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# High burden of infectious disease and antibiotic use in early life in Australian Aboriginal communities

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**A** boriginal and Torres Strait Islander people (hereafter respectfully referred to as Aboriginal Australians) experience significant barriers to achieving healthy lives. Throughout life, but particularly in the early years, healthy skin provides an effective barrier against external threats and pathogens. However, healthy skin is uncommon for Aboriginal children. Poor skin health has been linked to systemic issues such as crowded households, lack of access to working health hardware, and under-recognition of skin infections by healthcare providers.<sup>1,2</sup> High endemic prevalence of Group A *Streptococcus* (GAS) skin sores (prevalence 40–50%) brings a risk of acute invasive infection, acute post-streptococcal glomerulonephritis (APSGN) and the world's highest recorded incidence of acute rheumatic fever (ARF), which is 250–350 per 100,000 among Aboriginal children aged 5–14 years, and leads to rheumatic heart disease (RHD).<sup>3</sup>

This burden persists despite the existence of therapies and antimicrobials proven to be effective in this population context.<sup>4–7</sup> Over the past 20 years, a series of community-participatory interventions have been trialled to reduce the burden of skin sores in remote northern Australia. Notably, where successes have occurred in reducing prevalence of skin infections, the programs involved whole-of-

## Abstract

**Objective:** To quantify the childhood infectious disease burden and antibiotic use in the Northern Territory's East Arnhem region through synthesis and analysis of historical data resources.

**Methods:** We combined primary health clinic data originally reported in three separate publications stemming from the East Arnhem Healthy Skin Project (Jan-01 to Sep-07). Common statistical techniques were used to explore the prevalence of infectious conditions and the seasonality of infections, and to measure rates of antibiotic use.

**Results:** There was a high monthly prevalence of respiratory (mean: 32% [95% confidence interval (CI): 20%, 34%]) and skin (mean: 20% [95%CI: 19%, 22%]) infectious syndromes, with upper respiratory tract infections (mean: 29% [95%CI: 27%, 31%]) and skin sores (mean: 15% [95%CI: 14%, 17%]) the most common conditions. Antibiotics were frequently prescribed with 95% (95%CI: 91%, 97%) of children having received at least one antibiotic prescription by their first birthday, and 47% having received six antibiotic prescriptions; skin sores being a key driver.

**Conclusions:** Early life infections drive high antibiotic prescribing rates in remote Aboriginal communities.

**Implications for public health:** Eliminating skin disease could reduce antibiotic use by almost 20% in children under five years of age in this population.

**Key words:** infectious disease, antibiotic use, remote Aboriginal communities

community engagement with a broader focus on community participation in 'healthy skin days', rather than just screening and treating of individuals with skin infections.<sup>8,9</sup> While promising in the short term, initial benefits have not led to sustained improvements in health status in the Aboriginal communities involved, or more broadly. This absence of sustained benefit highlights ongoing

limitations in understanding relative contributions of, and interactions between, the underlying drivers of skin sore transmission and burden. These include social and environmental determinants such as housing, connectedness and mobility; scabies and other skin disorders associated with secondary infection risk; and access to healthcare and curative therapies.

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Structured mechanistic frameworks provided by mathematical and computational models enable the study of these and other factors to better understand skin infections in community settings. Unlike many other infectious conditions, there are no existing models of skin sore transmission. Development of such models has potential to advance the control and prevention of skin sores in high prevalence settings by allowing estimation of key parameters from existing datasets to inform *in silico* simulations of alternative community-driven healthy skin interventions.

To this end, we have revisited pivotal historical studies undertaken by the Menzies School of Health Research and community partners during the 2000s. Although individual datasets have previously been described,<sup>10-12</sup> they have not been analysed in aggregate. In this study, which is part of a larger program of related research, we use pooled data collected with a consistent methodology to describe the childhood burden of infectious disease presenting to primary care, with a particular focus on skin infections. This approach represents efficient information use at minimal additional cost, and importantly imposes a low participation burden on communities.

We have also used this opportunity to report on patterns of antibiotic use associated with clinic presentations for a variety of infectious syndromes in this dataset. There is increasing concern that high rates of antimicrobial use associated with the infectious disease burden in remote communities is driving selection for antimicrobial resistance (AMR). For example, a marked increase in the proportion of community-acquired *S. aureus* that are methicillin-resistant (MRSA) has

been observed in parts of northern Australia in recent years,<sup>13-17</sup> with some MRSA clones spreading to the rest of Australia and even overseas.<sup>18</sup> Such trends threaten our ability to effectively treat common and serious diseases, with grave implications for public health.<sup>19</sup>

There are few published data available on antibiotic use in Australian Aboriginal populations to inform assessment of the scope and appropriateness of prescribing in this context – a deficiency recognised in the National Antimicrobial Resistance Strategy Implementation Plan (Section 2.3).<sup>20</sup> A recent Australian Government report noted that antimicrobials supplied by Aboriginal and Torres Strait Islander health services were generally not captured under the Pharmaceutical Benefits Scheme or the Repatriation Pharmaceutical Benefits Scheme, used to monitor the use of antibiotics.<sup>21</sup> There is thus a clear need to better understand the level of antibiotic prescription in Aboriginal populations.

## Methods

### Aims

We aimed to more clearly delineate the drivers of the high infectious disease burden and associated antimicrobial prescribing in remote Northern Territory (NT) Aboriginal communities through synthesis of historical data resources curated by Menzies School of Health Research (Menzies).

### Study population

Data were originally collected as part of the East Arnhem Healthy Skin Project (EAHSP) conducted from 2004 to 2007 by Menzies in partnership with five remote communities.<sup>4,22</sup>

The EAHSP aimed to reduce the prevalence of scabies, skin sores and tinea, with a comprehensive program including annual mass community scabies treatment days, combined with routine screening and treatment of skin infections. For infants and young children whose carers provided consent, all clinic attendance records from birth up to 4.75 years of age for children born from January 2001 to December 2005 were retrospectively audited. Analyses of three separate but overlapping cohorts have been published by Kearns et al.,<sup>10</sup> McMeniman et al.<sup>11</sup> and Clucas et al.<sup>12</sup> The communities, ages of participants and duration of follow-up differed between these cohorts (Table 1). Ethics approval to access the datasets was granted by the Human Research Ethics Committee of the Northern Territory Department of Health and Families and the Menzies School of Health Research (Approval number 2015-2516).

### Data preparation

Datasets from the three publications were combined (Figure 1). At each clinic presentation we assumed a child did not have a particular condition if no infection status was recorded for that condition. Only participants with clinic records audited for at least 12 months were included. Children recruited after 1 January 2006, the end of a predetermined period of active enrolment, were omitted from the dataset due to a change in ascertainment practice.<sup>4</sup> In order to use the most informative period of data collection, we only included months with a minimum of 90 enrolled children for analyses of prevalence and seasonality (i.e. January 2002 to September 2005).

Table 1: Characteristics and enrolment criteria of datasets.

Study	Clinic data collection	Ages of longitudinal follow-up	Notes on enrolment criteria	Number of children					Total
				A	B	C	D	E	
Kearns et al. <sup>10</sup>	Jan 01–Dec 06	Birth to 1 year	Required to have ≥ 1 clinic presentation in each quarter of their first year of life*	47	91	43	40	61	282
McMeniman et al. <sup>11</sup>	Feb 01–Sep 07	Birth to 2 years	All children born between 2001 – 2005 (for whom consent had been obtained) were included	-	-	59	-	-	59
Clucas et al. <sup>12</sup>	Jan 02–Sep 05	Birth up to 4.75 years	As births were included from Jan-01, not all children were followed from birth	76	-	-	-	89	165
<b>Combined dataset</b>	Jan 01–Sep 07	Birth up to 4.75 years	Data from children that were included in more than one publication were linked and counted as a single record	76	91	59	40	89	355
Estimated community population				800	2,100	1,000	1,000	1,000	5,900

Notes:

\*considered to not unduly bias towards sick children because reflects minimum number of visits for a well child (e.g. for immunisations), high attendance/immunisation rates documented and considerable proportion of presentations were for non-infectious causes.

Note: the numbers presented in this table represent the study population used in our analysis, i.e. after we applied the exclusion criteria detailed in Figure 1.

**Analysis**

Indications for clinic presentation and associated treatment were reported for the combined dataset, and the modifying influences of age, community of residence and seasonality were explored. We classified presentations into broad infectious syndromes: respiratory, skin and ear disease. Infectious syndromes were further stratified: respiratory – upper respiratory tract infection (URTI), pneumonia/lower respiratory tract infection (LRTI) and throat infection; and skin – skin sores (impetigo), scabies and fungal infections. Monthly prevalence of infectious syndromes and conditions were calculated as the number of monthly cases divided by the number of monthly enrolled children (Supplementary File – Formula 1); each child could only contribute once per month to the prevalence for a condition. Prevalence was plotted to estimate the burden of disease and explore seasonality across the entire sample population and within communities (Supplementary File – Formula 2). Seasonality of infectious condition presentations was explored statistically using the Walter & Elwood test.<sup>23,24</sup>

Finally, we assessed the overall burden of antibiotic prescribing in this cohort, and the proportion of prescribing attributable to skin sore and respiratory indications. We assumed that antibiotics would not have been prescribed at clinic presentations when the only recorded indications were scabies or fungal infection. Simple linear regression was used to test the association between the monthly skin sore prevalence and the monthly proportion of children prescribed antibiotics. The proportion of antibiotic prescriptions that could be averted if skin sores were eliminated was calculated as the difference between the mean monthly proportion of children prescribed antibiotics and the constant of the regression model (i.e. when skin sore prevalence is equal to 0%). While the antibiotic used was not specified in any study, route of administration was recorded in two of the three studies.<sup>10,11</sup>

Confidence intervals (CIs) were calculated as exact binomial CIs. Data were analysed using Stata 14.2.<sup>25</sup>

**Results**

**Characteristics of dataset population**

We included 355 children, born between January 2001 and December 2005 (inclusive),

from five communities in the East Arnhem region from publications by Kearns et al.,<sup>10</sup> McMeniman et al.<sup>11</sup> and Clucas et al.<sup>12</sup> (Table 1 and Supplementary Figure 1). Different follow-up times and study populations led to changes in the population characteristics over time (Supplementary Figures 2 and 3). The combined dataset had 783 person-years of follow-up, comprised of 261 person-years in the 0–1-year-old age group (n=342), 245 person-years for 1–2-year-olds (n=303), 168 person-years for 2–3-year-olds (n=232), 87 person-years for 3–4-year-olds (n=139) and 22 person-years for 4–4.75-year-olds (n=58). The median follow-up time was 24 months (IQR: 13–40).

**Clinic presentation patterns**

The number of clinic presentations was highest during the first year of life with a median of 20 visits per child (IQR: 13–28, n=313). The number of presentations fell in each successive year to a median of 17 (IQR: 10–22, n=180) visits in the second year of life, 9 (IQR: 5–15, n=72) visits in the third year of life and 5 (IQR: 3–9, n=29) visits in the fourth year of life.

**Burden of disease**

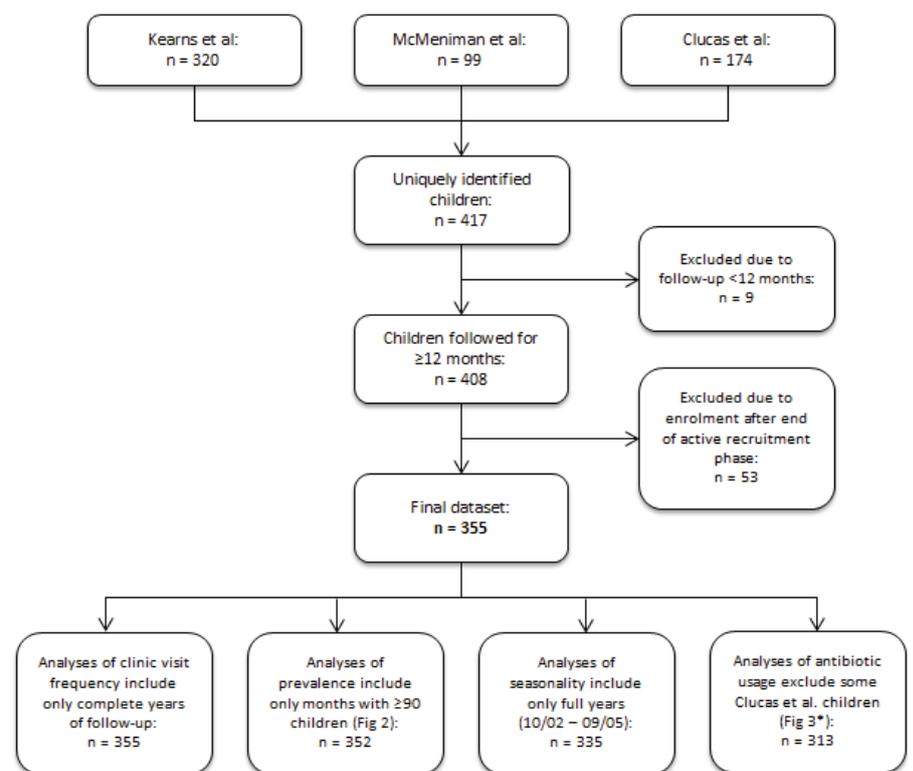
**Prevalence of skin and respiratory infections**

From January 2002 to September 2005, monthly prevalence of respiratory infections (URTIs, pneumonia/LRTI, throat) ranged from 18–50% (mean: 32% [95%CI: 30%, 34%]), while the prevalence of skin infections (skin sores, scabies, fungal) was comparatively lower (mean: 20% [95%CI: 19%, 22%], range: 12–34%), see Figure 2.

For skin infections, skin sores (mean: 15% [95%CI: 14%, 17%]) had a higher prevalence than scabies or fungal infections (Figure 2). For respiratory infections, URTIs (mean: 29% [95%CI: 27%, 31%]) had a higher prevalence than LRTI and throat infections (both, mean: 3% [95%CI: 2%, 4%]).

Monthly skin and respiratory infection prevalences demonstrated some variation over time across all communities (Supplementary Figures 4 and 5). The age distribution of studied children varied by community, given different study inclusion criteria and follow-up durations (Table 1). However, all communities included children in their first year of life. Compared with

Figure 1: Flow diagram explaining process of merging datasets and identifying children for inclusion in analyses.



Note:  
\*See notes in Figure caption.

other communities, community D had a higher average prevalence of skin infectious syndromes during the first year of life (31% [95%CI: 30%, 32%]), in particular skin sores (22% [95%CI: 20%, 23%]) and scabies (23% [95%CI: 22%, 25%]), see Supplementary Table 1. Community D also had a lower average prevalence of respiratory infectious syndromes during the first year of life (33% [95%CI: 31%, 35%]), particularly pneumonia/LRTI (8% [95%CI: 7%, 9%]) than the other four communities.

### Seasonality

We found only a minimal amount of seasonal variation in skin sore prevalence (amplitude of 11% from the mean) that did not reach statistical significance (Walter & Elwood test:  $p=0.05$ ), see Supplementary Table 2 and Supplementary Figure 6. Seasonality of pneumonia/LRTI was detected; however, the goodness of fit was extremely poor ( $p=0.01$ ; Supplementary Table 2 and Supplementary Figure 7).

### Antibiotic prescriptions

Antibiotics were prescribed regularly from birth and 95% (95%CI: 91%, 97%) of children had received at least one antibiotic prescription during the first 12 months of life (Figure 3 and Supplementary Figures 8 and 9). By four months of age, 58% (95%CI: 52%, 63%) of children had received at least one

antibiotic prescription and 47% (95%CI: 41%, 53%) had received at least six prescriptions by their first birthday. By their first birthday, 51% (95%CI: 45%, 57%) of children had received one antibiotic prescription when skin sores were the sole presenting condition (compared to 36% (95%CI: 30%, 41%) for URTIs), see Supplementary Figure 9. Antibiotics were prescribed in 33% of all consultations.

We found a strong association between an increased burden of skin sores and an increase in antibiotic prescriptions (Supplementary Figure 10). The mean monthly proportion of children prescribed antibiotics was 31%, and the constant of our linear regression model was 25%. Therefore, we estimate that eliminating skin sores in these communities could result in at least a 6% absolute (or 19% relative) decrease in antibiotic prescriptions.

While prescriptions for respiratory indications decreased dramatically as children aged, antibiotic prescriptions for skin sores remained consistently high over the observation period. In the fourth year of life, 41% (95%CI: 24%, 61%) of children presenting solely with skin sores were prescribed antibiotics at least once, compared with 7% (95%CI: 1%, 23%) of children presenting only with URTI (Supplementary Figure 11). Ear disease remained a predominant indication for antibiotic prescription throughout the first

four years of life; in each of these years, more than 50% of children were prescribed at least one course of antibiotics at a clinic visit where ear disease was recorded.

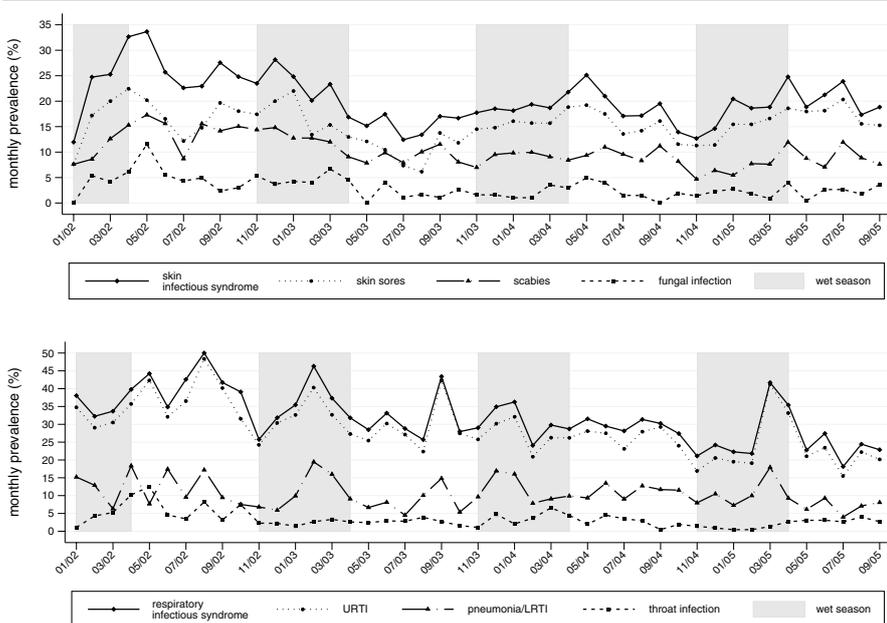
The route of administration of antibiotics prescribed was recorded as either topical, oral or injection. The majority of antibiotics were administered orally (especially for respiratory indications and ear disease); however, an antibiotic injection was most common for children with only skin sores recorded (Supplementary Figure 12). When the only recorded indication was skin sores, 64% of antibiotics were administered as an injection. Although the antibiotic is not specified in the data, these injections almost certainly represent intramuscular benzathine penicillin, which was the first line recommended therapy for skin sores in regional guidelines. Furthermore, half the children who received antibiotics when no indication was recorded were prescribed an oral antibiotic; no indication was recorded in 9% of prescriptions. These results were similar in each community.

### Conclusions

Although early childhood is universally a time of exposure to many infections, constant occurrences of bacterial infections with their associated antibiotic treatment can result in detrimental consequences. Aboriginal children living in remote communities in the East Arnhem region experience a substantial burden of early life infections, with URTI and skin sores the most commonly presenting clinical conditions affecting 96% and 86% of the study population, respectively. This infectious disease burden is associated with a high frequency of antibiotic prescription, with all infants in our study receiving at least one prescription, and almost half prescribed six antibiotics in the first year of life. Skin sores were a substantial driver of antibiotic prescription, especially from three months of age and persisting to the fourth year of life.

Prevalence trends in each community were similar; however, community D recorded a high prevalence of skin conditions (particularly scabies). A related analysis demonstrated the age of first infection with scabies was significantly younger in community D,<sup>26</sup> indicating that richer understanding of the heterogeneity of community-specific drivers of infection is needed to ensure interventions are tailored to meet the needs and priorities of each community.

**Figure 2: Top: monthly prevalence of skin sores, scabies and fungal infections as well as the combined prevalence of skin infectious syndromes; Bottom: monthly prevalence of URTI, throat infection and pneumonia/LRTI infections as well as the combined respiratory infectious syndromes (by month [January 2002–December 2005] and season [wet November–April, dry season May–October]).**

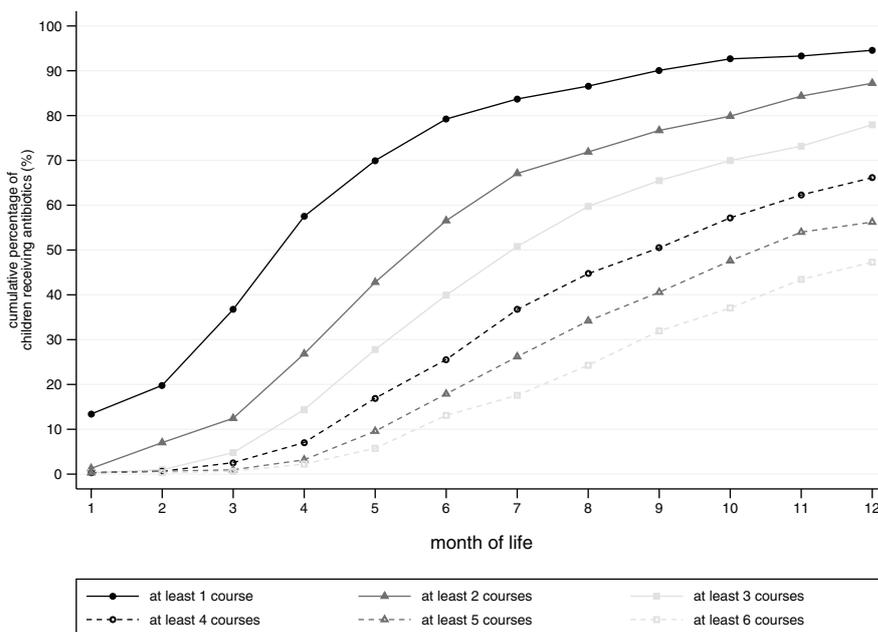


Prevalence of skin infections in our cohort is comparable to other research conducted both in Aboriginal communities and other low resource settings.<sup>27,28</sup> A recent study from the Solomon Islands reported 40% (95%CI: 34%, 47%) skin sore prevalence in children,<sup>29</sup> while Steer et al. reported the prevalence of impetigo in Fijian children to be 26% (95%CI: 24%, 27%).<sup>30</sup> The high prevalence of infectious diseases in these populations is thought to be caused by poor living conditions, household overcrowding, mobile communities and the tropical climate.<sup>31-34</sup>

Our results are consistent with the previously published analyses of these data.<sup>10-12</sup> In the screening study through which our participants were identified, Andrews et al.<sup>4</sup> also found no significant seasonality trends in the prevalence of pyoderma, with the mean wet season prevalence 35% (95%CI: 34%, 37%) and the mean dry season prevalence 36% (95%CI: 34%, 38%). Although there may be factors influencing seasonality for which we have not been able to account, our finding of seasonal patterns for pneumonia/LRTI suggests that if skin sore prevalence was subject to seasonal trends, our data would have been able to identify these trends. On this basis, inclusion of seasonality as a driver of infection in skin sore transmission models is not warranted.

Importantly, our analysis reports on antibiotic prescriptions and its correlation with the high burden of infectious disease in greater detail than the original publications. The high rates of antibiotic prescribing reflect the high burden of disease in these communities and the focus on solutions from the perspective of Western medicine. Antibiotic prescriptions were higher compared to other populations; a study in the US found approximately 35% of children had been exposed to antibiotics by the sixth month of life.<sup>35</sup> Another study from the US reported an antibiotic treatment rate of approximately two courses per person-year in children aged three months to three years.<sup>36</sup> While limited information was available regarding the specific antibiotics prescribed in our study, further evaluation of the appropriateness of prescribing in remote communities is needed to guide stewardship interventions relevant to this setting.<sup>37</sup> Ultimately, reductions in antibiotic use will only occur with reductions in the prevalence of infections, highlighting the importance of engaging with Aboriginal communities to better understand the social determinants underlying the infectious diseases burden.

Figure 3: Cumulative proportion of children who received up to and at least six antibiotic prescriptions over the first year of life – note: Clucas children born in 2001 not included since their health records did not begin from birth.



Exploration of traditional medicines such as tea tree oil for their laboratory and clinical efficacy against scabies may also serve as a connection point between Western and Aboriginal perspectives.<sup>38,39</sup>

This analysis was strengthened by pooling data from three separate but related studies. Each of these datasets was collected with very similar methodology and from the same geographical region. Combining these data substantially increased the number of children included, extended the person-time denominator and lengthened the observation period. Increased statistical power allowed us to investigate trends over time and enabled the comparison of epidemiological trends in different communities. However, although a large proportion of each community's under-five population was included over the follow-up period, the small sample size at some data points may have affected the accuracy of the monthly prevalence estimates.

Our analysis was limited by missing data in two ways. First, clinic records did not necessarily include the status of all health conditions, which is a limitation to be expected of a retrospective review. We assumed that if a disease was present, it would be noted, and thus all missing indications reflected an absence of disease; however, it is important to note that missing data is not evidence of good health. Second, the primary reason for the consultation was not known, meaning that the reason for

antimicrobial prescription was difficult to ascertain.

Normalisation of skin sores and scabies in remote communities where these infections are highly prevalent is a recognised cause of under-diagnosis and reporting.<sup>2</sup> Barriers to healthcare access may result in late or non-presentation with skin conditions, highlighting the need to form meaningful and lasting relationships with Aboriginal communities, and improve understanding of their diverse cultures and values to create a welcoming environment that recognises the importance of cultural beliefs and practices. These factors combined make it likely that our observations are an under-estimate of disease prevalence. In support of this assertion, the active screening program undertaken at the beginning of this study (Sep-04 to Sep-07) reported a skin sore prevalence of up to 60% in children younger than 15 years of age.<sup>4</sup> Efforts to highlight the importance of healthy skin and that link skin to cultural identity ('Our skin represents our pride and identity'; 'Our skin is who we are') should be encouraged (See IHHP – Meredin "Gotta Keep it Strong"; Available from <https://www.telethonkids.org.au/our-research/early-environment/infection-and-vaccines/skin-health/>).

### Implications for public health

Although the data analysed were collected 10 to 15 years ago, data collected during a

more recent clinical trial<sup>40</sup> and results of a systematic survey of skin sore prevalence<sup>41</sup> would suggest that there has been little change in the burden of skin infections in remote communities. This analysis has reaffirmed the burden of communicable disease and provided new knowledge on antibiotic usage in young Aboriginal children in East Arnhem.

Considering AMR is a major concern both in this setting and globally,<sup>42,43</sup> efforts to reduce the prevalence of infectious diseases, including skin conditions, will also reduce the need for antibiotic prescribing. Due to the severity of presentations in Aboriginal communities, it may not be appropriate to extrapolate antibiotic prescription recommendations from urban settings. For example, while topical therapy is recommended for skin sores in a recent Cochrane review,<sup>44</sup> this would be considered inappropriate in an Aboriginal community where lesions are more severe and where topical antibiotic use has been associated with rapid emergence of resistance.<sup>45</sup> To prevent selection for AMR in Aboriginal communities, culturally appropriate and sustainable strategies to reduce the underlying burden of infectious diseases need to be developed in collaboration with Aboriginal Australians.

Additionally, to ensure the appropriateness of prescribing in remote health clinics and reduce the progression of AMR, clinicians' antimicrobial prescribing behaviours must be more comprehensively understood. This work has motivated a collaborative research project funded by the NHMRC HOT NORTH consortium involving stewardship programs across all three northern Australian jurisdictions to adapt the National Antimicrobial Prescribing Survey audit tool<sup>46</sup> for use in Aboriginal Medical Services. These data will enable ongoing improvements in safety and quality of service delivery and inform development of antimicrobial stewardship priorities specific for Aboriginal and Torres Strait Islander health settings, currently absent from the national agenda. Misperceptions about antibiotic use and the term 'antimicrobial resistance' abound in the general public. It will be critical to develop culturally appropriate shared understandings of these concepts with Aboriginal communities.

There are also individual-level consequences of high levels of antibiotic use. Even single courses of antibiotics in children have been

shown to have an impact on risks for chronic disease.<sup>47</sup> The impact of such high levels of antibiotic use as described in this paper upon childhood microbiome and subsequent health for Aboriginal children remain to be elucidated.

The high burden of streptococcal skin infections is clearly linked to the high incidence of APSGN and likely ARF and RHD. We are unlikely to see reductions in these chronic conditions until the prevalence of skin infections is reduced. Longer-term surveillance of rates of APSGN and ARF/RHD should be incorporated into studies of interventions for improving skin health.

Our re-analysis of existing data resources has provided quantitative estimates of the prevalence of skin sores and its variation across the year, the population proportion prescribed antibiotics for skin sores, and has highlighted potential differences in drivers of transmission across communities. Further work is underway to synthesise findings of these and more recent studies to inform models of infection and treatment, including a current clinical trial incorporating both medical and environmental interventions to promote healthy skin (SToP: See, Treat and Prevent Scabies and Skin Sores, Telethon Kids Institute). Our overarching objective is to use historical and emerging insights to establish a model-informed evidence base that will support the participatory design of sustainable interventions to reduce the burden of skin sores and their sequelae.

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## Supporting Information

Additional supporting information may be found in the online version of this article:

**Supplementary File 1:** Formula 1.

**Supplementary File 2:** Formula 2.

**Supplementary Table 1:** Mean and 95% confidence intervals for prevalences of infectious conditions in each community.

**Supplementary Table 2:** Results of Walter & Elwood seasonality tests.

**Supplementary Figure 1:** Bar graph denoting number of participants enrolled in one or more studies, by community.

**Supplementary Figure 2:** Longitudinal representation of the median age distribution, number of enrolled study participants and their PHC presentations by month from January 2001 – December 2007.

**Supplementary Figure 3:** Longitudinal representation of number of enrolled participants in each of the five communities by study month.

**Supplementary Figure 4:** Prevalence of respiratory infectious syndromes (URTI, pneumonia/LRTI or throat) and skin infectious syndromes (skin sores, scabies or fungal) in each community (using a six-monthly rolling average).

**Supplementary Figure 5:** Prevalence of skin sores, scabies, URTI and pneumonia/LRTI in each community (using a six-monthly rolling average).

**Supplementary Figure 6:** The pooled number of skin sore and scabies cases occurring in each month between October 2002 and September 2005 plotted with the predicted number of cases.

**Supplementary Figure 7:** The pooled number of URTI, LRTI and diarrhoea cases occurring in each month between October 2002 and September 2005 plotted with the predicted number of cases.

**Supplementary Figure 8:** The percentage of consultations at which antibiotics were prescribed when any indication was recorded, and the sole indication which resulted in the greatest proportion of antibiotic prescriptions during that month of life.

**Supplementary Figure 9:** Cumulative proportion of children who received at least one antibiotic prescription, by infectious condition in the first year of life.

**Supplementary Figure 10:** Scatter plots showing relationship between monthly prevalence of skin sores (i.e. only skin sores recorded) and the proportion of children prescribed antibiotics.

**Supplementary Figure 11:** Proportion of children prescribed antibiotics stratified by year of life and by indication recorded at consultation.

**Supplementary Figure 12:** The number of antibiotics prescribed, by route and indications recorded at consultation.