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Burden of disease and barriers to comprehensive care for rheumatic heart disease in South Africa: an updated systematic review protocol

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ABSTRACT

Introduction Rheumatic heart disease (RHD) is responsible for a significant burden of cardiovascular morbidity and mortality, and remains the most common cause of acquired heart disease among children and young adults in low-income and middle-income countries. Additionally, the global COVID-19 pandemic has forced the emergency restructuring of many health systems, which has had a broad impact on health in general, including cardiovascular disease. Despite significant cost to the health system and estimates from 2015 indicating both high incidence and prevalence of RHD in South Africa, no cohesive national strategy exists. An updated review of national burden of disease estimates, as well as literature on barriers to care for patients with RHD, will provide crucial information to assist in the development of a national RHD programme.

Methods and analysis Using predefined search terms that capture relevant disease processes from Group A Streptococcal (GAS) infection through to the sequelae of RHD, a search of PubMed, Scopus, ISI Web of Science, Sabinet African Journals, SA Heart and Current and Completed Research databases will be performed. All eligible studies on RHD, acute rheumatic fever and GAS infection published from April 2014 to December 2022 will be included. Vital registration data for the same period from Statistics South Africa will also be collected. A standardised data extraction form will be used to capture results for both quantitative and qualitative analyses. All studies included in burden of disease estimates will undergo quality assessment using standardised tools. Updated estimates on mortality and morbidity as well as a synthesis of work on primary, secondary and tertiary prevention of RHD will be reported.

Ethics and dissemination No ethics clearance is required for this study. Findings will be disseminated in a peer-reviewed journal and submitted to national stakeholders in RHD.

PROSPERO registration number CRD42023392782.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This systematic review applies a broad search strategy and uses a mixed-methods approach to maximise capturing all relevant data on rheumatic heart disease (RHD) in South Africa.
⇒ By defining this work within two distinct objectives, the search strategies, analysis and reporting methods can be adjusted to the most appropriate tools for the relevant literature.
⇒ This review will provide current estimates and trends on the burden of disease from RHD in South Africa (objective one) and also allow further detail on the possible impact of the COVID-19 pandemic on the landscape of RHD in this country.
⇒ Studies dealing with challenges to implementing a national RHD programme (objective two) will involve a wide variety of literature from different disciplines, including non-governmental organisations and ministry of health documents. A broader, more inclusive search strategy is needed, which will likely produce significant heterogeneity and preclude a formal quality assessment, and may limit the ability to draw unbiased conclusions from the data. However, this objective requires a broad scan of the literature and an analytical approach focused on general concepts and common themes.

INTRODUCTION

Rheumatic heart disease (RHD) develops as a consequence of acute rheumatic fever (ARF) caused by infection with Group A Streptococcus (GAS). RHD is responsible for a significant burden of cardiovascular morbidity and mortality, and remains the most common cause of acquired heart disease in children, adolescents and young adults in low-income and middle-income countries (LMICs). The global prevalence of RHD has been rising steadily since 1990, reaching 40.5 million (95% uncertainty interval: 32.1 to 50.1 million) affected in 2019.[1] Despite the number of deaths due to RHD appearing to increase in recent years, there has been a reduction in disability-adjusted life years and years of life lost with a corresponding increase in years lived with a disability,[1] most likely due

to advances in surgery and diagnostics. There remains substantial global heterogeneity in the burden of RHD among regions, with sub-Saharan Africa showing minimal improvement over the 1990–2019 period according to the Global Burden of Disease (GBD) 2019 study's update on cardiovascular diseases.[1]

In recognition of RHD as a significant, preventable cause of mortality and morbidity globally, the World Heart Federation (WHF) released a position statement in 2013 on its intention to reduce premature mortality from RHD by 25% in those aged<25 years by 2025 (25×25<25 goal).[2] Five key strategic targets were identified: comprehensive register-based control programmes, global access to benzathine penicillin G, identification and development of public figures as 'RHD champions', expansion of RHD training hubs and support for GAS vaccine development.[2] Subsequently, the WHO released a resolution at the 2018 World Health Assembly (WHA) urging member states to undertake similar key actions, including accelerating multisectoral efforts focused on prevention, improved disease surveillance and good-quality data collection and analysis that facilitate appropriate follow-up and contribute to a broader understanding of the global disease burden.[3]

The sub-Saharan African region has seen significant financial and political change in recent decades, with the pace of per capita income growth in LMICs economies accelerating rapidly, substantially above that of advanced economies.[4] Since the transition to democracy in South Africa (SA) in 1994, there have also been significant advances within the healthcare sector, with various new primary healthcare initiatives and a renewed focus on improved healthcare delivery which may impact on the profile of RHD in the country.

Although RHD was long thought to have its hotspot in Africa in the sub-Saharan region,[5] as supported by findings in the GBD 2019 study,[1] RHD appears to be endemic across the continent.[6] Despite high rates of morbidity and mortality from RHD in East Africa, there is evidence of critical data gaps in the areas of GAS and ARF epidemiology as well as healthcare usage patterns and their determinants.[7] Stakeholders across multiple sectors and countries are involved in addressing RHD in this region, highlighting the complexity and need for collaboration in building national RHD programmes in Africa.[8] Earlier data from Johannesburg (1976) and Cape Town (1981), SA showed a prevalence of approximately 7 per 1000 in school-aged children by cardiac auscultation.[9 10] Surgical reports from the pre-1994 era reported significant morbidity and mortality of up to 8% per year, especially in the young.[11] A 2015 systematic review on RHD in SA found that the overall crude incidence of symptomatic RHD was 24.7 per 100 000 (95% CI 22.1 to 27.4) population per annum among adults (aged >13 years) in Soweto, while the prevalence of asymptomatic echocardiographic RHD in schoolchildren was 20.2 cases per 1000 children (95% CI 15.3 to 26.2) in Cape Town.[12] The 60-day mortality after admission with acute heart failure due to RHD was 24.8% (95% CI 13.6% to 42.5%) and 180-day mortality was 35.4% (95% CI 21.6% to 54.4%).[12] Postoperative all-cause mortality at 30 days was 2% (95% CI 0.0% to 4%), with post-surgical survival was over 75% at 5 years, and over 70% at 10 years.[12] Cause-specific mortality rate per 100 000 population decreased from 1.27 (95% CI 1.17 to 1.39) in 1997 to 0.7 (95% CI 0.63 to 0.78) in 2012.[12] As children with RHD live longer and are diagnosed earlier, prevalence of RHD has increased in SA with better postoperative survival over the last two decades. However, despite an estimated total cost of RHD care at tertiary centres of US$2 million in 2017[13]—of which surgery costs accounted for 65%—no cohesive national RHD strategy has yet emerged in SA.

The global COVID-19 pandemic has forced the emergency restructuring of many health systems including funding mechanisms, which has had a broad impact on health in general, including cardiovascular disease.[14] An updated systematic review will reveal any impact of these changes on RHD in SA, as well as clarifying the ongoing trends in incidence, prevalence and outcomes and identifying barriers to care for those affected since the previous review in 2015.[12]

OBJECTIVES

Objective one: burden of disease from RHD, GAS infection and ARF in SA

Our primary objective is to review the most recent estimates of the incidence of newly diagnosed cases and the prevalence of existing RHD in SA, using studies published since the 2015 systematic review until December 2022, which is approximately 3 years after the onset of the global COVID-19 pandemic. Secondary objectives include characterising the fatal and non-fatal outcomes of RHD in SA (including but not limited to heart failure, atrial fibrillation (AF) and infective endocarditis (IE)), using case-fatality rates and cause-specific mortality rates and identifying trends in the RHD burden over the same period.

Objective two: challenges to implementing a comprehensive national RHD programme

In addition, information on the challenges faced by SA in responding to the 2018 WHA RHD resolution[15] will be captured using the 5×5 framework for RHD programmes proposed by Reach (Rheumatic Heart Disease, Evidence, Advocacy, Communication and Hope www.stoprhd.org).[16] Specifically, this framework addresses prevention and control efforts at four levels (baseline, primary, secondary and tertiary),[16] with five main strategic areas identified: system/structure such as governance and finance; social determinants of health; inputs such as health workforce and access to medicines; current clinical services for RHD at all levels with appropriate monitoring and evaluation, and impact or burden of disease from RHD. The last area will already be addressed in objective one, and so this objective focuses on the preceding four strategic areas.

METHODS

This review protocol was registered with the PROSPERO International Prospective Register of systematic reviews http://www.crd.york.ac.uk/PROSPERO), prior to the start of data collection and extraction.

Objective one: burden of disease from RHD, GAS infection and ARF in SA

This updated review will be designed to best control for the confounding selection and publication biases,[17 18] with the findings reported using the Meta-analysis of Observational Studies in Epidemiology guidelines.[19] Where available, findings of randomised controlled trials will undergo a separate meta-analysis if there is sufficient data.

Inclusion and exclusion criteria

Similar methods to the previous 2015 systematic review will be employed.[20] Any study reporting on the incidence or prevalence of RHD, that had been conducted in SA and published in English with patient recruitment already completed between March 2014 and December 2022 will be considered for inclusion. Studies during this same period that investigate burden of disease from GAS infection and ARF will also be considered.

Although RHD does not affect children younger than 3 years of age, there is no age restriction for the patient population. We will include any study that estimates one or more of the following epidemiological measures of disease burden from RHD, GAS infection and ARF: incidence, prevalence, remission rate, relative risk of mortality (ie, excess mortality) or cause-specific mortality. In addition, we will consider any study of cardiovascular morbidity that quantified the attributable proportion of RHD, ARF or GAS cases, but is limited to disaggregated data pertaining to these conditions. The burden of RHD among pregnant South Africans will be included as estimates were last reported in 2014.[21 22]

The prevalence of RHD has previously been defined by screening programmes of subclinical disease in asymptomatic populations.[23–25] Hospital-based studies, however, focus on clinical disease in symptomatic populations. As far as possible, we intend to elucidate diagnostic methods in both echocardiography screening studies and hospital-based studies. In the context of RHD, improvement in severity of valvular disease is due exclusively to medical, percutaneous or surgical intervention, requiring an exploration of the surgical literature for rates of disease regression versus long-term progression (ie, leading to mortality). Based on clinical experience, the most significant morbid outcomes of RHD include heart failure, ischaemic/thromboembolic or haemorrhagic stroke, AF, IE and valve repair or replacement.

Studies will be excluded if they focus on degenerative heart valve disease or rheumatological conditions other than RHD. Autopsy and necropsy studies will be omitted because consent rates are low for these procedures in SA, and their conclusions about mortality patterns are highly likely to be biased. Editorials, commentaries and case reports will be excluded, but their reference lists will be searched for additional references worth consideration for inclusion. While the WHO recommends considering the inclusion of disease register data in burden-of-disease studies, there is evidence that such data collection is unreliable and not representative of the general population.[26] From previous experience, rheumatic fever registers tend to exclude information regarding RHD and are thus excluded from our analysis.[20] Although the latest SA Demographic and Health Survey (2016) does not contain primary data on RHD, we will use the mortality data in this review.[27]

Search strategy

Using predefined search terms that capture relevant disease processes from GAS infection through to the sequelae of RHD (see table 1), the three largest databases relevant to the South African population will be searched: PubMed, ISI Web of Science and Scopus. The search strategy for this review is consistent with the original search strategy employed by Zühlke *et al*,[20] but has been updated to include terms relevant to ARF and GAS and is informed by the strategy employed by Moloi *et al* for their 2016 systematic review of RHD in Africa.[28] Additionally, to identify relevant conference proceedings, theses and abstracts, a search of the following archives at the University of Cape Town's Health Sciences Library will be performed: Current and Completed Research (SA), SA Heart and Sabinet African Journals (which covers all South African publications, including those not currently indexed). The search process will be managed using the online Rayyan platform and search results will be exported to EndNote V.20 software as reference manager. Vital registration data from Statistics SA will also be collected. Although vital statistics can be flawed, the GBD study considers these an important source of mortality data and incorporates specific methods for handling misclassifications and inconsistencies.[29] Finally, a manual snowballing search of all reference lists of studies included in the final review will be performed. Given previous experience with the 2015 review,[12] a substantial amount of 'grey' literature on RHD is anticipated and so the database search strategy is kept intentionally broad. Contact will be made with other South African cardiovascular disease researchers and practitioners, as well as with international experts on RHD, in order to identify unpublished works or to obtain additional information. All published and unpublished data will be subject to the same quality assessment and data extraction process.

Following an independent review of the titles and abstracts of the search results from all databases by two researchers (SM and LA), a secondary review of the full-text manuscripts of potentially eligible reports will be performed. A tertiary review will be conducted, where potential discrepancies over the final inclusion list will be resolved by consensus discussion between the two primary reviewers (SM and LA), with arbitration by a third reviewer (LJZ) if required.

Table 1 Search strategy

Database	Search terms	Limits
PubMed	((((rheumatic heart disease(Title/Abstract)) OR (rheumatic heart disease(MeSH Terms))) OR ((acute rheumatic fever(Title/Abstract)) OR (acute rheumatic fever(MeSH Terms)))) OR ((Strep sore throat(Title/Abstract)) OR (Strep infect*(Title/Abstract)) OR (streptococc*(Title/Abstract)))) AND ((South Afric*(Title/Abstract)) OR (Eastern Cape(Title/Abstract)OR Free State(Title/Abstract)OR Gauteng(Title/Abstract)OR KwaZulu-Natal(Title/Abstract)OR Limpopo(Title/Abstract)OR Mpumalanga(Title/Abstract)OR Northern Cape(Title/Abstract)OR North West(Title/Abstract)OR Western Cape(Title/Abstract)))	Limited to English and humans. Restricted to March 2014 to December 2022
ISI Web of Science	((((TS=(rheumatic heart disease)) OR TS=(acute rheumatic fever)) OR TS=(streptococc*)) OR TS=(Strep sore throat OR Strep infect*)) AND (CU=(South Africa))	
Scopus	((TITLE-ABS-KEY(rheumatic heart disease) OR TITLE-ABS-KEY(acute rheumatic fever) OR TITLE-ABS-KEY((Streptococc*) OR (Strep sore throat) OR (Strep infect*)))) AND (TITLE-ABS-KEY(South Africa))	
Current and Completed Research	((rheumatic heart disease) OR (rheumatic fever) OR (streptococc*) OR (Strep sore throat) OR (Strep infect*)) AND (South Africa)	
Sabinet African Journals	((rheumatic heart disease) OR (rheumatic fever) OR (streptococc*) OR (Strep sore throat) OR (Strep infect*)) AND (South Africa)	
SA Heart	Manual search of titles over March 2014 to December 2022	
Statistics South Africa	Manual search of all reports on causes of death in South Africa published 2014–2022	

Quality assessment and risk of bias

All studies deemed eligible for inclusion will undergo quality assessment using study design-specific tools from the Joanna Briggs Institute.[30] The purpose of these checklists is to assess the methodological quality of a study and to determine the extent to which a study has addressed the possibility of bias in its design, conduct and analysis. The quality assessment can then inform synthesis and interpretation of the results of the study within the systematic review. The number of questions vary among tools, but cover the sampling of study groups, identification and adjustment for confounders, allocation of interventions, validity and reliability of results and methods to address loss to follow-up, etc. A study must meet at least 80% of applicable criteria in order to be considered of 'adequate quality', but studies will not be excluded from this review based on the outcome of the quality assessment.

Data extraction

A standardised data extraction form—developed for this review and based on the template used for the original review by Zühlke *et al* in 2015[12]—will be used to extract information from included articles that will be independently duplicated (ie, not split between the two authors) in order to improve reliability. The data extraction form will capture basic study characteristics, including objectives, study population, sample size, years and location of study, as well as study design. Disease-related parameters, including hospitalisation, secondary events, surgical interventions and mortality will be recorded too. Where study data are unclear, the original author of the manuscript will be contacted to clarify the findings. Where not provided, CIs will be incorporated into the formula $SE=(upper\ limit-lower\ limit)/3.92$ or calculated using the cii command in Stata V.17. Where not stated, RHD mortality per 100 000 will be calculated as follows: RHD deaths/mid-year population. Where population number is not stated, this will be calculated by using age-specific incidence rates and cases stated in the original paper as follows: 100 000 × (number of cases/incidence per 10^5).

Data synthesis and analysis

Prevalence data from individual studies will be combined according to the Mantel-Haenszel method using random-effects meta-analysis, given the anticipated heterogeneity with prevalence studies. Heterogeneity will be evaluated using the χ^2-based Q statistic (significant for $p<0.1$) and the I^2 statistic (>50% to be indicative of 'notable' heterogeneity).[31] Meta-analysis will be conducted using the *MetaProp* command[32] using Stata (V.17). We will perform the Freeman-Tukey double arcsine transformation to ensure stabilisation of the variance of study prevalence; the transformation is essential in minimising influence

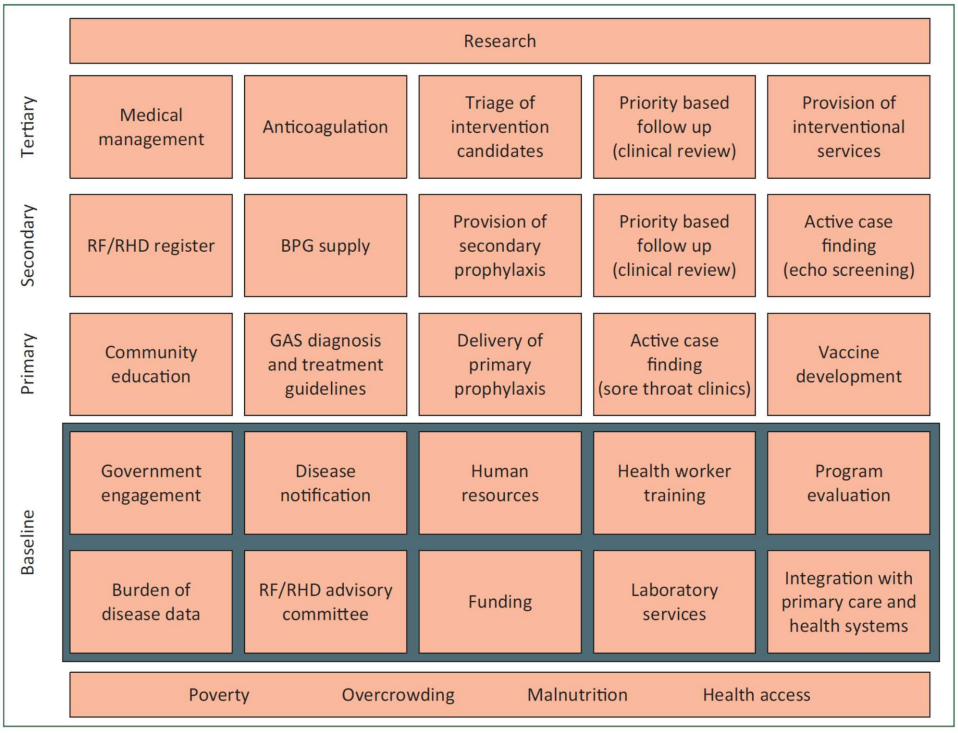

Figure 1 A conceptual framework for comprehensive, register-based RHD control programmes (derived from Wyber, 2013). BPG, benzathine penicillin; GAS, Group A Streptococcus; RF, rheumatic fever; RHD, rheumatic heart disease.

from studies with outliers before data are pooled.[32 33] To minimise publication bias, we will conduct an extensive literature search to identify completed studies or ongoing studies with preliminary results. If we include more than 10 studies, we will investigate publication bias by generating a funnel plot and using Egger's test to assess funnel plot asymmetry.[34]

Objective two: challenges to implementing a comprehensive national RHD programme

As conceptualised by Wyber in 2013,[16] this objective will look at 24 of the 25 specific facets of a comprehensive RHD programme, excluding burden of disease (figure 1). The search strategy will be informed by the systematic review protocol published by Moloi *et al*,[28] which identified stakeholders in RHD in Uganda and Tanzania using a mixed-methods approach that included case series, reports, editorials/commentaries and grey literature.[8]

Inclusion and exclusion criteria, search strategy and data management

Like objective one, all studies on RHD published between March 2014 and December 2022 (inclusive) are eligible for inclusion, with no age restriction on patient population. Studies during this same period that investigate relevant aspects of GAS infection and ARF, from preventative strategies to diagnosis and management will also be considered. The same limitation to English and human subjects will be applied. However, no restrictions in terms of study or publication type will be made as this objective requires a broad scan of the literature to ascertain information pertinent to the implementation of a national RHD programme. Articles unrelated to the topics of RHD, GAS, ARF, SA and health services will be excluded. Articles already included in burden of disease estimates (ie, objective one) will also be excluded unless they explicitly deal with the remaining 24 facets of a national RHD programme.

The same search strategy for databases as per objective one will be employed (table 1) and results will be managed via the online Rayyan platform and EndNote V.20 software as above. It is anticipated that the same initial results will be returned from each database search as per objective one. The search will be managed using the online Rayyan platform and search results will be exported to EndNote V.20 software as reference manager. The title and abstracts will be reviewed by two independent researchers (SM and LA), with HM acting as arbitrator, using the following categories:

- *Category one:* factors influencing diagnosis.
- *Category two:* factors influencing treatment or referral.
- *Category three:* factors influencing adherence and retention in long-term care.

These three categories reflect the pathway of care that patients undergo from GAS infection through to the sequelae of RHD. Barriers at each point of care highlight issues that can then be captured under the five main strategic areas listed in section *Objective two: challenges to implementing a comprehensive national RHD programme*. For example, factors influencing diagnosis (category one) could fall under system, inputs or current clinical services which overlap, but require involvement from multiple stakeholders to effect change. All other articles will be

excluded. No quality assessment or risk of bias assessment will be performed as this review is intended to provide broad comment on a national RHD strategy in SA, and all available information may be useful at this stage. SA also has a robust research community with much of the literature produced by known stakeholders and experts in the field of RHD. As such, it is anticipated that any grey literature, commentaries and editorials published in peer-reviewed journals will have input from one of these expert sources.

Data extraction, synthesis and analysis

Two reviewers will review the full text of each article and enter relevant information into a template for data extraction under the 5×5 framework for objective two. The information collected for each theme will then be combined following discussion by the two reviewers with any disputes mediated by a third reviewer.

The qualitative data will then undergo inductive analysis for overarching themes and inconsistencies, and reported under the five main strategic areas listed in section *Objective two: challenges to implementing a comprehensive national RHD programme*. If any numerical estimates are provided, they will be assessed to see if a formal quantitative meta-analysis is feasible, employing similar methods to objective one.

Presenting and reporting of results

For both objectives, flow diagrams summarising the study selection process and detailing reasons for exclusion will be used as per 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines for reporting systematic reviews.[35] This protocol as well as the final systematic review will be published in a peer-reviewed journal as was done with the previous 2015 systematic review.[12 20] Additionally, this review may help to inform the further development of national RHD programmes, by mapping the current burden of disease from RHD, ARF and GAS infection, associated trends in morbidity and mortality, and challenges faced in South Africa for effective prevention and control of RHD.

Outcomes

Objective one: burden of disease from RHD, GAS infection and ARF in SA

Incidence

We will tabulate crude age-specific incidence estimates per 100 000 person-years in summary tables, along with their 95% CIs. To estimate pooled median incidence rates and assess for heterogeneity, we will fit random effects models to log-transformed observed incidence in Stata V.17 (StataCorp, Texas, USA). We will obtain estimates of the median incidence and 25th and 75th percentiles of the distribution of true incidence by back-transforming the log estimates to the original incidence scale.

Prevalence

The pooled overall age-specific prevalence of RHD, GAS infection and ARF per 1000 persons will be calculated and expressed with a 95% CI, when appropriate. It is well known that, in screening for and diagnosing RHD, auscultation has limited sensitivity compared with echocardiography, which is the current reference test.[23] Therefore, we will report only screening data detected by echocardiography, using the 2012 WHF criteria.[36]

Data on both fatal and non-fatal outcomes will be expressed in the pooled analysis. We will tabulate estimates of crude age-specific mortality rates from ARF and RHD per 100 000 persons per year, along with their 95% CIs. Attributable proportions and the relative risks of fatal and non-fatal outcomes will be calculated when data were available, and 95% CIs will be generated using the 'cii' command in Stata V.17. A measure of the consistency of results will be included and, in cases where data are not amenable to meta-analysis, a narrative summary will be presented. Any trends will be reported on, either using meta-analytical methods such as meta-regression, if possible, or a detailed quantitative assessment.

Objective two: challenges to implementing a comprehensive national RHD programme

Findings will be reported under the five main strategic areas listed in section *Objective two: challenges to implementing a comprehensive national RHD programme*. General conclusions will be drawn using inductive analysis to comment on the current state of a national RHD programme in SA and the challenges faced in meeting the goals set by the 2018 WHA resolution on RHD. Where robust numerical estimates are found, a quantitative meta-analysis will be performed if feasible. Alternatively, reported estimates with their study context and limitations will be provided.

Patient and public involvement

There was no direct patient or public involvement in the design of this protocol and none is anticipated in the course of the review.

DISCUSSION

Strengths and limitations of proposed review

There are several strengths to this systematic review. This protocol applies a broad search strategy and uses a mixed-methods approach to maximise capturing all relevant data on RHD in SA. By defining this work within two distinct objectives, the search strategies, analysis and reporting methods can be adjusted to the most appropriate tools for the relevant literature. This review will provide current estimates and trends on the burden of disease from RHD in SA (Objective one) and also allow further detail on the possible impact of the COVID-19 pandemic on the landscape of RHD in this country.

As with any study, several limitations are anticipated. Studies dealing with challenges to implementing a national RHD programme (Objective two) will involve a wide variety of literature from different disciplines, including non-governmental organisations and ministry of health documents. In addition, we intend to use key

networks to identify relevant unpublished literature which may limit the reproducibility of this review. However, a broader, more inclusive search strategy is needed, which will likely produce significant heterogeneity and preclude a formal quality assessment, and may limit the ability to draw unbiased conclusions from the data. However, this objective requires a broad scan of the literature and an analytical approach focused on general concepts and common themes.

Dissemination and anticipated impact

This systematic review will produce current estimates of the burden of disease, including major causes of morbidity and mortality, from RHD, GAS infection and ARF in SA. This review will also produce a narrative synthesis on published literature addressing a range of challenges from primary through secondary to tertiary prevention efforts for RHD in the South African context. The conclusions of this review will be critical in providing national stakeholders, public health officials and policymakers with pooled contemporary data on RHD and its antecedent conditions of GAS infection and ARF, as well as possible comment on the impact of the COVID-19 pandemic on both the burden of disease and the restructuring of health services within the country. This information is essential in developing a national RHD programme, particularly in identifying priorities and opportunities within the existing health system. The results of this review will inform national policy and provide public health officials with appropriate targets for primary and secondary prevention through diagnosis to chronic and specialised care for patients living with RHD. It is vital that any national health programme, particularly one that ambitiously seeks to address both prevention and treatment of RHD, is well-integrated into the existing health system, although this appears to be only partially achieved even in settings that are less resource-constrained than SA.[37] This work will also help identify key areas for future research across sectors, which may encourage further collaboration among national stakeholders in RHD. The results of the proposed systematic review will be published in a peer-reviewed journal, allowing for wider dissemination beyond SA, which will feed into the current information on the profile of RHD in Africa.[7 8]

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Contributors LJZ and MEE conceived of the review. SM wrote the first draft and took primary responsibility for all subsequent revisions. LA, HM, RW, JA, DAW, MEE and LJZ contributed input to the various versions on search strategy, risk of bias assessments and planned analytical strategy. LJZ and MEE provided key scientific and statistical oversight of the protocol. All authors approved the final version of the protocol and gave permission for publication.

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Competing interests None declared.

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