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ORIGINAL ARTICLE



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

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**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 ECG 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 $FJ91.6 million (approximately US$47.7 million). Productivity losses from premature mortality constituted the majority of costs (71.4%). Indirect costs were 27-fold 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:** cost of illness, economics, rheumatic fever, rheumatic heart disease, 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] RHD 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 from 1985 to 2005 found the prevalence of RHD in school-aged children to be 3.5 per 1000, which is 10-fold higher than in high-income countries.[3,4] In Fiji, the prevalence of RHD is even higher, at 8.4 per 1000.[5] Hospitalization 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 and 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 $NZ38 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. By 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 US Centers for Disease Control (US CDC) and WHO 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 which 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 grounded in empirical data—primary data on ARF/RHD disease burdens and healthcare 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 1 January 2008–31 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 people 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 ECG 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 1 January 2013. Cases were identified for 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 program, all of whom were included in our analyses because all of them 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 comorbidity 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 ECG clinic registers at the two specialist referral divisional hospitals (where most ECG 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 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 STATA version 12.1 (StataCorp LP, College Station, TX, USA). 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 of 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 maximization.[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 a 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 1 January 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 chose a cost-of-illness approach because it provides a detailed picture of the use of different types of human and economic resources because of the presence of a disease in a country. Cost-of-illness approaches are 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 to 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 diseases. The direct costs of healthcare 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 non-intensive 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 micro-costing approach, establishing the unit costs by summing up each single cost-contributing component. We chose a micro-costing rather than a gross-costing approach because the former is generally more accurate.

As the exact amounts of some resources used (e.g. vials of penicillin) were not available to us, costs for each hospital admission, outpatient visit or surgery were estimated using the 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. the 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 healthcare unit costs estimated in this study. Travel costs were included in direct healthcare expenditures.

In addition to the direct costs of healthcare 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 separately estimated indirect costs as productivity losses due to healthcare utilization (e.g. time spent in a hospital) and productivity losses because of morbidity experienced outside a healthcare setting. We assumed that all patients hospitalized for heart failure and half of those hospitalized for arrhythmia would have heart failure classified as at least New York Heart Association Stage II, which has previously been associated with a loss of 132 out of 260 working days per year.[28] Finally, based on previous studies, we assumed 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 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 gender-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

**Table 1.** Unit cost estimates ($FJ)

| Disease | Fixed cost per case ($FJ) | Cost/day non-ICU ($FJ) | Cost/day ICU ($FJ) |
|---|---|---|---|
| *Inpatient costs* | | | |
| ARF[a] | 133 | 84 | 106 |
| RHD | | | |
| No complication[b] | 45 | 84 | 170 |
| Heart failure[c] | 67 | 84 | 148 |
| Arrhythmia[c] | 67 | 84 | 148 |
| Stroke[d] | 111 | 84 | 170 |
| Endocarditis[e] | 175 | 106 | 112 |
| Surgery (international) | 23 418 | NA | NA |
| *Outpatient costs* | | | |
| ARF/RHD | 193 | NA | NA |

Note: medication costs (including antibiotics) were unable to be ascertained individually; they are included within the average cost/day of admission

[a]ARF admissions include baseline tests (FBE, ESR, CXR, ECG, throat swab (MC&S), ASOT [two]) and additional tests per day of ICU admission (FBE).

[b]RHD (no complications) admissions include baseline tests (FBE, CXR, ECG) and additional tests per day of ICU admissions (FBE, UEC, CXR, ABG)

[c]RHD with heart failure and arrhythmia admissions include baseline tests (FBE, UEC, ECG, CXR) and additional tests per day of ICU admission (FBE, UEC, CXR).

[d]RHD with stroke admissions include baseline tests (FBE, INR, blood glucose, CT brain, UEC, ECG) and additional tests per day of ICU admission (FBE, UEC, INR, CXR)

[e]RHD with endocarditis admissions include baseline tests (ECG [two], blood cultures [three], FBE, ESR, dental review), additional tests per day of non-ICU admission (FBE) and additional tests per day of ICU admission (FBE, IV fluids [3 L])

ABG, arterial blood gas; ARF, acute rheumatic fever; ASOT, antistreptolysin o titre; CT, computer tomography; CXR: chest X-ray; ESR, erythrocyte sedimentation rate; FBE, full blood examination; ICU, intensive care unit; INR, international normalized ratio; IV, intravenous; MC&S, microscopy, culture and sensitivity; NA, not applicable; RHD, rheumatic heart disease; UEC, urea, electrolytes and creatinine

**Table 2.** Cost components and sources of information.

| Cost component | Source of cost information |
|---|---|
| Intravenous fluids | Fiji Pharmaceutical and Biomedical Services Centre |
| Pharmaceuticals | |
| ECG | Fiji RHD Control Program and interview with an echo sonographer at CWMH |
| Radiology | Published literature[37] |
| Laboratory tests | |
| Inpatient admission (cost per day in hospital) | |
| Outpatient visit | |
| Dental outpatient visit | |
| Surgical costs in Fiji: mechanical valve, surgical equipment | Personal correspondence with Operation Open Heart (cardiac surgery team) |
| Surgical costs for international surgery | Fiji Ministry of Health |
| Fiji RHD Control Program | Program staff |

CWMH, Colonial War Memorial Hospital; RHD, rheumatic heart disease.

Program, which is funded by the Ministry of Health and organizes the nationwide secondary prevention program focusing on managerial functions and monitoring and evaluation. We included these program 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, 2619 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 (range 5–69) y. Among these patients,

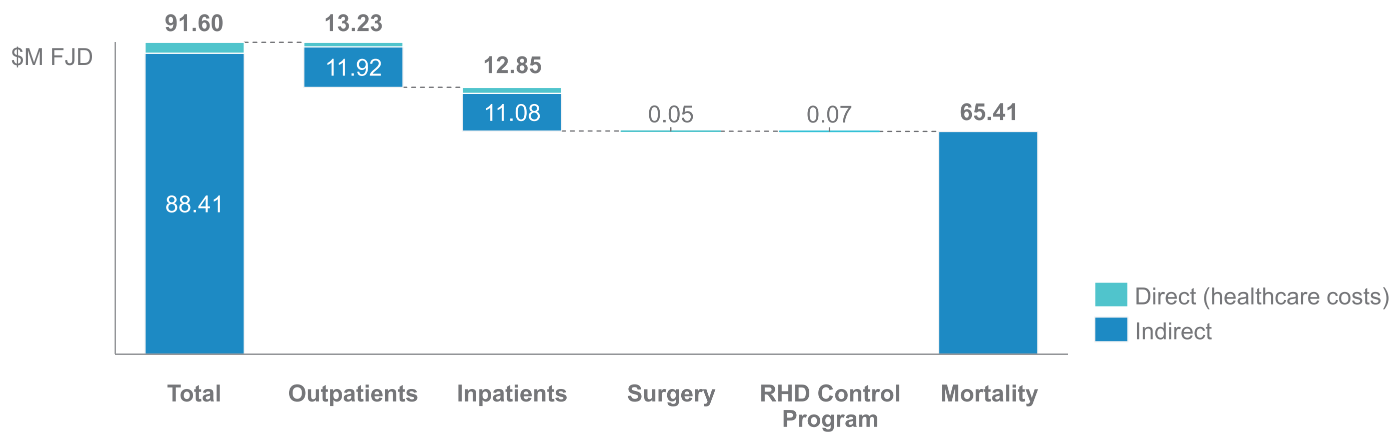


**Figure 1.** Cost-of-illness due to acute rheumatic fever (ARF) and rheumatic heart disease (RHD) in Fiji, 2008–2012 ($FJ million).

374 deaths were RHD-attributable during the 5-y study period. While 1195 ARF/RHD patients experienced at least one hospital admission (of a total of 2023 admissions), the remaining 1424 received only outpatient care during the 5-y period. This patient cohort is described in greater detail in a previous study.[17]

Figure 1 and Table 3 show the breakdown of the total costs, which are categorized as due to mortality, morbidity or other. The morbidity costs include: (1) direct costs of healthcare utilization and (2) indirect costs due to healthcare utilization and productivity losses due to morbidity experienced outside of healthcare 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 5-y period of 2008–2012 was approximately year-2010 $FJ91.6 million (or US$47.7 million using the 2010 average exchange rate)[31], equating to an average cost per patient of $FJ6995 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-fold larger than the total direct costs.

Total outpatient cost-of-illness was slightly higher than total inpatient cost-of-illness (year-2010 $FJ13.2 million versus $FJ12.9 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] one where RHD is an important and recognized clinical and public health problem,[6] it also 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 $FJ91.6 million. By comparison, the total Fiji GDP in year-2010 $FJ for the same period was $FJ25 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 GAS infection, could yield very large economic benefits 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 to 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 replacements. 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 a bottom-up) costing approach.[32] In Fiji (an upper middle income economy), we found that RHD cost an estimated US$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 US$11.6 million and US$8 million, respectively, of which a similar proportion were indirect costs (97, 88 and 83%, respectively). By contrast, a study in South

**Table 3.** Cost-of-illness due to acute rheumatic fever and rheumatic heart disease in Fiji, 2008–2012 ($FJ)

| Morbidity | Cost ($FJ) |
|---|---|
| **Outpatients** | |
| Direct costs, healthcare utilization | 1311 484 |
| Indirect costs, productivity loss | 11 919 018 |
| *Total* | *13 230 502* |
| **Inpatients** | |
| ***No complications*** | |
| Direct costs, healthcare utilization | 563 276 |
| Indirect costs, healthcare utilization | 147 370 |
| Indirect costs, productivity loss | 4836 417 |
| *Total* | *5547 063* |
| ***Heart failure*** | |
| Direct costs, healthcare utilization | 632 710 |
| Indirect costs, healthcare utilization | 166 223 |
| Indirect costs, productivity loss | 4196 216 |
| *Total* | *4 995 149* |
| ***Arrhythmia*** | |
| Direct costs, healthcare utilization | 150 762 |
| Indirect costs, healthcare utilization | 41 317 |
| Indirect costs, productivity loss | 654 610 |
| *Total* | *846 689* |
| ***Stroke*** | |
| Direct costs, healthcare utilization | 199 391 |
| Indirect costs, healthcare utilization | 53 068 |
| Indirect costs, productivity loss | 446 089 |
| *Total* | *698 548* |
| ***Endocarditis*** | |
| Direct costs, healthcare utilization | 218 433 |
| Indirect costs, healthcare utilization | 49 577 |
| Indirect costs, productivity loss | 491 770 |
| *Total* | *759 780* |
| ***Surgery*** | |
| Direct costs, healthcare utilization | 46 836 |
| Indirect costs, healthcare utilization | 843 |
| *Total* | *47 679* |
| **Total morbidity cost-of-illness** | **26 125 410** |
| **Mortality** | |
| Indirect costs, productivity loss | 65 408 069 |
| **Total mortality cost-of-illness** | **65 408 069** |
| **Fiji Rheumatic Heart Disease Control Program** | |
| **Total program cost** | **68 000** |
| **Grand total cost-of-illness** | **91 601 479** |

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 healthcare 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 aged <5 y, finding the total societal cost of a single episode of outpatient pneumonia to be an average of US$18.98 ($FJ28.46; 2008 US$ exchange rate).[34] 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 clear that the costs associated with outpatient management of this common childhood illness were far outweighed by the societal costs accrued by the average ARF/RHD patient each year (totaling $FJ6995).

The largest single component of total cost of ARF/RHD in Fiji is the cost of premature mortality. This suggests that at current levels of investment in treating ARF/RHD, Fiji's healthcare 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 cost-effectiveness of a GAS 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 GAS vaccine is known, our cost-of-illness results will continue to be valuable for policy, as they describe the total economic boost which would result if prevention interventions eliminated ARF and RHD from Fiji.

Our study has several limitations. First, 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 probably underestimated in our study.

Second, to ascertain mortality, we used cause of death as defined by the ICD-10 codes pertaining to RHD or ARF, or to an ICD-10 code for valvular heart disease or cardiac complications.[17] While we used a rigorous record linkage approach to amalgamate multiple sources of routine epidemiological data, some residual data inaccuracy probably persisted due to coding errors. 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 previous resource-allocation decisions.[36] However, cost-of-illness estimates have substantial value in that they measure the total economic losses which 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 currently 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 make comparisons 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 better accommodate 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 current estimate, which is slightly higher (i.e. US$30.4 million versus US$34.1 million per year), is likely to be more accurate because it is based on actual age of death rather than an amalgamation of 5-y age categories.

The results from this study are broadly generalizable to countries with demographic and epidemiological 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 a higher proportion of indirect costs. 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 RHD and ARF are high in Fiji, a country with among the highest documented prevalence of RHD 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 current levels of investment, Fiji's healthcare system cannot avert the major economic losses due to the disease. Access to evidence of these costs will help policymakers 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 to strengthen the global case for the development of a GAS vaccine as it signals likely vaccine demand through a demonstration of potential costs being averted should a vaccine become available.

**Authors' contributions** TB, ACS and DEB conceived the study; TB, RCH, TP, JK, DEB and ACS designed the study protocol; TB and RCH undertook the literature search; RCH and TP undertook the acquisition of data; RCH, TP and TB analyzed and interpreted data; RCH, TP, TB and ACS wrote the first draft of the manuscript; RCH, TP, TB, JK, DEB and 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, had full access to all the data and takes responsibility for the integrity of the data and the accuracy of the data analysis. The authors wish it to be known that, in their opinion, the first three authors (RCH, TP and TB) should be regarded as joint first authors.

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