Journal of the American Heart Association

ORIGINAL RESEARCH

Contemporary Incidence and Prevalence of Rheumatic Fever and Rheumatic Heart Disease in Australia Using Linked Data: The Case for Policy Change

Judith M. Katzenellenbogen, BSc (OT), BSc Hons (Epidemiol), MSc, PhD; Daniela Bond-Smith, BSc, MA, PhD; Rebecca J. Seth, BSc, Certificate Biostat; Karen Dempsey, BN, MPH, MAE, DrPH; Jeffrey Cannon, BSc (Hons), PhD; Ingrid Stacey, BSc (Hons), MBiostat; Vicki Wade, RN, MPH; Nicholas de Klerk, BSc, PhD; Melanie Greenland, BSc, MSc; Frank M. Sanfilippo, BSc, BPharm, PGradDipPharm, PhD; Alex Brown, MBChB, MPH, PhD; Jonathan R. Carapetis, MBBS, PhD; Rosemary Wyber, MBChB, MPH; Lee Nedkoff, BAppSc, GradDipBus, MPH, PhD; Joe Hung, MBBS (Hons), FRACP, FACC; Dawn Bessarab, BSW, PhD; Anna P. Ralph, BMedSci, MBBS, MPH, DTMH, PhD

BACKGROUND: In 2018, the World Health Organization prioritized control of acute rheumatic fever (ARF) and rheumatic heart disease (RHD), including disease surveillance. We developed strategies for estimating contemporary ARF/RHD incidence and prevalence in Australia (2015–2017) by age group, sex, and region for Indigenous and non-Indigenous Australians based on innovative, direct methods.

METHODS AND RESULTS: This population-based study used linked administrative data from 5 Australian jurisdictions. A cohort of ARF (age <45 years) and RHD cases (<55 years) were sourced from jurisdictional ARF/RHD registers, surgical registries, and inpatient data. We developed robust methods for epidemiologic case ascertainment for ARF/RHD. We calculated age-specific and age-standardized incidence and prevalence. Age-standardized rate and prevalence ratios compared disease burden between demographic subgroups. Of 1425 ARF episodes, 72.1% were first-ever, 88.8% in Indigenous people and 78.6% were aged <25 years. The age-standardized ARF first-ever rates were 71.9 and 0.60/100 000 for Indigenous and non-Indigenous populations, respectively (age-standardized rate ratio=124.1; 95% CI, 105.2–146.3). The 2017 Global Burden of Disease RHD prevalent counts for Australia (<55 years) underestimate the burden (1518 versus 6156 Australia-wide extrapolated from our study). The Indigenous age-standardized RHD prevalence (666.3/100 000) was 61.4 times higher (95% CI, 59.3–63.5) than non-Indigenous (10.9/100 000). Female RHD prevalence was double that in males. Regions in northern Australia had the highest rates.

CONCLUSIONS: This study provides the most accurate estimates to date of Australian ARF and RHD rates. The high Indigenous burden necessitates urgent government action. Findings suggest RHD may be underestimated in many high-resource settings. The linked data methods outlined here have potential for global applicability.

Key Words: Australia ■ epidemiology ■ ethnic ■ inequalities ■ linked data ■ rheumatic heart disease

In 2018, the World Health Organization (WHO)[1] prioritized the global control of acute rheumatic fever (ARF) and rheumatic heart disease (RHD), emphasizing the need for innovative solutions for prevention, improved access to health care and enhanced surveillance of this preventable disease. Internationally, the Global

Correspondence to: Judith Katzenellenbogen, BSc (OT), BSc Hons (Epidemiol), MSc, PhD, School of Population and Global Health, The University of Western Australia, Perth, Australia. E-mail: judith.katzenellenbogen@uwa.edu.au

Supplementary Materials for this article are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.120.016851

For Sources of Funding and Disclosures, see page 17.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- This Australian overview of the burden of acute rheumatic fever (ARF) and rheumatic heart disease (RHD)—using multiple person-linked administrative data sources—found substantial ethnic and subnational disparities and identified that the 2017 RHD prevalent counts for Australia (<55 years) produced by the Global Burden of Disease significantly underestimate the burden (1518 versus 6156 cases Australia-wide extrapolated from our study).
- Age-standardized ARF incidence (<45 years) was 124 times higher and RHD prevalence (<55 years) was 61 times higher among Indigenous compared with non-Indigenous Australians, with the burden substantially higher in northern, remote Australian regions.
- We provide the first detailed estimates of the burden in young non-Indigenous Australians showing that sporadic episodes still occur in the general population, with 29% of RHD cases <55 years occurring in non-Indigenous Australians. Disease severity and complication rates in this group were high.

What Are the Clinical Implications?

- Given known underdiagnosis of ARF, ongoing clinician education is needed to improve diagnostic capability, both in high-risk subpopulations in high-income countries and "low-risk" populations who appear to enter the health system at later stages of disease.
- The vast discrepancies in disease burden highlights ARF/RHD as an indicator of disadvantage requiring a comprehensive approach to ARF/RHD prevention, including addressing the socioeconomic and environmental conditions that underpin ARF/RHD burden and disparities.
- These data support Australian government and nongovernment (eg, https://endrhd.org.au/) efforts to mobilize resources to eliminate RHD in Australia by addressing upstream causes and clinical imperatives, supported by good surveillance systems.

Nonstandard Abbreviations and Acronyms

ARF	acute rheumatic fever
ASRR	age-standardized rate ratio
ERASE	End RHD in Australia: Study of Epidemiology
GBD	global burden of disease
ICD-10-AM	*International Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification*
IREG	Indigenous Region
NSW	New South Wales
NT	Northern Territory
RHD	rheumatic heart disease
SA	South Australia
START	Searching for a Technology-Driven Acute Rheumatic Fever Test
WA	Western Australia
WHO	World Health Organization

Burden of Disease (GBD) project provides the most comprehensive approximations of the global RHD burden. In 2017, they estimated 39.3 million cases of RHD, 285 517 RHD deaths, and 9.39 million disability-adjusted life-years.[2] Despite reductions of 47.5% in the burden between 1990 and 2015, large regional disparities persist,[2] with ARF hyperendemic in low- and middle-income countries where >80% of the world's ARF cases occur.[3,4] However, considerable gaps in knowledge about the burden of RHD still exist at country level, as estimates from the GBD often rely heavily on indirect methods using proxy socioeconomic markers rather than actual country-based epidemiologic data. Innovative methods of estimating disease burden can improve the accuracy of national estimates, with data linkage providing a potential mechanism.

In high-income countries, RHD is mainly found in older people who developed the disease before socioeconomic improvements and widespread use of antibiotics.[5] Simultaneously, some disadvantaged minority populations have a high burden of ARF and RHD,[3] including Indigenous populations,[6–8] people living in relative poverty, and immigrants from countries with endemic RHD. This applies in Australia, where ARF/RHD remains a critical public health problem among Aboriginal and Torres Strait Islander peoples (hereafter referred to as Indigenous).[6,9,10] Indigenous Australians comprise 3.3% of the population, have a median age of 23.0 years (versus 37.8 Australia-wide),[11] and a life expectancy 8 years lower than other Australians.[12] Additionally, >26% of the Australian population were born overseas, some from low- and middle-income countries with high RHD rates. Indeed, China, India, the Philippines, Vietnam, Malaysia, and South Africa rank among the top 10 countries of birth for Australian residents born overseas.[13] People with Māori or Pacific Islander ancestry, population groups also with high

RHD burden,[14] now comprise 1.5% (≈350 000 people) of the Australian population.[15]

In 2009, the Australian National Rheumatic Fever Strategy comprising jurisdictional control programs and a national supporting organization, RHDAustralia, were established, to support the delivery of high-quality ARF/RHD care. Subsequently, there has been increasing momentum for action on RHD among Indigenous Australians. This changing context led to the founding of END RHD, a coalition of peak bodies advocating for mobilization of government resources to eliminate RHD in Australia (https://endrhd.org.au/). Accurate estimates of the burden of ARF and RHD are critical to this effort and as a baseline for future monitoring.[16] To date, estimates have predominantly relied on data from unlinked ("stand-alone") hospital data sets,[6] mortality registries,[17] and jurisdiction-specific RHD registers,[18] with the majority of research undertaken in the Northern Territory (NT).[9,19,20] Consequently, data have been fragmented and incomplete, with no comprehensive national overview. The End RHD in Australia: Study of Epidemiology (ERASE) project[21] addresses this data gap. In this article, we substantively advance contemporary estimates of ARF/RHD burden. We provide the first multijurisdictional estimates of the morbidity burden of ARF and RHD in Australians aged <55 years, using diverse, linked administrative data covering 5 jurisdictions where 86% of Indigenous Australians live.[11] Specific objectives were to (1) provide a demographic and clinical profile of ARF episodes and prevalent RHD cases; (2) estimate and compare the first-ever and total incidence of ARF in people aged <45 years by Indigenous status, age, sex, jurisdiction; and (3) quantify the population incidence and prevalence of symptomatic RHD in those aged <55 years. In so doing, we aim to provide more comprehensive estimates of ARF/RHD morbidity burden to inform Australian policies and develop models of disease surveillance that may be adapted in other countries.

METHODS

Data, Materials, and Code Disclosure Statement

All details of the methods used in the analysis (program code or scripts for statistical packages), and materials used to conduct the research will be made available to any researcher for purposes of reproducing the results or replicating the procedure. Because of the sensitive nature of the linked data used in this study, requests to access the data set from qualified Australian researchers trained in human subject confidentiality protocols may be sent to the corresponding author at the University of Western Australia and will be subject to rigorous conditions. Ethics approvals for all linked data studies demand strict adherence to data security and confidentiality protocols. Additionally, emergence of new approaches to data sovereignty for Indigenous peoples (as outlined in the CARE Principles for Indigenous data governance at https://www.gida-global.org/care) necessitates recognition that "the emphasis on greater data sharing alone creates a tension for Indigenous peoples who are also asserting greater control over the application and use of Indigenous data and Indigenous knowledge for collective benefit."

Study Design

This multijurisdictional study of ARF and RHD incidence and prevalence uses retrospective, linked longitudinal administrative data.

Data Sources

The parent ERASE project derived all ARF and RHD cases from linked ARF/RHD registers, inpatient hospitalizations (*International Classification of Diseases, Tenth Revision, Australian Modification* [*ICD-10-AM*][22] codes I00–I09) and RHD-coded death registry data in 5 Australian jurisdictions (mid-2001–2018). Data sources and variables are further described in Katzenellenbogen et al.[21] Data from NT, Western Australia (WA), South Australia (SA), Queensland, and New South Wales (NSW) were probabilistically linked by separate jurisdiction-specific linkage units and harmonized across state and data sources. The WA linked data extend to only mid-2017 because of earlier completion of linkage. Availability of RHD register data was determined by the establishment dates of the jurisdictional registers, between 1998 (NT) and 2015 (NSW). Adult surgery registry data from the Australia–New Zealand Society of Cardio-thoracic Surgeons[23] provided additional data for the cohort. For the current study, case identification data were sourced from the ARF/RHD registers, Australia–New Zealand Society of Cardio-thoracic Surgeons, and hospital data. Death records determined vital status.

Cohort Definitions and Selection

Acute Rheumatic Fever

For ARF incidence, we identified a contemporary cohort of patients aged 3 to 44 years who had an ARF episode between 2015 and 2017 (WA mid-2014 to mid-2017). ARF is rare over 45 years,[3] with *ICD-10-AM* codes beyond this age having extremely low positive predictive value.[24] The start date of an ARF episode was defined by ARF diagnosis date recorded on the register or hospital admission date with a principal diagnosis of ARF (*ICD-10-AM* I00–I02). A unique

episode was defined as an ARF record >90 days from the previous one.[25] A first-ever ARF episode was based on the person not having a previously recorded ARF or RHD diagnosis. Thus, we excluded those with any historical ARF or RHD hospital record in the previous 13.5 years and those with evidence in the register of a previous episode. All other episodes were considered recurrences. Total ARF incidence was the sum of first-ever episodes and recurrences.

Rheumatic Heart Disease

We restricted RHD cases to those aged <55 years to focus on contemporary data for younger people affected by the disease in the post-1960s era of secondary prophylaxis treatment. People were categorized as RHD cases if they had a confirmed RHD diagnosis recorded in ARF/RHD registers, had an Australia-New Zealand Society of Cardio-thoracic Surgeons confirmation of rheumatic valvular disease, or were identified in hospital data based on *ICD-10-AM* codes. We previously reported on deficiencies in the *ICD* coding for RHD (*ICD-10-AM* I05-I09), resulting in high false-positive rates, particularly in non-Indigenous and older people.[24,26] Consequently, we developed a prediction model to identify hospital cases, using a large validation sample of people <60 years to address deficiencies in *ICD* codes for RHD.[27] The model is based on a generalized linear mixed-model structure with a binary outcome and a logistic link function and uses a range of *ICD-10-AM* codes in conjunction with demographic and clinical variables[27] (including hospital and year random effects) to predict which cases have an RHD diagnosis. The model reduced the false-positive rate from ARF cases misclassified as RHD from 0.59 to 0.27; similarly, for nonrheumatic valvular heart disease from 0.77 to 0.22. Overall, the model achieved strong discriminant capacity (area under the curve, 0.93) and maintained a similar robust performance during external validation (area under the curve, 0.88). The validation sample and prediction model have been published previously[27] and is summarized in Table S1. Thus, in the present study, cases captured by hospital data only were identified as probable RHD by the prediction model. RHD was considered a chronic condition that persisted after the first recorded RHD diagnosis date determined from all data sources.

A 13.5-year fixed "lookback" (clearance) period was used to identify first-ever RHD cases for each year from 2015 to 2017. Annual prevalent RHD cases were identified in 2015–2017 and included all people with an RHD record from any data source in the previous 14 years and alive at June 30 of each study year. The 3-year study period allowed capture of adequate numbers to calculate precise stratified population prevalence proportions. Given the numerators represent a 3-year period, we report mean annual numbers over the period but the person-based profile of RHD prevalent cases relates to 2017 only. Prevalent RHD cases were categorized as severe on the basis of a diagnosis of heart failure, recorded as severe in the ARF/RHD register, or receipt of a valvular procedure/surgery recorded in the register, hospital, or surgery records.

ARF or RHD

We identified any individual recorded any time in our data as having ARF or RHD ("prevalent ARF/RHD") to estimate the total number affected by this disease in their lives. All are at risk of recurrence, disease progression, and complications.

Variable Definitions

We grouped our cohort into 3 population categories: (1) Australian Indigenous, (2) internationally born in low- or lower-middle-income country or Māori/Pacific Islander, and (3) Other Australian.[21] Category 2 includes non-Indigenous populations known to be at high risk of ARF/RHD. To address known underidentification of Indigenous people in administrative records, we approximated an approach developed in WA,[28] maximizing predictive power of Indigenous status assignment using multiple administrative data sources. For non-Indigenous cases, data directly recording population category (eg, Māori/Pacific Islander, recorded in ARF/RHD registers) were used, where available. If unavailable, population category was assigned on the basis of the World Bank Country Income classification status (1996) of the person's recorded country of birth[29] (Table S1). A person was recorded as internationally born in low- or lower-middle-income country if the recorded country of birth was a low- or lower-middle-income country. The remaining people were classified as "Other Australian."

Residential post code, statistical area (level 2), locality, or clinic address was used for categorization into geographic areas of residence. Besides state/territory, region of residence was represented by Indigenous Region (IREG), the highest level of aggregation of the Indigenous Structure in the 2011 Australian Statistical Geographical Standard,[30] which we grouped into 9 categories (Table S1). Where post code or statistical area mapped across >1 IREG, people were allocated to the IREG that represents the largest population share of the post code/statistical area. People were also allocated to 5 geographic categories of the Accessibility/Remoteness Index of Australia[31] and quintiles of the Socio-economic Index

for Areas,[32] an area-level score of socioeconomic status derived from census variables. RHD complications were identified from all diagnosis fields in hospital records up to 1 year prior (because of the likelihood of complications developing before the first recorded diagnosis or hospitalization) or any time following the first RHD diagnosis date to end of follow-up (mid-2018).

Statistical Analysis

Baseline characteristics of Indigenous and non-Indigenous ARF episodes 2015–2017 and prevalent RHD cases as at mid-2017 were compared using t tests and chi-squared tests. The numerator for contemporary first-ever, total incidence, and prevalence was the sum of the yearly number of each of these case types over the 3 years 2015 through 2017.

The midyear Australian Bureau of Statistics Indigenous and non-Indigenous estimated populations for 2016[11] multiplied by 3 provided person-year estimates calculation of first-ever ARF, total ARF, and RHD incidence. The prevalence proportion was calculated as a 3-year average of prevalence at 2015, 2016, and 2017. Age-specific ARF and RHD incidence (0–44 years) and prevalence (0–54) estimates were used in conjunction with the WHO World Standard Population distribution[33] to calculate Indigenous and non-Indigenous age-standardized estimates and 95% CIs (calculated using a Poisson distribution for incidence rates and a normal distribution for reported prevalence ratios, incidence rate ratios, and prevalence ratios). Age-standardized prevalence, first-ever and total incidence rates, and rate and prevalence ratios were similarly calculated by jurisdiction, sex, and the 9 IREG categories. Any uncertainty arising from the use of the Australian Bureau of Statistics population estimates (as denominators for calculating rates) and the WHO Standard Population for age-standardization is considered negligible.

Recognizing our 14-year lookback period would miss earlier events/diagnoses, particularly in older people, we also restricted some estimates to people aged <25 years, substantially reducing the likelihood of missing historical records. Given WA's longer availability of data linkage,[34] we further undertook a sensitivity analysis to estimate the extent of overcounting of first-ever ARF episodes and undercounting of prevalent RHD cases in our main analysis. We assembled a similar WA cohort to our main 2015–2017 analysis but extended the lookback period for identifying incident events to a fixed length of 25 years.

Statistical Software

SAS 9.4 (SAS Institute, Cary, NC) was used for data manipulation and rate calculations. Figures and maps used R version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria).

Ethics

Human Research Ethics Committees of the Health Departments of all jurisdictions provided approval for the ERASE project. Aboriginal Ethics Committees from WA, SA, NT, and NSW approved the study, with support letters from peak bodies of the Aboriginal Community Controlled Health Services (Data S1). The requirement for consent of subjects was waived.

RESULTS

Profile of ARF Episodes 2015 to 2017

Of the 1425 ARF episodes identified in 2015–2017 (Table 1), 72.1% were deemed first-ever. Over half (54.1%) occurred in women, 88.8% in Indigenous people, and 78.6% were aged <25 years. Episodes peaked in the 0- to 14-year age group. A third of non-Indigenous episodes occurred in people born in low- and middle-income countries or Māori/Pacific Islander people. Eighty-two percent of episodes were recorded across Northern Australian regions, most of them in NT and Queensland. Seven in 10 episodes—predominantly Indigenous—occurred in people living in remote or very remote regions. Over two-thirds of non-Indigenous episodes occurred in metropolitan areas, exemplifying the differing distributions by Indigenous status ($P<0.001$). ARF episodes occurred in the most socially disadvantaged quintile for 71.5% of Indigenous people experiencing ARF but only 38.4% of non-Indigenous people. Eighty-five percent of Indigenous episodes were recorded on the register versus 42.8% in non-Indigenous people (with or without hospital records).

ARF recurrences comprised 27.9% of all ARF episodes in the 5-to-14 group (Figure S1), increasing to a third of episodes for 15- to 24-year-olds. For ages 25 to 34 and 35 to 44, recurrences accounted for half of all ARF episodes. Recurrences were low in the non-Indigenous population.

Profile of Prevalent RHD Cases

Table 2 shows profiles of 5574 people with RHD alive in mid-2017: 71.2% were Indigenous, and the remainder were classified as high- (internationally born in low- or lower-middle-income country/Maori/Pacific Islander, 16.7%) or low-risk (12.0%) non-Indigenous. Females comprised two-thirds of people with RHD. Indigenous people were younger (mean, 23.5 versus 34.3 years), more likely to be from remote/very remote and low socioeconomic status areas than non-Indigenous people (both

Table 1. Baseline Demographic and Broad Clinical Characteristics Associated With Episodes of ARF by Indigenous Status: 5 Australian Jurisdictions, 2015 to 2017

	Acute Rheumatic Fever Episodes			
	Total n (%)	Indigenous n (%)	Non-Indigenous n (%)	*P* Value
Total number episodes	1425 (100.0)	1265 (88.8)	159 (11.2)	
Mean age, y	16.8 (SD 9.5)	16.6 (SD 9.4)	18.6 (SD 10.6)	0.022
Age group, y				
0–14	761 (53.4)	689 (54.5)	72 (45.2)	0.072
15–24	359 (25.2)	312 (24.7)	46 (28.9)	
25–34	208 (14.6)	185 (14.6)	23 (14.5)	
35–44	97 (6.8)	79 (6.3)	18 (11.3)	
Sex				
Female	771 (54.1)	699 (55.3)	71 (44.7)	0.011
Population category (n=1 missing)				
Indigenous	1265 (88.8)	1265 (100.0)	n/a n/a	
ILIC*	53 (3.7)	N/A	53 (33.3)	
Other Australian	106 (7.4)	N/A	106 (66.7)	
State of residence				
NSW	82 (5.8)	28 (2.2)	54 (34.0)	<0.001
QLD	382 (26.8)	301 (23.8)	81 (50.9)	
SA	31 (2.2)	27 (2.1)	<5 (N/A)	
WA	171 (12.0)	165 (13.0)	6 (3.8)	
NT	759 (53.3)	744 (58.8)	15 (9.4)	
Remoteness index (n=74 missing)				
Major city	147 (10.9)	44 (3.7)	103 (68.2)	<0.001
Inner regional	34 (2.5)	21 (1.8)	13 (8.6)	
Outer regional	234 (17.3)	214 (17.8)	20 (13.3)	
Remote	261 (19.3)	248 (20.7)	13 (8.6)	
Very remote	675 (50.0)	673 (56.1)	<5 N/A	
Indigenous region category (n=1 missing)				
Northern Australia	1165 (81.8)	1132 (89.6)	33 (20.8)	<0.001
Metropolitan regions	156 (11.0)	48 (3.8)	108 (67.9)	
Other regions	103 (7.2)	84 (6.7)	18 (11.3)	
Social disadvantage (quintiles)* (n=77 missing)				
1–20 (most disadv)	914 (67.8)	856 (71.5)	58 (38.4)	<0.001
21–40	158 (11.7)	134 (11.2)	24 (15.9)	
41–60	176 (13.1)	145 (12.1)	31 (20.5)	
61–80	71 (5.3)	48 (4.0)	23 (15.2)	
81–100 (least disadv)	29 (2.2)	14 (1.2)	15 (9.9)	
Source of data				
Hospital only	285 (20.0)	194 (15.3)	91 (57.2)	<0.001
Register only	513 (36.0)	478 (37.8)	34 (21.4)	
Both	627 (44.0)	593 (46.9)	34 (21.4)	
Episode type				
Initial	1027 (72.1)	889 (70.3)	137 (86.2)	<0.001
Recurrent	398 (27.9)	376 (29.7)	22 (13.8)	
Years since first ARF diagnosis (3–44 y)				
0–5 y	1110 (88.3)	975 (87.1)	134 (97.8)	0.001

(Continues)

Table 1. Continued

	Acute Rheumatic Fever Episodes			
	Total n (%)	Indigenous n (%)	Non-Indigenous n (%)	*P* Value
6–10 y	96 (7.6)	94 (8.4)	<5 (N/A)	
>10 y	51 (4.1)	50 (4.5)	<5 (N/A)	
Years since first ARF diagnosis (<20 y) (n=560 missing)				
0–5 y	796 (92.0)	709 (91.1)	86 (100.0)	0.016
6–10 y	66 (7.6)	66 (8.5)	<5 (N/A)	
>10 y	<5 (N/A)	<5 (N/A)	<5 (N/A)	

ARF indicates acute rheumatic fever; N/A, not applicable; NSW, New South Wales; NT, Northern Territory; QLD, Queensland; SA, South Australia; and WA, Western Australia.

*ILIC=Pacific Islander, Maori, people born in low- and middle-income countries; social disadvantage based on area level Socio-economic Index for Australia scores[35]; Remoteness Index based on Accessibility Remoteness Index of Australia scores.[34]

P<0.001). Higher proportions of non-Indigenous than Indigenous people had severe RHD and history of valvular intervention (both *P*<0.001). A third of people with RHD had documented history of ARF, increasing to 76.5% when restricted to ages <20. Complications from RHD were proportionally higher in non-Indigenous people for all conditions considered and all age groups except heart failure and stroke in the 40-to-54 age group, although non-Indigenous numbers were small (Figure 1). A higher proportion of Indigenous women with RHD had experienced concurrent pregnancy.

Incidence Rates (<45 Years)

The age-specific incidence rate of ARF (both first-ever and total) and RHD peaked in the 5- to 14-year age group (Table 3; Figure 2). ARF reduced markedly with age but RHD incidence was relatively stable (between 3.2 and 3.7 new diagnoses per 100 000) from the age of 15 (Table 3). For first-ever ARF, Indigenous age-specific rates were 76 to 118 times higher than non-Indigenous rates (age-standardized rate ratio [ASRR] 0 to 44 years=98.7, 95% confidence interval [CI] 82.4–118.1) (Table 2). For total ARF incidence, age-standardized rates (ASR) were 71.9 (Indigenous) and 0.60 per 100 000 (non-Indigenous), with an ASRR of 124.1 (95% CI, 105.2–146.3). Restriction to <25 years had no impact on ASRR for first-ever ARF and slightly reduced ASRR for total ARF.

Our sensitivity analysis using a 25-year lookback period for WA identified an additional 2 of 104 ARF episodes that were not first-ever, both of which were Indigenous and occurring in the 25- to 34-year age group. This had no impact on age-standardized ARF first-ever rates (Table S2).

For RHD incidence, overall Indigenous to non-Indigenous ASRR was 49.0 (95% CI, 42.8–56.2) but higher (ASRR, 66.4, 95% CI, 53.0–83.2) for those <25.

Prevalence (<55 Years)

We identified a mean annual prevalence of ARF or RHD 2015–2017 pertaining to 7070 people <55 years (Table 4), 72.5% being Indigenous. Prevalence peaked in the 25- to 34year age group in the Indigenous population and at 45 to 54 years for the non-Indigenous population. After age-standardization, Indigenous people <55 years were 60.3 times (95% CI, 58.5–62.2) more likely to have been affected by these diseases than other Australians; 82.0 (95% CI, 77.0–87.2) when restricted to <25 years.

We identified an annual average of 5241 people <55 years with RHD (2185 severe) in the 5 jurisdictions covered by our data. Extrapolating from our age-specific prevalence, we estimate 6156 RHD cases Australia-wide (compared with 1518 from the 2017 GBD RHD prevalent counts for Australia (<55 years).[35] Overall, age-specific RHD prevalence increased with age (Table 4, Figure 1), particularly for the non-Indigenous population. After a steep initial increase, RHD prevalence in the Indigenous population was relatively stable from 25 years (Table 4). The age-standardized RHD prevalence in the Indigenous population (666.3 per 100 000) was 61.4 times higher (95% CI, 59.3–63.5) than that of the non-Indigenous population (10.9 per 100 000), increasing to 110.2 when restricted to <25 years.

The prevalence of severe RHD increased with age in both populations (Table 4, Figure 1), with age-specific prevalence ratios peaking at 25 to 34 (55.3). The age-standardized prevalence ratio was 30.8 (95% CI, 29.4–32.4) overall, increasing to 43.9 when restricted to <25 years.

In our sensitivity analysis, the longer lookback identified 378 additional RHD prevalent cases in WA as in mid-2017 (42.6% non-Indigenous) that were missed in the main analysis. Almost all were >25 years old in 2017 (89.2% ≥35 years), suggesting robust estimates <25 years and an underestimate of RHD prevalence in the older ages, particularly over the age of 34 years and disproportionately in the non-Indigenous population (Table S2).

Table 2. Baseline Demographic and Broad Clinical Characteristics Associated With Prevalent Cases of RHD Alive at Midyear 2017*, by Indigenous Status: 5 Australian Jurisdictions

	Total	Indigenous	Non-Indigenous	
	n (%)	n (%)	n (%)	*P* Value
Total number people	5574 (100.0)	3967 (71.2)	1601 (28.7)	
Mean age, y	26.58 (12.5)	23.46 (11.5)	34.3 (11.4)	<0.001
Age group, y				
0–14	417 (7.5)	362 (9.1)	56 (3.5)	
15–24	1071 (19.2)	946 (23.9)	124 (7.8)	
25–34	1275 (22.9)	1037 (26.1)	238 (14.9)	
35–44	1330 (23.9)	904 (22.8)	424 (26.5)	
45–54	1481 (26.6)	718 (18.1)	760 (47.5)	
Sex				
Female	3748 (67.2)	2665 (67.2)	1079 (67.4)	0.887
Population category (n=6 missing)				
Indigenous	3967 (71.3)	3967 (100.0)	N/A (N/A)	
LMIC†	930 (16.7)	n/a	930 (58.1)	
Other Australian	671 (12.1)	n/a	671 (41.9)	
State of residence				
NSW	876 (15.7)	159 (4.0)	717 (44.8)	<0.001
QLD	1879 (33.7)	1297 (32.7)	576 (36.0)	
SA	214 (3.8)	98 (2.5)	116 (7.3)	
WA	720 (12.9)	576 (14.5)	144 (9.0)	
NT	1885 (33.8)	1837 (46.3)	48 (3.0)	
Remoteness index (n=246 missing)				
Major city	1401 (26.3)	220 (5.8)	1178 (77.2)	<0.001
Inner regional	268 (5.0)	117 (3.1)	149 (9.8)	
Outer regional	877 (16.5)	733 (19.3)	144 (9.4)	
Remote	823 (15.5)	785 (20.7)	38 (2.5)	
Very remote	1959 (36.8)	1942 (51.2)	17 (1.1)	
Indigenous region category (n=10 missing)				
Northern Australia	3528 (63.4)	3366 (85.1)	162 (10.1)	<0.001
Metropolitan regions	1431 (25.7)	224 (5.7)	1202 (75.1)	
Other regions	605 (10.9)	367 (9.3)	237 (14.8)	
Social disadvantage (quintiles) (n=334 missing)				
1–20 (most disadv)	3051 (58.2)	2625 (69.9)	426 (28.7)	<0.001
21–40	785 (15.0)	493 (13.1)	292 (19.7)	
41–60	705 (13.5)	414 (11.0)	291 (19.6)	
61–80	429 (8.2)	157 (4.2)	272 (18.3)	
81–100 (least disadv)	270 (5.2)	64 (1.7)	205 (13.8)	
Source of RHD diagnosis				
Hospital only	2616 (46.9)	1258 (31.7)	1353 (84.5)	<0.001
Register only	1582 (28.4)	1441 (36.3)	140 (8.7)	
Both	1376 (24.7)	1268 (32)	108 (6.7)	
Years since first RHD diagnosis (3–54 y)				
0–5 y	2205 (39.6)	1448 (36.5)	756 (47.2)	<0.001
6–10 y	1586 (28.5)	1130 (28.5)	456 (28.5)	
>10 y	1783 (32.0)	1389 (35.0)	389 (24.3)	
Years since first RHD diagnosis (<20 y) (n=1050 missing)				

(Continues)

Table 2. Continued

	Total	Indigenous	Non-Indigenous	
	n (%)	n (%)	n (%)	*P* Value
0–5 y	703 (67.0)	604 (65.5)	99 (77.3)	0.029
6–10 y	299 (28.5)	274 (29.7)	25 (19.5)	
>10 y	48 (4.6)	44 (4.8)	<5 N/A	
Clinical history				
Record of ARF (<55 y)	1865 (33.5)	1724 (43.5)	141 (8.8)	<0.001
Record of ARF <20 y)‡	803 (76.5)	729 (79.1)	74 (57.8)	<0.001
History of ARF carditis	938 (16.8)	836 (21.1)	101 (6.3)	<0.001
Severe RHD	2295 (41.2)	1244 (31.4)	1046 (65.3)	<0.001
Valve intervention	1601 (28.7)	692 (17.4)	904 (56.5)	<0.001

ARF indicates acute rheumatic fever; N/A, not applicable; NSW, New South Wales; NT, Northern Territory; QLD, Queensland; RHD, rheumatic heart disease; SA, South Australia; and WA, Western Australia.

*RHD cases prevalent in 2017: shows people with RHD alive at mid-2017 to avoid potential triple counting cases over 2015–2017 used for mean annual prevalence proportions calculated in Table 3.

†ILIC=Pacific Islander, Maori, people born in low- and middle-income countries; social disadvantage based on area level Socio-economic Index for Australia scores[32]; remoteness Index based on Accessibility Remoteness Index of Australia scores.[31]

‡n=4524 missing.

Male-Female Differences

Indigenous age-standardized ARF incidence rates were higher in females than males (ASRR, 1.4; 95% CI, 1.2–1.5) (Figure 3). This sex differential did not apply to non-Indigenous people (ASRR, 0.9; 95% CI, 0.6–1.2). For RHD, ASRs were higher in females than males for both populations: Indigenous ASRR=1.9 (95% CI, 1.7–2.2); non-Indigenous ASRR=1.7 (95% CI, 1.3–2.1).

Geographic Differences in Incidence and Prevalence

Figure 4 provides an overview of the geographic distribution of age-standardized prevalence of ARF or RHD in the 5 Australian jurisdictions. The prevalence was substantially higher among Indigenous compared with total populations living in all jurisdictions and regions. The highest prevalence was estimated for the Indigenous population of NT (3544.8 per 100 000), with similar prevalence among Indigenous people of WA (1012.3 per 100 000) and Queensland (862.1 per 100 000). The highest prevalence of ARF or RHD was seen in Northern Australian IREG regions for both the total and Indigenous-only populations, particularly the 2 NT subregions. ARF/RHD was least prevalent in metropolitan areas (17.4 per 100 000 in the total population and 154.5 per 100 000 in the Indigenous population).

DISCUSSION

This article provides an unprecedented national overview of ARF and RHD in Australia using multiple linked data sources. This provides new insights into the epidemiology of this largely preventable disease. Our results confirm the endemic burden, with Indigenous Australians continuing to be overwhelmingly and disproportionately represented (89% and 71% of ARF and RHD, respectively) and at least 60 times more likely to be affected by either of these diseases. Age-standardized first-ever incidence rates for ARF and RHD were 99 and 49 times higher, respectively, in Indigenous compared with other Australians. This differential undoubtedly contributes to the high disparities in stroke,[36,37] atrial fibrillation,[38,39] and heart failure[40] among younger Indigenous versus non-Indigenous Australians. The study also provides the first detailed estimates of the burden in non-Indigenous Australians—both immigrants and other traditionally high- and low-risk groups—showing that this heterogeneous group also needs attention in any national approach. Overwhelmingly, our findings highlight the importance of addressing the socioeconomic and environmental conditions that underpin ARF/RHD burden and disparities nationally and internationally.

Previous Australian estimates were limited to stand-alone sources, which provided partial, often skewed data. Register-based estimates miss hospital-only recorded events,[18,41] the majority of which pertain to non-Indigenous patients. The most comprehensive previous studies used cohorts identified in NT registers only,[9] whereas ours is more broadly representative. Despite the different methods previously used for data collection in the different jurisdictions and data sources, all consistently show similar age patterns, orders of magnitude in disparities between population groups and the 2-fold sex differentials.

Globally, robust data on ARF/RHD rates are sparse, with most countries with high burden relying on

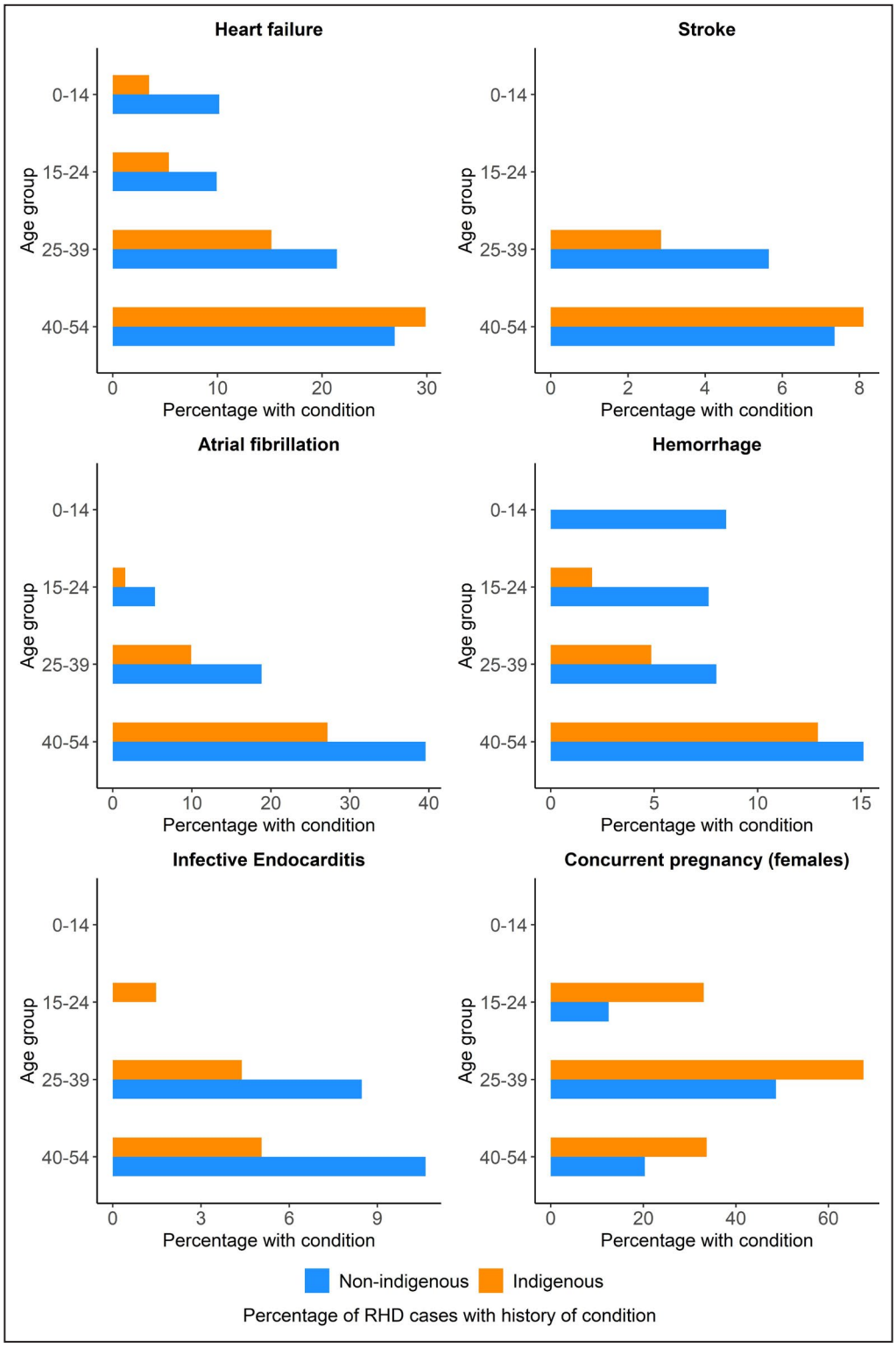

Figure 1. Percentage of prevalent RHD cases in mid-2017 with a history of complications of RHD and concurrent RHD and pregnancy, by age group and Indigenous status.
RHD indicates rheumatic heart disease.

intermittent echocardiogram surveys or indirect methods used by the GBD.[2] The 2017 RHD prevalent counts for Australia (<55 years) produced by the GBD project[35] significantly underestimate the burden (1518 versus 6156 Australia-wide extrapolated from our study). This suggests that RHD may be underestimated in some

Table 3. Crude, Age-Specific and Age-Standardized Incidence Per 100 000 Population for ARF and RHD, by Indigenous Status: 5 Australian Jurisdictions, 2015 to 2017

	Total		Indigenous		Non-Indigenous		
	N*	Per 100 000 (95% CI)	N*	Per 100 000 (95% CI)	N*	Per 100 000 (95% CI)	Rate Ratio (95% CI)
First-ever ARF							
0–4	37	1.1 (0.8–1.5)	33	13.3 (8.8–17.8)	<5	N/A	N/A
5–14	575	8.9 (8.2–9.7)	515	107.6 (98.3–116.9)	60	1.0 (0.8–1.3)	107.0 (81.9–139.8)
15–24	238	3.6 (3.1–4.0)	200	48.8 (42.0–55.5)	37	0.6 (0.4–0.8)	82.6 (58.2–117.3)
25–34	118	1.6 (1.3–1.8)	98	32.5 (26.1–38.9)	20	0.3 (0.2–0.4)	117.8 (72.8–190.5)
35–44	59	0.9 (0.6–1.1)	43	18.4 (12.9–23.9)	16	0.2 (0.1–0.4)	75.9 (42.7–134.7)
(0–44) crude†	1027	3.3 (3.1–3.5)	889	53.2 (49.8–56.8)	133	0.5 (0.0–0.6)	
ASR (0–44)	n/a	3.6 (3.4–3.8)	n/a	49.3 (46.0–52.6)	N/A	0.5 (0.4–0.6)	98.7 (82.4–118.1)
ASR (0–24)	n/a	5.3 (4.9–5.6)	n/a	65.8 (61.1–70.5)	N/A	0.7 (0.5–0.8)	98.4 (80.0–121.2)
Total ARF							
0–4	40	1.2 (0.8–1.6)	36	14.5 (9.8–19.3)	<5	N/A	N/A
5–14	721	11.2 (10.4–12.0)	653	136.4 (126.0–146.9)	68	1.1 (0.9–1.4)	119.7 (93.3–153.7)
15–24	359	5.4 (4.8–5.9)	312	76.1 (67.6–84.5)	46	0.7 (0.5–1.0)	103.7 (76.1–141.3)
25–34	208	2.8 (2.4–3.1)	185	61.3 (52.5–70.1)	23	0.3 (0.2–0.5)	193.3 (125.4–298.2)
35–44	97	1.4 (1.1–1.7)	79	33.8 (26.3–41.2)	18	0.3 (0.2–0.4)	123.9 (74.3–206.8)
(0–44) crude†	1425	4.6 (4.4–4.9)	1265	75.6 (71.6–79.9)	155	0.5 (0.5–0.6)	n/a
ASR (0–44)	n/a	4.9 (4.7–5.2)	n/a	71.9 (67.9–75.9)	N/A	0.6 (0.5–0.7)	124.1 (105.2–146.3)
ASR (0–24)	n/a	6.9 (6.5–7.3)	n/a	88.5 (83.0–94.0)	N/A	0.8 (0.6–0.9)	113.6 (93.8–137.4)
First-ever RHD							
0–4	5	0.2 (0.0–0.3)	5	2.0 (0.3–3.8)	0	N/A	N/A
5–14	282	4.4 (3.9–4.9)	234	48.9 (42.6–55.2)	48	0.8 (0.6–1.0)	60.8 (44.6–82.9)
15–24	245	3.7 (3.2–4.1)	202	49.3 (42.5–56.1)	43	0.7 (0.5–0.9)	71.8 (51.7–99.8)
25–34	240	3.2 (2.8–3.6)	153	50.7 (42.7–58.7)	86	1.2 (0.9–1.4)	42.8 (32.8–55.7)
35–44	246	3.6 (3.2–4.1)	136	58.1 (48.4–67.9)	110	1.7 (1.4–2.0)	34.9 (27.2–44.9)
(0–44) crude†	1018	3.3 (3.1–3.5)	730	43.7 (40.5–46.9)	287	1.0 (0.9–1.1)	N/A
ASR (0–44)	N/A	3.3 (3.1–3.5)	n/a	45.5 (42.1–48.9)	N/A	0.9 (0.8–1.0)	49.0 (42.8–56.2)
ASR (0–24)	N/A	3.3 (3.0–3.5)	n/a	39.7 (36.0–43.4)	N/A	0.6 (0.5–0.7)	66.4 (53.0–83.2)

ARF indicates acute rheumatic fever; ASR age-standardized rate; N/A, not applicable; and RHD, rheumatic heart disease.
*Sum of cases 2015–2017.
†To maintain anonymity, totals do not include cells that are <5.

high-resource settings, particularly where pooled nationwide RHD data can obscure critically important within-country variation.

Our study compellingly illustrates the potential of using the increasingly sophisticated routine data being collected and linked in a range of countries for case identification, resource utilization and outcomes. Such potential is not restricted to high-income countries[42]; health data linkage has been demonstrated in many low- and middle-income countries.[43–46] Linked data can support surveillance of high-risk subpopulations and regions where high disease burdens in particularly disadvantaged sectors might otherwise go unrecognized. This also applies to high-risk immigrant, refugee, and displaced communities in high-resource settings beyond Australia.[47] The clinician-informed methods developed for the ERASE project[21] have uniquely addressed problems with *ICD-10-AM* codes[24] for RHD by developing robust, sophisticated prediction modeling[27] and applied harmonizing approaches to deal with discrepancies between data sets. These methodologic approaches can be adapted for other contexts to support WHO's call for improved surveillance and action.

Currently, few low- and middle-income countries have the clinical, administrative, and technological infrastructure for comprehensive data linkage. However, concrete steps can be and have been taken to improve data collection and health information systems with the

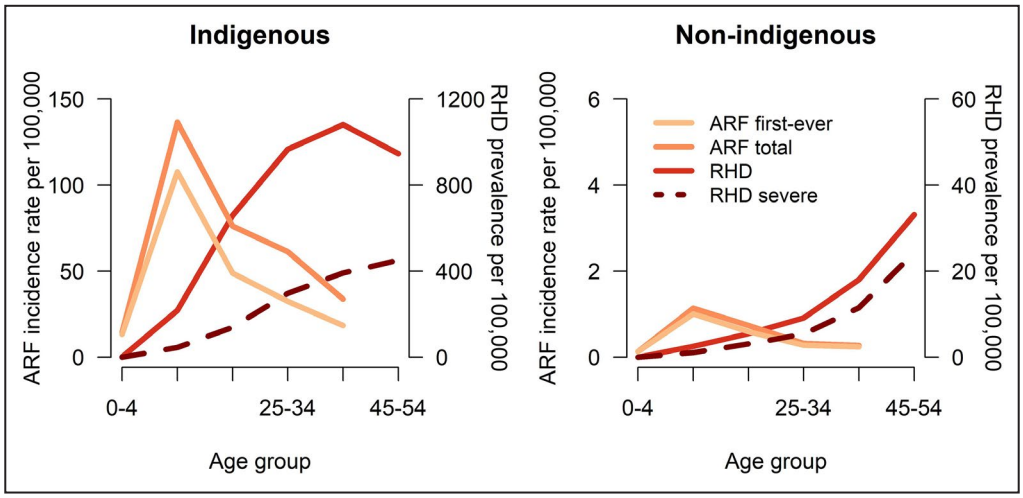

Figure 2. Age-specific incidence of ARF and prevalence of RHD in 5 Australian jurisdictions, by Indigenous status, 2015 to 2017.
ARF total includes first-ever episodes of ARF plus ARF recurrences. Severe RHD includes RHD cases who were recorded as having been in heart failure, received at least 1 cardiac valvular intervention or were recorded on RHD register as being severe. ARF or RHD includes any live person with a history of either ARF or RHD. ARF indicates acute rheumatic fever; and RHD, rheumatic heart disease.

aspirational goal of more comprehensive surveillance. This may offer a more sustainable and health system strengthening based approach than alternative approaches to measuring prevalence such as echocardiography screening. Incremental steps toward data linkage capacity include establishment and maintenance of population-based RHD registers; diagnostic coding of health encounters (hospital admissions, primary health care visits), and collection and analysis of vital statistics. Zambia, Uganda, and Fiji are examples of RHD-endemic countries where electronic health care information systems and registers are in use.[48] Electronic data capture is one of the key enablers that can allow these separate data sources to form the components of more comprehensive surveillance, potentially leading to opportunities for data linkage. Such improved data can be used to advocate for actions to address the sociopolitical and health system factors impacting on RHD.

Contemporary incidence in non-Indigenous Australians previously had limited attention. We show that sporadic episodes still occur in the general population, with 11% of ARF and 29% of RHD cases occurring in non-Indigenous Australians. Maori, Pacific Islanders, and those internationally born in low- or lower-middle-income country are recognized as being at risk, but only accounted for 33% of non-Indigenous ARF episodes and 58% of non-Indigenous RHD diagnoses. Indigenous status is the only ethnicity option provided in routinely collected Australian health administrative data sets.[49] Our method of identification likely underestimated non-Indigenous patients from communities at high risk of RHD. Additionally, as population estimates are not routinely available for specific non-Indigenous ethnic groups in Australia,[13] rates were not calculable. These findings suggest that while specific prevention strategies tailored for recognised at-risk non-Indigenous populations are needed, clinicians also require ongoing education to be able to recognize cases occurring in the broader population. Similarly, stronger attempts should be made to monitor high-risk subpopulations in high-income countries.

Unexpectedly, the percentage of non-Indigenous prevalent patients who had severe disease (65%) was greater than their Indigenous counterparts (31%). Figure 1 shows that this finding was true across all broad age groups. This and the higher proportions who had various RHD-related complications suggest that the threshold for identification and hospitalization among non-Indigenous patients might be higher and that RHD and complication risk might be underestimated. Higher mortality among Indigenous cases with RHD also likely reduced severe RHD numbers. There might be a pool of non-Indigenous RHD cases being missed, either undiagnosed or managed outside hospital/registers or that they only present when they have advanced disease. The sensitivity analysis of WA data using a longer lookback also suggests that our main results missed proportionally more non-Indigenous cases. Further research is necessary to determine the size of this cohort and whether they are receiving appropriate care.

Given the known issue of ARF underdiagnosis, particularly where clinicians are unfamiliar with the condition, nationwide ongoing clinician education should be introduced to improve awareness and clinical

Table 4. Mean Annual Crude, Age-Specific, and Age-Standardized Prevalence per 100 000 People With a History of ARF or RHD; RHD, and Severe RHD, by Indigenous Status: 5 Australian Jurisdictions, 2015 to 2017

	Total		Indigenous		Non-Indigenous		
	N*	Per 100 000 (95% CI)	N*	Per 100 000 (95% CI)	N*	Per 100 000 (95% CI)	Prevalence Ratio (95% CI)
ARF or RHD							
0–4	5	0.4 (0.2–0.6)	4	4.8 (2.1–7.6)	<5	n/a	n/a
5–14	938	43.6 (42.0–45.3)	812	508.9 (488.8–529.1)	126	6.3 (5.7–7.0)	80.5 (72.3–89.8)
15–24	1711	76.9 (74.8–79.0)	1441	1054.4 (1023.1–1085.6)	266	12.8 (11.9–13.6)	82.7 (76.7–89.2)
25–34	1525	60.5 (58.8–62.3)	1219	1211.9 (1172.8–1250.9)	302	12.5 (11.7–13.3)	97.0 (90.2–104.3)
35–44	1399	61.4 (59.5–63.2)	934	1197.9 (1153.8–1242.0)	463	21.0 (19.9–22.1)	57.0 (53.4–60.8)
45–54	1492	66.8 (64.9–68.8)	715	1007.6 (965.2–1050.0)	771	35.6 (34.2–37.1)	28.3 (26.7–30.0)
(0–54) crude†	7070	56.5 (55.7–57.2)	5126	815.5 (802.7–828.4)	1928	16.2 (15.8–16.6)	n/a
ASP (0–54)	N/A	55.3 (54.5–56.0)	N/A	881.3 (867.2–895.3)	N/A	14.6 (14.2–15.0)	60.3 (58.5–62.2)
ASP (0–24)	N/A	48.0 (46.9–49.0)	N/A	620.8 (606.1–635.6)	N/A	7.6 (7.1–8.0)	82.0 (77.0–87.2)
RHD							
0–4	<5	n/a	<5	n/a	<5	N/A	
5–14	396	18.4 (17.4–19.5)	346	216.9 (203.7–230.0)	50	2.5 (2.1–2.9)	86.7 (73.1–103.0)
15–24	1015	45.6 (44.0–47.2)	901	658.8 (634.1–683.6)	113	5.4 (4.9–6.0)	121.3 (108.4–135.8)
25–34	1196	47.5 (45.9–49.0)	972	966.6 (931.7–1001.6)	220	9.1 (8.4–9.8)	106.1 (97.5–115.5)
35–44	1241	54.4 (52.7–56.2)	843	1080.7 (1038.8–1122.6)	396	18.0 (17.0–19.0)	60.0 (56.0–64.3)
45–54	1393	62.4 (60.5–64.3)	671	945.1 (904.0–986.2)	717	33.1 (31.7–34.5)	28.5 (26.8–30.3)
(0–54) crude†	5241	41.9 (41.2–42.5)	3733	594.1 (583.1–605.0)	1496	12.6 (12.2–13.0)	n/a
ASP (0–54)	N/A	39.5 (38.8–40.1)	N/A	666.3 (653.9–678.8)	N/A	10.9 (10.5–11.2)	61.4 (59.3–63.5)
ASP (0–24)	N/A	25.4 (24.6–26.1)	N/A	346.1 (335.0–357.2)	N/A	3.1 (2.9–3.4)	110.2 (100.3–121.1)
Severe RHD							
0–4	<5	N/A	<5	N/A	<5	N/A	N/A
5–14	93	4.3 (3.8–4.9)	72	45.1 (39.1–51.1)	21	1.1 (0.8–1.3)	42.2 (31.9–55.8)
15–24	255	11.4 (10.6–12.3)	190	138.7 (127.4–150.1)	65	3.1 (2.7–3.6)	44.6 (37.9–52.5)
25–34	429	17.0 (16.1–18.0)	298	296.3 (276.9–315.7)	130	5.4 (4.8–5.9)	55.3 (49.1–62.3)
35–44	560	24.6 (23.4–25.7)	305	391.2 (365.9–416.5)	253	11.5 (10.7–12.3)	34.0 (30.9–37.5)
45–54	848	38.0 (36.5–39.5)	320	450.3 (421.8–478.7)	525	24.3 (23.1–25.5)	18.5 (17.1–20.1)
(0–54) crude†	2185	17.5 (17.0–17.9)	1184	188.4 (182.3–194.6)	994	8.4 (8.1–8.7)	n/a
ASP (0–54)	n/a	15.7 (15.3–16.1)	n/a	219.1 (211.9–226.4)	n/a	7.1 (6.9–7.4)	30.8 (29.4–32.4)
ASP (0–24)	n/a	6.2 (5.9–6.6)	n/a	72.6 (67.5–77.7)	n/a	1.7 (1.5–1.9)	43.9 (38.2–50.5)

ARF or RHD includes anyone with a history of either of these conditions. ARF indicates acute rheumatic fever; ASP, age-standardized prevalence; and RHD, rheumatic heart disease.

*Mean annual number of cases 2015–2017.

†To maintain anonymity, totals do not include cells that are <5.

diagnostic capability. The science to develop a diagnostic test for ARF is currently being pursued through the trans-Tasman START (Searching for a Technology-Driven Acute Rheumatic Fever Test) study (Carapetis JR, personal communication, 2019).

ARF recurrences were substantially lower for non-Indigenous patients. The current secondary prevention efforts focusing on Australian Indigenous populations provided under the Rheumatic Fever Strategy do not appear to be effective in improving equity. As in many other countries, adherence is suboptimal across diverse settings.[50,51] Secondary prophylaxis with benzathine benzylpenicillin, including adherence support and ensuring supply, is the basis of secondary prevention,[52] but must be coupled with community-led engagement and education.[53] Addressing the social and environmental determinants of recurrent streptococcal infections,[54] incorporating Indigenous knowledge and strengths into programs[55] and improving access to timely health care for these infections[16,56] would further reduce recurrences.

The stark 2-fold higher prevalence of RHD in females is consistent across populations, reflecting the female risk for autoimmunity[57] and possibly higher exposure to group A *Streptococcus* during child rearing.[3]

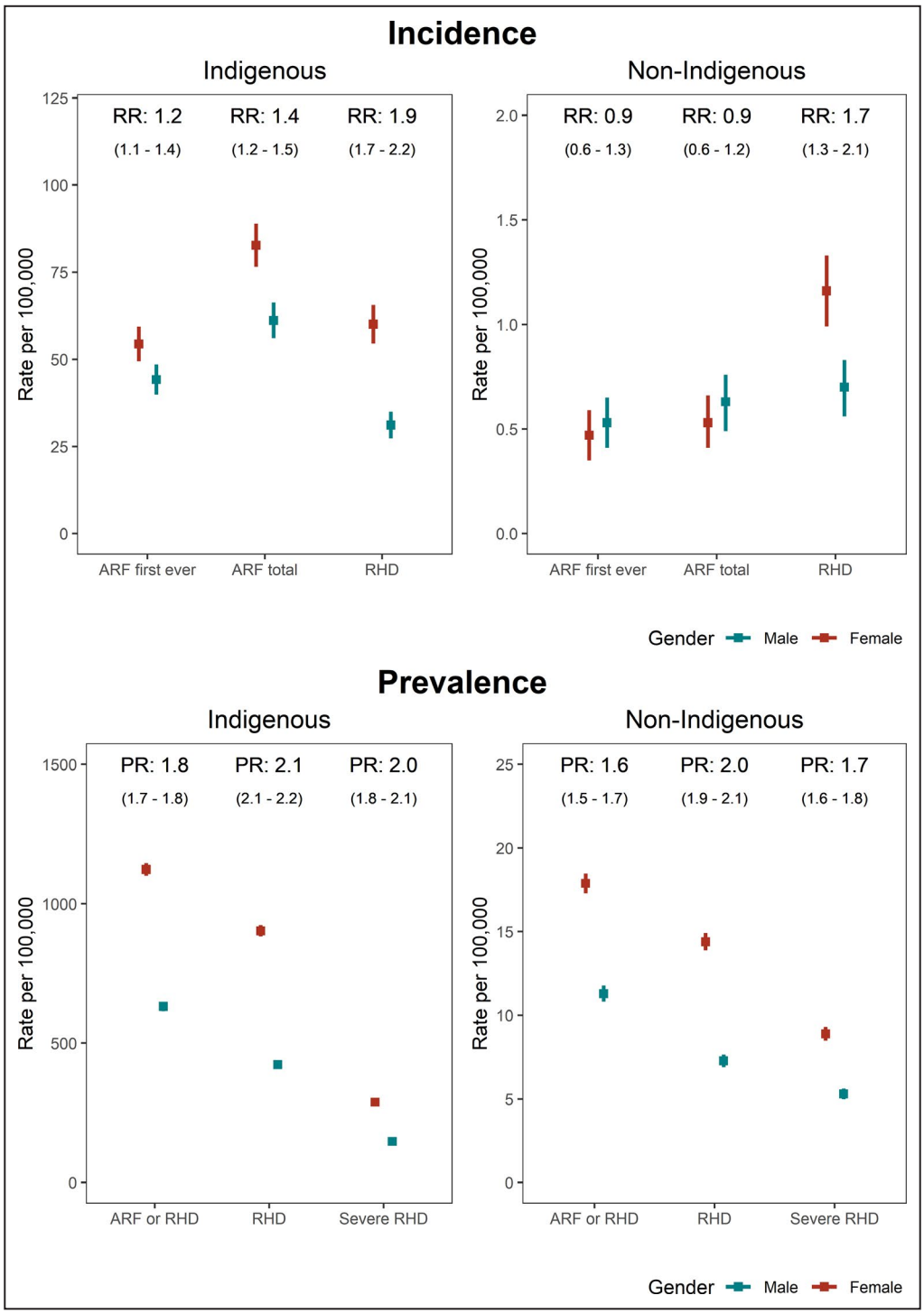

Figure 3. Sex differentials in the age-standardized incidence and prevalence of ARF and RHD in 5 Australian jurisdictions, by Indigenous status.
ARF total includes first-ever episodes of ARF plus ARF recurrences. Severe RHD includes RHD cases who were recorded as having been in heart failure, received at least 1 cardiac valvular intervention or were recorded on RHD register as being severe. ARF or RHD includes any live person with a history of either ARF or RHD. ARF indicates acute rheumatic fever; PR, prevalence ratio; RHD, rheumatic heart disease; and RR, rate ratio.

Innovative ways of identifying affected women need to be developed and intensified primary and secondary prevention pursued, particularly given the high risk of complications during pregnancy.[58–60]

The relatively high complexity among non-Indigenous cases challenges some current guidelines that assume that endocarditis risk is lower in non-Indigenous than Indigenous people with RHD. Our findings

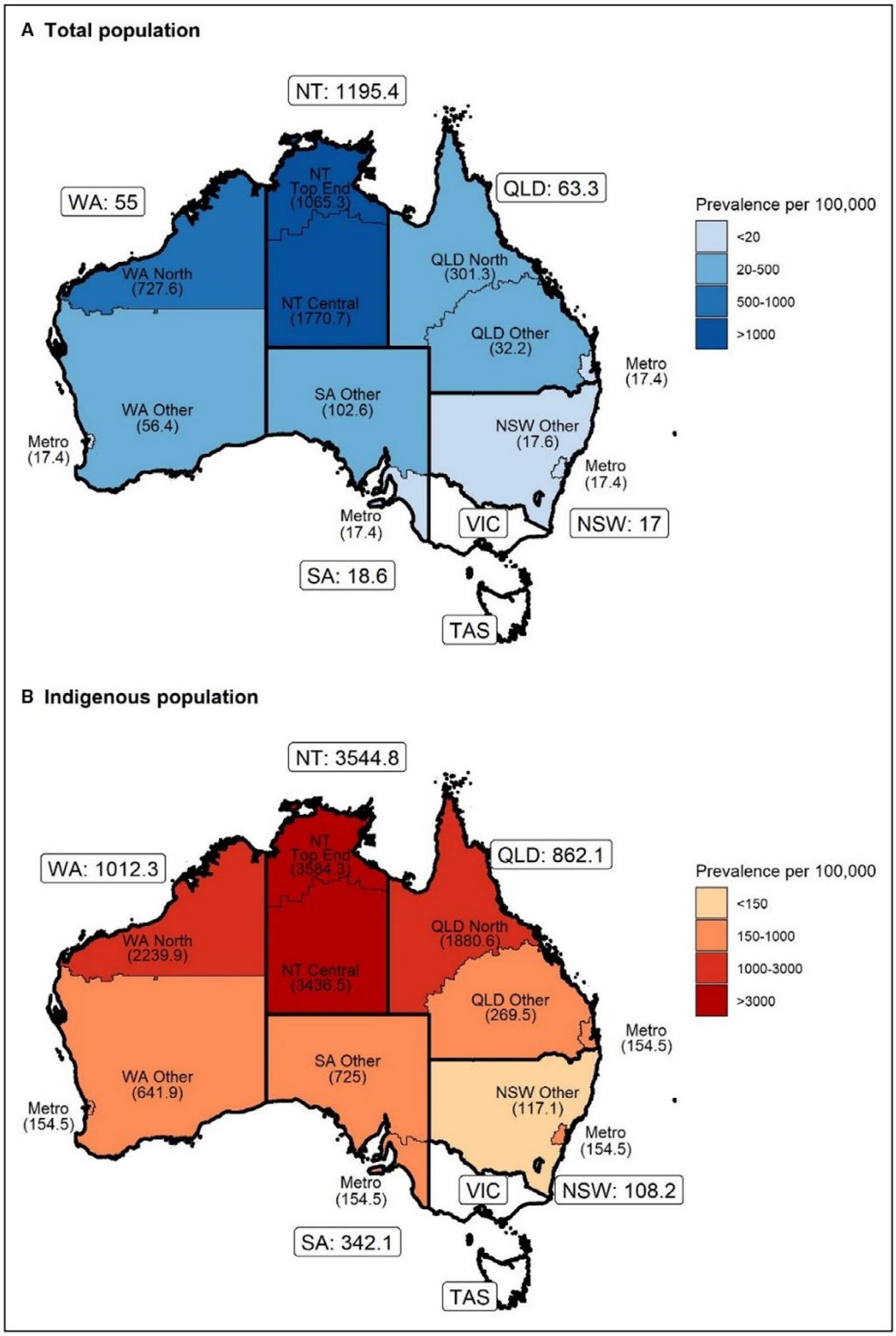

Figure 4. Total population (A) and Indigenous (B) age-standardized prevalence (per 100 000) of acute rheumatic fever or rheumatic heart disease in five Australian jurisdictions, by Indigenous Region Categories.

Within jurisdictional geographic regions are aggregations of 33 separate Indigenous Regions provided by the Australian Bureau of Statistics (see Data S1). NSW indicates New South Wales; NT, Northern Territory; QLD, Queensland; SA, South Australia; TAS Tasmania; VIC, Victoria; and WA, Western Australia.

have resulted in a move to broaden endocarditis prophylaxis in recently released guidelines to recommend antibiotics during certain high-risk dental procedures to all people with RHD.[52] Previous Australian guidelines recommended this prophylaxis only for people with RHD who are Indigenous or deemed socially disadvantaged.

Strengths and Weaknesses

The use of linked data across federated Australian jurisdictions, while innovative, will inevitably have shortcomings inherent in administrative data collated and analyzed retrospectively. We undertook substantial methodological development to address limitations in the *ICD-10* discharge codes for RHD to enable epidemiologically valid and replicable case definitions, which is not as robust as clinically validated cases. This is most likely to have affected the non-Indigenous patients with RHD, requiring a more stringent threshold to be classified as a case by our modeling. This might partly explain the more severe profile in non-Indigenous patients, although our extensive sensitivity analyses do not support this explanation. We used a 14-year lookback to accrue hospitalized cases over time to estimate prevalence, which provided relatively complete accrual of younger cases but will have missed those who were not registered and were hospitalized for RHD before our lookback window. The extent of this bias is moderate, as shown by our analysis of WA data using a longer lookback period. Similarly, we would also have misclassified some prevalent or repeat cases as first-ever diagnoses, thus underestimating recurrences as a proportion of all ARF episodes among older cases. The longer lookback analysis shows that this is likely to have had minimal impact on ARF incidence rates. It is possible we missed some symptomatic ARF episodes and milder RHD that were completely managed in primary care; however, this is likely to be relatively rare for ARF, given that it was notifiable for most of the study period and guidelines recommend hospitalization for ARF.[61] True RHD prevalence will be underestimated, as shown in screening studies in Northern Australia,[62] where half the cases identified on echocardiography had not been previously diagnosed. Some misclassification of regions of residence might also have occurred because of limitations and variation in geographic data provided by the linkage units or migration of patients. This particularly affects cases residing in South Australia who might be counted in Central Northern Territory where they have treatment, thus underestimating SA rates. Furthermore, our findings are also not fully representative of Australia, as Tasmania, Victoria, and the Australian Capital Territory were not included. However, our data represent 86% of the Indigenous Australian population and through extrapolation using our RHD age-specific prevalence estimates to the populations (<55 years) of these jurisdictions, we estimate 6156 people living with diagnosed RHD nationally. This study has focused exclusively on the morbidity burden of ARF and RHD; future studies will report on the corresponding mortality burden among Australians using a range of methodological approaches to allow appropriate monitoring of deaths in this population.

Policy Implications and Initiatives

This study contributes to the RHD Endgame Strategy, intended to eliminate ARF and RHD as a public health priority for Indigenous people in Australia. “End RHD” is taking this agenda forward, advocating for an increased scope of the Rheumatic Fever Strategy to address the environmental and economic factors perpetuating the ongoing disparities of this and other diseases. These study results, as well as the methods employed, build the case for policy change for a comprehensive approach to disease control with increased resources and ongoing surveillance. Importantly, while linked data methods advance epidemiologic estimates, the way these sensitive data are governed, reported, disseminated, and used to improve outcomes, need direction from Indigenous organizations and groups.[63] Consequently, our dissemination and translation plans include engagement with Indigenous peak bodies and communities to share data for smaller geographic areas and support innovative local solutions.

CONCLUSIONS

This study provides the most comprehensive epidemiologic picture of ARF and RHD in Australia to date, incorporating hospital-only cases previously excluded from register-based estimates. This allows greater confidence in subnational estimates of disease caseloads across geographic and ethnic divides and can guide how resources should be directed. The vast discrepancies between population groups highlights ARF/RHD as an indicator of disadvantage in this affluent country that urgently requires a more comprehensive approach to ARF/RHD prevention. Besides providing this baseline, the data linkage approach and the methods outlined here can be used and refined to track progress toward our goal of reducing and eventually eliminating ARF and RHD in high-risk communities and in the general Australian population. Reducing the burden of ARF and RHD, based on sound knowledge of true rates, is urgently required both in Australia and more globally. At the international level, the study

provides an example of what is possible in countries with some level of data infrastructure. In this way, the study supports the WHO's call to arms to address ARF and RHD.

ARTICLE INFORMATION

Received May 12, 2020; accepted August 10, 2020.

Affiliations

From the The University of Western Australia, Perth, Australia (J.M.K., D.B.-S., R.J.S., I.S., N.d.K., F.M.S., L.N., J.H., D.B.); Telethon Kids Institute, Perth, Australia (J.M.K., J.C., N.d.K., A.B., J.R.C., R.W.); Menzies School of Health Research, Charles Darwin University, Darwin, Australia (K.D., V.W., A.P.R.); University of Oxford, United Kingdom (M.G.); South Australian Medical Research Institute, Adelaide, Australia (A.B.); The University of Adelaide, Australia (A.B.); and The George Institute for Global Health, Sydney, New South Wales, Australia (R.W.).

Acknowledgments

The authors working on this paper have been supported by many collaborators across Australia, including Christopher Reid, Mellise Anderson, Elizabeth Geelhoed, Daniel Williamson, Angelita Martini, Kalinda Griffiths, Jess de Dassell, Fadwa Al-Yaman, Anne Russell, Hideo Tohira, Pamela Bradshaw, Sara Noonan, Emma Haynes, and Alice Mitchell. The authors value the support/endorsement provided to the project by the following peak bodies representing the Aboriginal Community Controlled Health sector: Aboriginal Medical Services Alliance Northern Territory, Kimberley Aboriginal Medical Service (the health service serving the high-burden region of WA), Aboriginal Health Council of South Australia, and Aboriginal Health and Medical Research Council (NSW). We also received support from the Aboriginal divisions of Queensland and WA Health Departments. We are committed to providing feedback to these organizations ensuring that the findings are accessible and provide the evidence needed for policy that can reduce the burden of ARF and RHD in Australia. We acknowledge that figures and other statistics represent the loss of health and human life with profound impact and sadness for people, families, community, and culture. We hope that the "numbers story" emanating from this project can augment the "lived stories" that reflect the voices of people with RHD and their families, thus jointly contributing to evidence to erase suffering from ARF and RHD in Australia. The authors also wish to thank the staff of the data linkage units of the State and Territory governments (WA, SA-NT, NSW, Queensland) for linkage of the data. We thank the State and Territory Registries of Births, Deaths and Marriages, the State and Territory Coroners, and the National Coronial Information System for enabling Cause of Death Unit Record File data to be used for this project. Further, we thank the data custodians and data managers for the provision of the following data:

1. Inpatient hospital data (5 States and Territories).
2. Emergency Department data (5 States and Territories).
3. RHD registers (5 States and Territories).
4. ANZ Society of Cardiac & Thoracic Surgeons data base (single data source from 5 States and Territories).
5. Royal Melbourne Children's Hospital Paediatric Cardiac Surgery data base (single data source for RHD pediatric patients from SA and NT receiving surgery in Melbourne).
6. Primary health care data from NT Department of Health.

Sources of Funding

This project received funding from the National Health and Medical Research Council through project grant (#114652) and seed funds from the End-RHD Centre for Research Excellence and HeartKids. Katzenellenbogen is supported by a Heart Foundation of Australia Future Leader Fellowship (#102043). Ralph (#1142011) and Nedkoff (#1110337) are supported by a National Health and Medical Research Council Fellowships. Wyber is supported by a National Health and Medical Research Postgraduate Scholarship (#1151165).

Disclosures

None.

Supplementary Materials

Data S1
Tables S1–S2
Figure S1

REFERENCES

1. World Health Organization. *Seventy-First World Health Assembly A71/25*. Resolution adopted on 25 May 2018 for provisional agenda 12.8 by Director General on 12 April 2018. Geneva: World Health Organization; 2018.
2. Watkins DA, Johnson CO, Colquhoun SM, Karthikeyan G, Beaton A, Bukhman G, Faorousanfar MH, Longnecker CT, Mayosi BM, Mensah GA, et al. Global, regional and national burden of rheumatic heart disease, 1990–2015. *N Engl J Med*. 2017;377:713–722.
3. Carapetis JR, Beaton A, Cunningham MW, Guilherme L, Karthikeyan G, Mayosi BM, Sable C, Steer A, Wilson N, Wyber R, et al. Acute rheumatic fever and rheumatic heart disease. *Nat Rev Dis Primers*. 2016;2:15084.
4. Carapetis JR, Steer AC, Mulholland EK, Weber M. The global burden of group A streptococcal diseases. *Lancet Infect Dis*. 2005;5:685–694.
5. Kaplan E. Global assessment of rheumatic fever and rheumatic heart disease at the close of the century. *Circulation*. 1993;88:1.
6. Australian Institute of Health and Welfare. *Rheumatic Heart Disease and Acute Rheumatic Fever in Australia: 1996–2012*. Canberra: AIHW; 2013.
7. Oliver J, Pierse N, Baker MG. Estimating rheumatic fever incidence in New Zealand using multiple data sources. *Epidemiol Infect*. 2015;143:167–177.
8. Gordon J, Kirlew M, Schreiber Y, Saginur R, Bocking N, Blakelock B, Haavaldsrud M, Kennedy C, Farrell T, Douglas L, et al. Acute rheumatic fever in First Nations communities in northwestern Ontario: social determinants of health "bite the heart." *Can Fam Physician*. 2015;61:881–886.
9. Lawrence JG, Carapetis JR, Griffiths K, Edwards K, Condon JR. Acute rheumatic fever and rheumatic heart disease: incidence and progression in the Northern Territory of Australia, 1997 to 2010. *Circulation*. 2013;128:492–501.
10. Australian Medical Association. *2016 AMA Report Card on Indigenous Health—A Call to Action to Prevent New Cases of Rheumatic Heart Disease in Indigenous Australia by 2031*. Barton: AMA; 2016.
11. Australian Bureau of Statistics. *Estimates of Aboriginal and Torres Strait Islander Australians, June 2016*. Canberra: ABS; 2018. Table 3238.0.55.001.
12. Australian Bureau of Statistics. *Life Tables for Aboriginal and Torres Strait Islander Australians*. Canberra: ABS; 2019:2015–2017.
13. Australian Bureau of Statistics. *Census of Population and Housing: Reflecting Australia—Stories From the Census*. Canberra: ABS; 2016. Report No.: 2071.0.
14. Wilson N. Rheumatic heart disease in indigenous populations—New Zealand experience. *Heart Lung Circ*. 2010;19:282–288.
15. Batley J. Devpolicyblog [Internet]. 2017. Available at: https://devpolicy.org/2016-census-reveal-about-pacific-islands-communities-in-australia-20170928/ Accessed January 12, 2020.
16. Wyber R, Katzenellenbogen JM, Pearson G, Gannon M. The rationale for action to end new cases of rheumatic heart disease in Australia. *Med J Aust*. 2017;207:322–323.
17. Colquhoun SM, Condon JR, Steer AC, Li SQ, Guthridge S, Carapetis JR. Disparity in mortality from rheumatic heart disease in indigenous Australians. *J Am Heart Assoc*. 2015;4:e001282. DOI: 10.1161/JAHA.114.001282.
18. Australian Institute of Health and Welfare. *Acute Rheumatic Fever and Rheumatic Heart Disease in Australia*. Canberra: AIHW; 2019. Cat. no: CVD 86.
19. Carapetis JR, Wolff DR, Currie BJ. Acute rheumatic fever and rheumatic heart disease in the top end of Australia's Northern Territory. *Med J Aust*. 1996;164:146–149.
20. He VY, Condon JR, Ralph AP, Zhao Y, Roberts K, de Dassel JL, Currie BJ, Fittock M, Edwards KN, Carapetis JR. Long-term outcomes from acute rheumatic fever and rheumatic heart disease: a data-linkage and survival analysis approach. *Circulation*. 2016;134:222–232.
21. Katzenellenbogen JM, Bond-Smith D, Cunneen R, Dempsey K, Cannon J, Nedkoff N, Sanfilippo FM, Ralph AP, De Klerk N, Hung J, et al. The End Rheumatic Heart Disease in Australia—Study of Epidemiology

(ERASE) Project: data sources, case ascertainment and cohort profile. *Clin Epidemiol*. 2019;11:1–14.
22. World Health Organization. *International Statistical Classification of Diseases and Health Related Problems, Tenth Revision, Australian Modification*. 5th ed. Geneva: WHO; 2016.
23. Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS). National Cardiac Surgery Database Melbourne: CCRE, Monash University; 2010. Available at: https://anzscts.org/national-database/. Accessed January 20, 2020.
24. Katzenellenbogen JM, Nedkoff L, Canon J, Kruger D, Pretty F, Carapetis JR, Dempsey KE, de Dassel J, Anderson M, de Klerk N, et al. Low positive predictive value of ICD-10 codes in relation to rheumatic heart disease: a challenge for global surveillan. *Int Med J*. 2019;49:400–403.
25. Rheumatic Fever Working Party of the Medical Research Council of Great Britain and American Council on Rheumatic Fever and Congenital Heart Disease: American Heart Association. The evolution of rheumatic heart disease in children: five-year report of a co-operative clinical trial of ACTH, cortisone and aspirin. *Can Med Assoc J*. 1960;83:781–789.
26. Fitz-Gerald JA, Ongzalima CO, Ng A, Greenland M, Sanfilippo FM, Hung J, Katzenellenbogen JM. A validation study: how predictive is a diagnostic coding algorithm at identifying rheumatic heart disease in Western Australian hospital data? *Heart Lung Circ*. 2020;29: E194–E199.
27. Bond-Smith D, Cunneen R, de Klerk N, Nedkoff L, Anderson M, Hung J, Cannon J, Griffiths K, Katzenellenbogen JM. Development and evaluation of a prediction model for ascertaining rheumatic heart disease status in administrative data. *Clin Epidemiol*. 2020;12:717–730.
28. Christensen D, Davis G, Draper G, Mitrou F, McKeown S, Lawrence D. Evidence for the use of an algorithm in resolving inconsistent and missing Indigenous status in administrative data collections. *Aust J Soc Issues*. 2014;49:423–443.
29. World Bank. World Bank Country and Lending Groups. Washington, DC: World Bank. Report No. Available at: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups. Accessed January 19, 2019.
30. Australian Bureau of Statistics. *Australian Statistical Geography Standard (ASGS)*. Canberra: ABS; 2011. Cat Number 1216.0.
31. Australian Institute of Health and Welfare. *Rural, Regional and Remote Health: a Guide to Remoteness Classification*. Canberra: AIHW; 2004. Cat no. PHE 53.
32. Australian Bureau of Statistics. *Information Paper: Census of Population and Housing—Socio-Economic Indexes for Areas, Australia*. Canberra: ABS; 2003. Cat no. 2033.055.001.
33. Ahmad OB, Boshci-Pinto C, Lopez AD, Murray CJL, Lozano R, Inone M. Age standardization of rates: a new WHO standard. Geneva: WHO; 2001. GPE Discussion Paper Series: No. 31.
34. Holman CD, Bass AJ, Rouse IL, Hobbs MS. Population-based linkage of health records in Western Australia: development of a health services research linked database. *Aust N Z J Public Health*. 1999;23:453–459.
35. Global Burden of Disease Study 2017 (GBD 2017) Results. [Internet]. Institute for Health Metrics and Evaluation (IHME); 2018. Available at: http://ghdx.healthdata.org/gbd-results-tool. Accessed February 20, 2020.
36. Balabanski AH, Newbury J, Leyden JM, Arima H, Anderson CS, Castle S, Cranefield J, Paterson T, Thrift AG, Katzenellenbogen J, et al. Excess stroke incidence in young Aboriginal people in South Australia: pooled results from two population-based studies. *Int J Stroke*. 2018;13:811–814.
37. You J, Condon JR, Zhao Y, Guthridge S. Incidence and survival after acute myocardial infarction in Indigenous and non-Indigenous people in the Northern Territory. *Med J Aust*. 2009;190:298–302.
38. Katzenellenbogen JM, Teng TH, Lopez D, Hung J, Knuiman MW, Sanfilippo FM, Hobbs MS, Thompson SC. Initial hospitalisation for atrial fibrillation in Aboriginal and non-Aboriginal populations in Western Australia. *Heart*. 2015;101:712–719.
39. Wong CX, Lee SW, Gan SW, Mahajan R, Rangnekar G, Pathak RK, Twomey D, Schultz C, Ganesan AN, Brooks AG, et al. Underuse and overuse of anticoagulation for atrial fibrillation: a study in Indigenous and non-Indigenous Australians. *Int J Cardiol*. 2015;191:20–24.
40. Woods JA, Katzenellenbogen JM, Davidson PM, Thompson SC. Heart failure among Indigenous Australians: a systematic review. *BMC Cardiovasc Disord*. 2012;12:99.
41. Agenson T, Katzenellenbogen JM, Seth R, Dempsey K, Anderson M, Wade V, Bond-Smith D. Case ascertainment on Australian registers for acute rheumatic fever and rheumatic heart disease. *Int J Environ Res Public Health*. 2020;17:5505.
42. Milea D, Azmi S, Reginald P, Verpillat P, Francois C. A review of accessibility of administrative healthcare databases in the Asia-Pacific region. *J Mark Access Health Policy*. 2015;3:28076.
43. International Population Data Linkage Network. Data Linkage Centres (tabulated) 2020. Available at: https://www.ipdln.org/data-linkage-centres. Accessed January 20, 2020.
44. Kamaluddin NA, Abd Rahman MF, Várhelyi A. Matching of police and hospital road crash casualty records—a data-linkage study in Malaysia. *Int J Inj Contr Saf Promot*. 2019;26:52–59.
45. Mehta U, Heekes A, Kalk E, Boulle A. Assessing the value of Western Cape Provincial Government health administrative data and electronic pharmacy records in ascertaining medicine use during pregnancy. *S Afr Med J*. 2018;108:439–443.
46. Parks T, Kado J, Miller AE, Ward B, Heenan R, Colquhoun SM, Barnighausen TW, Mirabel M, Bloom DE, Bailey RL, 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 Negl Trop Dis*. 2015;9:e0004033.
47. Doukky R, Abusin SA, Bayissa YA, Kelly RF, Ansari AH. Rheumatic heart disease in modern urban America: a cohort study of immigrant and indigenous patients in Chicago. *Int J Cardiol*. 2014;175: 178–180.
48. Wyber R, Kado J. Rheumatic Heart Disease Control Programs, Registers, and Access to Care. In: Dougherty S, Carapetis J, Zühlke L, Wilson N, eds. *Acute Rheumatic Fever and Rheumatic Heart Disease*. St Louis: Elsevier; 2020:235–259.
49. Australian Institute of Health and Welfare. Australian Burden of Disease Study: impact and causes of illness and death in Aboriginal and Torres Strait Islander people 2011 [Internet]. Canberra: AIHW; 2016. Available at: https://www.aihw.gov.au/reports/burden-of-disease/illness-death-indigenous-australians/contents/table-of-contents. Accessed December 16, 2019.
50. de Dassel JL, de Klerk N, Carapetis JR, Ralph AP. How many doses make a difference? An analysis of secondary prevention of rheumatic fever and rheumatic heart disease. *J Am Heart Assoc*. 2018;7:e010223. DOI: 10.1161/JAHA.118.010223.
51. Woods J, Katzenellenbogen JM. Adherence to secondary prophylaxis among patients with acute rheumatic fever and rheumatic heart disease. *Curr Cardiol Rev*. 2019;15:239–241.
52. RHDAustralia (ARF/RHD Writing Group), National Heart Foundation of Australia, Cardiac Society of Australia and New Zealand. *The 2020 Australian Guideline for Prevention, Diagnosis and Management of Acute Rheumatic Fever and Rheumatic Heart Disease*. 3rd ed. Darwin: RHDAustralia, Menzies School of Health Research; 2020.
53. Haynes E, Marawili M, Marika BM, Mitchell AG, Phillips J, Bessarab D, Walker R, Cook J, Ralph AP. Community-based participatory action research on rheumatic heart disease in an Australian Aboriginal homeland: evaluation of the "On track watch" project. *Eval Program Plann*. 2019;74:38–53.
54. Coffey PM, Ralph AP, Krause VL. The role of social determinants of health in the risk and prevention of group A streptococcal infection, acute rheumatic fever and rheumatic heart disease: a systematic review. *PLoS Negl Trop Dis*. 2018;12:e0006577.
55. Haynes E, Mitchell A, Enkel S, Wyber R, Bessarab B. Voices behind the statistics: a systematic literature review of the lived experience of rheumatic heart disease. *Int J Environ Res Public Health*. 2020;17:E1347.
56. Cannon J, Bessarab DC, Wyber R, Katzenellenbogen JM. Public health and economic perspectives on acute rheumatic fever and rheumatic heart disease: can we afford 'business as usual'? *Med J Aust*. 2019;211:250–252.
57. Wilhelmson AS, Rodriguez ML, Stubelius A, Fogelstrand P, Johansson I, Buechler MB, Lianoglou S, Kapoor VN, Johansson ME, Fagman JB, et al. Testosterone is an endogenous regulator of BAFF and splenic B cell number. *Nature Commun*. 2018;9:2067.
58. Beaton A, Okello E, Scheel A, DeWyer A, Ssembatya R, Baaka O, Namisanvu H, Njeri A, Matovu A, Namagembe I, et al. Impact of heart disease on maternal, fetal and neonatal outcomes in a low-resource setting. *Heart*. 2019;105:755–760.

59. Subbaiah M, Sharma V, Kumar S, Rajeshwari S, Kothari SS, Roy KK, Sharma JB, Singh N. Heart disease in pregnancy: cardiac and obstetric outcomes. *Arch Gynecol Obstet*. 2013;288:23–27.
60. Sullivan E, Vaughan G, Li Z, Peek MJ, Carapetis JR, Walsh W, Frawley J, Rémond M, Remenyi B, Jackson Pulver L, et al. The high prevalence and impact of rheumatic heart disease in pregnancy in First Nations populations in a high-income setting: a prospective cohort study. *BJOG*. 2020;127:47–56.
61. RHDAustralia (ARF/RHD Writing Group), National Heart Foundation of Australia, Cardiac Society of Australia and New Zealand, 2012. *Australian Guideline for Prevention, Diagnosis and Management of Acute Rheumatic Fever and Rheumatic Heart Disease*. 2nd ed. Darwin: RHDAustralia, Menzies School of Health Research; 2012.
62. Roberts K, Maguire G, Brown A, Atkinson D, Remenyi B, Ilton M, Wheaton G, Kelly A, Kumar RK, Carapetis J. Echocardiographic screening for rheumatic heart disease in high-risk and low-risk children: results of the Australian gECHO study. *Glob Heart*. 2014;1:e19.
63. Kukutai T, Taylor J, eds. *Indigenous Data Sovereignty: Towards an Agenda*. Canberra: Australian National University Press; 2016.

SUPPLEMENTAL MATERIAL

Data S1.

Supplemental Methods

Model for predicting RHD case for inclusion in cohort

Background:

Previous research has raised substantial concerns regarding the validity of the International Statistical Classification of Diseases and Related Health Problems (ICD) codes (ICD-10 I05-I09) for rheumatic heart disease (RHD) due to likely misclassification of non-rheumatic valvular disease (non-rheumatic VHD) as RHD. There is currently no validated, quantitative approach for reliable case ascertainment of RHD in administrative hospital data.

Methods:

A comprehensive dataset of validated Australian RHD cases from Queensland, Northern Territory, Western Australia and South Australia was compiled and linked to inpatient hospital records with a RHD ICD code (2000-2018, n=7555).

A prediction model was developed based on a generalized linear mixed model structure with a binary outcome and a logistic link function considering an extensive range of demographic and clinical variables including:

- individual RHD codes
- diagnosis position
- sex
- age continuous and categorical
- hospital type (private, public)
- private hospital insurance
- population category (Indigenous, other high-risk, low-risk)
- residential remoteness
- SES
- concurrent ARF code
- concurrent heart failure code
- history of congenital heart disease
- ARF ever recorded
- heart failure ever recorded
- non-invasive valvular procedure
- valvular surgery ever recorded

The final model included the underlined variables and hospital and year random effects.

The model was validated internally using randomly selected cross-validation samples and external data. Conditional optimal probability cut-points were calculated, maximising discrimination separately for high-risk versus low-risk populations.

Result:

The proposed model reduced the false-positive rate (FPR) from acute rheumatic fever (ARF) cases misclassified as RHD from 0.59 to 0.27; similarly for non-rheumatic VHD from 0.77 to 0.20. Overall, the model achieved strong discriminant capacity (AUC: 0.93) and maintained a similar robust performance during external validation (AUC: 0.88). This prediction model is not a clinical tool; suitable areas of application include: research, advocacy and policy development and evaluation.

A FULL DESCRIPTION OF THIS WORK HAS BEEN PUBLISHED IN OPEN ACCESS AT:

https://doi.org/10.2147/CLEP.S241588

Bond-Smith D, Cunneen R, de Klerk N, Nedkoff L, Anderson M, Hung J, et al. Development and evaluation of a prediction model for ascertaining rheumatic heart disease status in administrative data. Clinical Epidemiology. 2020;(12):717-30.

List of countries included in categorisation as Low and Lower-Middle Income Countries in this paper

Afghanistan	Egypt, Arab Rep.	Macedonia, FYR	Sierra Leone
Albania	El Salvador	Madagascar	Slovak Republic
Algeria	Equatorial Guinea	Malawi	Solomon Islands
Angola	Eritrea	Maldives	Somalia
Armenia	Estonia	Mali	South Sudan
Azerbaijan	Ethiopia	Marshall Islands	Sri Lanka
Bangladesh	Fiji	Mauritania	St. Vincent and the Grenadines
Belarus	Gambia, The	Micronesia, Fed. Sts.	Sudan
Belize	Georgia	Moldova	Suriname
Benin	Ghana	Mongolia	Swaziland
Bhutan	Grenada	Montenegro	Syrian Arab Republic
Bolivia	Guatemala	Morocco	Tajikistan
Bosnia and Herzegovina	Guinea	Mozambique	Tanzania
Botswana	Guinea-Bissau	Myanmar	Thailand
Bulgaria	Guyana	Namibia	Timor-Leste
Burkina Faso	Haiti	Nepal	Togo
Burundi	Honduras	Nicaragua	Tonga
Cabo Verde	India	Niger	Tunisia
Cambodia	Indonesia	Nigeria	Turkey
Cameroon	Iran, Islamic Rep.	Northern Mariana Islands	Turkmenistan
Central African Republic	Iraq	Pakistan	Tuvalu
Chad	Jamaica	Panama	Uganda
China	Jordan	Papua New Guinea	Ukraine
Colombia	Kazakhstan	Paraguay	Uzbekistan
Comoros	Kenya	Peru	Vanuatu
Congo, Dem. Rep.	Kiribati	Philippines	Venezuela, RB
Congo, Rep.	Korea, Dem. Rep.	Poland	Vietnam
Costa Rica	Kosovo	Romania	West Bank and Gaza
Côte d'Ivoire	Kyrgyz Republic	Russian Federation	Yemen, Rep.
Croatia	Lao PDR	Rwanda	Zambia
Cuba	Latvia	Samoa	Zimbabwe
Djibouti	Lebanon	São Tomé and Principe	
Dominica	Lesotho	Senegal	

Dominican Republic	Liberia	Serbia	
Ecuador	Lithuania	Serbia and Montenegro (former)	

Table S1. Indigenous committees and organisations* providing support and ethics approval of the project.

	Aboriginal organisational support	**General Human Research Ethics Committees (HREC)**	**Aboriginal Ethics Committees**
Northern Territory	Aboriginal Medical Services Alliance Northern Territory	Top End HREC (Northern Territory), Menzies School of Health Research Central Australia HREC – reciprocal with Top End	Joint with Top End HREC
Western Australia	Kimberley Aboriginal Medical Service, including Kimberley Aboriginal Health Planning Forum Research Sub-Committee Western Australia Aboriginal Health Directorate	Western Australian Human Research Ethics Committee (Department of Health)	Western Australian Aboriginal Health Ethics Committee
Queensland	Support through collaboration with Aboriginal and Torres Strait Islander Health Branch, Queensland Health	Prince Charles Hospital Human Ethics Committee	No dedicated Aboriginal ethics committee
South Australia	Aboriginal Health Council of South Australia	South Australia Department of Health and Ageing HREC	Aboriginal Health Research Ethics Committee
New South Wales	Aboriginal Health and Medical Research Council	NSW Population & Health Services Research Ethics Committee	Aboriginal Health and Medical Research Council Ethics Committee.
National	Cultural lead, Australian Heart Foundation		

*RHD Australia provided support for the project but is not an Indigenous organization/committee.

Table S2. Comparison of numbers and first-ever ARF rates and RHD prevalence 2015-2017 using 14 years versus 25 year lookback period in the Western Australian linked data

	Lookback 14 years			Lookback 25 years			Change in estimates		
	N	Rate	(95% CI)	N	Rate	(95% CI)	Addition cases	% Additional cases	% Increase in ASRR
First-ever ARF incidence:									
Total	104	2.4	(1.9 - 2.9)	102	2.4	(1.9 - 2.8)	-2	-2%	0%
Non-Indigenous	5	0.1	(0 - 0.2)	5	0.1	(0 - 0.2)	0	0%	0%
Indigenous	99	38.9	(31.2 - 46.7)	97	38	(30.4 - 45.6)	-2	-2%	-2%
Male	45	2.0	(1.4 - 2.6)	44	2	(1.4 - 2.5)	-1	-2%	0%
Female	58	2.8	(2.1 - 3.5)	57	2.7	(2 - 3.5)	-1	-2%	-4%
0-4	3	0.6	(0 - 1.2)	3	0.6	(0 - 1.2)	0	0%	0%
5-14	59	6.1	(4.5 - 7.6)	59	6.1	(4.5 - 7.6)	0	0%	0%
15-24	22	2.2	(1.3 - 3.2)	22	2.2	(1.3 - 3.2)	0	0%	0%
25-34	14	1.2	(0.5 - 1.8)	12	1.0	(0.4 - 1.5)	-2	-14%	-17%
35-44	6	0.6	(0.1 - 1)	6	0.6	(0.1 - 1)	0	0%	0%
RHD prevalence:									% Increase in ASPR
Total	2140	35.3	(33.8 - 36.8)	2518	40.8	(39.2 - 42.4)	378	18%	16%
Non-Indigenous	449	7	(6.3 - 7.6)	610	9.3	(8.6 - 10.1)	161	36%	33%
Indigenous	1691	681	(648.5 - 713.6)	1908	778.2	(743.2 - 813.2)	217	13%	14%
Male	675	22.7	(21 - 24.4)	780	25.7	(23.9 - 27.6)	105	16%	13%
Female	1465	48.2	(45.7 - 50.7)	1738	56.2	(53.5 - 58.8)	273	19%	17%
0-4	< 5	n/a	n/a	< 5	n/a	n/a	n/a	n/a	n/a
5-14	165	17	(14.4 - 19.6)	168	17.3	(14.7 - 19.9)	3	2%	2%
15-24	444	45.1	(40.9 - 49.3)	448	45.5	(41.3 - 49.7)	4	1%	1%
25-34	523	43	(39.3 - 46.7)	557	45.8	(42 - 49.6)	34	7%	7%
35-44	513	48.4	(44.2 - 52.6)	641	60.5	(55.8 - 65.2)	128	25%	25%
45-54	495	48.6	(44.3 - 52.8)	704	69.1	(64 - 74.2)	209	42%	42%

ARF Acute Rheumatic Fever; RHD Rheumatic heart disease
ASRR age-standardised rate ratio; ASPR age-standardized prevalence ratio

Figure S1. Contribution of first-ever to total acute rheumatic fever (ARF) incidence counts by age and Indigenous status in five Australian jurisdictions, 2015-2017.