An outbreak of acute rheumatic fever in a remote Aboriginal community

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Submitted: 30 January 2023; Revision requested: 8 July 2023; Accepted: 12 July 2023

Abstract

Objectives: We describe the public health response to an outbreak of acute rheumatic fever (ARF) in a remote Aboriginal community.

Methods: In August 2021, the Northern Territory Rheumatic Heart Disease Control Program identified an outbreak of acute rheumatic fever in a remote Aboriginal community. A public health response was developed using a modified acute poststreptococcal glomerulonephritis protocol and the National Acute Rheumatic Fever Guideline for Public Health Units.

Results: 12 cases were diagnosed during the outbreak; six-times the average number of cases in the same period in the five years prior (n=1.8). Half (n=6) of the outbreak cases were classified as recurrent episodes with overdue secondary prophylaxis. Contact tracing and screening of 11 households identified 86 close contacts.

Conclusions: This outbreak represented an increase in both first episodes and recurrences of acute rheumatic fever and highlights the critical need for strengthened delivery of acute rheumatic fever secondary prophylaxis, and for improvements to the social determinants of health in the region.

Implications for Public Health: Outbreaks of acute rheumatic fever are rare despite continuing high rates of acute rheumatic fever experienced by remote Aboriginal communities. Nevertheless, there can be improvements in the current national public health guidance relating to acute rheumatic fever cluster and outbreak management.

Key words: acute rhematic fever, outbreak, public health response, group A *Streptococcus*, notifiable disease, rhematic heart disease

Introduction

Acute rheumatic fever (ARF) is an autoimmune response arising as a complication of infection of the pharynx, and possibly of the skin, by group A *Streptococcus* (GAS) bacteria.[1–3] It is a preventable disease,[4,5] driven by aspects of poverty.[1,6–9] In Australia, Aboriginal and Torres Strait Islander peoples in underserved and under-resourced regions experience the burden of ARF almost exclusively.[9] The mainstay of ARF case management is secondary prophylaxis with intramuscular (IM) benzathine benzylpenicillin G (BPG) injection every 21–28 days. This prevents GAS infection and subsequent recurrences of ARF. For every day that ARF prophylaxis is overdue, an individual is said to have days at risk.[2,10] If recurrences of ARF occur, cumulative damage to cardiac valves can be sustained,

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Aust NZ J Public Health. 2023; Online; https://doi.org/10.1016/j.anzjph.2023.100077

leading to rheumatic heart disease (RHD).[1,6] RHD is a chronic and debilitating condition,[11] a marker of extreme health inequity,[12] and poses a substantial economic burden to health systems.[13,14] In the Northern Territory (NT) of Australia, definite and probable diagnoses of ARF are notifiable diseases, under the *NT Notifiable Diseases Act 1981*.[15,16] Enhanced clinical and surveillance data are managed by the NT RHD Control Program via a Register as part of routine NT Government Department of Health surveillance and case-management activities. The Register, and associated infrastructure, also includes automated case cluster and outbreak detection. This surveillance system notifies the NT RHD Control Program if at least two cases of ARF, with onset dates within 28 days of each other occur in a small community.[17] On 28 August 2021, the NT RHD Control Program notified Miwatj Health Aboriginal Corporation (MHAC), an Aboriginal Community- Controlled Health Organisation, of a potential outbreak of ARF in a remote Aboriginal community within East Arnhem Land, NT. This alert was generated when four cases of ARF were detected in the community with onset dates within 28 days of each other. A public health response was developed using a modified acute poststreptococcal glomerulonephritis protocol,[18] and the Communicable Diseases Network Australia National ARF Guideline for Public Health Units (ARF SoNG).[1]

Methods

Setting

The outbreak occurred in a remote Aboriginal community in East Arnhem Land in the NT of Australia. The majority of residents of this community are linguistically diverse Yolŋu[19] people, who can be highly transient across the region, particularly between associated homelands. Homelands, or outstations, are "*small, decentralised communities of close kin, established by the movement of Aboriginal Peoples to land of social, cultural and economic significance to them*".[20] Primary health services are delivered in the affected region by MHAC and one homelands health service. Tertiary care is provided via aeromedical evacuation to Gove District Hospital and Royal Darwin Hospital, with limited specialist outreach services. ARF is endemic in the region, with routine NT RHD Control Program Register data demonstrating an average of 6.4 cases diagnosed each year during the five years preceding the outbreak. Of these previous cases, in the main community, an annual average of two cases occurred in children between the age of 5 and 14 years, a notification rate of 522 cases per 100,000 population in this age group. In contrast, in Australia, communities with high rates of ARF are defined as those with an annual incidence of 30 cases per 100,000 population in the same age group.[2]

Cases

We developed an outbreak case definition using clinical, temporal and geographic features. All cases were diagnosed using the 2020 Australian ARF diagnostic criteria for diagnosis of first known or recurrent episodes of definite, probable or possible ARF.[2] We classified outbreak ARF episodes as those with disease onset (defined as the date of ARF symptom onset), between 1 July and 15 October 2021, in individuals who had resided in or visited the affected community or associated homelands during this period. ARF cases meeting the outbreak case definition were initially identified and notified through routine primary healthcare. Enhanced passive surveillance was subsequently initiated on 28 August 2021 by provision of Health Alerts to MHAC with guidance to increase vigilance toward ARF-like clinic presentations. Outreach-based contact tracing was initiated on 1 September 2021, with close contacts screened for ARF-like symptoms. Cardiology outreach was also performed by a private cardiology provider during the first week of enhanced active surveillance. The purpose of echocardiographic screening was to identify close contacts with undiagnosed RHD. We compared the number of notified outbreak ARF cases (n=12) with notifications of ARF between the same period, 1 July to 15 October, (in the 5 years preceding the outbreak) (n=9). Using these notification data, we calculated the size of the increase in ARF notifications within this outbreak. A case-management spreadsheet was developed, which comprised data sourced from the NT RHD Control Program Register and the primary and tertiary care medical records.

Close contacts

We developed a close-contact definition to include individuals who stayed in the same household as a case during the at-risk period of four weeks preceding ARF onset. This included both permanent and occasional household members; occasional household members were defined and identified by the head of the household. This extended to any household a case stayed in during the defined at-risk period of four weeks prior to the onset. We developed a screening tool to capture identifiers and ARF risk factors (scabies, skin infections, pharyngitis and ARF-like symptoms) and the number of contacts per case and case household. Contact tracing and identification of close contacts was conducted via house-to-house screening of known residences of cases. Contact tracing was led by field teams comprised of staff from MHAC,[21] NT Health,[22] One Disease[23] and RHD Australia.[24] Each team involved one local Aboriginal Community Worker or Aboriginal Hheath Practitioner and two Remote Area or Registered Nurses. All local staff had family and cultural ties within the community and supported the incorporation of Yolŋu values during the outreach. All close contacts were assessed for scabies infections (including skin rash or burrows), skin infections (skin sores, infected bites, cellulitis), pharyngitis and any ARF-like symptoms (arthritis, arthralgia, Sydenham chorea, fever, shortness of breath, signs of heart failure). Where applicable, treatment was offered in line with the Central Australian Rural Practitioners Association (CARPA) treatment guidelines.[25] Additionally, close contacts with pharyngitis were offered pharyngeal swab collection, those with skin sores were offered skin-swab collection, and contacts under 20 years of age were offered pharyngeal swabs regardless of presence or absence of symptoms of pharyngitis. GAS isolates were referred by the routine diagnostic laboratory for further investigation. Health education was delivered verbally to households centred on the *Healthy Skin Story*[26] and the *Strong Heart Story*[27] in Yolŋu Matha (the predominant language group used in the region) and English. This was facilitated with RHD Australia health-promotion resources and anatomic heart models. The identities of close contacts were confirmed via consultation with ACWs, AHPs and by reviewing social connections documented in the MHAC medical record system, Communicare[28] (version 19.2.23.117). Communicare has phonetic search and relational social-connection capability; this identifies and cohorts individuals with known family and kin relationships and is critical to rapid contact tracing in this setting.

Community

Health Alerts were generated by NT Centre for Disease Control to inform relevant primary and tertiary care services. This included the local affected community and homeland clinics, urban Aboriginal Community Controlled Health Organisation services, District Medical Officers and Emergency, Infectious Disease, Cardiology and Paediatric departments. The purpose of these health alerts was to encourage a low threshold for medical evacuation of ARF-like presentations. GAS isolates recovered from any specimens collected at the clinic in the affected community during the outbreak period were retained and referred by the routine diagnostic laboratory to the Menzies School of Health Research for further investigation. At the tertiary level, it was recommended for inpatients from the affected community and associated homelands to have skin and pharyngeal swabs collected for GAS culture. Locally, in-services were delivered for school staff, which focussed on supporting teachers to identify when to send students to the clinic for review. Community awareness and support for public health measures was generated using Facebook and Yolŋu Radio, a key community media source, in Yolŋu Matha dialects and English. In supplement, *Take Heart Project*[29] video resources were shared in school in Yolŋu Matha dialects and English. The local clinic also distributed bars of soap via the school and provided hygiene advice. The local clinic recall lists for clients requiring IM BPG injection for ARF secondary prophylaxis were audited and used as a working list to deliver overdue secondary prophylaxis to those with days at risk, using an outreach approach.

Laboratory investigation

GAS isolates were grown on chocolate agar and underwent DNA extraction at the Menzies School of Health Research using a QIAamp DNeasy kit.[30] Whole genome sequencing was conducted by the Australian Centre for Ecogenomics using Nextera DNA flex libraries and sequencing via Illumina NovaSeq6000. In silico emm, typing was conducted on the short-read data by the Menzies School of Health Research using Antimicrobial Resistance Identification By Assembly (ARIBA) software[31] (version v2.14.4) and a custom database of emm sequences downloaded in May 2022 from the Centers for Disease Control and Prevention Streptococcus Laboratory.[32]

The name of the affected community, and associated homelands, have been omitted from external dissemination, in lieu of a clear process for obtaining community authorisation to publish identifying information. The description of the outbreak setting has also been restricted to remove opportunity for indirect identification.

This public health response was carried out under the powers of the *NT Public and Environmental Health Act 2011*[33].

Results

Cases

A total of 12 cases were diagnosed during the outbreak (11 definite and one probable ARF diagnosis), with onset between 1 July and 15 October 2021 (Table 1, **Figure 1**); six-times the average number of cases diagnosed during the same period in the five years prior (1.8). Half (n=6) of the outbreak cases were classified as new episodes and half as recurrent episodes. All recurrent episodes had days-at-risk arising from overdue ARF secondary prophylaxis (days at risk; range 1 to 207 days). All outbreak cases were Aboriginal, with a 1:1 female-to-male sex ratio and a median age of 16 years (range 10 to 34 years)

Table 1: Outbreak case characteristics.

Case characteristics	Case numbers
Diagnosis	Definite n=11
	Probable n=1
ARF status	First episode n=6
	Recurrent episode n=6 (days at risk range: 1–207)
RHD status	Previous diagnosis n=7
Age[a]	Median 16 years (range: 10–34 years)
Sex	Female n=6
	Male n=6
Indigenous status	Aboriginal but not Torres Strait Islander n=12
Case finding	Symptomatic presentation n=12
Hospitalisation	n=11
Time from symptom onset to diagnosis	Median: 6.5 days (range: 1–35 days)
Symptoms, signs and laboratory results[b]	Carditis[e] n=4
	Sydenham chorea[e] n=2
	Elevated ESR or CRP[f] n=8
	Elevated GAS titres[d] n=12
	Erythema marginatum[e] n=0
	Fever[g] n=4
	Pharyngitis[c] n=0
	Monoarthralgia, polyarthralgia, polyarthritis or aseptic monoarthritis[e] n=10
	Prolonged PR interval[e] n=3
	Subcutaneous nodules[e] n=0

Abbreviations: ARF: acute rheumatic fever; RHD: rheumatic heart disease; GAS: group A *Streptococcus; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein*.

2 Symptoms & signs at diagnosis.

[a]Age at onset.

[b]Determination.

[c]GAS-positive pharyngeal swab.

[d]Blood anti-deoxyribonuclease B (Anti-DNase B) and Antistreptolysin O titre (ASOT) tests.

[e]Clinical signs.

[f]Elevated erythrocyte sedimentation rate (ESR) ≥30mm/hour or elevated C-reactive protein (CRP) ≥ 30mg/L.

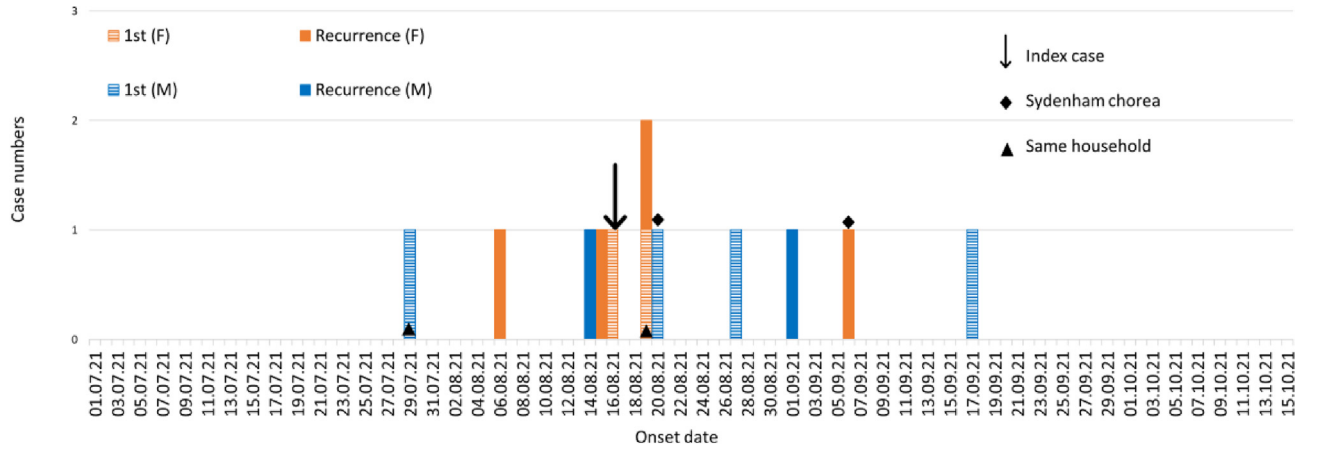
[g]Oral, tympanic or rectal temperature ≥38°C.

(Table 1). During standard care across the primary and tertiary care setting, 11 of the 12 outbreak cases had swabs collected for GAS culture (specimen collection site: pharyngeal n=9, skin sore n=1, unspecified n=1). Of these 11 specimens, one GAS isolate was cultured from a pharyngeal swab. In addition to the 12 diagnosed cases, three further ARF-like presentations were reviewed. Two were excluded as outbreak cases as clinical review found insufficient evidence to meet the diagnostic criteria for ARF, with one of these presentations found to have previously undiagnosed RHD. The third presentation under review had a history of polyarthralgia but was lost to follow-up.

Close contacts

Contact tracing conducted across 11 households identified 86 close contacts. One close contact was highly transient and unable to be located and screened. Of the 85 close contacts who were successfully screened, the following conditions/symptoms were found: scabies (n=9), skin sores (n=8), pharyngitis (n=1) and ARF-like symptoms (n=4). Treatment was provided to close contacts during contact tracing as per Central Australian Rural Practitioners

Figure 1: Epidemic curve of acute rheumatic fever outbreak cases (n=12) by sex and acute rheumatic fever status, East Arnhem Land Northern Territory, 1 July to 15 October 2021.



Association(CARPA) guidelines: 5% w/w permethrin for scabies, IM BPG injection or oral co-trimoxazole (if IM BPG declined) for skin sores and IM BPG injection for pharyngitis or as ARF secondary prophylaxis for previously diagnosed cases with days at risk. Close contacts identified as having symptoms consistent with ARF, such as polyarthralgia, were referred to the local clinic for assessment. The female-to-male sex ratio of close contacts was approximately 1:1 (n=45:41) with a median age of 25 years (range: 3–69 years). A total of 23 swab specimens were collected from close contacts (specimen collection site: pharyngeal n= 16, skin sore=7), with GAS isolates recovered from four of seven skin-sore specimens.

Community

At commencement of outreach on 1 September 2021, there were 50 active recalls in the Communicare medical records system for individuals with overdue ARF secondary prophylaxis. At conclusion of the outbreak on 15 October 2021, following both record auditing and outreach services targeting days-at-risk, approximately 30 recalls remained. During outreach, some individuals expressed hesitancy towards adherence to BPG for ARF secondary prophylaxis, some citing pain of injection and burden of follow-up as key barriers to accessibility. A total of 15 GAS isolates were recovered from specimens collected at the clinic in the affected community during the outbreak period. These isolates were retained and referred by the routine diagnostic laboratory to the Menzies School of Health Research for further investigation.

Laboratory investigation

A total of 17 isolates were analysed (n=3 isolates were unable to be sequenced, n=1 case, n=1 contact, n=1 community). In silico emm typing identified four emm sequence type (st) clusters, two of which involved both contact- and community-derived isolates. As case isolates are absent from this analysis, no further epidemiologic linkage was possible.

Discussion

We conducted a public health response to a 2021 outbreak of ARF in a remote Aboriginal community in East Arnhem Land in the NT of Australia. This outbreak represents an increase in both first episodes and recurrences of ARF. ARF is a preventable disease,[4,5] driven by aspects of poverty. However, the exact aspects of poverty and their roles in GAS infection and progression to ARF are unclear.[7] As such, the public health response to this outbreak was conducted with emphasis on the prevention and control of GAS infections. Due to the complexity of ARF and limited investigative capacity, a single cause, or causes, have not been identified.

We found that this outbreak exposed gaps in the cluster and outbreak-management section of the ARF SoNG.[1] At the foundation of these gaps is a lack of guidance to assist organisations in identifying when a public health response is required, and exactly what actions such a response should involve. These gaps may be addressed in two ways, firstly with improved sensitivity and specificity of the outbreak definition, and inclusion of end of outbreak criteria. Secondly, by provision of guidance for development of outbreak case and contact definitions and clear protocolisation of public health response activities. Globally, to the best of our knowledge at time of preparing this paper, only four ARF clusters or outbreaks have been reported in the literature in the 21st century.[34–37] These reports vary substantially in setting, outbreak, case and contact definitions, and public health response activities. This heterogeneity and paucity of the literature[1] reinforces the need for strong national guidance for public health units in relation to the management of ARF clusters and outbreaks. The first version of the ARF SoNG[1] was released in 2014 with a second version endorsed by Communicable Diseases Network Australia in 2017. Since 2017, the Australian guideline for prevention, diagnosis and management of ARF and RHD[2] has been revised, and literature around ARF and RHD has increased. To strengthen responses to future outbreaks, it is essential that the ARF SoNG is updated now.

This outbreak shows the value of household-level outreach-based public health responses, which appropriately include community members. The involvement of local Yolŋu staff, with family and cultural ties to the community, was vital for incorporation of Yolŋu values, and communication in-language, appropriate for the linguistically diverse setting. The effectiveness of this approach is demonstrated by the high-screening-coverage rate of 85 of 86 close contacts across 11 households. In addition, the embedment of health

education, and ARF secondary prophylaxis administration capacity within contact-tracing teams was a major strength of this response. This is considered critical in prevention of further ARF recurrences arising from overdue BPG injections, which accounted for half (n=6) of the outbreak cases. Ongoing outreach in the community, including household visits and discussion with family, remains an essential component of the day-to-day prevention and control of ARF.

We attempted to provide IM BPG injection to all individuals, with days-at-risk, at the whole of community level. However, consideration of those at greatest risk of recurrence may assist with improved establishment of priorities for resource allocation during public health response. Previous analyses of days-at-risk have identified that a longer duration of days at risk is a strong predictor of ARF recurrence.[38] On this basis, prioritisation of providing IM BPG injection to individuals based on their number of days-at-risk may be useful. Furthermore, any program for patients with overdue ARF secondary prophylaxis must be delivered in conjunction with education and promotion of pain-mitigation strategies to improve acceptability of ARF secondary prophylaxis. The deep IM injections of BPG are often painful,[2] the oral alternatives are less effective and less efficacious,[2] but it is possible to mitigate pain and fear associated with injection.[2,39]

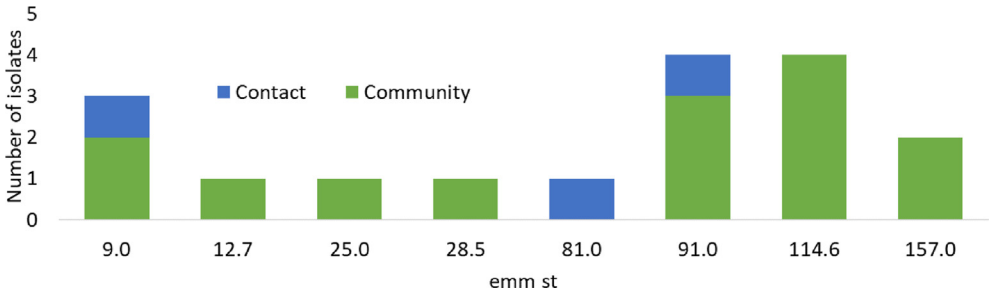
The remote setting is complex, and resources are constrained. Acute and primary care clinics currently do not have funding or capacity to deliver consistent outreach services targeting days-at-risk; however, this is considered critical to the prevention of ARF recurrences. Sustainable and dedicated ARF and RHD program funding continues to be a challenge. At the time of the outbreak, the three-year *Rheumatic Fever Strategy* (RFS) funding provided by the Australian Government to MHAC had ceased on 30 June 2021. This was followed by a funding gap of over one year. A 2021 independent evaluation of the RFS identified that "*stability in leadership and staffing is critical*" to the success of the RFS.[40] In this setting, inconsistent funding continues to negatively affect stability in leadership and staffing.

We must also reflect on the timing of this outbreak. East Arnhem Land had not yet experienced its first incursions and subsequent outbreaks of Coronavirus disease (COVID-19) at the time. However, the region had been affected by COVID-19 pandemic–associated health system shocks, an issue impacting remote settings and the NT more broadly. Changes in patterns of individual health-seeking behaviours and access to healthcare systems documented in other settings[41] may have also been at play here. These factors could have been drivers of reduced primary prevention activities, such as the treatment of GAS skin sores and pharyngitis, and provision of timely secondary ARF secondary prophylaxis. During the COVID-19 pandemic, the NT experienced a steady decrease in the coverage of ARF secondary prophylaxis.[42] In the community affected by this ARF outbreak, ARF secondary prophylaxis coverage decreased somewhat consistently from December 2020 from 35% to 25% of people with a prescription receiving at least 80% of IM BPG injections at commencement of the outbreak in July 2021.[42] As this ARF outbreak represents an increase to both first episodes and recurrences of ARF, consideration of potential reduction in both primary and secondary prevention accessibility and adherence is important.

The limited genotyping available from this outbreak was unable to determine if the increase in cases was associated with the introduction of a single rheumatogenic GAS strain. No GAS isolates were genotyped directly from ARF cases, and those genotyped from contacts and community members showed considerable diversity (**Figure 2**). This is consistent with the literature addressing GAS-strain diversity in regions with high rates of rheumatic heart disease in the NT of Australia.[43] Therefore, it remains possible that this outbreak did not arise due to a single strain of rheumatogenic GAS. Rather, it may reflect increased ARF cases caused by multiple circulating GAS genotypes resulting from the community circumstances noted earlier, including decreasing rates of ARF secondary prophylaxis and health-service-delivery issues linked to the COVID-19 pandemic. Similar considerations applied to the 2014 NT remote Aboriginal community outbreak.[37]

Ongoing and sustainable ARF prevention and control efforts are critical. Our core recommendations reflect those made by the Francis et al., 2019 report of a 2014 cluster of ARF in another remote Aboriginal community in the NT; "*ultimately, sustained reduction in rates of ARF and RHD require attention to the underlying social determinants, which predispose Aboriginal and Torres Strait Islander people in Australia to diseases of poverty*"[37]. Australia experiences some of the highest living standards in the world,[44] yet rates of ARF and RHD have not decreased.[9] Consideration of the profound influence of both historical and ongoing colonisation on the existence and perpetuation of differences in the determinants of health between Aboriginal and Torres Strait Islander peoples and non-Indigenous people in Australia[45–48] must be at the forefront when interpreting this paper. It is critical to improve both primordial and primary level prevention of ARF by addressing the social determinants of health. In doing so, the unacceptable morbidity, mortality and the

Figure 2: Group A streptococcal isolate (n=17) emm sequence types by contact status, East Arnhem Land Northern Territory, 1 July to 15 October 2021.



economic burden associated with ARF and its sequela RHD in Australia can be markedly reduced or ideally eliminated.

Funding statement

The primary author of this paper was funded via scholarship for Australian Field Epidemiology Training Program candidature. Scholarship funds were provided by MHAC, and were administered by the Australian National University. The outbreak response received no specific funding.

Ethical approval

Publication of the public health response, and its findings, is approved by MHAC and the Human Research Ethics Committee of the NT Department of Health and Menzies School of Health Research (Reference #HREC 2022-4330).

Acknowledgements

We would like to acknowledge and thank the affected community and associated homelands, along with cases, contacts and their families who welcomed field teams into their clinic and homes. Without their efforts, this public health response could not have been completed.

Conflicts of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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