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Active surveillance for rheumatic heart disease in endemic regions: a systematic review and meta-analysis of prevalence among children and adolescents

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Summary

Background Rheumatic heart disease accounts for up to 250 000 premature deaths every year worldwide and can be regarded as a physical manifestation of poverty and social inequality. We aimed to estimate the prevalence of rheumatic heart disease in endemic countries as assessed by different screening modalities and as a function of age.

Methods We searched Medline, Embase, the Latin American and Caribbean System on Health Sciences Information, African Journals Online, and the Cochrane Database of Systematic Reviews for population-based studies published between Jan 1, 1993, and June 30, 2014, that reported on prevalence of rheumatic heart disease among children and adolescents (≥5 years to <18 years). We assessed prevalence of clinically silent and clinically manifest rheumatic heart disease in random effects meta-analyses according to screening modality and geographical region. We assessed the association between social inequality and rheumatic heart disease with the Gini coefficient. We used Poisson regression to analyse the effect of age on prevalence of rheumatic heart disease and estimated the incidence of rheumatic heart disease from prevalence data.

Findings We included 37 populations in the systematic review and meta-analysis. The pooled prevalence of rheumatic heart disease detected by cardiac auscultation was 2·9 per 1000 people (95% CI 1·7–5·0) and by echocardiography it was 12·9 per 1000 people (8·9–18·6), with substantial heterogeneity between individual reports for both screening modalities (I^2=99·0% and 94·9%, respectively). We noted an association between social inequality expressed by the Gini coefficient and prevalence of rheumatic heart disease (p=0·0002). The prevalence of clinically silent rheumatic heart disease (21·1 per 1000 people, 95% CI 14·1–31·4) was about seven to eight times higher than that of clinically manifest disease (2·7 per 1000 people, 1·6–4·4). Prevalence progressively increased with advancing age, from 4·7 per 1000 people (95% CI 0·0–11·2) at age 5 years to 21·0 per 1000 people (6·8–35·1) at 16 years. The estimated incidence was 1·6 per 1000 people (0·8–2·3) and remained constant across age categories (range 2·5, 95% CI 1·3–3·7 in 5-year-old children to 1·7, 0·0–5·1 in 15-year-old adolescents). We noted no sex-related differences in prevalence (p=0·829).

Interpretation We found a high prevalence of rheumatic heart disease in endemic countries. Although a reduction in social inequalities represents the cornerstone of community-based prevention, the importance of early detection of silent rheumatic heart disease remains to be further assessed.

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Introduction

Rheumatic heart disease ranks among the leading causes of non-communicable diseases in low-income and middle-income countries and accounts for up to 250 000 premature deaths every year worldwide.[1] Acute rheumatic fever and rheumatic heart disease can be regarded as physical manifestations of poverty and social inequality. Although largely eliminated in high-income countries, three quarters of children aged 15 years or younger grow up in parts of the world where rheumatic heart disease is endemic.[1–3] Rheumatic heart disease accounts for the greatest cardiovascular-related loss of disability-adjusted life-years among 10–14-year-olds worldwide[4] and continues to be a major public health challenge in low-income and middle-income countries.

Acute rheumatic fever is caused by an abnormal autoimmune response to group A streptococcal pharyngitis, which can manifest as arthritis of the large joints, affect the skin and the brain, and cause cardiac inflammation of the valvular apparatus. Recurrent bouts of oligosymptomatic acute rheumatic fever can insidiously lead to clinically silent valvular disease through different morphological and functional stages, ultimately resulting in severe valvular damage and heart failure. Secondary antibiotic prophylaxis is the most effective therapeutic strategy for acute rheumatic fever and rheumatic heart disease in low-income and middle-income countries[2] and

will probably remain so until underlying risk factors—such as overcrowding, poor hygiene, and limited access to health care—are reduced by socioeconomic change. One target of the WHO global action plan for the prevention and control of non-communicable diseases[5] is relative reduction of non-communicable disease mortality by 25% by the year 2025. Since rheumatic heart disease accounts for a substantial proportion of global non-communicable diseases, the implementation of comprehensive rheumatic heart disease control programmes in low-income and middle-income countries is a priority.

We aimed to summarise evidence from population-based observational studies of rheumatic heart disease among children and adolescents from endemic countries and to identify knowledge gaps. Specifically, we aimed to assess the effect of different screening modalities on estimated prevalence.

Methods

Search strategy and selection criteria

We searched Medline, Embase, the Latin-American and Caribbean System on Health Sciences Information, African Journals Online, and the Cochrane Database of Systematic Reviews on July 22, 2014, for population-based studies on rheumatic heart disease published in English, French, Spanish, Dutch, or Portuguese between Jan 1, 1993, and June 30, 2014. We restricted the search period to the past 20 years, to be representative of the present prevalence of rheumatic heart disease. The search protocol is shown in the appendix. Inclusion criteria were a population-based study design; a sample size of at least 500 individuals; inclusion of children at least 5 years old and adolescents younger than 18 years; and reporting on prevalence of rheumatic heart disease. We excluded studies primarily reporting on streptococcal infections, acute rheumatic fever, or results after intervention or surgery for rheumatic heart disease. Two authors (MR and TP) screened all titles and abstracts, reviewed full-text articles, and assessed their eligibility for inclusion. Disagreements between the two reviewers were resolved by discussion; a final decision was reached after mutual agreement between the two reviewers or was made by a third author (SS).

See Online for appendix

Data extraction

All data were independently extracted by two reviewers. Discrepancies in data extraction were resolved by mutual consensus. In addition to the extraction of socio-demographic characteristics and prevalence findings, we assessed methodological aspects of the included studies, such as sampling strategy, specification of the sampling frame, and screening protocol (eg, independent confirmation and masking).

We differentiated between clinically manifest and clinically silent rheumatic heart disease. We defined clinically manifest rheumatic heart disease as the presence of a heart murmur on cardiac auscultation that was consistent with echocardiographic evidence of rheumatic heart disease. Clinically silent rheumatic heart disease was defined by pathological regurgitation or mitral stenosis, or the detection of morphological changes, or both, consistent with rheumatic heart disease in the absence of a heart murmur. The prevalence of rheumatic heart disease was defined as the total burden of valvular lesions consistent with rheumatic heart disease in a specified population. The incidence of rheumatic heart disease is defined as the number of new cases diagnosed with rheumatic heart disease in a specified population and time period, irrespective of the presence or absence of signs or symptoms of acute rheumatic fever and must not be misinterpreted as the occurrence of new episodes of acute rheumatic fever, rather than rheumatic heart disease.

Statistical analysis

We compared the extracted data by meta-analysis in Stata version 13.1 (StataCorp, College Station, TX, USA) with the metan[6] and metareg[7] commands. We pooled logit transformed prevalence estimates using a random-effects model. Estimates were back transformed and expressed as conventional prevalence; therefore, 95% CIs are asymmetrical throughout. To account for heterogeneity due to the screening method (auscultation *vs* echocardiography) and the regional context, we estimated the I^2 summary statistics and report both the confidence and prediction intervals by subgroups. According to Higgins and colleagues,[8] I^2 values can be distinguished between low (25%), moderate (50%), and high (75%). The prediction intervals are calculated taking into account the between-study variance τ^2.[6]

We assessed the association between social inequality and rheumatic heart disease in a scatter plot of the Gini coefficient of the country and year in which the reported screening took place. The Gini coefficient measures the income distribution within a society on a scale of 0–1, where 0 represents perfect equality of distribution of income and 1 perfect inequality. A higher Gini coefficient is therefore equivalent to higher social inequality.[9] The data for the Gini index were extracted from a World Bank database.[10] The Gini coefficient does not show socio-economic disparities between ethnic communities within one country. We used Poisson regression to estimate the prevalence of rheumatic heart disease according to social inequality and report both unadjusted coefficients and coefficients adjusted for continent and screening methods.

In a sensitivity analysis, we measured the prevalence of rheumatic heat disease in school-based and community-based populations by meta-regression, with the difference in prevalence assessed by a two-sided Z test. We used data from studies that reported prevalence by age groups to estimate prevalence of rheumatic heart disease as a function of age. We first estimated prevalence by age for each study separately. For studies that reported prevalence for two age groups, we applied a Poisson

regression model, and for those with more than two age groups, we used fractional polynomial Poisson regression. The estimated prevalence per age category within each study was then estimated across studies.

Since no direct estimates of incidence were provided in individual studies, we estimated the incidence from prevalence using the method suggested by Leske and colleagues.[11] We estimated the overall incidence of rheumatic heart disease using the estimated prevalence per age category in two steps, as was done for the estimation of the prevalence by age: first within each study separately and then between the studies by meta-regression. We first estimated incidence by age within each study using the method suggested by Leske and colleagues[11] and then estimated incidence across all studies by meta-regression. We estimated the incidence using the three underlying assumptions of Leske and colleagues.[11] First, we assumed that the mortality rate was constant and did not depend on age. Second, we assumed that the mortality rate among children under 16 years was independent of rheumatic heart disease. Third, we assumed that there was no disease regression. We ignored possible enrolment in secondary prevention programmes or any natural healing and assumed that the disease progression was constant over time. The underlying assumptions represent a simplification of the complex physiopathology of rheumatic heart disease. The appendix includes further information regarding the estimation of the incidence. Finally, we estimated the prevalence of silent and manifest rheumatic heart disease using data from studies that reported prevalence according to both screening modalities and that used the WHO definition of rheumatic heart disease, which differentiates between silent (ie, possible) and manifest (ie, probable and definite) rheumatic heart disease.[2]

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. MR and TP had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

We identified 2928 publications, 85 of which were potentially eligible (figure 1). 33 articles describing 37 populations met the inclusion criteria and were included in the systematic review and meta-analysis;[12–44] four of the publications included data from two population-based studies each.[25,28,31,37] The appendix includes a summary of the methodological characteristics reported in the included studies. The sampling frame was specified in 28 (76%) populations and the sampling strategy was specified in 27 (73%). The primary sampling unit was schools in 34 (92%) populations and communities in three (8%).

In studies using cardiac auscultation as the primary means for screening, various reasons for referral were used. In some studies, children with any heart murmur (functional or pathological) were referred for echocardiographic examination, whereas in others children with pathological murmurs only were referred. Different criteria for echocardiographic detection of rheumatic heart disease were used across studies. In most studies rheumatic heart disease was only diagnosed if both pathological regurgitation of left-sided valves and morphological features were present, whereas in others, the diagnosis was made if isolated pathological regurgitation or isolated morphological features were present. Methodological characteristics and sample sizes of the individual studies are shown in

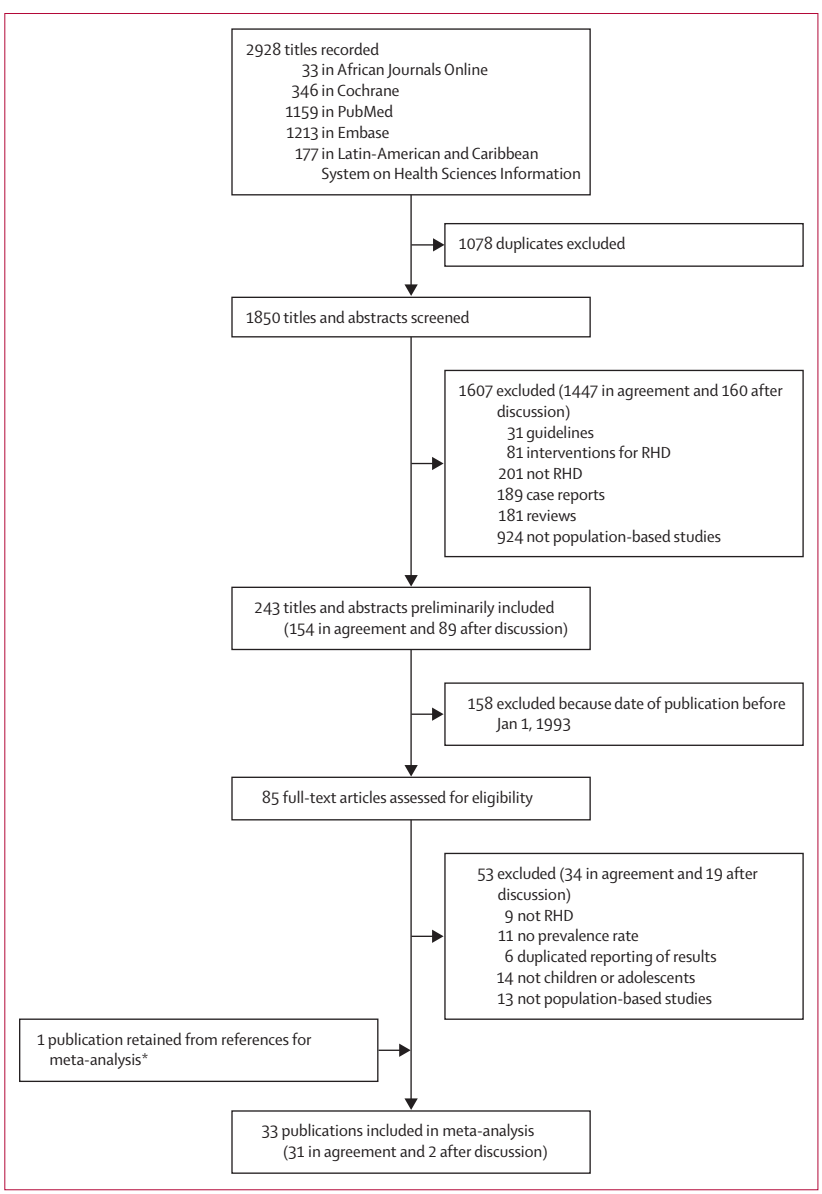

Figure 1: **Flow diagram of manuscript selection**
RHD=rheumatic heart disease. *Identified from the reference list from one article included in the meta-analysis during full-text assessment for eligibility.

the appendix, as are the clinical definition and echocardiographic criteria applied for case detection of rheumatic heart disease.

Among the 37 populations, 17 were from Asia, nine Africa, seven Oceania, three Latin America, and one Europe. The appendix summarises baseline characteristics

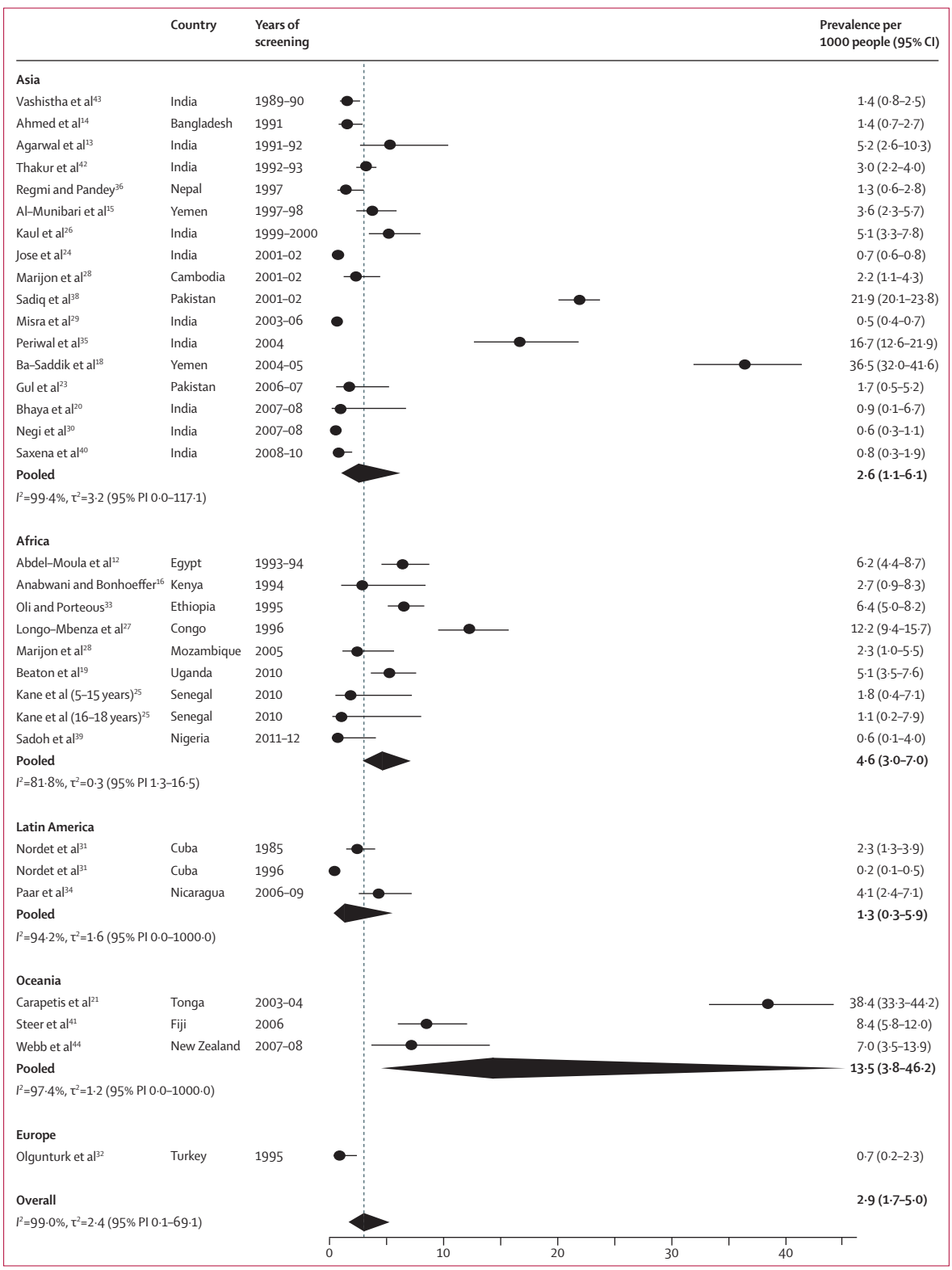

Figure 2: **Prevalence of rheumatic heart disease in studies in which patients were screened using cardiac auscultation**
Prevalence estimated from logit transformed data; therefore, 95% CIs are asymmetrical. PI=prediction interval.

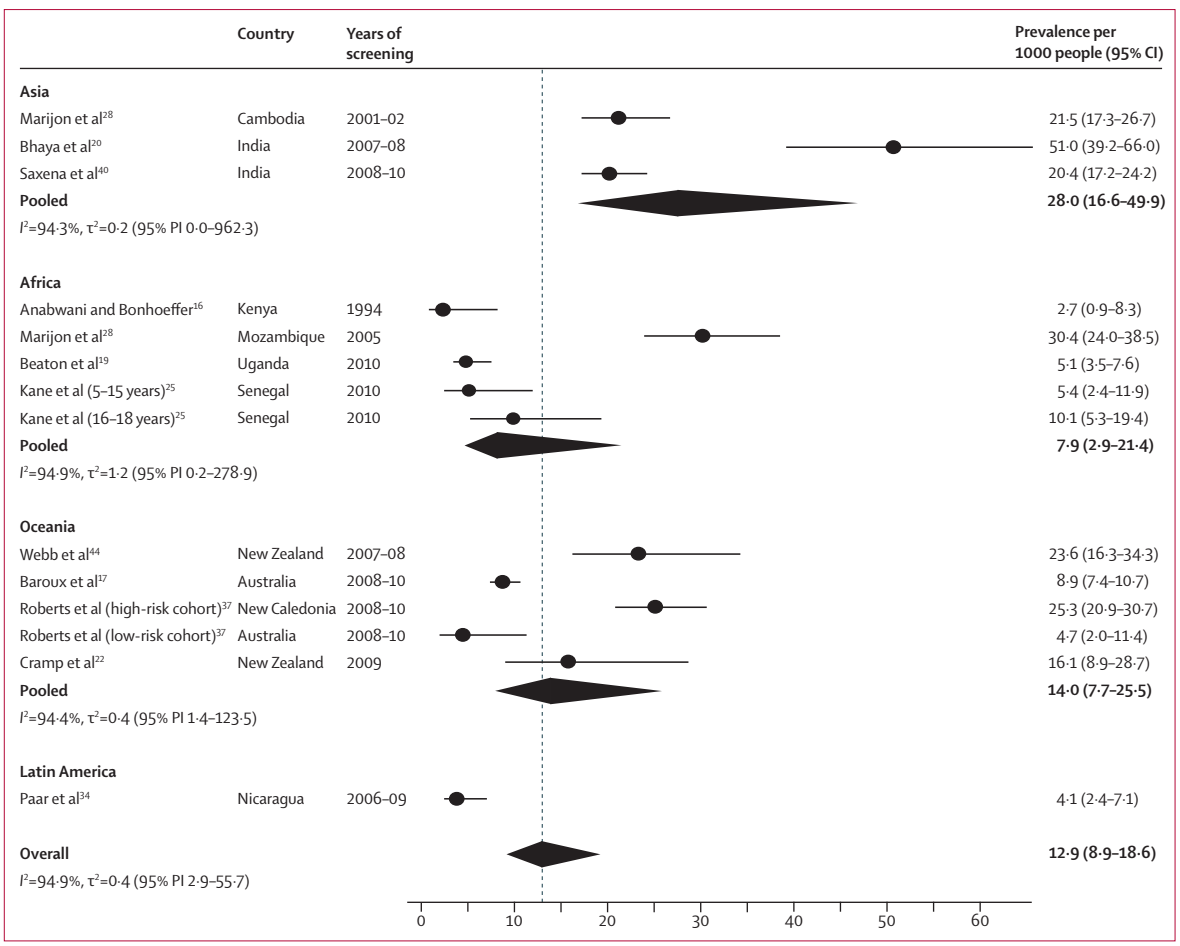

Figure 3: **Prevalence of rheumatic heart disease in studies in which patients were screened using echocardiography**
Prevalence estimated from logit transformed data; therefore, 95% CIs are asymmetrical. PI=prediction interval.

of the included studies. The mean age of the study population, as reported in 20 studies, was 11 years (SD 2), and the median proportion of boys, as reported in 27 studies, was 53% (IQR 49–56). Valvular involvement of the detected cases of rheumatic heart disease was reported in 27 studies. A mean of 65% (SD 31) of children and adolescents had mitral regurgitation, 21% (SD 18) had aortic regurgitation, and 15% (SD 22) had mitral stenosis.

Active surveillance with echocardiography was done in 14 studies, whereas in 23 studies individuals were screened for the presence of rheumatic heart disease by cardiac auscultation primarily, and eventually referred for further assessment only in case of a cardiac murmur. In ten studies, screening was done using both cardiac auscultation and echnocardiography. Findings were confirmed independently in 29 studies. The pooled prevalence of rheumatic heart disease detected by cardiac auscultation was 2·9 per 1000 people (95% CI 1·7–5·0; figure 2) and by echocardiography it was 12·9 per 1000 people (8·9–18·6; figure 3). The heterogeneity of reported prevalence in different studies from different continents was high for both studies in which rheumatic heart disease was detected by cardiac auscultation (I^2=99·0%; figure 2) and in those in which it was detected by echocardiography (I^2=94·9%; figure 3). In the sensitivity analysis, we found no significant interaction between prevalence in school-based and community-based active surveillance programmes (p=0·200).

The prevalence of clinically silent rheumatic heart disease (21·1 per 1000 people, 95% CI 14·1–31·4) was about seven to eight times higher than that of clinically manifest disease (2·7 per 1000 people, 1·6–4·4; figure 4). The prevalence of rheumatic heart disease by age groups was provided in 15 publications.[17–19,21,25–27,30,36,37,39–43] The prevalence of rheumatic heart disease progressively increased with advancing age, from 4·7 per 1000 people (95% CI 0·0–11·2) at age 5 years, to 21·0 per 1000 people (6·8–35·1) at 16 years (figure 5). Prevalence and incidence per study as a function of age are summarised in the appendix. On the basis of estimates of prevalence per age category, we estimated an overall incidence rate of 1·6 per 1000 people (95% CI 0·8–2·3), which remained constant across age categories (range 2·5, 95% CI

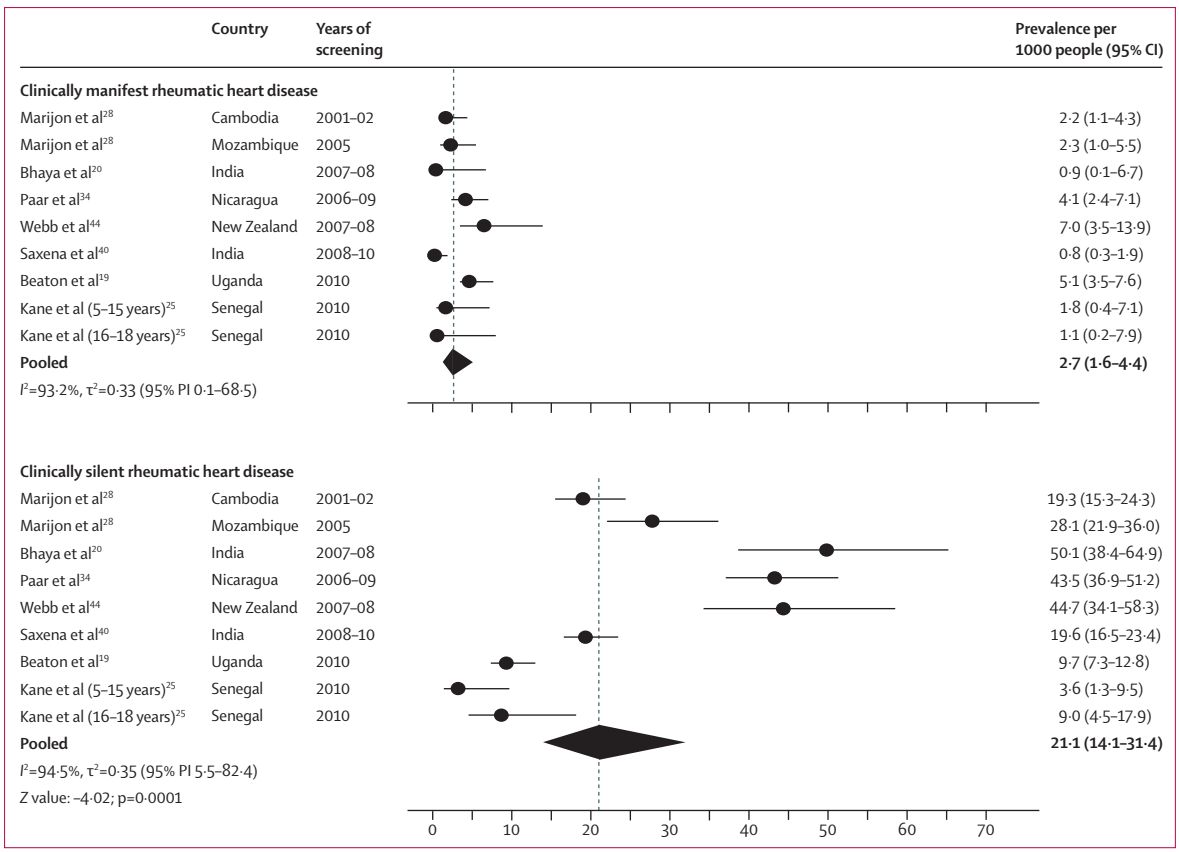

Figure 4: **Prevalence of clinically silent and clinically manifest rheumatic heart disease**
Prevalence in studies in which patients were screened using echocardiography. Prevalence estimated from logit transformed data; therefore, 95% CIs are asymmetrical. This analysis only included studies that reported prevalence of both silent and manifest rheumatic heart disease. PI=prediction interval.

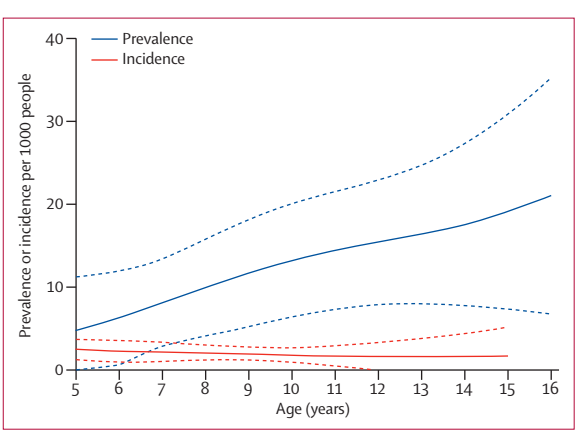

Figure 5: **Prevalence and incidence of rheumatic heart disease according to age**
Dashed lines are 95% CIs. 95% CIs have been truncated to zero in case of negative values. This analysis only included studies that reported prevalence by age groups.

1·3–3·7 in 5-year-old children to 1·7, 0·0–5·1 in 15-year-old adolescents).

The prevalence of rheumatic heart disease by sex was provided in 14 publications (38%).[13,17–19,26,27,33,35,36,38,40–43] There were no significant differences in the overall prevalence between girls (10·1 per 1000 people, 95% CI 6·6–13·5) and boys (9·5 per 1000 people, 6·0–13·1; p=0·829). The prevalence in those who were screened by auscultation was 7·8 per 1000 people (95% CI 2·9–12·8) among boys and 7·7 per 1000 people (3·3–12·2) among girls (p=0·977). Screening by echocardiography resulted in a prevalence of 13·9 per 1000 people (95% CI 8·3–19·5) among girls and 12·3 per 1000 people (7·2–17·4) among boys (p=0·662).

Prevalence of rheumatic heart disease varied by social inequality measured by the Gini coefficient (p=0·0002; figure 6). An increment of 0·1 of the Gini coefficient was associated with an increase in prevalence by a factor of 1·4 (95% CI 1·2–1·6). The association between Gini coefficient and prevalence of rheumatic heart disease persisted after adjusting for continent (p<0·0001) and screening method (p=0·049).

Discussion

In this systematic review and meta-analysis of population-based studies of endemic regions across Oceania, Asia, Africa, Latin America, and Europe we noted a high prevalence of rheumatic heart disease, with substantial heterogeneity between findings. Prevalence of rheumatic heart disease progressively increased between the ages of 5 years and 16 years, with a stable incidence rate, and that

of clinically silent rheumatic heart disease was seven to eight times higher than that of clinically manifest disease. Additionally, differences in estimated prevalence represented economic disparities and were associated with social inequality.

Reported prevalence of rheumatic heart disease among children and adolescents in endemic regions of the world ranged up to 5%, with substantial heterogeneity between populations. The differences in reported prevalence seem to represent true disparities in disease burden and are affected by methodological discrepancies in the undertaking of the studies, different methods and definitions applied for case detection, and the timeline of included data.

Several of the included studies had limited methodological strength and statistical precision at different levels. Most studies were underpowered to assess prevalence with adequate accuracy because of a small number of selected schools of communities or a small number of participants, or both. The setting (urban or rural) was not specified in most studies, which might introduce a latent bias into our prevalence estimates. Compared with urban areas, the prevalence of rheumatic heart disease seems to be higher in rural settings.[28,34] A quarter of studies omitted to adequately report the sampling strategy of the study population, which might further affect the reproducibility of the presented findings. Studies with sampling on the basis of school lists might underestimate the true burden of disease since school attendance is associated with socioeconomic status, a major risk factor for rheumatic heart disease.[37] However, in a sensitivity analysis, we found no significant interaction between prevalence in school-based and community-based active surveillance programmes. In a subset of studies, the difference between the sample of eligible pupils and the number of effectively screened students because of missing consent or failure to re-examine absentees from school in a repeat screening visit might have contributed to an underestimation of the actual burden of disease.

Differences in definitions and criteria for the diagnosis of rheumatic heart disease,[45,46] training of the examiner,[21] and utility of handheld or standard portable devices[47] have been outlined previously. Cardiac auscultation is an ineffective method of screening for rheumatic heart disease, regardless of the expertise of the auscultator.[48] Differentiation between innocent and suspicious or pathological murmurs can be challenging. In a staged screening protocol, sensitivity of auscultation to detect any cardiac murmur was higher when done by medical students than by paediatricians (96·4% *vs* 80·0%), although this came at the expense of lower specificity (1·3% *vs* 20·6%). In a second stage, classification of the previously detected murmurs into innocent or suspicious murmurs by a trained paediatrician increased the specificity to detect rheumatic heart disease from 20·6% to 65·1%, but reduced sensitivity from 80·0% to 46·4%.[21] A high level of suspicion for any heart murmur or a more rigorous referral strategy for echocardiographic

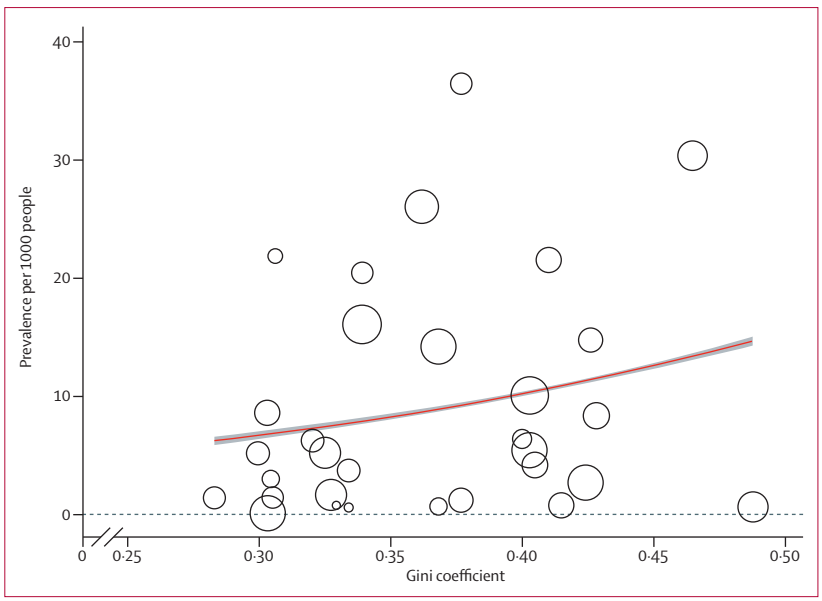

Figure 6: **Prevalence of rheumatic heart disease according to social inequality**
The size of the bubbles corresponds to the sample size of the reported study. The red line represents the estimated prevalence of rheumatic heart disease according to income distribution, with the 95% CI in grey.

confirmation might therefore have substantially affected documented prevalence in studies in which cardiac auscultation was used as the primary screening method. Accordingly, of the four studies reporting the highest prevalence of rheumatic heart disease by screening auscultation,[18,21,35,38] findings from three suggested that children and adolescents with any heart murmur (functional and pathological) were referred for echocardiography.[21,35,38] Similarly, prevalence of rheumatic heart disease identified on echocardiography might vary according to the diagnostic criteria used. The combined use of doppler-based and morphology-based criteria (any amount of valvular regurgitation noted in at least two planes associated with at least two of the following morphological signs: leaflet restriction, subvalvular thickening, or valvular thickening) had a three to four times higher rate of detection of subclinical rheumatic heart disease compared with the exclusive use of doppler-based criteria (regurgitant jet >1 cm in length, regurgitant jet in at least two planes, mosaic colour jet with a peak velocity >2·5 m/s, and persisting jet throughout systole or diastole) in a cohort of 2170 children screened in Mozambique.[49] Although in most studies pathological regurgitation of left-sided valves in combination with morphological features was deemed diagnostic for rheumatic heart disease, in other studies, isolated pathological regurgitation or isolated morphological features was sufficient for case detection. Moreover, interobserver reliability of screening findings was assessed in only 22% of studies.

Echocardiography for active surveillance has important benefits above and beyond the increased sensitivity and specificity compared with cardiac auscultation. The process involves common definitions and criteria for

diagnosis, independent and masked confirmatory assessments, and structured documentation. However, whereas in most studies in our analysis independent confirmation of preliminary findings from on-site screening was done by a second assessor masked or unmasked to the suspected diagnosis, not all studies reported confirmation of their findings.

Prevalence of rheumatic heart disease has declined over the past few decades.[50] A decline in disease burden might have contributed to the noted heterogeneity in reported prevalence, since the retained studies had been done over a timespan of over 20 years.

Consistent with findings from previous reports, we noted a continuous increase in the prevalence of rheumatic heart disease with advancing age;[19,25] however, this prevalence estimate must be interpreted with caution. The age range selected for active surveillance was determined by years of school attendance in most studies, and data on prevalence of rheumatic heart disease among adolescents in their late teens are scarce. Data from Senegal suggested a numerically higher prevalence of rheumatic heart disease among adolescents aged 16–18 years (10·1 per 1000 people, 95% CI 4·6–19·2) compared with children aged 5–15 years (5·4 per 1000 people, 2·0–11·7) and a numerically higher amount of advanced disease in adolescents (89%) than in children (33%; p=0·08).[25] These results were in line with those from a community-based screening programme in Pakistan.[51]

Corresponding with the steady increase in prevalence with advancing age, we estimated a constant incidence rate across age categories between 5 years and 15 years. The incidence estimate has to be interpreted in view of several limitations. First, any imprecision in approximated prevalence by age would directly transfer to the estimation of incidence. Second, the model used for the estimation of incidence did not account for mortality secondary to rheumatic heart disease and assumed a constant mortality rate independent of age. Finally, the model did not take into consideration the regression of disease that has been noted in several studies.[20,34,40,52] Notwithstanding, the estimated incidence of 1·6 per 1000 people is consistent with the reported incidence in Northern Territory, Australia.[53]

Several studies have reported a higher prevalence of rheumatic heart disease among women than men.[13,51,54–58] In contrast to findings from two previous community-based studies among predominantly young adults,[13,51] we did not document sex-related differences in prevalence of rheumatic heart disease in children in the present analysis of primarily school-based observational studies. A difference in sex-related prevalence ratios between children and adults might be explained by under-schooling of girls or a greater cumulative exposure to β-haemolytic streptococci of young, child-rearing mothers compared with men. Alternatively, differences in the diagnostic capacity of different screening modalities between females and males might contribute to the difference in sex-specific prevalence among children and adults. Since data on rheumatic heart disease among adults typically refers to clinically manifest disease as detected by auscultation, rather than to subclinical disease, a higher rate of echocardiographic false-negative findings among girls compared with boys might explain the noted sex difference as much as a higher rate of false-negative findings during auscultation in men compared with women. Because of limited data, we could not analyse whether there were differences in prevalence according to sex and age or investigate the relation between sex and the primary sampling unit (school-based versus community-based).

We noted a prevalence of clinically silent rheumatic heart disease that was seven to eight times higher than that of clinically manifest disease. In the absence of a history of acute rheumatic fever, a large proportion of silent cases is representative of latent disease, detected only by active echocardiographic surveillance. The low sensitivity of cardiac auscultation for detection of rheumatic heart disease and the resulting under-estimation of the disease burden have been highlighted in several studies.[19,20,25,28,34,40] However, the natural course and the prognostic effect of latent rheumatic heart disease need to be further elucidated. Longitudinal studies of children diagnosed with rheumatic heart disease in observational studies are limited by the small number of patients, high proportion of children lost to follow-up, and short duration of follow-up to a maximum of 2 years. Regression was noted in about a third of children with early stages of disease and was predominantly associated with a reduction of mitral regurgitation, whereas morphological changes were less likely to improve;[34,40,59,60] disease progression occurred in 5–15% of children.[34,40,59] The identification of children at risk of disease progression remains challenging. Advanced stages of disease and valvular morphological abnormalities, young age at initial diagnosis, and high anti-streptolysin O titres are associated with an increased risk of disease progression.[59,60] Timely implementation of secondary prevention strategies for silent rheumatic heart disease can prevent or slow the progression of valvular lesions.[59–61]

Differences in the estimated prevalence are suggestive of economic disparities and are associated with social inequality. A higher Gini index—a measure of the extent to which income and expenditures are distributed within a population—is associated with a higher prevalence of rheumatic heart disease. However, heterogeneity across neighbouring geographical regions with similar socio-economic backgrounds suggests under-reporting of the disease and might result from competition for limited resources with other non-communicable diseases in many low-income and middle-income countries. Rheumatic heart disease causes the highest number of disability-adjusted life-years of all listed cardiovascular diseases among 10–14-year-olds (516·6 per 100 000 people, 95% CI 425·3–647·0) and the second highest number among children aged 5–9 years (362·0, 294·6–462·0).[4]

These figures underscore the fact that rheumatic heart disease continues to be a major contributor to loss of health among children. Neglect of rheumatic heart disease on a governmental level in many low-income and middle-income countries translates into under-representation of rheumatic heart disease in the peer-reviewed published work.

Prevention policies and institutionalised programmes are paramount for the control of rheumatic heart disease in endemic countries. In 2005, the Drakensberg Declaration[62] issued a call for the development of national programmes in Africa, focusing on raising awareness, surveillance, advocacy, and prevention. Community awareness and targeted education of major stakeholders play an integral part in the consistent implementation of dedicated prevention programmes. At the same time, integration of rheumatic heart disease into national non-communicable disease programmes with active disease surveillance is essential. Collaborative efforts have resulted in the Mosi-o-Tunya call to action,[63,64] which outlines a strategic roadmap for addressing the challenges of rheumatic heart disease in Africa.

The global targets of WHO offer a unique opportunity to return rheumatic heart disease to the clinical and scientific mainstream.[65,66] The ambitious targets set out in the WHO global action plan,[5] namely to reduce premature mortality related to non-communicable diseases by 25% by the year 2025, would be more achievable if a common approach was adopted and awareness of rheumatic heart disease raised by high-quality and congruent research methodology. There are no guidelines on the undertaking of active surveillance for rheumatic heart disease. Although academic publications about rheumatic heart disease have substantially decreased since the 1970s, the number of published research articles has steadily increased since the beginning of the 21st century. This increase in scientific attention might have an effect on research funding and might lead to the transformation of knowledge into tangible action consisting of commensurate funding for the establishment of national control programmes for rheumatic heart disease and equitable access to primary and secondary preventative treatment.

Contributors

MR, JE, NRS, OK, PJ, and TP conceived the study, including the development of the proposal and study methods. MR and TP coordinated the collection and management of the systematic review and were involved in the data extraction together with SS, GGS, and ES. MR, CJO'S, PJ, and TP led the writing of the manuscript and all authors contributed to its development and the interpretation of the analysis.

Declaration of interests

ES is the recipient of a Research Fellowship of the European Association of Percutaneous Cardiovascular Interventions of the European Society of Cardiology and a Research Grant of the Spanish Society of Cardiology. All other authors declare no competing interests.

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