TITLE: The cost-of-illness due to rheumatic heart disease: national estimates for Fiji

Rachel C Heenan[a,b], Tom Parks[c,d], Till Bärnighausen[e,f,g], Joseph Kado[h,i], David E Bloom[e], Andrew C Steer[a,b,j],*

[a] Centre for International Child Health, University of Melbourne, Royal Children's Hospital, Parkville 3052, Australia; [b] Department of General Medicine, Royal Children's Hospital Melbourne, Parkville 3052, Australia; [c] Faculty of Infectious and Tropical Diseases, London School of Hygiene & Tropical Medicine, London, WC1E 7HT; [d] Wellcome Centre for Human Genetics, University of Oxford, Churchill Hospital, Oxford OX3 7LE, United Kingdom; [e] Department of Global Health and Population, Harvard T.H. Chan School of Public Health, Boston 02115, United States; [f] Africa Health Research Institute, KwaZulu-Natal 4013, South Africa; [g] Institute of Public Health, Heidelberg University, Heidelberg 69120, Germany; [h] College of Medicine, Nursing and Health Sciences, Fiji National University, Suva, Fiji; [i] Telethon Kids Institute, Nedlands 6009, Australia; [j] Group A Streptococcal Research Group, Murdoch Children's Research Institute, Royal Children's Hospital, Parkville 3052, Australia

The authors wish it to be known that, in their opinion, the first three authors should be regarded as joint First Authors

[*] Corresponding author: Tel: +61 3 8341 6200; Email: Andrew.Steer@rch.org.au

ABSTRACT

Background

Rheumatic heart disease (RHD) is a chronic valvular heart disease that is responsible for a heavy burden of premature mortality in low- and middle-income countries. The total costs of RHD are important to health policy and research investment decisions. We estimate for the first time the total cost of RHD for Fiji (2008–2012), using a cost-of-illness approach and novel primary data on RHD disease burden and costs.

Methods

RHD cases were identified using probabilistic record linkage across four routine data sources: (1) the Fiji RHD Control Program, (2) national hospital admissions records, (3) the Ministry of Health database of cause-specific deaths, and (4) hospital echocardiographic clinic registers. For each individual with RHD, we obtained information on RHD hospital admissions, treatment, and death. We conducted a prevalence-based cost-of-illness analysis, including bottom-up assessment of indirect and direct (healthcare) costs.

Results

The estimated cost of RHD in Fiji for 2008–2012 was year-2010 FJD$91.6 million (~US$47.7 million). Productivity losses from premature mortality constituted the majority of costs (71.4%). Indirect costs were 27 times larger than the direct costs.

Conclusions

RHD leads to a heavy economic burden in Fiji. Improved prevention strategies for RHD will likely confer substantial economic benefits to the country.

KEYWORDS

Rheumatic Heart Disease, Rheumatic Fever, Cost of Illness, Economics, Pacific Islands

INTRODUCTION

Rheumatic heart disease (RHD) is a chronic cardiac valvular disease that follows acute rheumatic fever (ARF), an autoimmune, multisystem inflammatory disease of childhood triggered by infection with the bacterium group A streptococcus (GAS).[1] Rheumatic heart disease is a complex condition: many patients experience an asymptomatic phase following an episode of childhood ARF before developing heart failure in early adulthood.[1] The disease can also be complicated by atrial fibrillation, stroke, and infective endocarditis, and many patients require cardiac surgery.

While ARF and RHD are uncommon conditions in high-income countries, these diseases remain important causes of morbidity and mortality in many low- and middle-income countries.[2,3] A pooled estimate from the Pacific region over the years 1985 to 2005 found the prevalence of RHD in school-aged children to be 3.5 per 1 000, which is tenfold higher than in high-income countries.[3,4] In Fiji the prevalence of RHD is even higher, at 8.4 per 1,000.[5] Hospitalisation due to a complication of RHD is common in Fiji, and 10% of patients with RHD die during their admission.[6] Despite this heavy burden of ARF/RHD, very little is known about the economic impact of the disease.[2,3]

Several important factors suggest that RHD is a high-cost disease. The first is that RHD is a chronic illness. While RHD leads to premature death, most patients also experience many years of poor health and disability due to heart failure, arrhythmia, or stroke that leads to reduced productivity and quality of life, particularly in young adulthood.[6] The second is the clinical complexity of the disease. Outpatient management is intensive: patients require three to four weekly benzathine penicillin injections; many require medication for cardiac failure or anticoagulation. Admissions for RHD complications are frequent and lengthy.[6] Third, many patients require costly cardiac surgery. The average cost of RHD surgery in New Zealand is NZ$38 000,[7] and the Samoan and Tongan governments spend up to an estimated 15% of their health budget on overseas RHD surgery.[8]

Population-level control of ARF/RHD through primary prevention (diagnosis and treatment of GAS sore throat) and secondary prevention (regular benzathine penicillin to prevent further episodes of

ARF in patients with RHD) has been difficult to implement in most RHD-endemic low- and middle-income countries.[9] This has led to calls for the development of a GAS vaccine.[10,11] An effective GAS vaccine would prevent ARF/RHD by preventing the antecedent GAS infection. In contrast, the current primary and secondary prevention approaches for RHD control require epidemiological surveillance and case registration systems, community health education activities, significant additional human resources and training, and systems which monitor patient outcomes. Thus, vaccine-based prevention of RHD is likely to be substantially more successful than current prevention efforts in reducing the disease and economic burdens of RHD in endemic settings. The concrete prospect of a vaccine motivates our study.

Cost-of-illness studies are one of the most common study types in health policy and economics, and are often used by public health institutions, such as the Centers for Disease Control and World Health Organization, to inform decision-making and priority setting for health interventions.[12-16] Cost-of-illness studies are valuable in this regard, because they provide a detailed picture of the different types of resources consumed in an economy because of an illness. For a disease that can potentially be prevented with a vaccine in the near future, this information estimates the resources that disease prevention would free up for human and economic development by averting medical expenditures and productivity losses. Our objective here is to estimate the total national cost of ARF/RHD for the country of Fiji. Our estimation is deeply grounded in empirical data – primary data on ARF/RHD disease burdens and health care costs that we collected for the first time in Fiji – ensuring local validity and relevance of our findings. Ultimately, we hope that our estimation will provide important input into national and international policy decisions regarding ARF/RHD.

MATERIALS AND METHODS

This cost-of-illness study sought to determine the cost of ARF/RHD in Fiji during the period 1st January 2008 – 31st December 2012. This time period was chosen to align with and build on the findings of a published record-linkage cohort study determining cause-specific mortality for persons diagnosed with RHD.[17] Specifically, we estimated how many individuals were known to be suffering

from the condition during the study period and how many were hospitalized or died. Cases and events were ascertained from routine data by probabilistic linkage of routine health records from the Fiji RHD Control Program register, the national patient information system, a database of death certificates, and echocardiography clinic registers. Cost data were derived from published literature, Fijian government reports, and interviews with Fijian government employees.

Cases and events

Individuals were eligible for the study if they had attended a hospital or clinic in Fiji and been diagnosed with ARF or RHD before January 1, 2013. Cases were identified for the period 2008–2012 from four sources of data. First, we included all individuals known to the Fiji RHD Control Program's centralized register of ARF and RHD cases. This includes individuals for whom the diagnosis was questionable as indicated by qualifying terms such as "suspected" or "borderline" as well as cases detected by screening programme, all of whom were included in our analyses because all cost the health system. We also included patients from a list held by the Fiji RHD Control Program of individuals who had undergone cardiac surgery performed by visiting international teams. Second, we included all individuals with a diagnosis of ARF and/or RHD in hospital ICD-10–coded discharge diagnoses obtained from the country's national public-sector hospital patient information system.[18] Third, we included individuals whose death certificate mentioned ARF or RHD as the cause of death or co-morbidity based on a database of ICD-10-coded medical death certificate diagnoses held by the Ministry of Health. Fourth, we included individuals with a RHD diagnosis recorded in echocardiographic clinic registers at the two specialist referral divisional hospitals (where most echocardiography is performed).[17]

For each individual with a diagnosis of ARF or RHD ascertained from at least one of these sources, we obtained information for the period 2008-2012 about hospital admissions for complications of RHD and death from any cause using the patient information system, medical certificates of deaths, and cardiac surgeries using lists supplied by visiting surgical teams and from the Ministry of Health.

To avoid counting admissions for complications more than once, we merged these admissions into a single episode.

Data linkage

All individual-level data were exported from their original format into StataCorp's Stata version 12.1. Using a purpose-designed probabilistic algorithm each record was linked to a national health number.[17] As described previously, we used a variety of identifier fields including names, dates and demographics that referred to the same individual.[17] To reduce the number of possible matched records we sorted (termed 'blocking') by finding groups individuals with similar names and similar ages. The likelihood of a true match was estimated under the Fellegi-Sunter model of record-linkage using expectation maximisation.[19] From this a posterior probability was calculated taking into account addition information, including locality, age, gender and ethnicity. As is standard, record pairs achieving a posterior probability of 50% or more were considered a match.[17]

Eligibility

Broadly, cases were included under four categories: (1) those who had ARF without record of RHD or complications, (2) those with firm evidence of RHD who were not hospitalized for the condition during the study, (3) those who were hospitalized for RHD, and (4) other individuals known to the Fiji RHD Control Program receiving treatment for RHD/ARF on an outpatient basis without firm evidence of either diagnosis. Because of the uncertainty of their diagnosis, the latter group was excluded from estimates of admissions for complications. In addition, patients who had died before January 1, 2008 were excluded. Finally, patients who could not be matched to a valid national health number were included in counts of the number of cases and the number of deaths but excluded from estimates of admissions for complications.

Cost-of-illness approach

We choose a cost-of-illness approach, because it provides detailed picture of the use of different types of human and economic resources because of the presence of a diseases in a country. Cost-of-illness

approaches are a recommended for health policy support by major public health institutions, such as the US CDC and WHO.[12-16] Cost-of-illness approaches have recently been used in several powerful studies estimating the human and economic resources that are used because of potentially preventable diseases.[20-24] The cost-of-illness approach is particularly well-suited for estimating the societal losses associated with potentially preventable diseases, because it provides a quantification of the resources that would become available to a country if a disease disappeared.

Within the family of cost-of-illness methods, we made the following choices. We conducted a prevalence-based study on the cost of ARF/RHD, including both established and new disease. The direct costs of health care utilization and the indirect costs of productivity losses were included in the cost-of-illness estimation. Lost expected future earnings resulting from premature mortality were assigned to the year when the death occurred. We chose a prevalence rather than an incidence-based approach because our primary data on RHD include both established and new cases of RHD and cannot be used to distinguish between the two. The study is a bottom-up rather than a top-down cost-of-illness study, because we measured the quantity of health inputs used and multiplied by the unit costs of these inputs to derive total cost estimates.

We took a comprehensive perspective to cost estimation: We attempted to include as many types of costs of illness – such as transport costs, outpatient consultation costs, and inpatient costs – as we could given the available data. In particular, we measured empirically the total number of admissions and hospital days (in intensive care units and in nonintensive care) by type of disease (ARF; RHD without complication; and RHD with heart failure, arrhythmia, stroke, or endocarditis). We further measured additional surgical costs. Finally, we collected data on the number of outpatient visits for ARF/RHD diagnosis and treatment and the cost per outpatient visit. To estimate unit costs we used a microcosting approach, establishing the unit costs by summing up each single cost contributing component. We chose a micro- rather than a gross-costing approach because the former is generally more accurate.

As the exact amount of some resources used (e.g.: vials of penicillin) was not available to us, costs for each hospital admission, outpatient visit, or surgery were estimated using relevant guidelines for ARF, RHD, and heart failure, stroke, and infective endocarditis (Table 1).[25-27] These guidelines were adapted to local practices and resource limitations by an experienced physician who has treated ARF/RHD patients in Fiji for many years. Costs for each component in a hospitalization, outpatient visit, or surgery were obtained from published literature; government reports (e.g., Fiji Pharmaceutical and Biomedical Services Centre); and interviews with Ministry of Health staff, key healthcare workers, administrative personnel at Fiji's largest hospital (the Colonial War Memorial Hospital, Suva), and cardiac surgery team members (Table 2). Patient public transport costs were estimated through interviews with health staff, based on a random sample of 1% of patients from the Fiji RHD Control Program register.

Cost-of-illness estimation

We assumed that ARF/RHD cases continued unless they ended in death and that the RHD-specific mortality rates were uniform throughout the study period. All costs were discounted at an annual rate of 3% to the year 2010, the midpoint of the study period. Table 1 shows the health care unit costs estimated in this study. Travel costs were included in direct health care expenditures.

In addition to the direct costs of health care utilization, we estimated indirect costs due to productivity losses resulting from ARF/RHD. We valued productive work days lost to ARF/RHD morbidity and mortality at the daily per-capita gross domestic product (GDP) in the year when the ARF/RHD event occurred. We estimated separately indirect costs as productivity losses due to health care utilization (e.g., time spent in a hospital), and productivity losses because of morbidity experienced outside a health care setting. We assumed that all patients hospitalised for heart failure and half of those hospitalised for arrhythmia would have at least New York Heart Association Stage II which has previously been associated with loss of 132 out of 260 working days per year.[28] Finally, we assumed based on previous studies that 25% of all stroke patients did not return to work after the stroke event.[29]

Economic losses due to premature death were estimated as the discounted per-capita Gross Domestic Product (GDP) streams from the calendar year in which a death occurred into the future (i.e. the present value of a person's future economic activity). To estimate the future years over which these productivity losses occurred, we used the age of death from the subset of patients whose deaths could be attributed to ARF/RHD. Productivity losses started in the calendar year of death. For each individual, we used the sex-specific life expectancy at the age of death[30] to determine the calendar year in which the productivity losses due to premature mortality ended.

In addition to the individual patient costs and productivity losses, we also measured the spending on the Fiji RHD Control Program, which is funded by the Ministry of Health and organizes the nationwide secondary prevention programme focusing on managerial functions and monitoring and evaluation. We included these programme costs in the cost-of-illness estimate because secondary prevention would become obsolete if successful primary prevention was achieved with a vaccine.

RESULTS

In total, 2 619 patients met the inclusion criteria. Of these, 56% were female. 64.9% were of iTaukei (Indigenous) ethnicity, 29% were of Indian ethnicity, and the remainder were other ethnicities. The mean age was 25 years ranging 5-69 years. Among these patients, 374 deaths were RHD-attributable during the 5-year study period. While 1 195 ARF/RHD patients experienced at least one hospital admission (total 2 023 admissions), the remaining 1 424 individuals received only outpatient care during the five-year period. This patient cohort is described in further detail in a previously published study.[17]

Figure 1 and Table 3 show the breakdown of the total costs, which are categorised as due to mortality, morbidity or other. The morbidity costs include: (1) direct costs of health care utilization; and (2) indirect costs due to (a) health care utilization and (b) productivity losses due to morbidity experienced outside health care settings. These cost estimates are shown for ARF/RHD outpatients,

for five different types of ARF/RHD-related admissions, as well as for surgeries. In addition, we show the total cost of premature mortality, and cost of the Fiji RHD Control Program. The estimated total cost of ARF/RHD for the five-year period 2008-2012 was approximately year-2010 Fiji$91.6 million (or US$47.7 million using the 2010 average exchange rate)[31], equating to an average cost per patient of FJD$6 995 annually. The largest cost item to the Fiji economy was the productivity losses from premature mortality, which constitute 71.4% of the total cost-of-illness for the period. The total indirect costs of illness were 27 times larger than the total direct costs.

Total outpatient cost-of-illness was slightly higher than total inpatient cost-of-illness (year-2010 Fiji$13.2M versus 12.9M million respectively). Heart failure was the most costly inpatient complication, comprising more than a third of total inpatient cost-of-illness. For all complicating conditions, productivity losses comprised the bulk of the costs, ranging from 63.9% to 87.2% of total costs.

DISCUSSION

This is one of the first studies to assess the cost-of-illness of ARF and RHD in a low- or middle-income country. While this study is of particular value to Fiji, a country which has among the highest documented prevalence of RHD in the world,[5] and where RHD is an important and recognized clinical and public health problem,[6] it provides a valuable evaluation framework and an indication of the economic burden of ARF/RHD in low and middle-income countries.

The total cost-of-illness over the observation period 2008–2012 was very large at year-2010 Fiji$91.6 million. In comparison, the total Fiji GDP in year-2010 Fiji$ for the same period was $25 062 million, thus the cost-of-illness due to ARF/RHD was about one third of one percent of GDP. This finding suggests that an effective intervention to prevent ARF/RHD, such as a vaccine against group A streptococcal infection, could yield very large economic benefit for Fiji, depending on the cost of such an intervention.

The total cost of ARF/RHD is largely driven by productivity losses, which account for 96.5% of the total cost-of-illness. This finding is not surprising given the significant premature mortality caused by RHD and the chronic and debilitating natural course of the disease, with severe complications such as heart failure and stroke commonly occurring before or during the productive middle years of life.

While surgical costs are relatively low as a proportion of total cost-of-illness, they are still substantial on a per-patient basis and may be a barrier for individual patients to access surgical care. Even higher proportional costs for surgery have been found in studies of the economic burden of RHD in high-income countries. A recent study in New Zealand found that 72% of the cost of all RHD admissions was attributable to valve surgery.[7] Visiting teams of cardiac surgeons run surgical "camps" in Fiji twice a year, and occasionally patients are flown overseas for valve replacement. However, despite these international aid efforts, a considerable proportion of the need for valve surgery is not met in Fiji, explaining the low proportional (but high per-patient) costs of surgery in the country. Increasing the availability of surgery may prove cost-effective in Fiji because of the high cost burden of premature death that timely surgery can avert.

Global data on the cost-of-illness due to RHD are scarce. The findings from the only other study of the cost-of-illness of RHD in low income countries, using Indian and Ugandan data, were consistent with our results, despite their use of a top-down (rather than bottom-up) costing approach.[32] In Fiji (an upper-middle income economy) we found that RHD cost an estimated USD$11.4 million per million population per year, while in Uganda (a low-income economy) and India (a lower-middle income economy) these costs were USD$11.6 and USD$8 million respectively, and a similar proportion were indirect costs (97%, 88% and 83% respectively). In contrast, a study in South Korea found a substantially smaller proportion of indirect costs (39%) compared with our study in Fiji.[33] This difference is unsurprising as the direct costs of RHD-related health care utilization in a high-income setting such as South Korea are comparatively larger because fewer cases remain undetected or untreated and treatment intensity is high. Therefore, productivity losses due to mortality and

morbidity start earlier in the life course in Fiji than in South Korea. This underscores the importance of prevention programs in low- and middle-income countries.

To date, there is only one other study on the economic burdens of diseases for Fiji. This study examines the cost of episodes of outpatient pneumonia in children <5 years, finding the total societal cost of a single episode of outpatient pneumonia to be an average of USD$18.98 (FJD$28.46; 2008 dollars).[34] This study underscores the significant burden of ARF/RHD: a child could have new episodes of outpatient pneumonia on two of every three days in a year, and still the economic burden of their illnesses (FJD$6 856) would fall slightly short of the costs accrued by the average ARF/RHD patient in our cohort (FJD$6 995; assumes minimal change in value between 2008 and 2010 $FJD). While the two studies are not directly comparable (our study takes a human capital approach, while the study of childhood pneumonia measures loss of household income directly), it is noteworthy that the costs to society associated with ARF/RHD appear to far outweigh those associated with the outpatient management of this common childhood illness.

The largest single component of total cost of ARF/RHD in Fiji is the cost of premature mortality. This suggests that at present levels of investment in treating ARF/RHD, Fiji's health care system cannot avert the major economic losses due to the disease. Secondary prevention programs should be well funded to prevent the progression of mild RHD to severe RHD disease and premature mortality.

At present, the empirical data needed for a cost-effectiveness of a group A streptococcus vaccine to prevent ARF and RHD are lacking. In this situation, cost-of-illness estimates provide an important basis for policy and planning for future vaccine campaigns, as well as for other prevention interventions. Once the cost-effectiveness of a group A streptococcus vaccine is known, our cost-of-illness results will continue to be valuable for policy – they describe the total economic boost that would result if prevention interventions eliminated ARF and RHD from Fiji.

Our study has several limitations. Pregnancy-related RHD complications were excluded from the study, as linking such admissions to underlying RHD was not possible using our data sources and methodology. The contribution of pregnancy to clinical decompensation of RHD is well recognized,[35] so this omission implies that the economic burden of RHD is likely underestimated in our study.

Secondly, to ascertain mortality, we used cause of death defined by the ICD10 codes pertaining to RHD or ARF, or to an ICD10 code for valvular heart disease or cardiac complications.[17] While we used a rigorous record linkage approach to amalgamate multiple sources of routine epidemiologic data, some residual data inaccuracy likely persisted due to coding error. Theoretically, this leaves a risk that some of the burden attributed to ARF/RHD should have been attributed to a different cause.

There are also several limitations inherent in the cost-of-illness methodology itself. In particular, cost-of-illness studies have been criticized because the cost estimates depend on past resource allocation decisions.[36] However, cost-of-illness estimates have substantial value in that they measure the total economic losses that could be avoided due to successful prevention efforts. We also followed the "human capital approach" of valuing life at per-capita GDP. The human capital approach leads to an underestimate of cost-of-illness because human life has many other values in addition to market productivity. Unfortunately, good holistic valuations of life are presently not available for most low- and middle-income countries. In this situation, the valuation of life as average per-capita GDP has several advantages, including setting a conservative lower-bound estimate, and the ability to compare with other studies. We took a comprehensive perspective to our cost estimation. However, the available data did not allow us to include all types of costs. For instance, we lacked data to estimate the costs of home improvements to accommodate better a patient suffering from RHD. Our cost-of-illness numbers for ARF/RHD in Fiji are thus an underestimate of the true costs of this disease. This, in turn, implies that our estimates are conservative when used to inform policy decisions on ARF/RHD prevention. Moreover, given that we included many of the most important types of direct and indirect costs of ARF/RHD it is unlikely that our underestimation is severe. Finally, we published an earlier estimate of the costs associated with mortality.[17] However, the present estimate, which is

slightly higher (i.e. $30.4M versus $34.1M per year), is likely to be more accurate because it is based on actual age of death rather than amalgamation of five-year age categories.

The results from this study are broadly generalizable to countries with demographic and epidemiologic features similar to Fiji. RHD is predominantly a disease of the poor and so is common in low- and middle-income countries. The main barrier to generalizability is that Fiji is wealthier than many other countries with high RHD burdens, particularly in sub-Saharan Africa. In lower-income countries the direct costs of ARF/RHD are likely to represent a lower proportion of total costs, and indirect costs higher. Further studies of cost-of-illness are needed, particularly in sub-Saharan African countries and other settings where RHD is endemic. Overall ARF and RHD impose a large economic burden in Fiji and the largest contributions to this burden are the indirect costs of productivity losses, in particular due to premature mortality. Our results suggest that improved and novel primary and secondary prevention strategies for RHD would be economically highly beneficial in Fiji.

CONCLUSIONS

This study provides evidence that the cost-of-illness of rheumatic heart disease and acute rheumatic fever are high in Fiji, a country with among the highest documented prevalence of rheumatic heart disease in the world. We found that the majority of the costs are indirect and attributable to premature mortality. Heart failure was the most costly complicating condition. Surgical costs only contributed a small amount to overall costs, due to relatively few people accessing surgical care. The high total costs of RHD suggest that at present levels of investment, Fiji's health care system cannot avert the major economic losses due to the disease. Access to evidence of these costs helps policy makers improve the effectiveness of resource allocation decisions. Specifically, these data may support further investment in cost-effective primary and secondary prevention strategies. Furthermore, this evidence helps strengthen the global case for the development of a group A streptococcal vaccine, as it signals likely vaccine demand through a demonstration of potential costs averted should a vaccine become available.

AUTHORS' STATEMENTS

Authors' contributions

The authors contributed in the following ways: TB, ACS, DEB conceived the study; TB, RCH, TP, JK, DEB, ACS designed the study protocol; TB and RCH undertook the literature search; RCH and TP undertook the acquisition of data; RCH, TP and TB analysed and interpreted data; RCH, TP, TB and ACS wrote initial manuscript draft; RCH, TP, TB, JK, DEB, ACS provided critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript. ACS is a guarantor of this work and had full access to all the data, and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Competing interests

There are no conflicts of interest to disclose for any author.

Ethical approval

This work was approved by the Oxford Tropical Research Ethics Committee (1055-13) and the Fiji National Research Ethics Review Committee (2013-89).

Figure 1: Cost-of-illness due to ARF & RHD in Fiji, 2008-2012 ($M FJD):

(see attached .pptx file)

Waterfall chart showing dollar amount (in millions of Fiji dollars) contributed by each of the major types of costs (across outpatient stays, inpatient stays, surgery, RHD control program, and mortality), and segmented into direct and indirect costs.

ARF: acute rheumatic fever; FJD: Fiji dollars; RHD: rheumatic heart disease

Table 1: Unit cost estimates (FJD$)

(see attached .docx file)

Table 2: Costs components and sources of information

(see attached .docx file)

Table 3: Cost-of-illness due to acute rheumatic fever and rheumatic heart disease in Fiji, 2008-2012 (FJD$)

(see attached .docx file)

REFERENCES

1. *Rheumatic fever and rheumatic heart disease: report of a WHO Expert Consultation Geneva.* Geneva: World Health Organisation;2004.
2. Carapetis JR. Rheumatic heart disease in developing countries. *N Engl J Med.* 2007;357(5):439-441.
3. Carapetis JR, Steer AC, Mulholland EK, Weber M. The global burden of group A streptococcal diseases. *Lancet Infect Dis.* 2005;5(11):685-694.
4. Steer AC, Carapetis JR, Nolan TM, Shann F. Systematic review of rheumatic heart disease prevalence in children in developing countries: the role of environmental factors. *J Paediatr Child Health.* 2002;38(3):229-234.
5. Steer AC, Kado J, Wilson N, et al. High prevalence of rheumatic heart disease by clinical and echocardiographic screening among children in Fiji. *J Heart Valve Dis.* 2009;18:327-335.
6. Steer AC, Kado J, Jenney AW, et al. Acute rheumatic fever and rheumatic heart disease in Fiji: prospective surveillance, 2005-2007. *Med J Aust.* 2009;190(3):133-135.
7. Milne RJ, Lennon D, Stewart JM, Vander Hoorn S, Scuffham PA. Mortality and hospitalisation costs of rheumatic fever and rheumatic heart disease in New Zealand. *J Paediatr Child Health.* 2012;48:692-697.
8. Colquhoun SM, Carapetis JR, Kado JH, Steer AC. Rheumatic heart disease and its control in the Pacific. *Expert Rev Cardiovasc Ther.* 2009;7(12):1517-1524.
9. Steer AC, Carapetis JR. Prevention and treatment of rheumatic heart disease in the developing world. *Nat Rev Cardiol.* 2009;6(11):689-698.
10. Bisno AL, Rubin FA, Cleary PP, Dale JB. Prospects for a group A streptococcal vaccine: rationale, feasibility, and obstacles--report of a National Institute of Allergy and Infectious Diseases workshop. *Clin Infect Dis.* 2005;41(8):1150-1156.
11. *Group A streptococcal vaccine development: current status and issues of relevance to less developed countries.* Geneva: World Health Organization, Department of Child and Adolescent Health and Development;2005.
12. Department of Immunization, Vaccines, and, Biologics. *WHO Manual for estimating the economic burden of seasonal influenza.* Geneva: World Health Organization;2016.
13. Lane R, Soyemi A. Five-Part Webcast on Economic Evaluation. 2017; https://www.cdc.gov/dhdsp/evaluation_resources/economic_evaluation/index.htm. Accessed 18 August, 2019.
14. Rice DP. Estimating the cost of illness. *American Journal of Public Health and the Nations Health.* 1967;57(3):424-440.
15. Tarricone R. Cost-of-illness analysis. What room in health economics? *Health Policy.* 2006;77(1):51-63.
16. Clabaugh G, Ward MM. Cost-of-illness studies in the United States: a systematic review of methodologies used for direct cost. *Value Health.* 2008;11(1):13-21.
17. Parks T, Kado J, Miller AE, et al. Rheumatic Heart Disease-Attributable Mortality at Ages 5–69 Years in Fiji: A Five-Year, National, Population-Based Record-Linkage Cohort Study. *PLOS Neglected Tropical Diseases.* 2015;9(9):e0004033.
18. Roberts G, Irava W, Tuiketei T, et al. *The Fiji Islands Health System Review.* Manila: World Health Organization, Regional Office for the Western Pacific;2011.
19. Fellegi IP, Sunter AB. A Theory for Record Linkage. *Journal of the American Statistical Association.* 1969;64(328):1183-1210.
20. Bommer C, Heesemann E, Sagalova V, et al. The global economic burden of diabetes in adults aged 20-79 years: a cost-of-illness study. *The lancet Diabetes & endocrinology.* 2017;5(6):423-430.
21. Ozawa S, Portnoy A, Getaneh H, et al. Modeling The Economic Burden Of Adult Vaccine-Preventable Diseases In The United States. *Health affairs (Project Hope).* 2016;35(11):2124-2132.

22. Ozawa S, Clark S, Portnoy A, et al. Estimated economic impact of vaccinations in 73 low- and middle-income countries, 2001-2020. *Bulletin of the World Health Organization.* 2017;95(9):629-638.
23. Sarker AR, Sultana M, Mahumud RA, et al. Economic costs of hospitalized diarrheal disease in Bangladesh: a societal perspective. *Glob Health Res Policy.* 2018;3:1-1.
24. Lesyuk W, Kriza C, Kolominsky-Rabas P. Cost-of-illness studies in heart failure: a systematic review 2004-2016. *BMC cardiovascular disorders.* 2018;18(1):74.
25. *RHD Australia (ARF/RHD writing group), National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand. Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease (2nd edition).* 2012.
26. Jauch EC, Saver JL, Adams HP, Jr., et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke; a journal of cerebral circulation.* 2013;44(3):870-947.
27. Hoen B, Duval X. Clinical practice. Infective endocarditis. *New Engl J Med.* 2013;368(15):1425-1433.
28. Spannheimer A, Goertz A. Economic evaluation of torasemide in congestive heart failure in Germany. *Value in Health: The Journal of the International Society for Pharmacoeconomics and Outcomes Research.* 1998;1(1):51.
29. Hackett ML, Glozier N, Jan S, Lindley R. Returning to paid employment after stroke: the Psychosocial Outcomes In StrokE (POISE) cohort study. *PLOS One.* 2012;7(7):e41795.
30. World Health Organization. Life tables by country: Fiji. *Global Health Observatory Data Repository* 2016; http://apps.who.int/gho/data/?theme=main&vid=60560. Accessed 25 March, 2018.
31. OANDA. OANDA Historical Rates. https://www.oanda.com/fx-for-business/historical-rates. Accessed 5 May, 2017.
32. Sandhu AT, G K, Bolger A, Okello E, Kazi DS. Abstract 19839: Clinical and Economic Burden of Rheumatic Heart Disease in Low-Income Nations: Estimating the Cost-of-Illness in India and Uganda. *Circulation.* 2014;130(Suppl 2):A19839-A19839.
33. Seo HY, Yoon SJ, Kim EJ, Oh IH, Lee YH, Kim YA. The economic burden of rheumatic heart disease in South Korea. *Rheumatol Int.* 2013;33(6):1505-1510.
34. Temple B, Griffiths UK, Mulholland EK, Ratu FT, Tikoduadua L, Russell FM. The cost of outpatient pneumonia in children <5 years of age in Fiji. *Tropical Medicine & International Health.* 2012;17(2):197-203.
35. North RA, Sadler L, Stewart AW, McCowan LM, Kerr AR, White HD. Long-term survival and valve-related complications in young women with cardiac valve replacements. *Circulation.* 1999;99(20):2669-2676.
36. Drummond M. Cost-of-illness studies: a major headache? *Pharmacoeconomics.* 1992;2(1):1-4.