a consistent prevalence in all endemic areas. This meta-analysis differs from prior work by focusing exclusively on echocardiographic screening studies, examining RHD severity and morphological features, and addressing sex disparities in latent RHD. By directly comparing prevalence across subgroups, we confirmed previous knowledge and highlighted vulnerable populations—(i) females, (ii) individuals in rural areas, (iii) students in public schools, and (iv) low-income households. Additionally, latent RHD prevalence exceeded twice in patients aged 10 years or older compared to younger individuals.

Chronic RHD exhibits a higher prevalence among females, with at least a 2:1 ratio (5, 9, 10). Previous studies including patients with rheumatic mitral stenosis, a late stage of RHD, reveal an even higher female predominance, exceeding 80% (10, 79). However, ARF, the primary precursor to RHD, has not been reported as more prevalent in female children and adolescents; most studies suggest a 1:1 ratio (4). Our study extends the findings of a prior meta-analysis, which, via univariate meta-regression, revealed an association between female sex and latent RHD diagnosis (80). In our investigation, this finding was confirmed through a first direct comparison of latent RHD prevalence across sexes, with a ratio female/male of 1.4:1. In summary, current literature supports that (i) ARF has approximately a 1:1 female/male ratio, our meta-analysis showed that it is (ii) 1.4:1 in latent RHD and is well-known that (iii) chronic it is at least 2:1. These findings suggest a tendency towards a higher prevalence of RHD progression in females.

Environmental factors may contribute to the increased risk in females, given the more frequent role of women in caring for children and younger siblings outside their household, which may expose them to a greater risk of group A streptococcus infections (4, 81). In addition, females typically are also more susceptible to autoimmune conditions, which may contribute to these outcomes (82). A recent study conducted proteomic analysis on 30 cardiac valves from patients without RHD and compared them to valves affected by RHD (5). This investigation revealed a higher presence of prothymosin-alpha in RHD-related valve pathologies (5). Notably, this protein, which plays an important pathogenetic role in streptococcal antigen

presentation by HLA molecules and CD8 lymphocyte activation, is linked to estrogen receptor alpha activity, suggesting its potential role as a regulator of the female predisposition to developing RHD (5).

RHD exerts a greater burden on low-to-middle-income nations (14). This may be secondary to superior healthcare in middle-to-high-income nations, including prompt treatment for streptococcal sore throats more widespread implementation of secondary prophylaxis with penicillin, and better living conditions that avoid overcrowding (81). Disparities in healthcare support can also be observed within regions of the same country. Our study revealed, by direct comparison, a heightened prevalence of latent RHD among children from rural areas, those attending public schools, and those from low-income families, all of whom exhibit increased health vulnerability. The study with the highest latent RHD prevalence included African refugees residing in Italy and unveiled a prevalence of 21%, which is tenfold greater than the overall prevalence in our analysis (69). This can indicate the environmental vulnerability associated with the disease and immigrant population.

The WHO first proposed echocardiographic screening criteria for RHD in 2005, introducing the concepts of definite, probable, and possible disease based on echocardiographic findings and epidemiological factors such as residence in endemic areas or a history of ARF. In 2012, the WHF released updated criteria (19), defining only borderline and definite RHD, based solely on echocardiographic parameters (see [Supplementary Appendix](#)). In our analysis, the prevalence by WHO criteria (eight studies) was 24 per 1,000 (95% CI 13–40; $I^2 = 97\%$), and by WHF criteria (46 studies) 25 per 1,000 (95% CI 19–32; $I^2 = 98\%$), with no significant difference. However, rates varied among studies, and Spitzer et al. (66) did a direct comparison in a Peruvian cohort and found prevalence rates of 19.7/1,000 (WHO) vs. 3.9/1,000 (2012 WHF). Most recently, the 2023 WHF classification introduced four stages (A–D) reflecting valve morphology and regurgitation severity (15). This staging recognizes RHD as a spectrum, enhancing the understanding of disease progression. Nevertheless, none of the included studies were performed after the adoption of the new WHF criteria.

Latent RHD was categorized into two groups according to 2012 WHF criteria: definite and borderline (19). Within the definite category, there are further subdivisions, namely mild, moderate, and severe, each associated with distinct disease progression patterns and outcomes. Moderate and severe RHD exhibit a higher propensity for disease progression and are linked to increased mortality (83). One study followed latent RHD patients for over one year, revealing that, during the follow-up, 40% of those with moderate to severe definite RHD experienced disease progression, and 10% succumbed to the condition (83). A meta-analysis on disease progression reported a 7.5% progression rate in definite RHD, with 60% remaining stable; however, one limitation was the variability in follow-up durations across studies (80). Therefore, a large amount of latent RHD patients improve without any treatment. In our pooled analysis, 41% of individuals with definite RHD had

moderate-severe disease. The overall prevalence of definite RHD by WHF among screened children is 9 cases per 1,000, and with moderate-severe definite RHD at 41%, it is plausible that more than 3 children out of every 1,000 in endemic regions may have a more severe form of the disease.

Definite RHD could benefit from a screening program: (i) it typically manifests later in life, stemming mainly from childhood ARF (4); (ii) there is a disease progression, advancing from borderline latent RHD to definite latent RHD and ultimately clinical RHD (80); (iii) Current evidence supports that secondary prophylaxis can prevent disease progression (11), and (iv) sensitive diagnostic examinations as echocardiogram are available for detection (12). Efforts to combat RHD could greatly benefit from the identification of a biomarker. The Leducq Foundation is currently funding multi-center research groups aimed at discovering a biomarker for ARF that could be utilized for effective screening. Nonetheless, some challenges persist, such as the need for specialized echocardiogram interpretation, more studies on secondary prophylaxis, and the necessity for further data to determine the optimal age for screening initiation, as the timing of maximum treatment effectiveness remains uncertain. Our meta-analysis unveiled a higher prevalence of latent RHD in children aged 10 years and older when compared with those younger than 10 years ([Supplementary Figure S6](#)). This outcome aligns with expectations, given that the disease exhibits progressive development over time, with a significant proportion of ARF cases occurring between the ages of 5 and 15 years.

Our study contributes to the discussion on public health strategies for RHD prevention, such as echocardiographic screening and subsequent penicillin prophylaxis. Before these approaches can be implemented as public policy, further studies are needed to assess cost-effectiveness and to compare screened and treated groups with unscreened populations. Based on our findings, initial screening efforts could focus on high-risk settings, such as rural areas, low-income families, and children attending public schools, who are likely to benefit the most. Additionally, a promising strategy to provide region specific data and further understand disease burden is the development of high-quality RHD databases, such as the ARG1 from Egypt (84).

Two previous meta-analyses (2014 and 2019) examined the global prevalence of latent RHD (80, 85). However, the current meta-analysis provides a more focused and comprehensive approach by narrowing the scope to echocardiogram-based screening studies in endemic regions. This strategy allowed us to delve deeper into at-risk groups, identifying higher susceptibility among females, public school children, rural residents, and individuals from low-income families. Additionally, we assessed prevalence patterns based on echocardiogram criteria, mitral lesion types, and the prevalence of moderate and severe cases. Importantly, our systematic search incorporated 24 new studies, screening over 85,000 individuals, significantly expanding the evidence base since the last global meta-analysis. This updated and detailed perspective highlights emerging trends and provides critical insights to guide targeted interventions and policy development in high-burden regions.

Our study has limitations. As a worldwide systematic review, we utilized data with varying inclusion criteria, ethnicities, baseline characteristics, and risk factors. While these factors contributed to a broader result, they also increased heterogeneity. To mitigate this, we only included studies that used echocardiogram as a screening tool due to its high sensitivity compared to other methods. Nevertheless, the consistency of overall prevalence across the endemic areas despite different clinical and geographic settings suggests that the current results are reproducible. Furthermore, we scrutinized the findings by constructing a meta-regression with several potential confounding or modifier variables. Ultimately, the heterogeneity may simply be secondary to different regional prevalences between studies.

Conclusion

The present study reveals a higher prevalence of RHD in females, consistent with patterns observed in chronic RHD. By highlighting the early-stage female predominance in latent RHD, our study provides support for the concept that gender disparity in RHD emerges at an early stage, preceding the onset of heart valve damage. Moreover, there is a higher prevalence in children from rural areas, public schools, and low-income families, emphasizing the need for targeted interventions in these vulnerable populations.

Data availability statement

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author.

Author contributions

AM: Formal analysis, Writing – original draft, Project administration, Investigation, Conceptualization, Methodology, Writing – review & editing. AP: Conceptualization, Data curation, Investigation, Writing – review & editing, Writing – original draft. PM: Project administration, Writing – review & editing, Writing – original draft, Supervision, Investigation. WN: Data curation, Methodology, Writing – review & editing, Writing – original draft, Investigation. AN: Writing – review & editing, Formal analysis, Investigation, Data curation, Methodology, Writing – original draft. NF: Investigation, Writing – review & editing, Methodology, Data curation, Writing – original draft. GG: Supervision, Investigation, Writing – review & editing, Methodology, Writing – original draft. RC: Writing – original draft, Methodology, Writing – review & editing, Supervision, Investigation. AL: Investigation, Writing – review & editing, Data curation, Writing – original

draft, Methodology. EA: Writing – review & editing, Supervision, Writing – original draft, Methodology. RL: Supervision, Methodology, Writing – review & editing, Writing – original draft. MN: Methodology, Supervision, Writing – original draft, Writing – review & editing.

Funding

The author(s) declare that financial support was received for the research and/or publication of this article. Supported in part by the Leducq Foundation PRIMA (Preventing Rheumatic Injury bioMarker Alliance) Network grant 22ARF02. The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The author(s) declared that they were an editorial board member of Frontiers, at the time of submission. This had no impact on the peer review process and the final decision.

Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fcvm.2025.1615158/full#supplementary-material>

References

- Remenyi B, Carapetis J, Wyber R, Taubert K, Mayosi BM, World Heart Federation. Position statement of the world heart federation on the prevention and control of rheumatic heart disease. *Nat Rev Cardiol.* (2013) 10(5):284–92. doi: 10.1038/nrcardio.2013.34
- Ou Z, Yu D, Liang Y, Wu J, He H, Li Y, et al. Global burden of rheumatic heart disease: trends from 1990 to 2019. *Arthritis Res Ther.* (2022) 24(1):138. doi: 10.1186/s13075-022-02829-3
- Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, et al. Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 study. *J Am Coll Cardiol.* (2020) 76(25):2982–3021. doi: 10.1016/j.jacc.2020.11.010
- 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. doi: 10.1038/nrdp.2015.84
- Passos LSA, Jha PK, Becker-Greene D, Blaser MC, Romero D, Lupieri A, et al. Prothymosin alpha: a novel contributor to estradiol receptor alpha-mediated CD8+ T-cell pathogenic responses and recognition of type 1 collagen in rheumatic heart valve disease. *Circulation.* (2022) 145(7):531–48. doi: 10.1161/CIRCULATIONAHA.121.057301
- Mutarelli A, Armelin L, Pantaleão AN, Nogueira A, Machado CJ, Silva JLP, et al. Temporal trends in the epidemiology of acute rheumatic fever: a nationwide analysis from 2008 to 2022. *Arq Bras Cardiol.* (2025) 122(7):e20240763. doi: 10.36660/abc.20240763
- Sadiq NM, Afshan G, Qureshi AU, Sadiq M. Current clinical profile of acute rheumatic fever and recurrent acute rheumatic fever in Pakistan. *Pediatr Cardiol.* (2024) 45(2):240–7. doi: 10.1007/s00246-023-03378-5
- Lawrence JG, Carapetis JR, Griffiths K, Edwards K, Condon JR. Acute rheumatic fever and rheumatic heart disease: incidence and progression in the northern territory of Australia, 1997 to 2010. *Circulation.* (2013) 128(5):492–501. doi: 10.1161/CIRCULATIONAHA.113.001477
- Negi PC, Kandoria A, Asotra S, Ganju NK, Merwaha R, Sharma R, et al. Gender differences in the epidemiology of Rheumatic Fever/Rheumatic heart disease (RF/RHD) patient population of hill state of northern India; 9 years prospective hospital based, HP-RHD registry. *Indian Heart J.* (2020) 72(6):552–6. doi: 10.1016/j.ijhi.2020.09.011
- Nunes MCP, Tan TC, Elmariyah S, Lodi-Junqueira L, Nascimento BR, do Lago R, et al. Net atrioventricular compliance is an independent predictor of cardiovascular death in mitral stenosis. *Heart.* (2017) 103(23):1891–8. doi: 10.1136/heartjnl-2016-310955
- Beaton A, Okello E, Rwebembera J, Grobler A, Engelman D, Alepere J, et al. Secondary antibiotic prophylaxis for latent rheumatic heart disease. *N Engl J Med.* (2022) 386(3):230–40. doi: 10.1056/NEJMoa2102074
- Marijon E, Ou P, Celermajor DS, Ferreira B, Mocumbi AO, Jani D, et al. Prevalence of rheumatic heart disease detected by echocardiographic screening. *N Engl J Med.* (2007) 357(5):470–6. doi: 10.1056/NEJMoa065085
- Ekure EN, Amadi C, Sokunbi O, Kalu N, Olusegun-Joseph A, Kushimo O, et al. Echocardiographic screening of 4107 Nigerian school children for rheumatic heart disease. *Trop Med Int Health.* (2019) 24(6):757–65. doi: 10.1111/tmi.13235
- Kumar RK, Antunes MJ, Beaton A, Mirabel M, Nkomo VT, Okello E, et al. Contemporary diagnosis and management of rheumatic heart disease: implications for closing the gap: a scientific statement from the American Heart Association. *Circulation.* (2020) 142(20):e337–57. doi: 10.1161/CIR.0000000000000921
- Rwebembera J, Marangou J, Mwita JC, Mocumbi AO, Mota C, Okello E, et al. 2023 World heart federation guidelines for the echocardiographic diagnosis of rheumatic heart disease. *Nat Rev Cardiol.* (2024) 21(4):250–63. doi: 10.1038/s41569-023-00940-9
- Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Br Med J.* (2021) 372:n71. doi: 10.1136/bmj.n71
- Cumpston M, Li T, Page MJ, Chandler J, Welch VA, Higgins JP, et al. Updated guidance for trusted systematic reviews: a new edition of the cochrane handbook for systematic reviews of interventions. *Cochrane Database Syst Rev.* (2019) 10(10):ED000142. doi: 10.1002/14651858.ED000142
- Scheel A, Miller KM, Beaton A, Katzenellenbogen J, Parks T, Cherian T, et al. Standardization of epidemiological surveillance of rheumatic heart disease. *Open Forum Infect Dis.* (2022) 9(Suppl 1):S50–6. doi: 10.1093/ofid/ofac250
- Reményi B, Wilson N, Steer A, Ferreira B, Kado J, Kumar K, et al. World heart federation criteria for echocardiographic diagnosis of rheumatic heart disease—an evidence-based guideline. *Nat Rev Cardiol.* (2012) 9(5):297–309. doi: 10.1038/nrcardio.2012.7
- Hoy D, Brooks P, Woolf A, Blyth F, March L, Bain C, et al. Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement. *J Clin Epidemiol.* (2012) 65(9):934–9. doi: 10.1016/j.jclinepi.2011.11.014
- Sterne JAC, Sutton AJ, Ioannidis JPA, Terrin N, Jones DR, Lau J, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *Br Med J.* (2011) 343:d4002. doi: 10.1136/bmj.d4002
- Balduzzi S, Rücker G, Schwarzer G. How to perform a meta-analysis with R: a practical tutorial. *BMJ Ment Health.* (2019) 22(4):153–60. doi: 10.1136/ebmental-2019-300117
- Allen M, Allen J, Naseri T, Gardner R, Tolley D, Allen L. A rapid echocardiographic screening protocol for rheumatic heart disease in Samoa: a high prevalence of advanced disease. *Cardiol Young.* (2017) 27(8):1599–605. doi: 10.1017/S1047951117000907
- Francis JR, Fairhurst H, Yan J, Fernandes Monteiro A, Lee AM, Maurays J, et al. Abbreviated echocardiographic screening for rheumatic heart disease by nonexperts with and without offsite expert review: a diagnostic accuracy study. *J Am Soc Echocardiogr.* (2023) 36(7):733–45. doi: 10.1016/j.echo.2023.02.007
- Corsenac P, Heenan RC, Roth A, Rouchon B, Guillot N, Hoy D. An epidemiological study to assess the true incidence and prevalence of rheumatic heart disease and acute rheumatic fever in New Caledonian school children. *J Paediatr Child Health.* (2016) 52(7):739–44. doi: 10.1111/jpc.13185
- Scheel A, Ssinabulya I, Aliku T, Bradley-Hewitt T, Clauss A, Clauss S, et al. Community study to uncover the full spectrum of rheumatic heart disease in Uganda. *Heart.* (2019) 105(1):60–6. doi: 10.1136/heartjnl-2018-313171
- Gemechu T, Parry EHO, Yacoub MH, Phillips DIW, Kotit S. Community-based prevalence of rheumatic heart disease in rural Ethiopia: five-year follow-up. *PLoS Negl Trop Dis.* (2021) 15(10):e0009830. doi: 10.1371/journal.pntd.0009830
- Nascimento BR, Sable C, Nunes MCP, Diamantino AC, Oliveira KKB, Oliveira CM, et al. Comparison between different strategies of rheumatic heart disease echocardiographic screening in Brazil: data from the PROVAR (rheumatic valve disease screening program) study. *J Am Heart Assoc.* (2018) 7(4):e008039. doi: 10.1161/JAHA.117.008039
- Bhaya M, Panwar S, Sharma A, Chaudhary D, Singh S, Beniwal R, et al. Comparison of the newer proposed diagnostic score with the world heart federation criteria for echocardiographic detection of rheumatic heart disease. *Echocardiography.* (2019) 36(12):2259–64. doi: 10.1111/echo.14547
- Saxena A, Desai A, Narvencar K, Ramakrishnan S, Thangjam RS, Kulkarni S, et al. Echocardiographic prevalence of rheumatic heart disease in Indian school children using world heart federation criteria—a multi site extension of RHEUMATIC study (the e-RHEUMATIC study). *Int J Cardiol.* (2017) 249:438–42. doi: 10.1016/j.ijcard.2017.09.184
- Ali S, Domi S, Abbo B, Abbas R, Bushari T, Al Awad K, et al. Echocardiographic screening for rheumatic heart disease in 4 515 Sudanese school children: marked disparity between two communities. *Cardiovasc J Afr.* (2018) 29(5):273–7. doi: 10.5830/CVJA-2018-022
- Atalay S, Tutar E, Uçar T, Topçu S, Köse SK, Doğan MT. Echocardiographic screening for rheumatic heart disease in Turkish schoolchildren. *Cardiol Young.* (2019) 29(10):1272–7. doi: 10.1017/S1047951119002075
- Kane A, Mirabel M, Touré K, Périer MC, Fazaa S, Tafflet M, et al. Echocardiographic screening for rheumatic heart disease: age matters. *Int J Cardiol.* (2013) 168(2):888–91. doi: 10.1016/j.ijcard.2012.10.090
- Colquhoun SM, Kado JH, Remenyi B, Wilson NJ, Carapetis JR, Steer AC. Echocardiographic screening in a resource poor setting: borderline rheumatic heart disease could be a normal variant. *Int J Cardiol.* (2014) 173(2):284–9. doi: 10.1016/j.ijcard.2014.03.004
- Huang JH, Favazza M, Legg A, Holmes KW, Armsby I, Eliapo-Unutoa I, et al. Echocardiographic screening of rheumatic heart disease in American Samoa. *Pediatr Cardiol.* (2018) 39(1):38–44. doi: 10.1007/s00246-017-1724-4
- Ali SKM, Mohamed SH, Mohammedain H, Haj AMA. Echocardiographic surveillance of rheumatic heart disease in west and north darfur compared with kassala state: socioeconomic or genetic differences? *Sudanese J Paediatr.* (2022) 22(2):131. doi: 10.24911/SJP.106-1657904885
- Beaton A, Okello E, Lwabi P, Mondo C, McCarter R, Sable C. Echocardiography screening for rheumatic heart disease in Ugandan schoolchildren. *Circulation.* (2012) 125(25):3127–32. doi: 10.1161/CIRCULATIONAHA.112.092312
- Karki P, Uranw S, Bastola S, Mahato R, Shrestha NR, Sherpa K, et al. Effectiveness of systematic echocardiographic screening for rheumatic heart disease in Nepalese schoolchildren: a cluster randomized clinical trial. *JAMA Cardiology.* (2021) 6(4):1. doi: 10.1001/jamacardio.2020.7050
- Ploutz M, Lu JC, Scheel J, Webb C, Ensing GJ, Aliku T, et al. Handheld echocardiographic screening for rheumatic heart disease by non-experts. *Heart.* (2016) 102(1):35–9. doi: 10.1136/heartjnl-2015-308236

40. Ali S, Awadallah H, Hamim AA, Hussein HA, Sunni MAAA, Bushari T, et al. Handheld echocardiography for screening and control of rheumatic heart disease study in gezira state, Sudan: a double approach model. *Cardiovasc Diagn Ther.* (2018) 8(4):500. doi: 10.21037/cdt.2018.07.04
41. Godown J, Lu JC, Beaton A, Sable C, Mirembe G, Sanya R, et al. Handheld echocardiography versus auscultation for detection of rheumatic heart disease. *Pediatrics.* (2015) 135(4):e939–944. doi: 10.1542/peds.2014-2774
42. Bhaya M, Panwar S, Beniwal R, Panwar RB. High prevalence of rheumatic heart disease detected by echocardiography in school children. *Echocardiography.* (2010) 27(4):448–53. doi: 10.1111/j.1540-8175.2009.01055.x
43. Baroux N, Rouchon B, Huon B, Germain A, Meunier JM, D'Ortenzio E. High prevalence of rheumatic heart disease in schoolchildren detected by echocardiography screening in New Caledonia. *J Paediatr Child Health.* (2013) 49(2):109–14. doi: 10.1111/jpc.12087
44. Francis JR, Fairhurst H, Hardefeldt H, Brown S, Ryan C, Brown K, et al. Hyperendemic rheumatic heart disease in a remote Australian town identified by echocardiographic screening. *Med J Aust.* (2020) 213(3):118–23. doi: 10.5694/mja2.50682
45. Voleti S, Adelbai M, Hovis I, Colyer J, Burns KM, Lewis EO, et al. Novel handheld ultrasound technology to enhance non-expert screening for rheumatic heart disease in the republic of Palau: a descriptive study. *J Paediatr Child Health.* (2021) 57(7):1089–95. doi: 10.1111/jpc.15409
46. Webb RH, Wilson NJ, Lennon DR, Wilson EM, Nicholson RW, Gentles TL, et al. Optimising echocardiographic screening for rheumatic heart disease in New Zealand: not all valve disease is rheumatic. *Cardiol Young.* (2011) 21(4):436–43. doi: 10.1017/S1047951111000266
47. Bertaina G, Rouchon B, Huon B, Guillot N, Robillard C, Noël B, et al. Outcomes of borderline rheumatic heart disease: a prospective cohort study. *Int J Cardiol.* (2017) 228:661–5. doi: 10.1016/j.ijcard.2016.11.234
48. Choudhary D, Panwar SR, Gupta BK, Panwar RB, Gupta R, Bhaya M, et al. Prevalence and follow-up of subclinical rheumatic heart disease among asymptomatic school children in a north-western district of India based on the world heart federation echocardiographic criteria. *Echocardiography.* (2021) 38(7):1173–8. doi: 10.1111/echo.15035
49. Saxena A, Ramakrishnan S, Roy A, Seth S, Krishnan A, Misra P, et al. Prevalence and outcome of subclinical rheumatic heart disease in India: the RHEUMATIC (rheumatic heart Echo utilisation and monitoring actuarial trends in Indian children) study. *Heart.* (2011) 97(24):2018–22. doi: 10.1136/heartjnl-2011-300792
50. Kotit S, Said K, ElFaramawy A, Mahmoud H, Phillips DIW, Yacoub MH. Prevalence and prognostic value of echocardiographic screening for rheumatic heart disease. *Open Heart.* (2017) 4(2):e000702. doi: 10.1136/openhrt-2017-000702
51. Kazahura PT, Mushi TL, Pallangyo P, Janabi M, Kisenge R, Albaghdadi M, et al. Prevalence and risk factors for subclinical rheumatic heart disease among primary school children in Dar es Salaam, Tanzania: a community based cross-sectional study. *BMC Cardiovasc Disord.* (2021) 21(1):610. doi: 10.1186/s12872-021-02377-9
52. Kumari NR, Raju IB, Patnaik AN, Barik R, Singh A, Pushpanjali A, et al. Prevalence of rheumatic and congenital heart disease in school children of Andhra Pradesh, south India. *J Cardiovasc Dis Res.* (2013) 4(1):11. doi: 10.1016/j.jcdr.2012.11.003
53. Yadeta D, Hailu A, Haileamlak A, Gedlu E, Guteta S, Tefera E, et al. Prevalence of rheumatic heart disease among school children in Ethiopia: a multisite echocardiography-based screening. *Int J Cardiol.* (2016) 221:260–3. doi: 10.1016/j.ijcard.2016.06.232
54. Engel ME, Haileamlak A, Zühlke L, Lemmer CE, Nkepu S, van de Wall M, et al. Prevalence of rheumatic heart disease in 4720 asymptomatic scholars from South Africa and Ethiopia. *Heart.* (2015) 101(17):1389–94. doi: 10.1136/heartjnl-2015-307444
55. Paar JA, Berrios NM, Rose JD, Cáceres M, Peña R, Pérez W, et al. Prevalence of rheumatic heart disease in children and young adults in Nicaragua. *Am J Cardiol.* (2010) 105(12):1809–14. doi: 10.1016/j.amjcard.2010.01.364
56. Cosimo Marco Campanale CMC, Di Gioia G, Di Maria S, Marullo F, Fittipaldi M, Creta A, et al. Australasia Medical Journal. (Accessed 2024 November 17). Prevalence of Rheumatic Heart Disease in North Madagascar: An echocardiographic screening in young and adult populations. Available from: Available online at: doi: 10.21767/AMJ.2017.3047
57. Ngaidé AA, Mbaye A, Kane A, Ndiaye MB, Jobe M, Bodian M, et al. Prevalence of rheumatic heart disease in Senegalese school children: a clinical and echocardiographic screening. *Heart Asia.* (2015) 7(2):40–5. doi: 10.1136/heartasia-2015-010664
58. Musuku J, Engel ME, Musonda P, Lungu JC, Machila E, Schwaninger S, et al. Prevalence of rheumatic heart disease in Zambian school children. *BMC Cardiovasc Disord.* (2018) 18(1):135. doi: 10.1186/s12872-018-0871-8
59. Mucumbitsi J, Bulwer B, Mutesa L, Ndahindwa V, Semakula M, Rusingiza E, et al. Prevalence of rheumatic valvular heart disease in Rwandan school children: echocardiographic evaluation using the world heart federation criteria. *Cardiovasc J Afr.* (2017) 28(5):285–92. doi: 10.5830/CVJA-2017-007
60. Hosseini S, Samiei N, Tabib A, Bakhshandeh H, Rezaei Y, Parsaee M, et al. Prevalence of structural heart diseases detected by handheld echocardiographic device in school-age children in Iran: the SHED LIGHT study. *Glob Heart.* (2022) 17(1):39. doi: 10.5334/gh.1121
61. Shrestha NR, Karki P, Mahto R, Gurung K, Pandey N, Agrawal K, et al. Prevalence of subclinical rheumatic heart disease in eastern Nepal: a school-based cross-sectional study. *JAMA Cardiol.* (2016) 1(1):89–96. doi: 10.1001/jamacardio.2015.0292
62. Roberts KV, Maguire GP, Brown A, Atkinson DN, Remenyi B, Wheaton G, et al. Rheumatic heart disease in indigenous children in northern Australia: differences in prevalence and the challenges of screening. *Med J Aust.* (2015) 203(5):221.e1–7. doi: 10.5694/mja15.00139
63. Davis K, Remenyi B, Draper AD, Dos Santos J, Bayley N, Paratz E, et al. Rheumatic heart disease in Timor-Leste school students: an echocardiography-based prevalence study. *Med J Aust.* (2018) 208(7):303–7. doi: 10.5694/mja17.00666
64. Marijon E, Celermajer DS, Tafflet M, El-Haou S, Jani DN, Ferreira B, et al. Rheumatic heart disease screening by echocardiography: the inadequacy of world health organization criteria for optimizing the diagnosis of subclinical disease. *Circulation.* (2009) 120(8):663–8. doi: 10.1161/CIRCULATIONAHA.109.849190
65. Johannsen RA, Kaltenborn ZP, Shroff GR. Saving time saves lives! A time focused evaluation of a single-view echocardiographic screening protocol for subclinical rheumatic heart disease. *Int J Cardiol.* (2022) 351:111–4. doi: 10.1016/j.ijcard.2021.12.031
66. Spitzer E, Mercado J, Islas F, Rothenbühler M, Kurmann R, Zürcher F, et al. Screening for rheumatic heart disease among Peruvian children: a two-stage sampling observational study. *PLoS One.* (2015) 10(7):e0133004. doi: 10.1371/journal.pone.0133004
67. Mirabel M, Bacquelin R, Tafflet M, Robillard C, Huon B, Corsenac P, et al. Screening for rheumatic heart disease: evaluation of a focused cardiac ultrasound approach. *Circ Cardiovasc Imaging.* (2015) 8(1):e002324. doi: 10.1161/CIRCIMAGING.114.002324
68. Hunter LD, Pecoraro AJK, Doubell AF, Monaghan MJ, Lloyd GW, Lombard CJ, et al. Screening for subclinical rheumatic heart disease: addressing borderline disease in a real-world setting. *Eur Heart J Open.* (2021) 1(3):oeab041. doi: 10.1093/ehjopen/oeab041
69. Condemni F, Rossi G, Lupiz M, Pagano A, Zamatto F, Marini S, et al. Screening of asymptomatic rheumatic heart disease among refugee/migrant children and youths in Italy. *Pediatr Rheumatol Online J.* (2019) 17(1):12. doi: 10.1186/s12969-019-0314-9
70. Chatard JC, Dubois T, Espinosa F, Kamblock J, Ledos PH, Tarpinian E, et al. Screening rheumatic heart disease in 1530 New Caledonian adolescents. *Journal of the American Heart Association: Cardiovascular and Cerebrovascular Disease.* (2020) 9(9):e015017. doi: 10.1161/JAHA.119.015017
71. 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(2):67. doi: 10.1136/heartasia-2016-010847
72. Lu JC, Sable C, Ensing GJ, Webb C, Scheel J, Aliku T, et al. Simplified rheumatic heart disease screening criteria for handheld echocardiography. *J Am Soc Echocardiogr.* (2015) 28(4):463–9. doi: 10.1016/j.echo.2015.01.001
73. Francis JR, Whalley GA, Kaethner A, Fairhurst H, Hardefeldt H, Reeves B, et al. Single-View echocardiography by nonexpert practitioners to detect rheumatic heart disease: a prospective study of diagnostic accuracy. *Circ Cardiovasc Imaging.* (2021) 14(8):e011790. doi: 10.1161/CIRCIMAGING.120.011790
74. Chillo P, Mutagaywa R, Nkya D, Njelekela M, Kwasigabo G, Kahabuka F, et al. Sub-clinical rheumatic heart disease (RHD) detected by hand-held echocardiogram in children participating in a school-based RHD prevention program in Tanzania. *BMC Cardiovasc Disord.* (2023) 23(1):155. doi: 10.1186/s12872-023-03186-y
75. Kaltenborn ZP, Zewde A, Kirsch JD, Yates M, Tessier KM, Nemec E, et al. The impact of a handheld ultrasound device in a rheumatic heart disease screening program in Ethiopia. *POCUS J.* (2023) 8(2):193–201. doi: 10.24908/pocus.v8i2.16390
76. Beaton A, Lu JC, Aliku T, Dean P, Gaur L, Weinberg J, et al. The utility of handheld echocardiography for early rheumatic heart disease diagnosis: a field study. *Eur Heart J Cardiovasc Imaging.* (2015) 16(5):475–82. doi: 10.1093/ehjci/jeu296
77. Sanyahumbi A, Beaton A, Guffey D, Hosseinipour MC, Karlsten M, Minard CG, et al. Two-year evolution of latent rheumatic heart disease in Malawi. *Congenit Heart Dis.* (2019) 14(4):614–8. doi: 10.1111/chd.12756
78. Cramp G, Stonehouse M, Webb R, Webb R, Chaffey-Aupouri G, Wilson N. Undetected rheumatic heart disease revealed using portable echocardiography in a population of school students in Tairarwhiti, New Zealand. *N Z Med J.* (2012) 125(1363):53–64.
79. Nunes MCP, Hung J, Barbosa MM, Esteves WA, Carvalho VT, Lodi-Junqueira L, et al. Impact of net atrioventricular compliance on clinical outcome in mitral stenosis. *Circ Cardiovasc Imaging.* (2013) 6(6):1001–8. doi: 10.1161/CIRCIMAGING.112.000328
80. Noubiap JJ, Agbor VN, Bigna JJ, Kaze AD, Nyaga UF, Mayosi BM. Prevalence and progression of rheumatic heart disease: a global systematic review and meta-

analysis of population-based echocardiographic studies. *Sci Rep.* (2019) 9(1):17022. doi: 10.1038/s41598-019-53540-4

81. Brown A, McDonald MI, Calma T. Rheumatic fever and social justice. *Med J Aust.* (2007) 186(11):557–8. doi: 10.5694/j.1326-5377.2007.tb01052.x

82. Angum F, Khan T, Kaler J, Siddiqui L, Hussain A. The prevalence of autoimmune disorders in women: a narrative review. *Cureus.* (2020) 12(5):e8094. doi: 10.7759/cureus.8094

83. Beaton A, Aliku T, Dewyer A, Jacobs M, Jiang J, Longenecker CT, et al. Latent rheumatic heart disease: identifying the children at highest risk of unfavorable

outcome. *Circulation.* (2017) 136(23):2233–44. doi: 10.1161/CIRCULATIONAHA.117.029936

84. Kotit S, Yacoub MH. The aswan rheumatic heart disease reGIstry: rationale and preliminary results of the ARGi database. *Front Cardiovasc Med.* (2023) 10:1230965 (p. 1–5). doi: 10.3389/fcvm.2023.1230965

85. Rothenbühler M, O'Sullivan CJ, Stortecky S, Stefanini GG, Spitzer E, Estill J, et al. Active surveillance for rheumatic heart disease in endemic regions: a systematic review and meta-analysis of prevalence among children and adolescents. *Lancet Glob Health.* (2014) 2(12):e717–726. doi: 10.1016/S2214-109X(14)70310-9