

The Health Systems Barriers and Facilitators for RHD Prevalence



An Epidemiological Meta-Analysis From Uganda and Tanzania

Annesinah H. Moloji*, Sumaya Mall^{†,‡}, Mark E. Engel*, Renae Stafford[§], Zhang Wan Zhu^{||}, Liesl J. Zühlke*,[¶] David A. Watkins[#]

Cape Town, South Africa; Stellenbosch, South Africa; Johannesburg, South Africa; Mwanza, Tanzania; Kampala, Uganda; Seattle, WA, USA

ABSTRACT

Background: Rheumatic heart disease (RHD) is an important and preventable cause of cardiovascular disease.

Objectives: As part of a recent RHD initiative in Uganda and Tanzania, we systematically reviewed group A streptococcal disease (GAS), acute rheumatic fever (ARF), and RHD in these countries.

Methods: Using a systematic review and meta-analysis/meta-synthesis, we searched PubMed, Embase, and grey literature for quantitative and qualitative studies conducted in Uganda and Tanzania that included individuals affected by GAS, ARF, and RHD. We pre-specified 3 sets of outcomes: 1) disease epidemiology; 2) barriers and facilitators to health care; and 3) stakeholder identification and engagement. Study descriptors, outcomes, and interest, and quality assessments were recorded. For the first objective, we conducted random-effects meta-analyses. For the second objective, we produced a narrative synthesis of themes. No studies contained data on the third objective.

Results: Of 293 records identified, 12 met our inclusion criteria (9 for objective 1 and 3 for objective 2). Most quantitative studies were at moderate or high risk of bias, and only 1 of 2 qualitative studies was high quality. We estimated the prevalence of RHD to be 17.9 (95% confidence interval [CI]: 4.0 to 41.2) per 1,000 individuals. The most frequent nonfatal sequelae were heart failure, pulmonary hypertension, and atrial fibrillation. Case-fatality rates in medical and surgical wards were 17% (95% CI: 13% to 21%) and 27% (95% CI: 18% to 36%), respectively. Barriers and facilitators to GAS and RHD care were identified in the domains of individual knowledge, family support, provider communication and knowledge, and system design.

Conclusions: RHD remains endemic in Tanzania and Uganda, and symptomatic RHD is associated with high rates of morbidity and mortality. We have identified critical data gaps in the areas of GAS and ARF epidemiology as well as health care utilization patterns and their determinants.

Rheumatic heart disease (RHD) is a chronic inflammatory disease of the heart valves that usually results from recurrent episodes of acute rheumatic fever (ARF). The origins of ARF can be traced to untreated group A streptococcal (GAS) pharyngitis [1-3]. RHD can be prevented by treating GAS pharyngitis with benzathine penicillin. In turn, the incidence and severity of RHD can be reduced with prophylactic penicillin, preventing further cardiovascular damage and, thus, the need for surgical repair or replacement of damaged valves [1].

Many individuals miss the opportunity to prevent RHD and first present to care with advanced heart failure or other complications [1]. This is because RHD is often latent in its early years [1,4]. Furthermore, in low- and middle-income countries such as Tanzania and Uganda, RHD treatment and prevention is complicated by lack of access to evidence-based interventions at different levels of

care [5]. RHD is estimated to cause between 233,000 and 294,000 deaths globally each year, mostly in Africa, South Asia, and Pacific Island nations [6].

For RHD to be prevented and properly managed in nations where it remains endemic and where resources for adequate prevention and control are especially scarce, strong policies are required that adequately recognize RHD and devote resources to its prevention and control [7]. Decision makers in these settings require up-to-date information about the epidemiology of GAS, ARF, and RHD as well as specific contextual information about local health care delivery patterns and barriers and facilitators to care. Systematic reviews are an integral aspect of needs assessments that answer these questions. Ideally, such reviews capture quantitative as well as qualitative data sources—both of which are essential to health systems research—and integrate them within an overarching narrative.

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This work was funded by the Medtronic Foundation through support to RhEACH and RHD Action. From the *Department of Medicine, Groote Schuur Hospital and Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa; †Centre for Evidence Based Health Care, Faculty of Health Sciences, Stellenbosch University, Stellenbosch, South Africa; ‡Division of Epidemiology and Biostatistics, School of Public Health, University of the Witwatersrand, Johannesburg, South Africa; §Touch Foundation, Mwanza, Tanzania; ||Department of Adult Cardiology, Uganda Heart Institute, Kampala, Uganda; ¶Department of Paediatrics, Red Cross War Memorial Children's Hospital, University of Cape Town, Cape Town, South Africa; and the #Division of General Internal Medicine, University of Washington, Seattle, WA, USA. Correspondence: D. A. Watkins (davidaw@uw.edu).

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TABLE 1. Database search strategies

	Subject	Search Terms
PubMed search strategy		
1	Group A β -hemolytic <i>streptococcal</i> , acute rheumatic fever, rheumatic heart disease	"Pharyngitis"[MeSH] OR pharyngitis OR sore throat OR strep OR group a β -hemolytic streptococcal OR "streptococcus pyogenes"[MeSH] OR group a streptococcus OR group a streptococcal infection OR "impetigo" [MeSH] OR impetigo OR group a streptococcus skin infection OR rheumatic fever OR "rheumatic fever" [MeSH] OR rheumatic heart disease OR "rheumatic heart disease" [MeSH]
2	Service delivery	Accessibility of health services OR availability of health services OR attitudes to health OR barrier* OR delivery of health care OR facilitator* OR health OR "health behavior" [MeSH] OR health care OR health care quality, access, and evaluation OR "health care personnel" OR health education" [MeSH] OR patient compliance OR patient education OR professional knowledge OR obstacle*
3	Stakeholder analysis	Collaboration or health policy or mapping or "policy"[mesh] or policy or stakeholder
4	Country	Uganda OR Ugandan OR Tanzania OR Tanzanian
Search		1 AND 4
Search		1 AND 2 AND 4
Search		1 AND 3 AND 4
	Filters: Publication date from January 1, 1995.	
EMBASE search strategy		
1	Group A β -hemolytic <i>streptococcal</i> , acute rheumatic fever, rheumatic heart disease	"Group A streptococcal infection"/exp OR "streptococcus group a"/exp OR "group A streptococcal infection" OR "streptococcus group A" OR "pharyngitis"/exp OR "pharyngitis" sore throat OR "impetigo" OR "impetigo"/exp OR "group A streptococcus skin infection"/exp OR "rheumatic fever"/exp OR "rheumatic fever" OR "rheumatic heart disease"/exp OR "rheumatic heart disease"
2	Service delivery	"Accessibility of health services" OR "availability of health services" OR "attitudes to health" OR "barrier" OR "delivery of health care" OR "facilitator" OR "health" OR health behavior OR "health care" OR "health care quality, access, and evaluation" OR "health care personnel" OR health education OR "patient compliance" OR "patient education" OR "professional knowledge" OR "obstacle"
3	Stakeholder analysis	"collaboration" OR "health policy" OR "mapping" OR "policy" OR "stakeholder"
4	Country	Uganda OR Ugandan OR Tanzania OR Tanzanian
Search		1 AND 4
Search		1 AND 2 AND 4
Search		1 AND 3 AND 4
	Filters: Publication date from January 1, 1995.	

MeSH, medical subject heading.

*Wildcard term as per database notation.

In September 2015, RHD Action (www.rhdaction.org) was launched as a coalition of global organizations working with all relevant stakeholders to reduce premature mortality from RHD and contributing to both the World Health Organization's 25 \times 25 goal and the World Heart Federation's 25 \times 25 <25 goal. Partners in 2 African countries—Uganda Heart Institute in Uganda and Touch Foundation in Tanzania—received seed funding to conduct RHD demonstration projects. As part of the needs assessment process for these projects, we conducted a systematic review of the published data that adapts a previously published protocol [8].

Our review had 3 broad objectives: 1) to quantify the burden of GAS, ARF, and RHD in Tanzania and Uganda; 2) to describe the patient and provider health care experience with GAS, ARF, and RHD in these countries; and 3) to identify the types of stakeholders who currently are, or need to be, engaged when designing and implementing RHD programs in these communities. This review deals with objectives 1 and 2 using standard systematic review methods for synthesizing quantitative and qualitative research [9,10]. Because we did not identify any primary published data on objective 3, the issue of stakeholders will be addressed in a separate report.

METHODS

This review is registered in the PROSPERO (International Prospective Register of Systematic Reviews) as CRD42016032852. It adheres to the recommendations of the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) statement [11].

Search strategy

Our search strategy was adapted from the approach used in the original protocol by Moloi et al. [8]. In brief, we searched for studies that: 1) estimated specific epidemiological outcomes related to GAS, ARF, and RHD (see the following text); or 2) elicited from patients or health care providers the perceived barriers and facilitators to care of these conditions. We exchanged country-specific terms for the Africa-wide “filter” listed in our original protocol to retrieve studies from Uganda or Tanzania. The complete search strategy for PubMed and Embase is provided in Table 1. We consulted in-country experts to obtain, where possible, relevant nongovernmental organization reports, death notifications, theses, and other unpublished works. Finally, we hand-searched the reference lists of all full-text reports. Our last search was conducted on April 30, 2016.

Study inclusion criteria

Studies were included in this review if they provided data on 1 or both of our stated objectives. For objective 1, we pursued case series, cross-sectional studies, and cohort studies that measured GAS, ARF, or RHD. For GAS, we were interested in pharyngitis incidence or prevalence of GAS among cases of pharyngitis. We only considered studies that defined symptomatic GAS using a clinical prediction rule, throat culture, or rapid antigen test [12]. For ARF, we were interested in incidence and mortality. We only considered studies that defined ARF according to the 1992 Jones criteria and its subsequent revisions [13] except for the latest revision of the criteria, which are still being introduced into clinical practice [14]. For RHD, we were interested in general prevalence, mortality, and prevalence of specific nonfatal outcomes: heart failure, pulmonary hypertension, stroke, atrial fibrillation, and infective endocarditis. For prevalence, we considered echocardiography-based screening studies conducted at the community level. We allowed flexibility in the case definition of RHD, since this field has evolved significantly over the past decade, including revisions to diagnostic criteria using echocardiography [15-17]. For morbidity and mortality, we considered all types of studies, although we only included studies in which RHD was diagnosed by a clinician with echocardiographic confirmation.

For objective 2, we developed a conceptual model of the potential barriers and facilitators at the patient, health care provider, and health system level for GAS, ARF, and RHD care (Table 2). This framework was used to organize the specific barriers and facilitators identified in the

TABLE 2. Conceptual model for objective 2 (barriers and facilitators to care)

	Patients	Health Care Providers	Health Systems
Initial decision to seek care	✓	✓	✓
Factors influencing diagnosis	✓	✓	✓
Factors influencing treatment and/or referral	✓	✓	✓
Factors influencing adherence and retention in long-term care	✓	✓	✓

published data. We primarily sought out phenomenological and ethnographic (qualitative) studies, but because these were scarce, we also considered studies that quantified specific barriers and facilitators.

Exclusion criteria

We excluded all case reports, editorials, and commentaries. If study data were published in multiple papers, we excluded all but the most complete and recent version of the dataset in question. Because we sought contemporary data to guide program development, we excluded studies published prior to 1995. Finally, we excluded studies that were published in languages other than English.

Data extraction and management

Authors in sets of 2 (A.H.M. and D.A.W.; A.H.M. and S.M.) independently screened all of the titles, abstracts, and full-text papers for objectives 1 and 2, respectively. They independently extracted data from all included full-text papers for the respective objectives. Contradictions at each stage of screening were resolved through consensus and arbitration by 2 other authors (M.E.E. and L.J.Z.) when necessary. We used different standardized data extraction forms and quality assessment worksheets for objectives 1 and 2 (Online Table 1). We managed search results using Covidence (Melbourne, Victoria, Australia).

Quality appraisal

We used 3 separate quality assessment tools that were relevant to the various designs of the included studies (Online Table 2). These are different than the tools outlined in our original protocol [8].

To assess population-based studies, we employed a quality assessment tool for evaluating prevalence studies suggested by Hoy et al. [18] and adapted by Werfalli et al. [19]. Briefly, the assessment tool evaluates risk of bias related to internal validity, external validity, and generalizability of the study results. Werfalli et al. [19] added a quantitative scoring system that categorizes high-risk studies as those with an overall score of 0 to 5 points, moderate risk as 6 to 8 points, and low risk as >8 points.

For case series, we used a case series tool adapted from the National Institutes of Health [20]. We categorized the

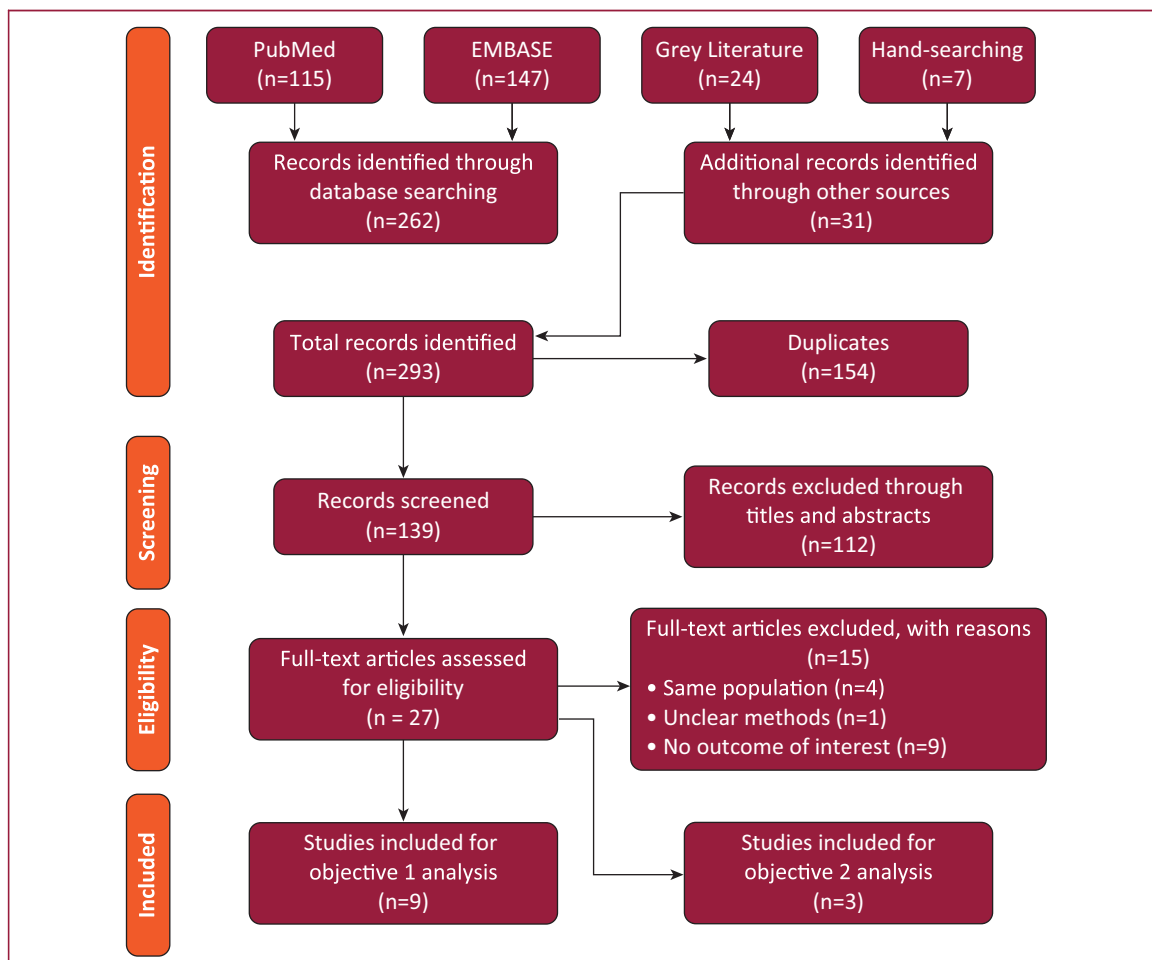


FIGURE 1. PRISMA flow diagram.

case series studies as having a high risk of bias if they had a combined score of 0 to 3 points, moderate risk of bias if they had a combined score of 4 to 6 points, and low risk of bias if they had a combined score of >7 points.

We used the Critical Appraisal Skills Programme criteria to evaluate evidence from qualitative studies as detailed in the original protocol [8,21]. We categorized studies as having an overall score of more than 8 points as good quality and those with an overall score of 0 to 5 points as poor quality.

Data synthesis and analysis

For objective 1, we pooled individual estimates of each outcome. Each set of outcome estimates (prevalence ratio, frequency of sequelae, or case-fatality rates) was subjected to an inverse variance-weighted random effects meta-analysis. Variances were stabilized by means of double arcsine transformation. Heterogeneity was explored quantitatively by use of the I^2 statistic and qualitatively by considering variation due to study design, quality, case

definition, country, and year. Missing data for each study were described and discussed as to the extent to which they could alter the results. Where deemed necessary, we contacted the studies' authors to request for missing information. For objective 2, we conducted a 3-stage qualitative meta-synthesis as described in the original protocol [8].

RESULTS

Study retrieval

We retrieved 262 records from the electronic databases and another 31 records from hand-searching of relevant reference lists and "gray literature," including nongovernmental organization reports, theses, unpublished research, mortality statistics, and health surveys. Twelve studies were included in our final review, of which 9 contained data relevant to objective 1 and 3 to objective 2 (Fig. 1). For 15 excluded full-text reports, we document the reasons for exclusion in [Online Table 3](#).

TABLE 3. Characteristics of included studies

Study	Setting (Local, Social Context)	Population	Study Design	Outcome Reported	Quality Score
Studies included in the objective 1 analysis					
Beaton et al., 2012 [34]	Public schools across different socioeconomic groups in urban (Kampala) Uganda	School children age 5–16 yrs	Cross-sectional study	Prevalence of RHD	8
Beaton et al., 2015 [22]	5 public schools in rural (Gulu) Uganda	Primary school children	Cross-sectional study	Prevalence of RHD	6
Bienmoyo et al., 2012 [30]	8 districts with differing socioeconomic status in Uganda	School children age 7–20 yrs	Cross-sectional study	Prevalence of RHD	5
Damasceno et al., 2012 [28]	Tertiary, nonprofit hospital in urban (Kampala) Uganda	Patients older than 12 yrs admitted with dyspnea as the main complaint, and diagnosed with acute heart failure	Case series	Mortality from heart failure including RHD	6
Grimaldi et al., 2014 [23]	Tertiary, nonprofit hospital in urban (Kampala) Uganda	Patients referred for suspected heart disease	Case series	Morbidity and mortality from RHD including surgery	5
Makubi et al., 2014 [25]	Tertiary, nonprofit hospital in urban (Dar es Salaam) Tanzania	Patients diagnosed with heart failure. 73% of the patients were recruited from outpatients	Case series	Morbidity and mortality from RHD including surgery	7
Nyawawa et al., 2010 [26]	Cardiovascular center at a referral hospital in urban (Dar es Salaam) Tanzania	Cardiac patients who underwent cardiac operations between May 2008 and June 2009 in Muhimbili National Hospital	Case series	Morbidity and mortality from surgery including RHD	5
Okello et al., 2013 [27]	Main referral hospital for cardiovascular disease in urban (Kampala) Uganda	Adults age 15–60 yrs diagnosed with RHD	Case series	Morbidity from RHD	7
Okello et al., 2015 [29]	Main referral hospital for cardiovascular disease in urban (Kampala) Uganda	Adults age 15–60 yrs diagnosed with RHD	Case series (follow-up)	Morbidity and mortality from RHD	7
Studies included in the objective 2 analysis					
Bergmark et al., 2010 [24]	National referral hospital in urban (Dar es Salaam) Tanzania	Inpatients, outpatients, and parents of patients with RHD age 3–29 yrs	Individual interviews	Barriers to GAS management	5
Huck et al., 2015 [31]	National referral hospital in urban (Kampala) Uganda	RHD patients who are part of the RHD registry at the Uganda Heart Institute. The patients receive monthly benzathine penicillin G and are at different levels of adherence	Semistructured focus groups	Facilitators and barriers to RHD management	8
Musoke et al., 2013 [32]	National referral hospital in urban (Kampala) Uganda	RHD patients age 5–55 yrs who are eligible to continue prophylaxis for a period not less than 1 yr from the time of recruitment and consented to the study were recruited	Cross-sectional study	Facilitators and barriers to RHD management	7

GAS, group A streptococcal disease; RHD, rheumatic heart disease.

Characteristics of studies included in objective 1

Seven peer-reviewed papers [22,23,25–28,34] and 2 unpublished reports [29,30] were included in objective 1 (Table 3).

Three were cross-sectional studies conducted in schools to examine the prevalence of RHD [22,30,34]; 2 using the 2006 World Health Organization/National Institutes of Health criteria [30,34], and 1 using the 2012

World Heart Federation criteria [22]. None of the studies used auscultation. Two of the cross-sectional studies were conducted in Uganda (urban Kampala [34] and rural Gulu [22]). The other study was conducted in 8 districts of Tanzania with differing socioeconomic and cultural backgrounds [30]. It should be noted that these studies are only representative of those communities and not the country as a whole. The age range of participants was 5 to 20 years.

We found no data on prevalence in adults. In addition, no studies reported on GAS or ARF.

The remaining 6 studies were case series of RHD patients [23,25-29]. Four were conducted in Kampala, Uganda, and the other 2 in Dar Es Salaam, Tanzania. The age range of participants was 13 to 60 years. We found no data on rates of sequelae in children.

We contacted authors of 4 of the studies to request extra data. Damasceno et al. [28] provided us with data on acute heart failure and RHD. Nyawawa et al. [26] provided us with data on cardiac surgery and RHD. The Bienmoyo Foundation [30] provided us with aggregated data on the prevalence of RHD. Makubi et al. [25] provided us with data on heart failure and RHD.

Quality assessment of studies included in objective 1

Three cross-sectional studies reported on the prevalence of RHD in school children. All were conducted at the community level in areas previously deemed to be endemic. Risk of bias in these studies ranged from low-to-moderate (Uganda studies) to high (Tanzania study). Six case series reported on RHD fatal and nonfatal outcomes. All were samples from tertiary hospitals. Risk of bias was high in 2 studies and moderate in the other 4 studies. The factors most frequently implicated in higher risk of bias were inadequate description of participant recruitment, inadequate follow-up, and inadequate description of methods. Figure 2 illustrates the factors influencing risk of bias across these studies.

Prevalence

The combined prevalence of RHD among school children in Tanzania and Uganda was estimated at 18 (95% confidence interval [CI]: 4 to 41) per 1,000 individuals (Fig. 3). Our estimate contained statistically significant heterogeneity. The outlier study, which found a higher prevalence, was conducted in a rural area. This suggests but does not confirm a socioeconomic gradient in RHD in these countries.

Frequency of nonfatal sequelae

Forest plots of the estimated frequencies of RHD sequelae are presented in Figure 4. Pulmonary hypertension was observed in 30% (95% CI: 25% to 35%). Atrial fibrillation was observed in 32% (95% CI: 3% to 71%); amongst these studies, Okello et al. [29] was an outlier, with an estimate of 64% compared with 14% to 21% in the other 2 studies, leading to significant heterogeneity in the pooled estimate. Stroke was observed in 1% (95% CI: 1% to 2%), and 1 study found that 50% of stroke patients had concurrent atrial fibrillation [27]. Infective endocarditis was observed in 3% (95% CI: 2% to 4%) and heart failure in 41% (95% CI: 37% to 45%).

Case-fatality rates

We estimated the RHD case-fatality rate at 19% (95% CI: 13% to 27%) across 4 studies (Fig. 5). When the aggregated data were subanalyzed as nonsurgical versus surgical outcomes (2 studies each), the estimated case-fatality rates were 17% (95% CI: 13% to 21%) and 27% (95% CI: 18% to 36%), respectively. Both subgroups estimates, as well as the overall estimate, had some evidence of heterogeneity ($I^2 = 85%$ and $55%$, respectively).

Characteristics of studies included in objective 2

Of the 3 studies included in objective 2, 2 were qualitative [24,31] and 1 was quantitative [32] in design. Each study included a population of RHD patients, and 1 study also included children with GAS [24]. Two studies described facilitators and barriers to RHD treatment and care in Uganda: 1 using semistructured focus groups [31], and the other, individual survey questionnaires [32]. The third study explored barriers to GAS treatment in Tanzania through in-depth qualitative interviews [24]. None of the studies reported on ARF.

Quality assessment of studies included in objective 2

The focus group discussion study in Uganda was deemed to be of high quality, and the cross-sectional quantitative study in Uganda was deemed to have low risk of bias. The individual interview study in Tanzania was deemed to be of low quality. Figure 2 illustrates the various aspects of quality across these studies. The reported data on GAS and RHD were not sufficient to conduct a meta-synthesis of the patient and provider experience, so we discuss the findings in the following narrative.

Barriers and facilitators to care in Uganda

Huck et al. [31] reported health behaviors, attitudes, and health systems issues related to adherence to monthly secondary prophylaxis. They found that on an individual level, patients continued their RHD medication because of reminder systems, personal motivation, experience with or information about adherence to other daily medications, and not wanting to miss many injections. On the interpersonal level, adherence was enabled by family/friends encouragement, material support, and having a good relationship with a health care provider. At the systems level, close proximity to a clinic facilitated care.

This study also identified lack of transportation money, pain of injections, and lack of perceived consequences from missing an injection as obstacles to adherence on an individual level. For those with human immunodeficiency virus, multiple appointments and regimens of multiple medications were an added hindrance. Interpersonal factors that obstructed treatment included stigma from family/friends, lack of support, and the feeling of being a burden to caregivers. Poor communication and

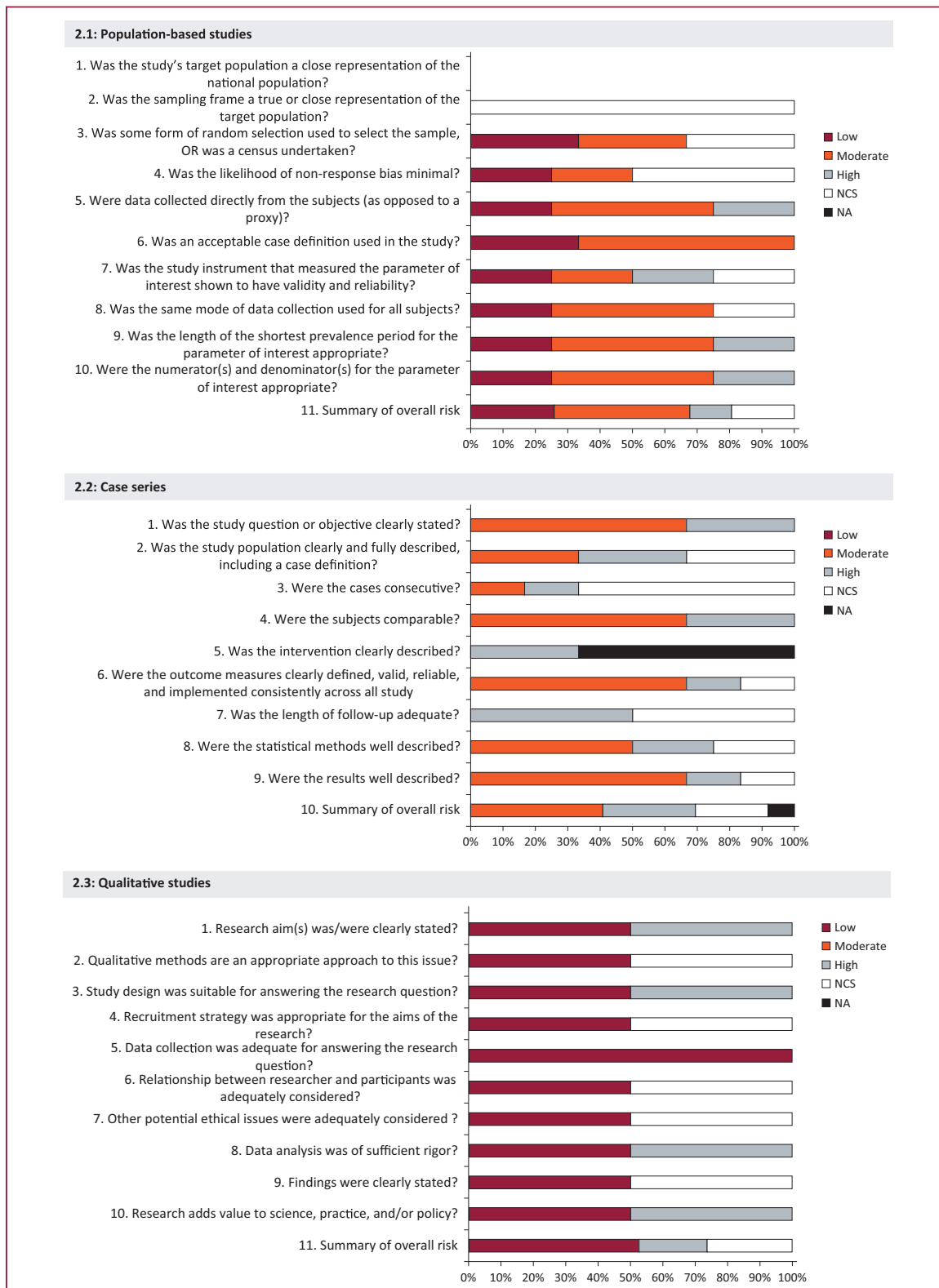


FIGURE 2. Assessment of risk of bias. NA, not applicable; NCS, not clearly stated (the article did not provide enough information to determine the answer to the particular quality-related question).

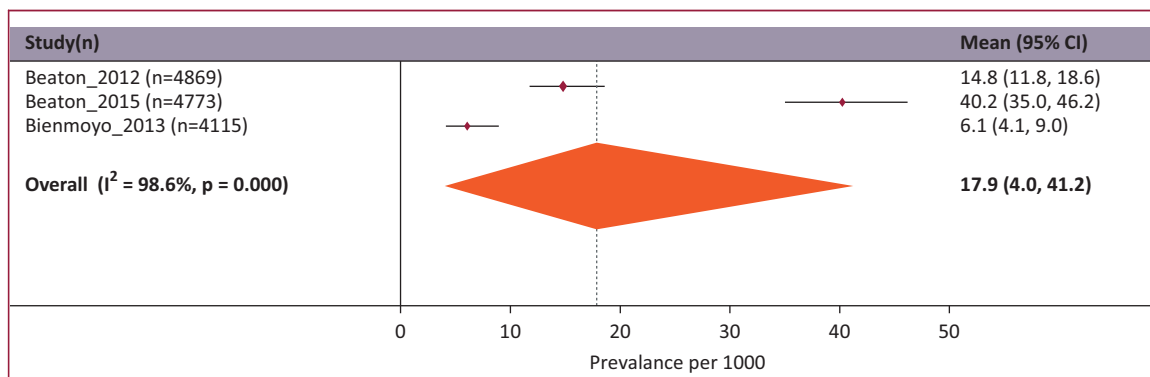


FIGURE 3. Prevalence of asymptomatic RHD in school children in Uganda and Tanzania. CI, confidence interval; RHD, rheumatic heart disease.

distrust of providers were also notable barriers. Finally, the health system barriers to adherence included lack of skilled/knowledgeable providers in the local community, long waiting times for appointments, and shortages of penicillin.

Similar results were reported by Musoke et al. [32] in a quantitative observational study that explored RHD treatment adherence in Uganda. In addition to the factors addressed in the previous text, these investigators found that treatment adherence improved with education. However, individual factors, such as age, sex, and previous exposure to penicillin, did not affect adherence.

Barriers and facilitators to care in Tanzania

Bergmark et al. [24] reported on practice patterns and barriers to diagnosing and treating GAS among clinicians, individuals with RHD, and family members. The study discovered that patients' lack of knowledge of GAS and its connection to RHD was a barrier to seeking medical care for sore throat. This study also identified, at the provider and systems level, a lack of resources to manage GAS. The authors asserted that the lack of resources was due to competing priorities of treating human immunodeficiency virus/acquired immunodeficiency syndrome and malaria.

DISCUSSION

RHD remains a leading cause of acquired heart disease in Africa, striking individuals in the prime of their lives and carrying major economic implications for households [6,33]. Comprehensive RHD control programs are cost-effective and have led to incredible gains in health in other regions of the world [35]. The present review represents a critical first step in mobilizing resources to control RHD in Tanzania and Uganda. We summarize recent evidence demonstrating that RHD remains endemic among children in these countries, and symptomatic cases among adults carry high rates of morbidity and mortality. Further, we highlight barriers to RHD prevention and control at the patient, provider, and health system levels. Our findings

answer the need for local, up-to-date, high-quality data on the epidemiology of RHD and related health system challenges and opportunities in these countries. Our review also identifies knowledge gaps in these countries that need to be addressed to develop RHD programs.

On the basis of 3 screening studies, we estimate that nearly 1.8% of schoolchildren in Tanzania and Uganda are affected by RHD. RHD appears to be more common in rural areas, although further research is needed to disentangle socioeconomic and geographical variations. The prevalence of RHD in Tanzanian and Ugandan adults is not known, which presents major challenges for health system planners looking to increase access to secondary prevention and tertiary care.

Across 6 studies of inpatients with RHD, nearly one-third of individuals had evidence of pulmonary hypertension and/or atrial fibrillation; a smaller proportion had stroke or endocarditis. Our most concerning result was that 41% had evidence of heart failure, which is a late finding in RHD that usually implies that the window for definitive surgical treatment has passed [36,37].

Similarly, we estimated high case-fatality rates from RHD among inpatients: 17% in medical wards and 27% in surgical wards. The latter is concerning because of the short follow-up interval in these studies, which implicates in-hospital, intraoperative, and early post-operative factors. Cardiac surgery programs in these two countries are nascent, and these data suggest there is still much to be done to reduce early surgical mortality to acceptable levels that are comparable with high-volume centers in other African countries.

Our review identified numerous challenges and some promising opportunities to improve RHD care in Tanzania and Uganda. Education of patients, families, and communities is clearly deficient, but education can be empowering and can have the effect of increasing care-seeking behavior among children with sore throat and individuals requiring secondary prophylaxis. As with other chronic diseases, interpersonal dynamics also seem to play a large part in positive or negative adherence behaviors around RHD.

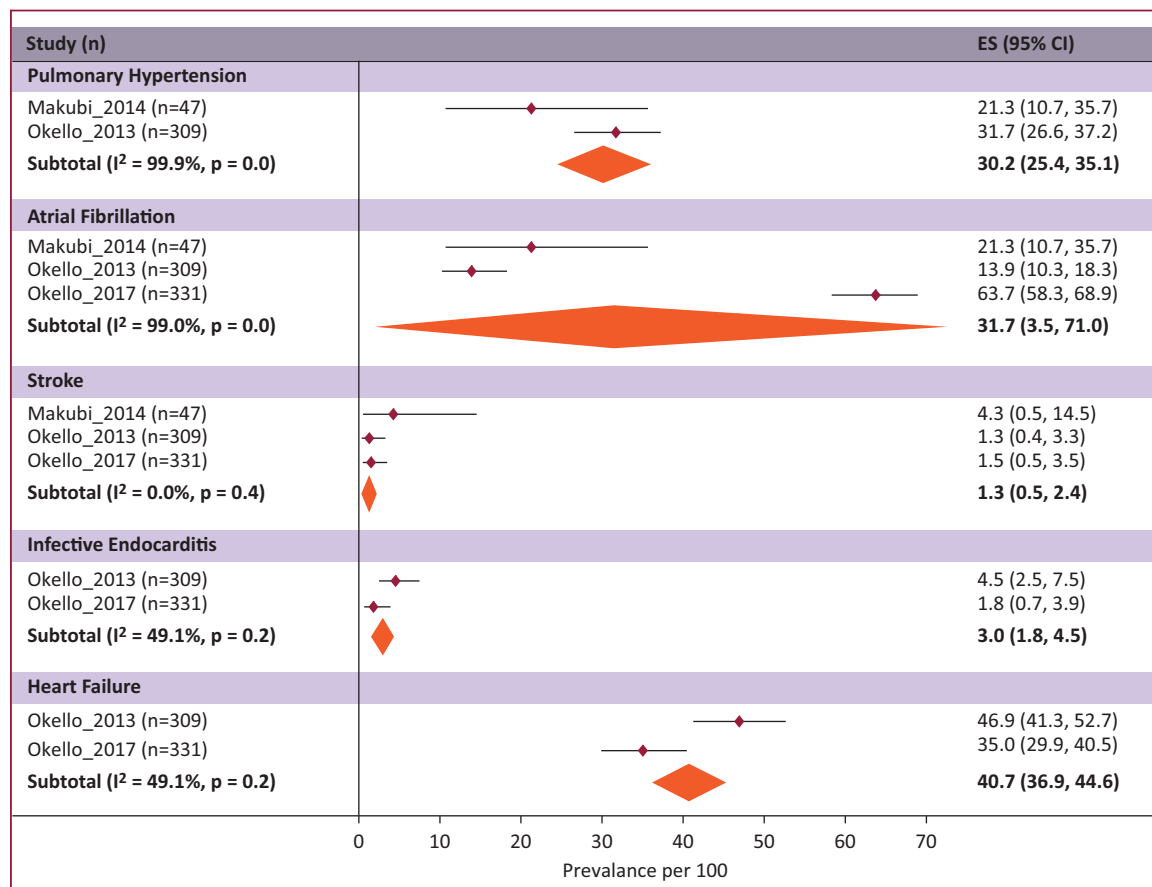


FIGURE 4. Frequencies of selected nonfatal sequelae among inpatients with RHD in Uganda and Tanzania. Abbreviations as in Figure 3.

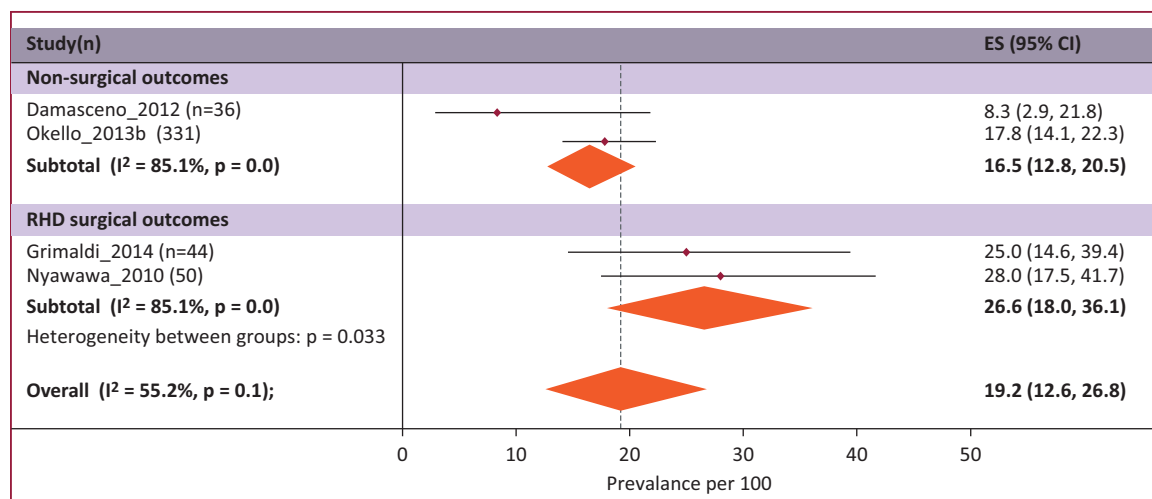


FIGURE 5. Nonsurgical and surgical case-fatality rates among inpatients with RHD in Uganda and Tanzania. Abbreviations as in Figure 3.

TABLE 4. Key data needs

Objective 1																		
	GAS		ARF				RHD											
	Incidence of GAS Pharyngitis	Prevalence of GAS Among Cases of Sore Throat	Incidence	Case-Fatality Rate			Incidence	Prevalence	Nonfatal Sequelae	Cardiac Surgery	Mortality (Case-Fatality)							
Tanzania	*	*	*	*	*	*	1	*	*	1								
Uganda	*	*	*	*	*	*	2	3	4	2								

Objective 2																		
	Tanzania									Uganda								
	Patients			Health Providers			Health Systems			Patients			Health Providers			Health Systems		
	GAS	ARF	RHD	GAS	ARF	RHD	GAS	ARF	RHD	GAS	ARF	RHD	GAS	ARF	RHD	GAS	ARF	RHD
Facilitators																		
Initial decision to seek care	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Factors influencing diagnosis	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Factors influencing treatment and/or referral	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Factors influencing adherence and retention in long-term care	*	*	*	*	*	*	*	*	*	*	*	2	*	*	2	*	*	2
Barriers																		
Initial decision to seek care	1	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Factors influencing diagnosis	*	*	*	1	*	*	1	*	*	*	*	*	*	*	*	*	*	*
Factors influencing treatment and/or referral	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
Factors influencing adherence and retention in long-term care	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Numbers denote the number of reports containing data on a specific outcome.
 *No data.

Some individuals experienced stigma and lack of support from their families or did not have positive interactions with providers. Yet, others seemed to navigate the system well and had productive relationships with providers. Still, in both countries, the health system was perceived to have inadequate resources for GAS treatment and secondary prophylaxis.

On the basis of our review, we identified key data gaps in Tanzania and Uganda (Table 4). At present, there are no data on GAS and ARF in either country, and there are relatively fewer data on fatal and nonfatal RHD in Tanzania compared with Uganda. In both countries, data on health-seeking behaviors are particularly sparse.

CONCLUSIONS

We found that RHD remains endemic in Tanzania and Uganda and that these health systems have much to do to address current gaps in care. Our review proposes an agenda for prospective data collection and lays the foundation for interventions that could ultimately eradicate ARF and reduce the burden of RHD.

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APPENDIX

ONLINE TABLE 1. Data extraction form

Data Extraction Form: Objective 1 Results								
Prevalence of Rheumatic Heart Disease								
Study ID	Total sample recruited			Withdrawals and exclusions		Total sample analyzed		# of new cases of RHD over period
Nonfatal and fatal outcomes of RHD without cardiac surgery								
Study ID	Cases of RHD	Heart failure	Congenital heart disease	Pulmonary hypertension	Stroke	Infective endocarditis	Atrial fibrillation	Death
Nonfatal and fatal outcomes of RHD cardiac surgery								
Study ID	Cases of RHD	Heart failure	Congenital heart disease	pulmonary hypertension	Stroke	Infective endocarditis	Atrial fibrillation	Death
Data Extraction Form: Objective 2 Results				Patients	Health Providers	Health Systems	Notes	
Facility (primary, referral to higher level facility, surgical intervention)								
Unit of analysis (individual interviews, focus groups)								
Research question undertaken?								
Framework if used								
Facilitators to treatment adherence?								
Barriers to treatment adherence?								

ONLINE TABLE 2. Quality assessment tools

Criteria Used for Assessment of Population-Based Studies [17]	Point
1. Was the study's target population a close representation of the national population in relation to relevant variables?	1
2. Was the sampling frame a true or close representation of the target population?	1
3. Was some form of random selection used to select the sample, OR, was a census undertaken?	1
4. Was the likelihood of non-response bias minimal?	1
5. Were data collected directly from the subjects (as opposed to a proxy)?	1
6. Was an acceptable case definition used in the study?	1
7. Was the study instrument that measured the parameter of interest shown to have reliability?	1
8. Was the same mode of data collection used for all subjects?	1
9. Was the length of the shortest prevalence period for the parameter of interest appropriate?	1
10. Were the numerator(s) and denominator(s) for the parameter of interest appropriate	1
Risk of assessment quantitative score [18] 0–5 points: high risk 6–8 points: moderate risk >8 points: low risk	
Criteria Used for Assessment of Case-Series Studies [19]	Points
1. Was the study question or objective clearly stated?	1
2. Was the study population clearly and fully described, including a case definition?	1
3. Were the cases consecutive?	1
4. Were the cases comparable?	1
5. Was the intervention clearly described?	1
6. Where the outcome measures clearly defined, valid, reliable and implemented consistently across all study participants?	1
7. Was the follow-up adequate?	1
8. Were the statistical methods well-described?	1
9. Were the results well described?	1
Case-series studies risk of assessment quantitative score 0–3 points: high risk 4–6 points: moderate risk >7 points: low risk	
Criteria Used for Assessment of Qualitative Studies [20]	Points
1. Research aim(s) was/were clearly stated?	1
2. Qualitative methods are an appropriate approach to this issue?	1
3. Study design was suitable for answering the research question?	1
4. Recruitment strategy was appropriate for the aims of the research?	1
5. Data collection was adequate for answering the research question?	1
6. Relationship between researcher and participants was adequately considered?	1
7. Other potential ethical issues were adequately considered?	1
8. Data analysis was of sufficient rigor?	1
9. Findings were clearly stated?	1
10. Research adds value to science, practice, and/or policy?	1
Qualitative studies risk of assessment quantitative score 0–5 points: high risk 6–8 points: moderate risk >8 points: low risk	

ONLINE TABLE 3. Characteristics of excluded studies

Study	Reason for Exclusion
Same population	
Godown et al., 2015 [1]	The population and results of interest are the same as Beaton 2015
Lui et al., 2015 [2]	The population and results of interest are the same as Beaton 2015
Okello et al., 2014 [3]	The results are same as those published in the studies by Beaton 2014
Zuhlke et al., 2015 [4]	The Uganda population results are the same as those reported by Okello et al., 2014
Unclear methods	
Grimaldi et al., 2013 [5]	Letter to the editor, it has no methods section.
No outcome of interest	
Beaton et al., 2014 [6]	Study reports progression of asymptomatic RHD; no information on prevalence/severity
Braitto et al., 2004 [7]	Study only reports on GAS carriage
Kisenge et al., 2011 [8]	Study does not report on outcomes of interest
Longenecker et al., 2014 [9]	Study is about the management of RHD in Uganda
Lubega, 2014 [10]	Study focuses on echocardiography characteristics; no outcomes of interest
Melkert et al., 2015 [11]	Study reports on changes in maternal mortality, not related to RHD.
Nayiga et al., (no date) [12]	Study only reports on GAS carriage, it does not report on symptomatic cases
Ploutz et al., (no date) [13]	Study focus on echocardiography awareness and acceptability; no outcomes of interest
Zachariah et al., (no date) [14]	RHD biomarker study
Zhang et al., 2013 [15]	Study does not report on outcomes of interest

GAS, group A streptococcal disease; RHD, rheumatic heart disease.

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