Risk factors for group A streptococcal pharyngitis and skin infections: A case control study

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Summary

Background Group A streptococcal (GAS) infections can trigger an immune-mediated response resulting in acute rheumatic fever (ARF). The role of social and environmental risk factors for GAS pharyngitis and skin infections are not well understood. This study aimed to identify factors associated with GAS pharyngitis and skin infections, and to determine if these are the same as those for ARF.

Methods A case-control study, including 733 children aged 5-14 years, was undertaken between March 2018 and October 2019 in Auckland, New Zealand. Healthy controls (n = 190) and symptomatic cases including GAS pharyngitis (n = 210), GAS seronegative carriers (n = 182), and GAS skin infections (n = 151) were recruited. Trained interviewers administered a comprehensive, pre-tested, face-to-face questionnaire.

Findings Multivariable analysis identified strong associations between barriers to accessing primary healthcare and having GAS pharyngitis (adjusted OR 3.3; 95% CI 1.8-6.0), GAS carriage (aOR 2.9; 95% CI 1.5-6.0) or a GAS skin infection (aOR 3.5; 95% CI 1.6-7.6). Children who had GAS skin infections were more likely than all other groups to report living in a crowded home (aOR 1.9; 95% CI 1.0-3.4), have Māori or Pacific grandparents (aOR 3.0; 95% CI 1.2-7.6), a family history of ARF (aOR 2.2; 95% CI 1.4-3.3), or having a previous diagnosis of eczema (aOR 3.9; 95% CI 2.2-6.9).

Interpretation Reducing barriers to accessing primary healthcare (including financial restrictions, the inability to book an appointment, lack of transport, and lack of childcare for other children) to treat GAS pharyngitis and skin infections could potentially reduce these infections and lead to a reduction in their sequelae, including ARF. These strategies should be co-designed and culturally appropriate for the communities being served and carefully evaluated.

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Introduction

Rheumatic heart disease (RHD) or permanent cardiac damage can occur after a severe episode, or recurrent episodes of untreated acute rheumatic fever (ARF). An immune-mediated disease, ARF occurs as a delayed...
Acute rheumatic fever (ARF) has long been recognised as an immune-mediated complication of group A streptococcus (GAS) pharyngitis and more recently GAS skin infections. ARF has been shown to be associated with poverty, household crowding and poor access to primary healthcare. It is unknown if the risk factors for GAS pharyngitis and GAS skin infections are the same as those for ARF.

Risk factors associated with the development of ARF include household crowding,8,9 barriers to accessing health care,9 bed sharing,10 and a family history of ARF.9,11 However, there are considerable gaps in our knowledge about the risk factors for GAS pharyngitis and GAS skin infections and whether these factors differ from those associated with ARF.5,12 To date household crowding has been the most frequently assessed risk factor for GAS infections, followed by socioeconomic deprivation.13 An Australian study that investigated risk factors for sore throat and GAS pharyngitis (both serologically confirmed and GAS-positive culture), did not detect any association with household crowding, socioeconomic status or time spent in childcare or school.14 However, this study involved small families and was not adequately powered to measure effects of socioeconomic deprivation. A systematic review concluded that the weight of evidence supports a causative association between household crowding and the promotion of GAS transmission, and its rheumatic sequelae, but found no associations with dwelling characteristics (e.g. housing condition, dampness, ventilation, water, and electricity).15

An intensive ARF prevention programme that focused on sore throat management (GAS detection and treatment) operated in New Zealand between 2012 and 2017.15 This programme showed some success in areas where high coverage could be achieved. Identifying potentially modifiable risk factors for GAS pharyngitis and GAS skin infections is critical for the design of future evidence-based prevention programmes. Therefore, this study aimed to investigate the extent to which risk factors for GAS pharyngitis, GAS carriage, and GAS skin infections are the same as those for ARF, which will provide insights into whether interventions to reduce pharyngitis and skin infections are also likely to prevent ARF.

Methods

Study design and recruitment
This case-control study involved recruiting children aged 5-14 years, from March 2018 to October 2019, from the Auckland region (Waitemata, Auckland, and Counties Manukau District Health Boards) of New Zealand. Auckland is the largest city in New Zealand, with a population of approximately 1.6 million people at the 2018 census.16 At that time the city had a prioritized ethnic population mix of 12% Māori, 16% Pacific Peoples, 28% Asian, and 54% European/Other.16

The study aimed to recruit equal numbers of Māori, Pacific and New Zealand European/Other children, across three conditions of interest; GAS pharyngitis, GAS carriage, and GAS skin infections plus a set of healthy controls (Figure 1). Participants who had previously consented to being contacted for further research

Research in context

Evidence before this study
Acute rheumatic fever (ARF) has long been recognised as an immune-mediated complication of group A streptococcus (GAS) pharyngitis and more recently GAS skin infections. ARF has been shown to be associated with poverty, household crowding and poor access to primary healthcare. It is unknown if the risk factors for GAS pharyngitis and GAS skin infections are the same as those for ARF.

Added value of this study
This study is the first we are aware of to investigate risk factors for both GAS skin and throat infections in a single large cohort of children. Results highlight the importance of adequate access to primary healthcare in preventing these GAS infections. This is an important finding, as effective and timely treatment of GAS pharyngitis and potentially skin infections can prevent the development of GAS sequelae such as ARF, which has also recently been shown to be associated with barriers to accessing healthcare. Findings from this study also show the importance of adequate housing as a key strategy to reducing GAS skin infections, as children who had a GAS-positive skin culture were more likely to live in over-crowded homes.

Implications of all the available evidence
Findings from this study direct attention to the importance of reducing barriers to primary healthcare to facilitate effective treatment of GAS pharyngitis and skin infections and strategies to ensure an adequate supply of suitable housing to minimize household crowding. These interventions would likely reduce not only the number of children suffering from GAS pharyngitis and skin infections but potentially the number of children developing ARF.

sequelae to group A streptococcus (GAS) infection. In 2015, approximately 34 million people were estimated to be living with RHD, largely in low and middle-income countries and amongst vulnerable populations in some high-income countries.1 In New Zealand, ARF occurs almost exclusively in Indigenous Māori and Pacific children, who suffer some of the highest rates in the world.2 While ARF largely occurs in children, particularly those living in poverty, GAS pharyngitis, a known trigger for ARF, occurs globally across a wide range of age groups, ethnicities, and socioeconomic circumstances.3,4 GAS skin infections, which predominately occur in vulnerable children aged two-to-five years, have also been shown to be associated with ARF.5,6 The process by which GAS infections lead to ARF is poorly understood, but it appears priming of the immune system by repeated GAS exposure may be required.7
after taking part in the New Zealand Health Survey (a rolling population based survey with 14,000 participants per year) were recruited as healthy controls. Symptomatic children (sore throat or skin infection) who had recently visited a healthcare professional that resulted in a throat or skin swab being sent to the community laboratory for investigation were recruited. Families or household members of children were phoned by the laboratory (sole diagnostic service provider for the Auckland region) and invited to take part in the study. Details of potential participants, who consented to be contacted, were phoned by study investigators to arrange an initial home visit. Full details of the study protocol have been previously published. To determine if children who had a GAS-positive throat culture had true GAS seropositive pharyngitis or were GAS seronegative carriers (presumed viral pharyngitis with coincidental GAS carriage), blood samples were collected as soon as logistically possible after symptom onset, and a second blood sample obtained 2-4 weeks after the first home visit (i.e. 3-5 weeks after symptom onset). In addition, healthy controls had a throat swab taken for culture. Participants with GAS pharyngitis were defined as those that had a GAS-positive throat culture and either a two-fold or greater rise between acute (≤ 7 days) and convalescent (> 14 days) anti-streptolysin (ASO) or anti-DNase B (ADB) titres, or an ASO upper limit of normal (ULN) above 450 IU/ml or ADB ULN above 400 U/ml as previously defined. Healthy controls who had a sore throat or a skin infection in the previous four-weeks were excluded. However, included in the healthy control group were asymptomatic GAS carriers (11%) as this is representative of a healthy population.

**Data collection**

To identify potentially modifiable risk factors, all parents/caregivers of participants were interviewed face-to-face by experienced researchers, specifically trained for this study. The questionnaire was designed and previously used in the Rheumatic Fever Risk Factors Study (JVP 13/959), and drew on other pre-existing questionnaires where appropriate to maximise comparability.

**Exposure measures**

Composite measures that combined multiple questions were used for the following exposures: Exposure to damp and mould in the home; exposure to cold in the home; number of social gatherings outside the home; barriers to accessing primary healthcare experienced in the previous 12 months; and ARF health literacy. Structural household crowding was measured using the American Crowding Index. This index states that...
crowding occurs if there is more than one person per room, severe crowding occurs if there are more than 1.5 persons per room (excluding bathrooms, balconies, porches, foyers, hall-ways and half-rooms). The American Crowding Index provides a valid indicator of household crowding in the New Zealand setting and allows for international comparisons. Functional crowding was defined as the case or control sharing a sleeping room just to stay warm.

Statistical analysis
Statistical analysis was conducted in SAS version 9.4 (SAS Institute, Cary, NC). Logistic regression was used to investigate the independent association between each risk factor and each condition of interest (Table 2). Odds Ratios (OR) for occurrence of GAS pharyngitis, GAS carriage, GAS skin infection, and healthy controls were estimated in models and were adjusted for age (years), socioeconomic deprivation (NZiDep), sex (male/female) and ethnicity (prioritised). Prioritised ethnic grouping allocates individuals to a single ethnic group based on a prioritised order of Māori, Pacific Peoples, Asian, and European/Other. For example if an individual identifies as being both Māori and European, that person will be classified as Māori for the purposes of data analysis. In addition to the adjusting variables, the multivariable model included variables determined by stepwise regression, with collinear or non-significant variables removed. Environmental variables included: Structural crowding (crowded versus uncrowded); number of people sharing case/control’s bed (shared versus not shared); exposure to damp and mould in the home (damp/mould versus none). Health and nutritional variables included in the model were the number of vegetables eaten per day (none versus 1+); general health (poor/fair versus good/very good/excellent); and eczema (yes/no). Also included in the model were a family history of ARF (no/yes; blood relative with a history of ARF/RHD), grandparents with Māori/Pacific ethnicity (4 versus 1, 2, 3), and barriers to healthcare access (barriers versus no barriers). Barriers to accessing healthcare included the unaffordable cost of the appointment and prescription; the inability to book an appointment within 24 hours, lack of transport and lack of childcare for other children. Cultural and language barriers were not assessed.

Ethical approval
Ethics approval for this study was obtained from the New Zealand Health and Disability Ethics Committee (HDEC) (reference 17/NTA/262). Informed consent (from a parent or legal guardian) and assent (for children) was required for all participants. The ethics, study design, and operation were also reviewed by Māori and Pacific Governance Groups.

Role of the funding source
The funders of this study had no role in the study design, data collection, data analysis, interpretation, or writing of the report.

Results
Demographic characteristics
In total, 733 children were included in the study. Symptomatic cases included 210 children with sore throat, GAS-positive throat culture and raised ASO/ADB titres (GAS pharyngitis), 182 children with sore throat, GAS-positive throat culture and normal ASO/ADB titres (GAS carriers) and 151 children with skin infection and a GAS-positive skin culture. There were 190 healthy controls, who had not had a sore throat or a skin infection in the previous four-weeks. The mean age was 9.2 years (range 5 to 14 years), 56-2% of participants were male, and the sample had approximately one-third Māori (33.3%), Pacific (37.9%), and New Zealand European/Other (28.8%) children. The median household income ranged from $50,000–70,000 NZD. Almost two-thirds (61.8%) of participants were living in the least socioeconomic deprivation (NZiDep 0-1) (Table 1).

Preceding infections of the throat and skin
Table 2 reports risk factors for children with GAS pharyngitis, GAS carriage and GAS-positive skin culture, in comparison to healthy controls. All three symptomatic groups reported having a greater number of sore throats and skin infections in the previous 12 months than healthy controls. However, children with GAS pharyngitis reported having the most sore throats (aOR 2.5; 95% CI 1.0-4.6; 4) and children in the GAS-positive skin group were more likely to report having skin infections in the previous 12 months (aOR 135.0; 95% CI 56.0-325.4, indicating persistent skin infections.

Environmental exposures
Of the environmental exposures, household crowding was associated with all three symptomatic groups. Children with GAS pharyngitis (aOR 1.6; 95% CI 1.0-2.5), children who were GAS carriers (aOR 1.6; 95% CI 1.0-2.6) and children with GAS skin infections (aOR 2.4; 95% CI 1.5-4.1) were more likely than healthy controls to report living in a crowded or severely crowded home.

Health services access and use
Across all three symptomatic groups, children were more likely to report having greater barriers to primary healthcare than healthy children (Table 2). Children with GAS pharyngitis (aOR 3.0; 95% CI 1.7-5.3) or GAS skin infection (aOR 3.2; 95% CI 1.7-6.0) reported the
greatest barriers to healthcare. Despite a greater proportion of children in the GAS skin infection group belonging to a school with a school-based ARF prevention programme, the levels of knowledge about ARF were similar across all symptomatic groups (Table 2).

Health status, oral health, nutrition and family history
Children with GAS skin infections were more likely to report having poor or fair general health in the four-weeks prior to the interview than any of the other groups (aOR 3.0; 95% CI 1.0-9.3). They were also more likely to report having doctor-diagnosed eczema (aOR 4.4; 95% CI 2.6-7.3) Children with GAS pharyngitis (aOR 1.9; 95% CI 1.1-3.3) or GAS skin infections (aOR 2.5; 95% CI 1.4-4.6) were more likely to report a family history of ARF.

Multivariable risk factor analysis
Table 3 reports data from the multivariable analyses. Having GAS pharyngitis (aOR 3.3; 95% CI 1.8-6.0), GAS carriage (aOR 2.9; 95% CI 1.5-6.0) or having a GAS skin infection (aOR 3.5; 95% CI 1.6-7.6) all remained strongly associated with barriers to accessing primary healthcare. Those children who had GAS skin infection were more likely to report having a previous diagnosis of eczema (aOR 3.9; 95% CI 2.2-6.9) or be living in a crowded home (aOR 1.9; 95% CI 1.0-3.4). Children with GAS skin infections were also more likely to have Māori or Pacific grandparents (aOR 3.0; 95% CI 1.2-7.7) and a family history of ARF (aOR 2.2; 95% CI 1.1-4.3).

Discussion
This study is the first we are aware of to investigate risk factors for both GAS skin and throat infections in a single large cohort of children. Results highlight the importance of adequate access to primary healthcare in preventing these GAS infections. This is an important finding, as effective and timely treatment of GAS

| Variable | GAS pharyngitis (N = 182) | GAS skin infection (N = 178) | Healthy controls (N = 190) | Total (733) |
|----------|---------------------------|-------------------------------|-----------------------------|------------|
| Age      |                           |                               |                             |            |
| 5-9      | 127 (60.5)                | 101 (66.9)                    | 82 (43.2)                   | 419 (57.2) |
| 10-14    | 83 (39.5)                 | 50 (33.1)                     | 108 (56.8)                  | 314 (42.8) |
| Mean age (years) | 8.9                      | 8.7                           | 10.3                        | 9.2        |
| Sex      |                           |                               |                             |            |
| Male     | 124 (59.0)                | 84 (55.6)                     | 98 (51.6)                   | 412 (56.2) |
| Female   | 86 (41.0)                 | 67 (44.4)                     | 92 (48.4)                   | 321 (43.8) |
| Ethnicity (prioritized) |                     |                               |                             |            |
| Māori    | 80 (38.1)                 | 45 (29.8)                     | 58 (30.5)                   | 244 (33.3) |
| Pacific  | 73 (34.8)                 | 74 (49.0)                     | 70 (36.8)                   | 278 (37.9) |
| Asian    | 19 (9.0)                  | 13 (8.6)                      | 35 (18.4)                   | 86 (11.7)  |
| NZ European | 38 (18.1)               | 19 (12.6)                     | 27 (14.2)                   | 125 (17.1) |
| Household income |                     |                               |                             |            |
| <$20,001 | 16 (7.6)                  | 13 (8.7)                      | 10 (5.5)                    | 52 (7.1)   |
| 20,001-$50,000 | 46 (21.9)           | 54 (35.8)                     | 38 (20.9)                   | 177 (24.2) |
| 50,001-$70,000 | 25 (11.9)           | 17 (11.3)                     | 21 (11.5)                   | 85 (11.6)  |
| 70,001-$100,000 | 28 (13.3)          | 19 (12.6)                     | 29 (15.9)                   | 107 (14.6) |
| $100,001-$150,000 | 34 (16.2)           | 10 (6.6)                      | 35 (19.2)                   | 111 (15.1) |
| >$150,000 | 33 (15.7)                | 23 (15.2)                     | 32 (17.6)                   | 114 (15.6) |
| Median (NZD) | 50,000-70,000        | 50,000-70,000                 | 70,000-100,000              | 50,000-70,000 |
| Socioeconomic deprivation (NZDep score of caregiver) |     |                               |                             |            |
| 0 (least deprived) | 97 (46.2)            | 50 (33.1)                     | 87 (47.8)                   | 320 (43.7) |
| 1                   | 38 (18.1)                 | 30 (19.9)                     | 35 (19.2)                   | 133 (18.1) |
| 2       | 21 (10.0)                 | 13 (8.6)                      | 18 (9.9)                    | 78 (10.6)  |
| 3       | 18 (8.6)                  | 25 (16.6)                     | 8 (4.4)                     | 74 (10.1)  |
| 4       | 21 (10.0)                 | 17 (11.3)                     | 15 (8.2)                    | 66 (9.0)   |
| 5       | 10 (4.8)                  | 10 (6.6)                      | 8 (4.4)                     | 36 (4.9)   |
| 6 (most deprived) | 4 (1.9)              | 4 (2.7)                       | 7 (3.8)                     | 17 (2.3)   |

Table 1: Demographics of symptomatic cases and healthy controls, Auckland, New Zealand.
### Table 2 (Continued)

**Exposure (in four weeks prior to interview unless stated otherwise)**

| Exposure | GAS pharyngitis (N = 210) | GAS carries (N = 182) | GAS-positive skin culture (N = 151) | Healthy controls (N = 190) |
|----------|--------------------------|-----------------------|------------------------------------|--------------------------|
|          | N % OR (95% C.I.) aOR (95% C.I.) | N % OR (95% C.I.) aOR (95% C.I.) | N % OR (95% C.I.) aOR (95% C.I.) | N % OR (95% C.I.) aOR (95% C.I.) |
| **Procedural infections of throat and skin** | | | | |
| Number of tonsils removed at any time | 248 | 23.7 (0.0-56.0) | 9.9 (0.4-3.1) | 3.0 (0.1-0.9) | 3.0 (0.1-0.9) | 50 (0.1-5.0) | 50 (0.1-5.0) |
| **Practice** | | | | |
| Number of dental practices | 1 | 187 | 96.9 | 23 (0.0-56.0) | 25.2 (1.0-4.6) | 1.08 (0.5-2.2) | 1.08 (0.5-2.2) |
| Number of dental practitioners | 1 | | | | | | |
| **BMI and weight** | | | | |
| Body mass index | | | | |
| Average body mass index | 1 | 187 | 96.9 | 23 (0.0-56.0) | 25.2 (1.0-4.6) | 1.08 (0.5-2.2) | 1.08 (0.5-2.2) |
| **BMI and weight** | | | | |
| Height and weight | | | | |
| Average height and weight | | | | |
| **Health services access, use, and health literacy** | | | | |
| Number of health literacy programs | | | | |
| Average health literacy program | | | | |
| **Health status, oral health, and dental** | | | | |
| General health prior to interview | Good/very good/excellent | | | | | | |
| Poor | 200 | 95.2 | 1.0 (0.6-1.5) | 1.7 (0.6-3.6) | 1.9 (0.6-3.6) | 3.5 (0.2-10.0) | 3.0 (0.1-0.9) | 5.2 | 2.1 |
| **Number of health literacy programs** | | | | |
| Average number of health literacy programs | | | | |
| **Health status, oral health, and dental** | | | | |
| General health prior to interview | | | | | | | |
| Poor | 200 | 95.2 | 1.0 (0.6-1.5) | 1.7 (0.6-3.6) | 1.9 (0.6-3.6) | 3.5 (0.2-10.0) | 3.0 (0.1-0.9) | 5.2 | 2.1 |
| **Number of health literacy programs** | | | | |
| Average number of health literacy programs | | | | |
| **Health status, oral health, and dental** | | | | |
| General health prior to interview | | | | | | | |
| Poor | 200 | 95.2 | 1.0 (0.6-1.5) | 1.7 (0.6-3.6) | 1.9 (0.6-3.6) | 3.5 (0.2-10.0) | 3.0 (0.1-0.9) | 5.2 | 2.1 |
| **Number of health literacy programs** | | | | |
| Average number of health literacy programs | | | | |
| **Health status, oral health, and dental** | | | | |
| General health prior to interview | | | | | | | |
| Poor | 200 | 95.2 | 1.0 (0.6-1.5) | 1.7 (0.6-3.6) | 1.9 (0.6-3.6) | 3.5 (0.2-10.0) | 3.0 (0.1-0.9) | 5.2 | 2.1 |
| **Number of health literacy programs** | | | | |
| Average number of health literacy programs | | | | | | | |
| **Health status, oral health, and dental** | | | | |
| General health prior to interview | | | | | | | |
| Poor | 200 | 95.2 | 1.0 (0.6-1.5) | 1.7 (0.6-3.6) | 1.9 (0.6-3.6) | 3.5 (0.2-10.0) | 3.0 (0.1-0.9) | 5.2 | 2.1 |
| **Number of health literacy programs** | | | | |
| Average number of health literacy programs | | | | | | | |
| **Health status, oral health, and dental** | | | | |
| General health prior to interview | | | | | | | |
| Poor | 200 | 95.2 | 1.0 (0.6-1.5) | 1.7 (0.6-3.6) | 1.9 (0.6-3.6) | 3.5 (0.2-10.0) | 3.0 (0.1-0.9) | 5.2 | 2.1 |
| **Number of health literacy programs** | | | | |
| Average number of health literacy programs | | | | | | | |
pharyngitis and potentially skin infections can prevent the development of GAS sequelae such as ARF, which has also recently been shown to be associated with barriers to accessing healthcare. ARF remains relatively common in populations where access to healthcare is a known public health problem. Such barriers may also contribute to Māori and Pacific children suffering disproportionately higher rates of GAS skin infections, which may be associated with the alarmingly high rates of ARF also seen in these populations.

Findings from this study also show the importance of adequate housing as a key strategy for reducing GAS skin infections, as children who had a GAS-positive skin culture were more likely to live in overcrowded homes. Worldwide household crowding is often a marker of poverty and social deprivation. Crowding is associated with other infectious diseases, including tuberculous, diarrhea, gastroenteritis, and respiratory infections; it has also been shown to a modifiable risk factor in the development of ARF. Strategies to ensure an adequate supply of suitable housing to minimize household crowding would likely reduce not only the number of children suffering from skin infections but the number of children developing ARF.

It is not surprising that children who had a GAS-positive skin culture were more likely to report having a previous diagnosis of eczema, due to eczema disrupting the skin barrier and causing scratching. Thus special attention should be paid to eczema in children at high-risk of ARF. This would also be an opportunity to treat scabies infection, which also showed a positive association with GAS skin infection in this study and with ARF and is likely to be underdiagnosed. Interestingly children with GAS-positive skin infections were also more likely to have Māori or Pacific grandparents and a family history of ARF, which has also been reported in children who have ARF. Ensuring that Māori and Pacific children, particularly those with a family history of ARF, can easily get access to culturally appropriate healthcare for skin related conditions, should be prioritized to reduce the burden of skin infections but also potentially the burden of ARF in these communities.

This study does have some limitations. Bias may have occurred as those who consented to take part may have systematic differences from those who declined to take part. There also may be some residual confounding due to unmeasured or inaccurately measured exposures, but we anticipate that these are distributed evenly across the study groups. In addition, some recall bias is possible. There is also likely to be some social desirability bias with questions on risks for children (e.g. smoking indoors), which could result in differential reporting between cases and controls.

Findings from this study direct attention to the importance of reducing barriers to primary healthcare to facilitate effective treatment of GAS pharyngitis and skin infections. Strategies to reduce these barriers

### Table 2: Univariate association between individual risk factors and GAS pharyngitis, carriage and skin infection.

| Exposure (in four-weeks prior to interview unless stated otherwise) | No of participants | % | OR (95% CI) aOR (95% CI) |
|---------------------------------------------------------------|-------------------|---|------------------------|
| ARF factors                                                   |                   |   |                        |
| Family history of ARF                                         | Yes               | 47 | 2.32 (1.80-3.01) | 2.32 (1.80-3.01) |
| No                                                           | 156              | 76 | 1.00 (0.81-1.23) | 1.00 (0.81-1.23) |
| Number of grandparents with Māori/Pacific ethnicity           | 0-1               | 104 | 52 | 0.89 (0.65-1.23) | 0.89 (0.65-1.23) |
| 2-3                                                           | 92               | 43 | 1.12 (0.87-1.45) | 1.12 (0.87-1.45) |
| 4-5                                                           | 82               | 39 | 0.90 (0.67-1.25) | 0.90 (0.67-1.25) |
| 6+                                                            | 32               | 15 | 0.72 (0.46-1.16) | 0.72 (0.46-1.16) |
| Highest educational status                                     | Primary          | 47 | 2.32 (1.80-3.01) | 2.32 (1.80-3.01) |
| Secondary                                                    | 156             | 76 | 1.00 (0.81-1.23) | 1.00 (0.81-1.23) |
| Number of grandparents with Māori/Pacific ethnicity           | 0-1               | 104 | 52 | 0.89 (0.65-1.23) | 0.89 (0.65-1.23) |
| 2-3                                                           | 92               | 43 | 1.12 (0.87-1.45) | 1.12 (0.87-1.45) |
| 4-5                                                           | 82               | 39 | 0.90 (0.67-1.25) | 0.90 (0.67-1.25) |
| 6+                                                            | 32               | 15 | 0.72 (0.46-1.16) | 0.72 (0.46-1.16) |
| Table 2: Univariate association between individual risk factors and GAS pharyngitis, carriage and skin infection. |                   |   |                        |
should be co-designed and culturally appropriate for the communities they are serving to be successful. It will also be important to evaluate interventions fully. Recent large-scale sore throat management programmes in New Zealand, based on short-courses of oral antibiotics, have not so far resulted in consistent declines in ARF. Given the link between GAS pharyngitis and skin infections, better access to healthcare also has the potential to reduce ARF rates.

### Contributors
J.B. project managed the study, designed the analysis, interpreted the results and wrote the manuscript. N.M. designed the study and interpreted data. J.Z. conducted the data analysis. J.C. designed the study. D.S.P. led the Pacific Governance Group and interpreted data. J.C. designed the study and interpreted data. D.W. interpreted data. M.G.B. initiated and designed the study, interpreted the results and wrote the manuscript. N.M. J.B. project managed the study, designed the analysis. A.O. interpreted data. M.G.B. initiated and designed the study, and co-ordinated the data analysis. J.C. designed the study, D.S.P. led the Pacific Governance Group and interpreted data. J.C. designed the study and interpreted data. D.W. interpreted data. M.G.B. initiated and designed the study, obtained funding and interpreted the data. All authors have read and reviewed the manuscript.

### Data sharing statement
The study protocol is provided in the protocol paper. Individual participant data will be made available when the remaining analyses have been completed, upon reasonable requests directed to the corresponding author.

### Declaration of interests
The authors have no conflict of interest to declare.

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### Table 3: Multivariable association between risk factors and GAS pharyngitis, GAS carriage or GAS skin infection, adjusted for sociodemographic variables and all other risk factors included in the model.

| Risk factor                        | Units                  | GAS pharyngitis aOR (95%CI) | GAS carriers aOR (95%CI) | GAS positive skin aOR (95%CI) |
|------------------------------------|------------------------|-----------------------------|--------------------------|------------------------------|
| Eczema                             | Yes/no                 | 1.5 (0.9-2.5)               | 0.8 (0.4-1.4)            | 3.9 (2.6-9)                  |
| Barriers to accessing primary health care | Barriers versus no barriers | 3.3 (1.8-6.0)               | 2.9 (1.5-6.0)            | 3.5 (1.6-7.6)               |
| Grandparents with any Māori or Pacific ethnicity | 4 versus 0,1,2,3 | 1.5 (0.8-3.0)               | 1.3 (0.7-2.7)            | 3.0 (1.2-7.7)               |
| Family history of ARF (blood relative) | Yes/no                 | 1.5 (0.8-2.8)               | 1.4 (0.7-2.7)            | 2.2 (1.1-4.3)               |
| Structural household crowding      | Crowded versus         | 1.5 (0.9-2.4)               | 1.6 (1.0-2.8)            | 1.9 (1.0-3.4)               |
| (American Crowding Index)          | uncrowded              |                             |                          |                              |
| Exposure to damp and mould in the home | Damp/mould versus none | 1.4 (0.7-2.7)               | 1.1 (0.7-1.9)            | 1.3 (0.7-2.3)               |
| Number of vegetables per day       | None versus 1+         | 1.4 (0.7-2.7)               | 1.8 (0.9-3.4)            | 1.6 (0.8-3.3)               |
| Bed sharing                        | ≥1 versus no one       | 1.3 (0.8-2.3)               | 1.3 (0.8-2.2)            | 1.4 (0.8-2.6)               |
| General health                     | Poor/fair versus       | 1.2 (0.3-4.5)               | 2.2 (0.6-8.0)            | 1.6 (0.4-6.9)               |
|                                     | Good/very good/excellent |                             |                          |                              |

aOR are controlled for all listed risk factors, age, sex, ethnicity, and NZiDep.
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