The Cardiac Society of Australia and New Zealand

Heart Foundation™

New Zealand Guidelines for Rheumatic Fever

3. Proposed Rheumatic Fever Primary Prevention Programme

Evidence-based, best practice Guidelines on:

1. Diagnosis, Management and Secondary Prevention
2. Group A Streptococcal Sore Throat Management
3. **Proposed Rheumatic Fever Primary Prevention Programme**

Evidence-based, best practice New Zealand Guidelines for **Rheumatic Fever**

Evidence-based, best practice
New Zealand Guidelines for Rheumatic Fever

3. PROPOSED RHEUMATIC FEVER PRIMARY PREVENTION PROGRAMME

He korokoro ora he manawa ora,
Mo tatou katoa

(A healthy throat, a healthy heart for us all)

May 2009

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1. Foreword

Kia ora koutou katoa
Kei raro te aroha o to tatou atua
Rau rangatira ma nga mihi rangatira ki a koutou katoa
Tena koutou

These guidelines are an important step in controlling rheumatic fever. This disease among Māori is important for two reasons: Firstly, currently 0-20 year olds are the largest age-group for Māori and by 2021 will make up 28% of this national age group population. Secondly our tamariki (*children*)/rangatahi (*teens*) are critical in the resurgence of our culture, our reo (*language)*, our tikanga (*customs)* and ultimately what we are all striving for, our hauora (*health and wellbeing)*. It is unacceptable that our tamariki mokopuna living in New Zealand should suffer rates of rheumatic fever comparable to third world countries. These guidelines will give clinicians a standardised approach to managing the triggering illness for rheumatic fever and provide a tool for educating communities, and preventing and treating rheumatic heart disease, therefore going some way towards addressing the burden our children shoulder. (See http://www.heartfoundation.org.nz for guidelines).

It is my pleasure to be a part of the writing group to offer a tangata whenua perspective.

In addition I was asked to consider a whakatauki (*proverb)* to be used with the guidelines.

He korokoro ora he manawa ora
Mo tatou katoa

This translates to:
A healthy throat, a healthy heart for us all

This whakatauki highlights the importance for our whanau of treating sore throats seriously as there is a link between a sore throat and heart disease. It also highlights the importance to our whanau of the contagious nature of the disease and the impact that rheumatic heart disease has, not only on the patient, but on all those close to them. This is evident in the “a healthy heart for us all” (similar to the *one heart many lives* theme).

This whakatauki was chosen because it is succinct, and clearly establishes the link between prevention and disease.

Dr Lance O’Sullivan
Chairman
Te Hotu Manawa Māori
Member of Rheumatic Fever Guidelines Writing Group

2. Scope and Purpose of Guideline

This document aims to provide evidence-based guidelines for primary prevention of acute rheumatic fever (ARF) among New Zealanders.

Acute rheumatic fever is an autoimmune disorder which can occur after group A streptococcal (GAS) throat infections, in certain susceptible individuals. It is diagnosed using the Jones criteria and may involve the heart, joints and movement disorders (chorea), causing significant morbidity and mortality. It is most common in school-aged children, particularly among children living in situations where there is poverty and household crowding. In some children permanent heart valve damage and consequently rheumatic heart disease (RHD) may result. After an initial episode of rheumatic fever, the individual is at risk for future recurrences and requires years of follow up. For these reasons, guidelines for primary prevention of rheumatic fever are required.

Rheumatic fever is still common in New Zealand, especially among Māori and Pacific children, even though it has virtually disappeared in other industrialised countries. It causes significant disability, loss of quality of life and length of life and costs to individuals and their families and to society.

Primary prevention is a strategy that seeks to prevent disease occurring in the first instance rather than treating it once it has developed. In the case of ARF this means preventing GAS bacterial throat infections before they can initiate ARF.

Target groups which may be interested in this guideline include those which work with pharyngitis and rheumatic fever patients in the clinical setting:

- Paediatricians
- General practitioners
- Nurses
- Other community health workers
- Organisations which employ or represent these groups.

Those involved in policy and programme development:

- Ministry of Health
- District Health Boards
- Primary Health Organisations
- Public Health Service providers
- Managers of other health services.

Gaps between current practice and evidence

It has been ten years since the most recent comprehensive review of rheumatic fever primary prevention in the New Zealand setting.[1] Durham and Kljakovic's report for the Ministry of Health focused on the role of general practice and found there was no evidence that treating GAS pharyngitis in general practice had an impact on the incidence of ARF.[1] In the intervening years, New Zealand has continued to have high rates of rheumatic fever compared to other industrialised countries and the disease burden still rests inequitably on Māori and Pacific peoples. This guideline aims to review the evidence and suggest a new way forward in rheumatic fever primary prevention.

3. About the Guideline

Rheumatic fever is still common in New Zealand, even though it has virtually disappeared in other industrialised countries. It mainly occurs in Māori and Pacific children, in lower socioeconomic areas of the North Island.

Why New Zealand has such a high rate of ARF and why Māori and Pacific peoples are disproportionately affected, is not entirely clear. In international studies, a number of causative socioeconomic factors have been suggested, including poverty, housing, access to health care and there has been some research on genetic predisposition. As ARF is an ongoing concern in New Zealand, we have addressed these questions in the guideline (see Clinical and Public Health Questions section).

Disclaimer

This document has been produced by The National Heart Foundation of New Zealand and the Cardiac Society of Australia and New Zealand for health professionals. The statements and recommendations it contains are, unless labelled as "expert opinion", based on independent review of the available evidence. Interpretation of this document by those without appropriate health training is not recommended, other than at the request of, or in consultation with, a relevant health professional. This document provides evidence-based guidelines for the primary prevention of acute rheumatic fever in New Zealand.

In addition, the recommendations in this guideline are not intended to replace clinical judgment. Treatment of individuals should take into account co-morbidities, drug tolerance, lifestyle, living circumstances, cultural sensibilities and wishes. When prescribing medication, clinicians should observe usual contra-indications, be mindful of potential adverse drug interactions and allergies, monitor responses and ensure regular review.

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Outline of grading methodology used

Table 1 has been customised for use in this guideline, and is used where the writing group has assessed the evidence.

Table 1. Levels of Evidence for Clinical Interventions and Grades of Recommendation

LEVEL OF EVIDENCE	STUDY DESIGN
I	Evidence obtained from a systematic review of all relevant randomised controlled trials (RCT)
II	Evidence obtained from at least one properly designed randomised controlled trial
III-I	Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method)
III-2	Evidence obtained from comparative studies with concurrent controls and allocation not randomised (cohort studies), case-control studies, or interrupted time series with a control group
III-3	Evidence obtained from comparative studies with historical control, 2 or more single-arm studies, or interrupted time series with a parallel control group
IV	Evidence obtained from case series, either post-test or pre-test and post-test

GRADE OF RECOMMENDATION	
A	Rich body of high-quality randomised controlled trial (RCT) data
B	Limited body of RCT data or high-quality non-RCT data
C	Limited evidence
D	No evidence available – panel consensus judgement

Source: The levels of evidence and grades of recommendations are adapted from the National Institute of Health and Medical Research Council levels of evidence for clinical interventions and the US National Institute of Health clinical guidelines. Details can be found at www.nhlbi.nih.gov/guidelines/index.htm .

Guideline development process

This guideline was developed by a writing group comprising of experts in primary care, paediatric infectious diseases, public health and rheumatic fever. Selected individuals with experience in sore throat and ARF management, and relevant stakeholders were also involved. These included a range of general and specialist clinicians, nurses, Māori and Pacific professionals and lay representative groups.

This guideline has been produced for New Zealand and is endorsed by New Zealand organisations.

The evidence-based search strategies for rheumatic fever articles, including the Medline and Old Medline search strings, are described in detail in Appendix 1 and a full description is published seperately. Studies were restricted to those in humans and published in the English language, and included if they pertained to primary prevention schemes or any of the clinical questions. Further PubMed searches were made for the clinical questions.

There is no current plan to update this guideline.

Endorsing organisations

- The Cardiac Society of Australia and New Zealand
- The National Heart Foundation of New Zealand
- Pacific Islands Heartbeat
- Te Hotu Manawa Māori
- Rheumatic Fever Trust
- Te Ohu Rata o Aotearoa/Te Ora Māori Medical Practitioners Association
- New Zealand Nurses Organisation

Organisations consulted

- Community Board advising Counties Manukau DHB Māori Team
- New Zealand Ministry of Health
- Australian Society of Infectious Diseases
- Pasifika Medical Association
- Paediatric Society of New Zealand
- Royal Australasian College of Practitioners
- The Royal New Zealand College of General Practitioners

Organisations consulted for original school clinic sore throat programme (in 1996)

- School Boards of Trustees Association
- Primary Principals Association
- Post Primary Principals Association

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Declaration of competing interests and conflicts of interest

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4. Executive Summary

This document provides evidence-based guidelines for the primary prevention of acute rheumatic fever (ARF) in New Zealand.

Acute Rheumatic Fever is a disease of the immune system that can occur following throat infections caused by group A streptococcus (GAS) bacteria in susceptible individuals. It is most common in school-aged children, particularly among children living in situations where there is poverty and household crowding. ARF may cause inflammation of the heart, joints, and nervous system. In some children, permanent heart valve damage and consequently rheumatic heart disease (RHD) may result. After an initial episode of rheumatic fever, the individual is at risk of future recurrences and so requires many years of follow up.

Rheumatic fever is still common in New Zealand, especially among Māori and Pacific children, even though it has virtually disappeared in other industrialised countries. It causes significant disability, loss of quality of life and length of life and costs to individuals, their families and to society.

Primary prevention is a strategy that seeks to prevent disease occurring in the first instance rather than treating it once it has developed. In the case of ARF this means preventing GAS bacterial throat infections before they can initiate ARF.

Key Messages

- Treating GAS throat infections reduces the subsequent rate of development of ARF
- School, and mixed community and school-based GAS sore throat detection and treatment programmes are all effective in reducing rheumatic fever
- Crowding in the household is associated with an increased risk of developing rheumatic fever
- Some studies show a link between poverty and rheumatic fever, others do not
- There is some evidence linking poor quality housing and rheumatic fever, but definitions vary between studies and it is impossible to make recommendations for minimum standards of housing at this stage
- Māori and Pacific healthcare providers, school-based sore throat programmes and primary health care reforms have a role in improving access to healthcare for patients most at risk of rheumatic fever
- There is no convincing evidence that rheumatic fever is caused by skin infections
- There is no convincing evidence of a genetic cause of rheumatic fever and no reliable genetic markers of who is susceptible to the disease
- The role of seasonal antibiotic prophylaxis for recurrent GAS sore throats has not been proven
- Separate guidelines in this series, available to download from: www.heartfoundation.org.nz , address the following:
    - Group A streptococcal sore throat management, including diagnosis, management and a treatment algorithm
    - Rheumatic fever diagnosis, management and secondary prevention, including treatment algorithms.

5. Introduction

The rate of rheumatic fever in New Zealand, 3.8 per 100,000 in 2003, exceeds that in other western countries.[2] One hundred and forty-one new cases were reported in 2003, most of which occurred in the ten to14 year age group (n=82) and the five to nine year (n=27) age group.[2] Seventy cases occurred in Māori and 58 among Pacific peoples.[2] The geographic distribution of rheumatic fever in New Zealand is complex, and is summarised in the map in Appendix 2, and pockets of rheumatic fever are summarised in Appendix 3. The main areas of rheumatic fever occurrence are in lower socioeconomic areas of the North Island, in areas such as parts of Auckland, Waikato, Northland, the Bay of Plenty, Rotorua, Gisborne, Hawke's Bay and Porirua.

In comparison, rheumatic fever declined sharply in Denmark from the early 1960s.[3] In western Scotland, between 1976 and 1979, the rate was 0.6 per 100,000 children per year.[4] Del Mar et al estimated that it would have taken twelve general practitioners' working lifetimes to find one new case of rheumatic fever in western Scotland in the 1980s.[5] Studies from the last 20 years on the incidence of rheumatic fever in children around the world are summarised in Appendix 4.

Group A streptococcal (GAS) throat infections are the trigger for acute rheumatic fever (ARF).[6] It has not been possible to predict which patients will develop this post-streptococcal sequela. GAS infections from other sites, in particular the skin, have not been proven to cause rheumatic fever[6,7] although skin associated GAS have been found in the throats of patients developing rheumatic fever[8,9] and ARF is common in some populations with endemic skin disease.[8,10-12] The process by which GAS pharyngitis leads to rheumatic fever is poorly understood, but has been postulated to have an autoimmune basis.[13]

Treating GAS throat infections with appropriate antibiotics, aiming for eradication in most cases, reduces the likelihood of subsequent development of ARF. This has been demonstrated in a number of studies.[5,14-16] Shortly after the introduction of penicillin, epidemic rheumatic fever in the American armed forces was controlled using injectable penicillin.[17] A recent meta-analysis demonstrated this effect in a further nine studies, eight of which were in a military setting, that also used injectable penicillin.[18] Subsequently, observational studies in Baltimore,[19] Costa Rica[20] and the French Caribbean,[21] the latter two in low-resource settings, have shown ARF reduction.

Inner-city comprehensive primary care programmes were set up in Baltimore, USA in the 1960s. The rate of rheumatic fever decreased 60% between 1960 to 1964 and 1968 to 1970 in the programme areas, but was unchanged in the rest of the city. A ten year programme in the French Caribbean reduced the incidence of rheumatic fever by 78% in Martinique and 74% in Guadalupe. It appears the rate of rheumatic fever fell largely due to secondary prevention, although primary prevention measures also contributed. In Costa Rica, suspected GAS pharyngitis was diagnosed on clinical criteria alone i.e. no throat swabs were performed and patients were treated with intramuscular (IM) benzathine penicillin. New cases (first attacks) of rheumatic fever fell from 94 in 1970 to just four in 1991, which may or may not be a consequence.

Since ARF can be reduced by treating GAS sore throats with antibiotics and rheumatic fever is still a problem in New Zealand, national pharyngitis protocols have been developed (see http://www.heartfoundation.org.nz).

This guideline summarises evidence on the primary prevention of rheumatic fever as found by systematic searches of international literature which is relevant to New Zealand.

6. Clinical and Public Health Questions

There are a number of possible factors influencing the development of rheumatic fever, hence a number of possible interventions. These are examined in the questions below. Where possible, recommendations are made.

The clinical and public health questions are grouped according to the potential causes of ARF:

- Section A: Biological factors
- Section B: Healthcare systems and services
- Section C: Physical, social and economic environment (socioeconomic factors)
- Section D: Lifestyle factors.

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7. Section A: Biological Factors

Question 1. What is the evidence that new cases of acute rheumatic fever (ARF) can be prevented by treating group A streptococcal (GAS) throat infections?

Evidence statement
There is good evidence from randomised controlled trials (RCTs) that treating group A streptococcal (GAS) sore throats with antibiotics reduces the likelihood of developing acute rheumatic fever (ARF). These RCTs are shown in Appendices 5 and 6.

Appropriate antibiotics regimens are summarised in the Group A Streptococcal Sore Throat Management Guideline (2008), available to download from: http://www.heartfoundation.org.nz

Recommendation:	GAS sore throats should be treated with appropriate antibiotics to reduce the likelihood of the patient developing rheumatic fever
Recommendation grade:	A, for treating GAS sore throats with antibiotics
Evidence level:	I, for treating GAS sore throats with antibiotics

Question 2. In the prevention of rheumatic fever, is there a role for seasonal prophylactic treatment for GAS pharyngitis?

Evidence statement
There is limited evidence from two RCTs that this may be effective in a circumscribed community. The studies are summarised in Appendix 7.

Recommendation:	No recommendation is possible regarding seasonal prophylaxis
Recommendation grade:	D
Evidence level:	Insufficient evidence to make a judgement

Question 3. Do GAS skin infections (pyoderma/impetigo) cause ARF?

Whether there is a causal link between skin streptococcal infections and ARF has been debated. Key studies are detailed in Appendix 8 and referred to in the following questions.

Recent research from Australia suggests a possible link between skin streptococcal infections and rheumatic fever.[22] McDonald et al hypothesised that recurrent skin infections may immunise against throat colonisation and infection,[22] although this link has not been proven.[7]

Evidence statement
There is insufficient evidence that streptococcal skin infections cause ARF. Observations in Trinidad and Chile do not support this hypothesis.[11,23]

Recommendation:	No recommendation is possible
Recommendation grade:	C
Evidence level:	IV, insufficient evidence that impetigo/pyoderma causes rheumatic fever

Question 4. Is there evidence that M/*emm* types of GAS other than established "rheumatogenic" types are associated with ARF?

Over 20 years of epidemiologic evidence from Auckland, New Zealand, which has high ARF rates, supports *emm* 53 and 58 as aetiologic for ARF.[8,24] M53 also occurs with others including M1, M5 and M74 in Chilean ARF cases.[11] Studies which have shown associations between M/*emm* types and ARF are shown in Appendix 9.

Evidence Summary
Evidence from observational studies from two endemic areas suggests other M/*emm* types are associated with ARF.

Recommendation:	No recommendation possible
Recommendation grade:	C
Evidence level:	IV

Question 5. Do pyodermal strains of GAS cause ARF?

Evidence statement
Some of the same strains of GAS found on the skin can cause ARF when isolated from the throat. Studies on isolation of "pyodermal" GAS from the throat in ARF are shown in Table 2.

Table 2. Isolation of "Pyodermal" GAS from Throat in ARF

STUDY	TYPE	PLACE	INTERVEN-TION	OUTCOMES & CONCLUSIONS
Bisno AL et al. 1970[25]	Observation study	Tennessee, USA (APSGN and ARF occur in same population)	N/A	No ARF in summer (no GAS cultured from throat in these patients). "Pyodermal" isolates found in throat and skin in summer
Lennon D et al. 2008[24] submitted	Randomised controlled trial	Auckland, New Zealand	Sore throat clinics	*emm*/M58, 74, 75: well supported with appropriate incubation period and raised streptococcal titres. Also *emm*/M76, 92, 99 associated with ARF (1 case each) with raised antibody titres but preventable incubation periods. M/*emm* 58, 75 associated with pharynigitis and pyoderma in Martin et al 1994[9].
Martin DR et al. 1994[9]	Observation study	New Zealand	N/A	M6, 53, 55, 66, 89 also strongly associated with ARF ($p < 0.05$) are found commonly in pharyngitis and pyoderma in this study
Potter E et al. 1978[10]	Observation study	Trinidad	N/A	M11 primarily respiratory and M41 primarily pyodermal found in ARF cases (n=2) both found in both studies

Recommendation: No recommendation possible

Recommendation grade: B

Evidence level: II

Question 6. Does treating GAS skin infections prevent rheumatic fever?

Evidence statement, evidence level & recommendation:
Current data is insufficient to refute this statement. No conclusions or recommendations are able to be made

Question 7. Can some GAS strains cause both acute post streptococcal glomerulonephritis (APSGN) and ARF?

Evidence summary
Current data is insufficient to refute this statement. Some studies lend weak support. Studies relating to M/*emm* types associated with APSGN are shown in Appendix 10.

Recommendation: No recommendation possible

Recommendation Grade: C

Evidence level: III-3

Question 8. What is the evidence for genetic susceptibility for rheumatic fever?

Evidence summary

Clustering of cases of rheumatic fever in families has been documented for more than a century.[26-28] Familial clustering persists when socioeconomic factors and environment are controlled for.[29,30] It remains unclear precisely what factor or factors render a person particularly susceptible to rheumatic fever. Currently, susceptibility to rheumatic fever can only be defined by contracting the disease. The imperative behind the search for a marker for genetic susceptibility is to identify susceptible persons before rheumatic fever occurs.

Wilson and Schweitzer in 1937 proposed that susceptibility to rheumatic fever was transmitted in an autosomal recessive fashion, based on data of their own and British data from the Medical Research Council (MRC) (1927).[31] Stevenson & Cheeseman (1953) and Uchida (1953) both failed to confirm this, as did reanalysis of the data by Elandt-Johnson (1970).[32-34] Sit (1990) has also re-analysed these data sets and supports Wilson and Schweitzer's conclusion of classical Mendelian recessive transmission, with the caveat that effective antibiotic treatment is able to prevent the expression of disease susceptibility.[35]

Evidence statement & recommendation:
The evidence for genetic susceptibility to rheumatic fever is conflicting. Effective antibiotic treatment of streptococcal throat infection may prevent the expression of susceptibility

Recommendation grade: C

Evidence level: IV

Question 9. Is there a human leukocyte antigen (HLA) association with rheumatic fever?

Major histocompatability complex (MHC) class II antigens are present on antigen presenting cells and B lymphocytes, where they function as antigen receptors.

Carlquist et al performed a meta-analysis of studies of HLA DR frequencies in rheumatic heart disease (RHD).[36] This supported an association between class II alleles and the risk for RHD but concluded that considerable heterogeneity existed between different ethnic and racial groups. Subsequent studies support the observation that associations with HLA DR and DQ loci are stronger and more consistent in groups homogeneous for ethnicity and with respect to manifestations of rheumatic fever.[37-43]

Evidence statement & recommendation:
There is some evidence of an association between class II alleles and an increased risk of rheumatic fever, but no evidence to support population screening for the alleles at this stage

Recommendation grade: A, meta-analysis

Evidence level: I, meta-analysis

Question 10. Does the monoclonal antibody D8/17 define susceptibility to rheumatic fever?

Evidence suggests that there is an inherited susceptibility to rheumatic fever. This evidence is summarised in Appendix 11. The precise mechanism remains unclear. No universal HLA associations have been defined. The monoclonal antibody D8/17 may reliably detect patients with previous rheumatic fever or RHD in many populations, but technically remains a research tool at this time.

Zabriskie et al have described an alloantigen identified by a monoclonal antibody designated D8/17 that is present on the surface of B cells.[44,45] This antigen does not appear to be associated with any of the known HLA antigens. The monoclonal antibody identified the alloantigen on the surface of B cells of almost all patients with current or past rheumatic fever and only 14% of controls. First degree relatives had intermediate levels of expression.[46]

The D8/17 monoclonal antibody appears to be a consistent marker of past rheumatic fever in many populations. Intermediate levels are detected in first degree relatives, including relatives of patients with Sydenham's chorea, suggesting that the B cell marker is inherited.[47] An autosomal recessive mode of inheritance has been proposed.[46] Expression is highest in patients with ARF, suggesting the alloantigen may be upregulated during the disease process.[48]

Evidence statement:	No predictive marker for susceptibility to rheumatic fever has yet been defined
Recommendation grade:	B
Evidence level:	III-2

Question 11. Do recurrent sore throats increase the risk of a patient progressing to ARF?

Evidence statement
There are insufficient published data to answer this question with any degree of certainty. Studies listing sore throat episodes and rheumatic fever are in Appendix 12.

Recommendation:	There is insufficient evidence to make a recommendation; the scanty evidence of a link comes from what seems to be a single case-control study (published in 3 variations by Adanja and Vlajinac)[49-51]
Recommendation grade:	C
Evidence Level:	IV

Question 12: Is there a vaccine available for the control of GAS disease (which may prevent rheumatic fever)?

Evidence statement
No GAS vaccine has been marketed to date. However, recent clinical trials have been promising.[52]

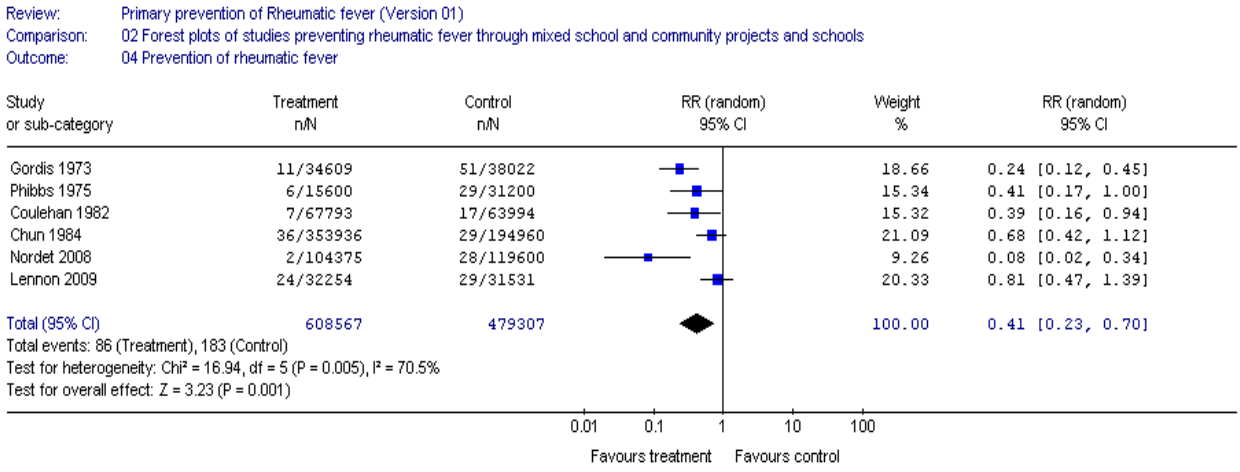
Recommendation:	No recommendations are able to be made, as possible vaccines are still under development

8. Section B: Healthcare Systems and Services

Question 13: What is the evidence that new cases of ARF can be prevented through school and/or community projects which involve GAS throat infection treatment?

Studies preventing rheumatic fever through school and/or community projects[19, 53-57] are summarized in Figure 1. Only studies with estimable relative risk (RR) have been included. Studies with no cases of rheumatic fever either in the control or the intervention group have been excluded (as the software defaults to a value other than zero). See Appendices 13 and 14 for studies included and rejected for the meta-analysis.

Figure 1. Forest plots of studies preventing rheumatic fever through school and/or community projects



***Study by Lennon 2009** has had the sample size adjusted to allow for the unit of randomization being school.

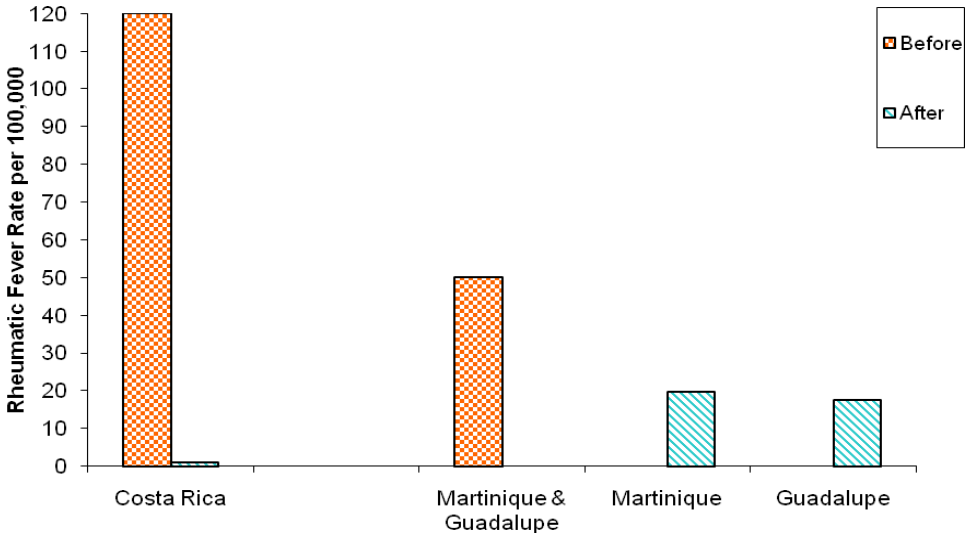
Source: Lennon et al. 2009, in press.[58]

Historically significant non-RCTs involving sore throat treatment for rheumatic fever prevention in low-resource settings are summarised in Table 3 and Figure 2 below. Studies on other community, mixed community and school studies for rheumatic fever prevention are summarisied in Appendices 15 and 16.

Table 3. Historically Significant Non-Randomised Controlled Trials Involving Sore Throat Treatment for Rheumatic Fever Prevention in Low-Resource Settings

STUDY	STUDY TYPE AND PROBLEMS	PLACE	INTERVENTION	OUTCOMES
Arguedas A et al. 1992[20]	Ecological study. Community wide rheumatic fever prevention intervention for Costa Rica as a whole. No blinding or randomisation. Data not well presented, graphs difficult to interpret. Unclear whether primary and secondary cases are counted together in rheumatic fever statistics	Costa Rica. 1970s-91 approx	IM benzathine penicillin given after GAS diagnosed on clinical grounds: fever or sore throat and examination showing halitosis, redness of pharynx and hypertrophy of tonsils with white exudate. Penicillin dose: 300,000 U IM for patients under 3 years old, 600,000 U for 3-5 year olds, 1,200,000 U for patients aged over 5 years. Erythromycin PO 30-40mg/kg per day, in 4 doses for 10 day regime	Not well quantified. 1950 rate of rheumatic fever: 120 cases per 100,000 inhabitants cited, fell to approx 1 per 100,000 inhabitants in 1990 (as read from bar graph p 570). Secondary prophylaxis not discussed
Bach JF et al. 1996[21]	Ecological study. Ignoring initial year of programme. Data not broken down as much as it could be in tables. Primary and secondary rheumatic fever not differentiated in some cases. Programme ran on both islands, no blinding or randomisation. Community wide intervention	French Caribbean. 1982-92. 10 year programme in Martinique and Guadalupe	Educational programme set up: targeted public and health care workers, included radio and TV broadcasts. Rheumatic fever register for primary and secondary cases set up (using Jones criteria). Free access to medical care. Secondary prevention as well as sore throat management	Initial rise 10-20% in children admitted with rheumatic fever - thought to be due to renewed attention paid to the disease, so reference year then taken as 1982. Overall: 78% reduction in rheumatic fever cases Martinique and 74% reduction in Guadeloupe

Figure 2. Historically significant uncontrolled rheumatic fever interventions in low–resource settings



Evidence statement
Both communitywide and combined school and community GAS sore throat interventions have reduced the incidence of new cases of ARF.

Recommendation:	Community and combined school and community sore throat treatment interventions could be expected to reduce the incidence of ARF by up to 60%
Recommendation grade:	B, for community and combined school and community based GAS sore throat interventions
Evidence level:	II, for community and combined school and community based GAS sore throat interventions. The studies are of varying quality and may not describe methodology in detail

Question 14: What is the evidence that new cases of ARF can be prevented by school-based programmes which involve GAS throat infection treatment?

Evidence statement
There is good evidence of the effectiveness of school-based GAS sore throat interventions at reducing the incidence of new cases of ARF. These studies are summarized in Appendices 14 and 16.

Recommendation:	School-based GAS detection and treatment interventions involving treating sore throats could be expected to reduce the incidence of ARF
Recommendation grade:	B, for school-based GAS sore throat interventions
Evidence level:	II, for school-based GAS sore throat interventions

Question 15: What is the evidence that in institutional settings, prophylactic treatment of GAS pharyngitis reduces the cases of rheumatic fever?

In general, prophylactic antibiotics to prevent the spread of GAS pharyngitis and subsequent rheumatic fever, were given to persons as they entered a closed, population-dense environment, such as juvenile detention centres or military barracks. These studies are summarised in Appendix 17.

Evidence summary
There is some evidence from large-scale military and institutional studies that prophylactic penicillin (IM or PO) can reduce the rate of rheumatic fever, where there is high prevalence of rheumatic fever and a large, potentially crowded population.

Recommendation:	Prophylactic antibiotics for GAS pharyngitis may be beneficial in some institutional situations. The risk of rheumatic fever needs to be weighed against the risk of antibiotic allergic reactions
Recommendation grade:	C
Evidence level:	IV, case series

Question 16: Does improving access to primary healthcare (as it is currently available) reduce the rate of rheumatic fever?

In the past, there has been no evidence that treating GAS pharyngitis in general practice has made a difference to rheumatic fever rates.[1] However, as GAS pharyngitis can cause rheumatic fever, it is important to examine the issues surrounding access to healthcare.

It is worth noting that if people do not consider sore throats important, they will not seek medical help for them, and this is a barrier in rheumatic fever prevention.

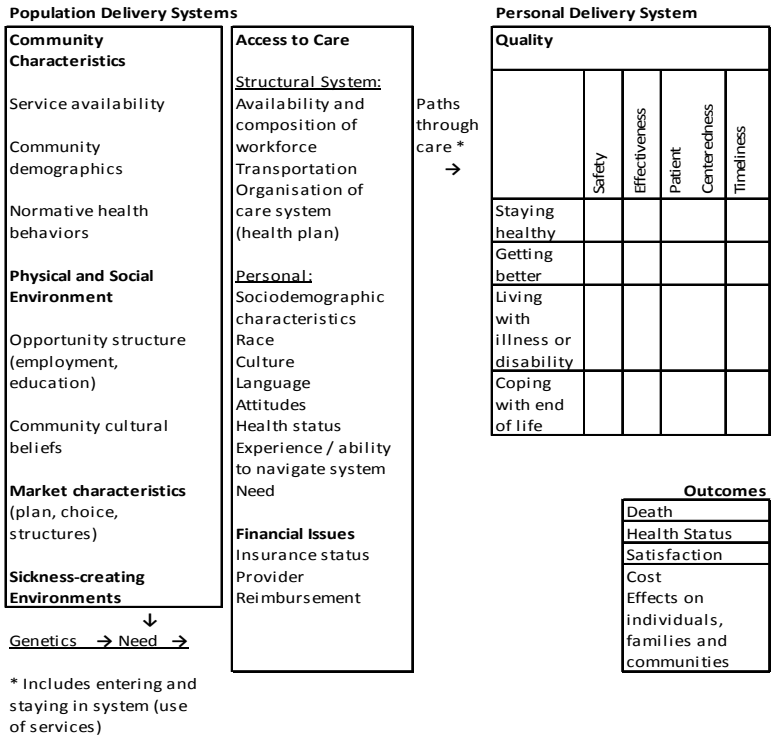
Community-wide interventions which have improved access to healthcare have shown a reduction in rheumatic fever rates in three classic studies.[19-21] See Table 3 and Figure 2.

The topic of healthcare access has been divided into four sections:
1. Background
2. Healthcare access and socioeconomically disadvantaged groups in New Zealand
3. Healthcare access and Māori and Pacific Peoples in New Zealand
4. Ways to improve access to healthcare in New Zealand.

1. Background

The topic of access to healthcare is controversial. What constitutes 'access' is debated and measured in a number of ways by different observers. Access to healthcare can include visiting general practitioners and filling prescriptions, but it can be more complex than this. Lurie has summarised several definitions of access to healthcare, indicators of access and factors which may impact on access.[59] It is a dynamic process with interactions between the individual and society and includes value judgements on outcomes, as summarised in Lurie's table Figure 3.

Figure 3. Relationship between population and personal delivery systems (after Lurie 2002)



Source: Reprinted with permission from Guidance for the National Healthcare Disparities Report © by the National Academy of Sciences, Courtesy of the National Academies Press, Washington, D.C. Accessed from: http://www.nap.edu/openbook/0309085195/html/1.htm

Lurie's table is a good starting point for discussions of healthcare access. However, in New Zealand, relationships with whanau and iwi should also be taken into consideration.

Defining the groups with special health needs, which most need access to healthcare in New Zealand, is not straightforward either. It is likely that individuals who do not access healthcare when required, for instance to have GAS pharyngitis treated, may be at increased risk of rheumatic fever. Pomare, writing in 1988, outlined six groups with special health care needs in the New Zealand setting: Māori, women, the socioeconomically disadvantaged (e.g. Māori), age (infants and the aged), the chronically disabled (with physical/sensory/mental handicaps) and those with geographic isolation (rural and urban).[60] These groups still have special needs today and have arguably been joined by others, including Pacific peoples and immigrants.

2. Healthcare access and socioeconomically disadvantaged groups in New Zealand

Classic studies in low socioeconomic settings in the French Caribbean, Costa Rica and Baltimore,[19-21] have shown a marked decrease in the rate of rheumatic fever when healthcare access was improved (see Table 3 and Figure 2).

From these studies and those in Appendix 18, it seems that there may be a link between reduced access to healthcare and the incidence of rheumatic fever, although it is difficult to quantify.

In New Zealand, lower income groups face barriers in accessing healthcare. Schoen used the 2001 Commonwealth Fund International Health Policy Survey to compare access to medical care in New Zealand, Australia, Canada, the United States and the United Kingdom.[61] This was a random cross sectional survey of 1,400 people. In New Zealand, those with below average incomes, found it extremely or very difficult to see a specialist, compared to those with above average incomes. They were more likely to not fill prescriptions and miss out on tests or treatment. Low income New Zealanders (24%) had medical problems but did not see the doctor and, unsurprisingly, had trouble paying medical bills. See Appendix 19 for further details.

3. Healthcare Access and Māori and Pacific Peoples in New Zealand

As well as low income groups, Māori and Pacific peoples face barriers in accessing healthcare. Using NZDep2001 deciles (which assess a number of markers for deprivation, see www.moh.org.nz) Hefford found that over 50% of Māori and Pacific peoples lived in the three most deprived deciles.[62] It is predominately Māori and Pacific peoples who are diagnosed with rheumatic fever in New Zealand (see Table 4).

Table 4. Notified Rheumatic Fever Cases in New Zealand 2003 (Initial Cases & Recurrences)

ETHNICITY	NUMBER OF CASES OF RHEUMATIC FEVER (TOTALS)	RATE PER 100,000 POPULATION
European	4	0.2
Māori	70	13.3
Pacific peoples	58	29.0
Other ethnicity	6	2.4
Unknown	5	-
Total-initial cases	141	3.8
Total-recurrences	2	0.1

Source: Adapted from Table 33 and page 32. Rheumatic fever cases in New Zealand 2003. From: Institute of Environmental Sciences and Research Ltd. Notifiable and other diseases in New Zealand, Annual Report 2003. Wellington: Ministry of Health. Downloaded from: http://www.surv.esc.cri.nz/PDF_surveillance/AnnSurvRpt/2003AnnualSurvRpt.pdf

Healthcare access and Māori

A recent report on Māori health, Tatau Khukura: Māori Health Chart Book (2006), gathered statistics from a number of sources.[63] The top six reasons Māori males and females aged 15 and over gave for not seeing a GP when they needed to were summarised.[63] The top reason was 'costs too much', given by over 50%.

There may also be a number of other cultural and social barriers which are difficult to quantify, including Treaty of Waitangi issues, which reduce the likelihood of Māori accessing healthcare. Māori socioeconomic indicators from 2001 are summarised in Appendix 20.

Ellinson-Loschmann discusses the differences in life expectancy between Māori and non-Māori and points out that a significant amount of Māori mortality is due to diseases for which healthcare is available, i.e. preventable diseases.[64]

Studies that have looked at Māori and access to healthcare in general terms are summarised in Appendix 21. None of these were RCTs.

Healthcare access and Pacific peoples

Studies which look at Pacific peoples and access to healthcare in general terms are summarised in Appendix 22. The Pacific Health Chart Book (2004), which collates Pacific health information from a number of sources, was reviewed.[65]

Apart from economic and practical reasons, there may also be cultural and linguistic barriers which reduce the likelihood of Pacific peoples accessing healthcare. Cook, in a study of Samoan immigrants to Hawaii from 1979 to 1981, identified two major barriers to them accessing healthcare.[66] He argued that a comprehensive alternative belief system was in place among the Samoan community which could explain and treat illness. Secondly, negative experiences (from unfamiliarity with procedures and from communication difficulties) with the health system in Hawaii had caused aversion to its use.[66]

4. Ways to improve access to healthcare in New Zealand

Possible solutions to improve access to healthcare in New Zealand include:

- Primary sector reform measures
- Moves to strengthen Māori and Pacific health providers
- Innovative community based strategies through marae, schools and churches.

Primary sector reform in New Zealand

The aim in primary sector reform has been to increase access to healthcare for groups with the greatest healthcare needs. Hefford summarises recent measures in primary healthcare reform, stating that there has been a move from fee-for-service (when visiting the healthcare provider such as a GP) towards capitation (practices are given a fee for each patient registered with the practice, with the idea being that patients are not charged at each visit).[62] There has also been a shift towards promotion of population health management and a not-for-profit infrastructure with community involvement.[62] Hefford points out that funding for the primary care sector is scheduled to rise by 43% over three years.[62] See Table 5 for further details.

Table 5. Reducing Disparities through Health Policy Reform

POLICY ELEMENT	HOSPITAL MECHANISM FOR REDUCING DISPARITIES
Lower co-payments	Reduce cost barriers to needed care
Services to improve access	Resources to implement new/additional services targeting high need groups
Project funding. Needs based health promotion funding	Fund projects aimed at, for example, housing, lifestyle change, risk reduction and community health initiatives
Capitation	General focus on population health, increased use and scope of nurses and allied health practitioners
Funding to care for medically complex patients	Funding is targeted to those from high need groups who are more likely to have medical complications
PHO obligation to work with and develop plans for groups with poorer health status	Implementation of specific services targeting deprived groups, Māori and Pacific
Community and Māori involvement in PHO governance	Involvement of minority groups in decision-making may increase appropriateness and attractiveness of care for disadvantaged groups
Performance indicators (policy element not yet fully developed)	Reward those who are providing effective services to high need individuals

Source: Table 5 reprinted from Health Policy, 72, Hefford M, Crampton P, Foley J. Reducing health disparities through primary care reform: the New Zealand experiment, 9-23. Copyright 2005, with permission from Elsevier Health.[62]

How has this reform been working? Hefford argues that healthcare access has improved access to healthcare for vulnerable groups. He states that 994,173 people have received subsidised care through this scheme, in the first 15 months after it was launched. Of these, it is estimated 400,000 would not previously have had subsidised primary healthcare (135,000 Māori and Pacific peoples, 52,000 living in the two most deprived deciles [nine and ten]).[62]

Māori and Pacific health providers

Māori and Pacific healthcare providers have been increasing in number in recent years and form part of the answer for access among these groups. The impact of Māori and Pacific healthcare providers is summarised in Appendix 23.

One in seven Māori adults in a 2002-03 survey had seen a healthcare worker from a Māori healthcare provider in the last 12 months, most commonly a doctor. The most frequently given reason was for a routine check-up. Most were satisfied or very satisfied with their visit.[67]

The main reason given by Māori for choosing to visit a Māori health provider, was feeling more comfortable talking to someone who understands their culture. One in 17 Māori adults had wanted to see a Māori health provider in the last 12 months, but were unable to.[67]

One in 11 Pacific adults had seen a healthcare worker at a Pacific health provider in the last 12 months. The most common reason was a routine check-up or health advice. Of those who visited a Pacific health provider, most were very satisfied or satisfied.[67]

The main reasons given by Pacific peoples for choosing to visit a Pacific health provider, was: 'I feel more comfortable talking to someone who understands my culture'. An unmet demand existed: 3.1% of Pacific adults had wanted or needed to see a Pacific health provider in the last 12 months, but were unable to.[67]

Crengle outlined the barriers to healthcare and solutions used in Māori primary care services.[68] Financial, geographic and transport barriers, cultural barriers and barriers within the healthcare system (among others) are discussed, along with possible solutions. Crengle's solutions include cheaper co-payments, e.g. making visits for under 16 year olds free, discounted medications and transporting patients to the clinic.[68]

Innovative community-based strategies through marae, schools, churches and public health actions

School-based GAS sore throat interventions

For a discussion of school GAS sore throat studies, see Question 14. There is RCT evidence of school sore throat programmes reducing rheumatic fever. If the rate of spread of GAS pharyngitis is between 19 to 50% within a household per month[69-72] (see Appendix 24 for more details), then public health notifications of this disease and throat swabbing household contacts may reduce the burden of streptococcal pharyngitis and potentially the burden of rheumatic fever.

Evidence summary

Primary health care reform and Māori and Pacific healthcare providers have improved access to healthcare providers. They do not address all barriers, such as transport and telephone access, which are encountered by those at risk of rheumatic fever. A meta-analysis of international studies of school-based interventions supports this approach (see Question 13 & 14).

Recommendation:	Primary healthcare reform and Māori and Pacific healthcare providers have not reduced the rate of rheumatic fever to date. Community-based, in particular school-based sore throat interventions, have been proven effective in rheumatic fever reduction in settings including New Zealand	
Evidence level and recommendation grade:	Evidence of a benefit (improvement in healthcare access) in the New Zealand setting from:	
	Evidence Level:	**Recommendation grade:**
Primary care reform:	Observational study evidence only	
School programmes:	I	A
Māori and Pacific health care providers:	IV	C

9. Section C: The physical, social and economic environment (Socioeconomic factors)

Question 17: Does reducing crowded living conditions help reduce the incidence of rheumatic fever?

International studies on crowding and rheumatic fever are summarised in Appendix 25. For New Zealand, the data on crowding per region is summarised in Appendix 26. There was considerable geographic variation, with Auckland having the most people per bedroom, 1.41.[73]

There is also good evidence, in a study of Auckland children, of a link between crowding and meningococcal disease.[74]

Evidence statement
There is evidence from comparative studies of a link between crowding in the home and rheumatic fever. Addressing crowding may have some impact on reducing the rate of rheumatic fever.

Recommendation:	Reducing household crowding could be expected to reduce the rate of rheumatic fever
Recommendation grade:	B
Evidence level:	III-2

Question 18: Is there a link between quality of housing and rheumatic fever? Does improving housing reduce the rate of rheumatic fever?

Studies of ARF and quality of housing are summarised in Appendix 27. None were RCTs.

Evidence statement
There is some evidence for a link between poor quality housing and rheumatic fever, but definitions of housing quality vary between studies. It is impossible to generalise enough to make a recommendation for a minimum standard of housing at this stage in New Zealand.

Recommendation:	It is not currently possible to recommend a minimum standard of housing which would make acquiring rheumatic fever less likely
Recommendation grade:	B
Evidence level:	III-2

Question 19: Is there a link between poverty and rheumatic fever? Would reducing poverty reduce rheumatic fever?

Studies on poverty and ARF are summarised in Appendix 28.

Evidence statement
Although suggestive of a link, studies do not show a clear-cut association. Rheumatic fever patients tend to have lower incomes, as do many of the controls. Some studies found an association and some did not. Due to the differences in currencies and comparison groups, it is not possible to establish a definitive association or to draw any conclusions for New Zealand. Poverty may feed indirectly into other factors which may impact on rheumatic fever, such as crowding, housing, nutrition, parental unemployment and poor access to healthcare.

Recommendation:	A minimum level of income, to reduce the likelihood of developing rheumatic fever, is unable to be definitively established for the New Zealand setting
Recommendation grade:	B
Evidence level:	III-2, case control

Question 20: Is there a link between unemployment and rheumatic fever?

Adanja et al in a case control study, found that 90.5% of rheumatic fever patients had both parents or just the father working, compared to 95.0% of controls (RR=1.0).[49] In the case of only the mother working or both parents being unemployed, 9.4% of rheumatic fever patients were in this situation, compared to 4.5% of controls (RR=10.37, p=0.00014). This showed there was a significant association between the occurrence of rheumatic fever and having both parents unemployed or only the mother employed. A further case control study gave a p value of 0.110 unemployment of parents as a risk factor for rheumatic fever (adjusted RR=2.08, 95% CI, 0.85-5.09), finding there was no significant association.[51]

Evidence statement
There is scanty research in this area, although it is suggestive of a link between both parents being unemployed or the father being unemployed and a patient having rheumatic fever.

Recommendation:	No recommendation possible
Recommendation grade:	B
Evidence level:	III-2

Question 21. Is there a link between parental education and rheumatic fever?

One case control study from Yugoslavia looked at this issue, published in two versions.[50,51] In the most recent article, Vlajinac found a link between the low education of the mother (less than four years of elementary school) and an adjusted relative risk (RR) of rheumatic fever of 2.52 (95% CI, 1.29-4.92).[51] Zaman found that cases of rheumatic fever had a parental schooling (years) on average 10.3 years and controls 17.8 years ($p<0.0001$) which was significant.[75] Meira prospectively studied patients with ARF to see which ones progressed to severe valvular disease and found an association between severe disease and a mother's schooling of less than four years (p=0.09, RR=1.77, 95% CI, 0.91-3.46).[76]

Evidence statement
There is insufficient evidence to generalise or make a definitive recommendation on the link between low levels of maternal education and rheumatic fever, as education levels vary between countries.

Recommendation:	No recommendation possible
Recommendation grade:	B
Evidence level:	III-2

10. Section D: Lifestyle Factors

Question 22: Does having a smoker in the house make rheumatic fever more likely to occur?

Evidence statement
There is insufficient published evidence to answer this question. A single Indian study found a link between the presence of a tobacco smoker in the household and the incidence of GAS pharyngitis in the children.[77] Evidence exists that the incidence of other respiratory illnesses, including meningococcal disease, is increased by the presence of smokers.[74,78]

Recommendation:	The writing group consensus is that streptococcal pharyngitis, like other respiratory illnesses, is likely to be exacerbated by smoking within the household and recommends cessation of smoking or smoking outdoors
Recommendation grade:	D
Evidence level:	Insufficient evidence

Question 23: Does improving nutrition have a role in reducing rates of GAS or in rheumatic fever?

Studies addressing the role of nutrition and ARF are summarised in Appendix 29.

Evidence summary
There has been some research on intake of various food items, particularly eggs,[79] nutritional deficiencies[50,75,80] and rheumatic fever, but the research is currently inconclusive. An association has been found between low body weight and/or thin arms and rheumatic fever in studies from Zaire, Bangladesh and Yugoslavia.[51,75,81] These studies may not seem relevant in the New Zealand context at first, with obesity a growing problem in the local population, but it must be remembered that it is possible to have nutritional deficiencies despite a high body mass index (BMI).

Recommendation:	It is not possible to recommend a certain diet or BMI to prevent rheumatic fever or reduce the risk of rheumatic fever recurrence, but a healthy balanced diet is recommended in general
Recommendation grade:	B
Evidence level:	III-2

Question 24: Do fomites (dust/clothing/bedding) have a role in the spread of GAS and therefore in rheumatic fever?

Evidence statement
Although this area has not been extensively researched, current thinking is that GAS is not significantly spread through contaminated fomites such as dust, bedding and furnishings.[82,83] In two key experimental studies, Perry did not find any evidence that dust or GAS contaminated blankets spread GAS pharyngitis.[84,85] Falck et al in a case-control study also found that hygienic measures, such as changing

toothbrushes and washing bedclothes, did not make any difference to the recurrence of GAS sore throat.[72] These studies are summarised in Appendix 30.

Recommendation:	The evidence for fomites causing GAS pharyngitis/rheumatic fever infection is inconclusive, so no recommendations are able to be made at this stage
Recommendation grade:	B
Evidence level:	III-2

11. Implementation of the Guideline

Driving forces

The drive to reduce the incidence of rheumatic fever and its sequel, rheumatic heart disease, a preventable chronic disease, has informed this guideline. About a third of rheumatic fever patients will present with moderate or severe heart disease, and ten to twenty percent will continue to have severe chronic heart disease, requiring intensive medical or surgical management for their shortened lifetimes. The burden of rheumatic fever is inequitably borne by Māori and Pacific peoples, especially children and youth. Rheumatic fever is a disease which New Zealand has failed to control.

Restraining forces

The following challenges will need to be met:

- Perception by many children, young people, parents and caregivers that sore throats are a minor ailment and do not have sequelae
- Barriers to primary care services and diagnostic tests
- Lack of knowledge by health professionals and lay public alike that rheumatic fever and rheumatic heart disease are preventable
- The need to wait until swab results are known before antibiotics are prescribed, therefore requiring more than one healthcare visit
- The cost of doctor visits and antibiotics for patients aged over six years
- The difficulty in completing a ten day course of antibiotics and patient dislike of intramuscular benzathine penicillin injections
- Avoiding unnecessary antibiotic prescribing in low ARF-risk patients
- Poorer socioeconomic circumstances (including a lack of transport or telephone) which may contribute to untreated sore throats and thus rheumatic fever
- Cost and complexity of investigation of families and household members in association with a case of recurrent GAS pharyngitis in a high risk population
- Streptococcal disease other than rheumatic fever is no longer a notifiable disease
- A lack of funding in New Zealand for rapid streptococcal throat swab diagnostic tests, and need for consideration of their effectiveness
- Other unknown factors.

Consultation

The following consultation was undertaken:

Relevant consumer groups and community agencies including Te Hotu Manawa Māori and Pacific Islands Heartbeat were consulted and reviewed the guideline. Prior to the Auckland school-based RCT for the prevention of rheumatic fever study (Lennon, unpublished), in 1996 there was consultation at St Stephen's church in Otara and Te Puea marae in Mangere regarding possible venues for sore throat clinics. The community feedback at that time backed schools as the preferred option. Both communities called for more information on rheumatic fever prevention and the consequences of rheumatic fever.

A community panel consultation meeting called by the Community Liaison Manager regarding rheumatic fever primary prevention was held at Counties Manukau District Health Board in Auckland on 16 February 2007. The feedback included the following points:

- The panel endorsed a strong need to improve community awareness around the prevention of rheumatic fever, particularly in children
- Best practice and proven capacity indicated a partnership with schools similar to that used by the meningococcal campaign and the school-based rheumatic fever prevention study
- The panel wondered whether rheumatic fever prevention, i.e. sore throat diagnosis and treatment, should be standardised as an in-school check that health nurses and other health related staff could administer
- Strong support was indicated for a more prominent presence and heightened awareness of ear, nose and throat clinics in schools
- The perceived risk of long term antibiotic treatment should be weighed against the risks of heart damage by rheumatic fever.

Suggested implementation strategies to reduce the rate of ARF in New Zealand

Populations at high risk of rheumatic fever:

- Māori and Pacific peoples
- Youth, especially those aged five to 14 years
- Those living in lower socioeconomic circumstance within the North Island, especially within parts of the Northland, Auckland, Waikato, Bay of Plenty, Rotorua, Gisborne, Hawke's Bay and the Wellington area.

From the evidence-based literature review provided in this guideline, the following should be instigated:

1. Nationwide Initiatives

- **Raise awareness that RHF/RHD is PREVENTABLE.** Raise awareness of sore throats as a trigger for rheumatic fever, a potentially fatal preventable disease and target this strategy to those in high-risk populations, through:
  - Development of health promotion materials, such as pamphlets, DVDs, videos, posters, appropriate for those at highest risk
  - Health promotion in schools and youth groups in high-risk areas
  - Awareness-raising through community and family groups in high-risk areas (whanau, iwi, marae and church groups and other appropriate vehicles).

- **Diagnose and treat streptococcal sore throats appropriately.** It is imperative that those at risk of rheumatic fever (principally Māori and Pacific youth living in lower socioeconomic areas of the North Island), who present with sore throats, are swabbed for GAS pharyngitis or treated empirically, with the approriate antibiotics for the appropriate duration. For diagnosis and antibiotic options, see Group A Streptoccocal Sore Throat Management Guideline algorithm available at: www.heartfoundation.org.nz.

- **Address the spread of GAS pharyngitis within households.** GAS pharyngitis is droplet-spread and the rate of GAS pharyngitis cross-infection within a household is between 19-50% (see Appendix 24).

  - Strengthen the case for household contact tracing to interrupt the spread of GAS following a case of rheumatic fever (see page 27: Rheumatic Fever Diagnosis, Management and Secondary Prevention Guideline).

  - The spread of GAS infection is therefore an important risk factor for the development of rheumatic fever in areas where there is a high incidence of rheumatic fever. Consequently, there may be value in changing the present status of GAS pharyngitis in the Health Act 1956 into a disease which is notifiable to the Medical Officer of Health.

  - Public health follow-up when three or more cases of GAS pharyngitis are reported from the same family or address within a three month period could be an extension of this process. It is recommended that GAS pharyngitis notifications to the Medical Officer of Health be trialled in areas at particularly high risk of rheumatic fever to determine the practicality and effectiveness of this intervention.

- **Training.** Ensure funding for training of health workforce persons to implement this guideline.

- **Circulation of rheumatic fever and sore throat guidelines.** This guideline and two related guidelines on Group A Streptococcal Sore Throat Management, and Diagnosis, Management and Secondary Prevention of Rheumatic Fever are available from The National Heart Foundation of New Zealand. They will be electronically circulated to relevant professional organisations and members of the writing group. These guidelines are free to download from: http://www.heartfoundation.org.nz

- Support for community development/partnership approaches (see next page)

- Reduction in the barriers to primary care for the at-risk population.

2. Assessment of rheumatic fever burden

Rheumatic fever prevention in communities: A community partnership approach. Areas with high rates and/or risk or rheumatic fever should be evaluated. These are usually lower socioeconomic, with a high Māori and/or Pacific population, in the North Island, and with high rates or rheumatic fever in previous years. It is recommended that Public Health Units in partnership with community paediatricians should:

- Carry out an annual analysis of rheumatic fever notifications and in particular assess the notification rates in communities where there are high numbers of Māori or Pacific peoples. Public health action needs to be considered once 5-14 year old notification rates **exceed 20 per 100,000**.

- Where the annualised rates of ARF in children aged 5-14 years over the last five years are **≥20 per 100,000**, early detection and **appropriate treatment of GAS pharyngitis** are required. Advocacy for strategies regarding socioeconomic determinants of health (such as housing) is required.

- Where the annualised rates of ARF in children aged 5-14 years are **≥50 per 100,000**, the feasibility of a **school-based sore throat programme** for rheumatic fever prevention should also be assessed. This requires a community partnership approach, including support from local paediatricians, iwi, Pacific providers, schools and primary care providers (see Table 6). If there is widespread support then seek funding from the District Health Board and the Ministry of Health.

- Where the population ARF rates do not reach the prevalence above, but the rates in the high risk populations of that area (particularly Māori and Pacific) exceed **20 per 100 000** then consideration should be given to relevant public health action with these communities.

3. School-based sore throat clinics

School-based streptococal sore throat clinics in communities at high risk of rheumatic fever in the North Island (refer to high-risk section above) could address problems with healthcare access and target the age groups most at risk of rheumatic fever. Throat swabs would be taken at school and antibiotics dispensed, with parental consent and a letter sent to the GP (see algorithm in Appendix 31). For correct throat swab technique, see Appendix 33.

City/suburban approach. This has been trialled in a New Zealand suburban setting. A school-based sore throat clinic RCT in decile 1 schools, including kura kaupapa Māori, was run by Lennon et al between 1998 and 2001 in South Auckland, involving 24,000 children (see Question 1 for further details). There was a 29% reduction in cases of ARF in the schools with clinics. This was not statistically significant as the study was very large but under powered. When this data was meta-analysed with data from three other school and community studies (before-after or with control groups), the numbers combined to show a reduction in cases of ARF in the clinic areas of 33% p=0.62, RR=0.67 (95%CI, 0.48-0.93), i.e. favours treatment (see Question 13, especially Figure 1 forest plot). Thus, rheumatic fever in an urban community setting is preventable.

Fine-tuning of the sore throat clinic model used in the South Auckland setting could include:

- Substitution of once-a-day amoxicillin in place of twice-daily penicillin to reduce costs.

- The sensitivity and specificity of rapid GAS diagnostic tests (compared to throat swabs cultured on sheep blood agar) in the New Zealand setting. Rapid tests need to be shown to be equal to swabs in effectiveness before they are able to be used with confidence (and without swab back-up) in a school programme. This could reduce laboratory costs.

- The South Auckland RCT was a community partnership overseen by the Rheumatic Trust Board (members were Colin Tukuitonga, Rea Wikiara, Shirley Maihi and Diana Lennon), with close consultation with Counties Manukau District Health Board, GPs, paediatricians, schools (principals and BOTs) and Māori Health providers (as in 1996). The Māori and Pacific communities were consulted at a day meeting at Te Puea Marae, Mangere and St Stephens Church, Otara. Any ongoing initiatives would require similar partnerships.

Rural/community approach. A school-based rheumatic fever primary prevention programme, utilising this community partnership approach has been successfully run in Whangaroa, a rural community in Northland by Dr Jonathan Jarman since 2002. Rheumatic fever rates were previously the highest in New Zealand and all patients were Māori. The disease has been eliminated from the area and the last case occurred in March 2002.

See Appendix 31 for a model for school sore throat clinics (urban and rural). See Appendix 32 for a guide for Public Health Units for selecting appropriate strategies for primary prevention of ARF in small towns and rural settings.

Table 6. Feasibility Assessment

1.	Is the epidemiology of the disease well described? • What are the numbers of cases and annualised rates for children aged 5-14 years over the last 10 years? • Are the numbers and/or rates increasing, decreasing or stable? • Are there ethnic disparities? • How do the rates compare with national rates? • Are there "hotspots" based on attendance at certain schools? • Is there a high level of population mobility?
2.	Is there community concern about rheumatic fever especially in the populations with the highest level of risk?
3.	Is there concern by local health care workers (PHOs, Iwi health providers, Pacific health providers and others) about the level of disease in the community and are they knowledgeable about its preventability?
4.	Do the local paediatricians support a rheumatic fever prevention programme in this community?
5.	Is the area well defined? Do schools mainly take children from the high incidence area?
6.	Is there a community agency that can act as the local "champion"?
7.	Can the local health providers, Iwi providers and regional public health provider work together in partnership with the community on this issue?
8.	Are the local schools knowledgeable about rheumatic fever and supportive of a school-based prevention programme?
9.	Are the District Health Board and the Ministry of Health aware of the level of disease in the area and know about: • The evidence supporting a school-based initiative from the meta-analysis of community intervention trials (including the New Zealand trial)? • The effectiveness of the Whangaroa rheumatic fever prevention programme which has eradicated rheumatic fever?

Measuring effectiveness and outcomes

Although there may be confounding variables, the primary outcome of the institution of this guideline ought to be the reduction in the incidence of ARF, particularly in targeted high-risk groups. Rheumatic fever is a notifiable disease and the incidence is monitored by the Ministry of Health in New Zealand.

Economic analysis

An economic analysis is due for completion later in 2007 and will be published separately.

[12. Appendices]

Appendix 1: Guideline search strategy

Overview

Relevant literature regarding sore throats and ARF was identified primarily using computerised databases described below, primarily PubMed. Publications were limited to those in the English language. Articles found through this methodology were then searched for relevant information and further articles identified through bibliographic references. A substantial physical library of sore throat and ARF references held at the School of Population Health was also reviewed for key articles.

The Search Strategy included:

- Medline was searched from 1966 to July week 4, 2006. Search string from New Zealand Guidelines Group included the terms; 'rheumatic fever', 'randomised controlled trials', 'controlled trials' and limits 'humans' and 'english language' which gave 85 hits.

- Old Medline to 1965 was searched for the term 'rheumatic fever', limits 'humans' and 'english language' and gave 7 hits. This was reviewed by two people (MK and DL).

- Cochrane, DARE Central and NHS EED and WHOLIS and www.clinicalevidence.com, www.cdc.gov and MOH were searched and specific topics were searched in www.pubmed.gov .

- Sore throat guidelines prepared by the Infectious Diseases Society of America,[15] the American Academy of Family Physicians and The American College of Physicians[86] and the 2003 Report of the Committee on Infectious Diseases by the American Academy of Pediatrics[87] and McIsaac's GAS pharyngitis criteria, based on Centor et al. 1981;[88] McIsaac et al. 2004,[16] were reviewed.

In 2004, a steering group met to agree that guidelines for rheumatic fever should be developed. In 2005 a similar group met agreeing that guidelines should be drawn up for acute rheumatic fever for New Zealand including secondary prophylaxis, sore throat management and primary prevention in addition to diagnosis and treatment.

- A writing group formed for the sore throat management guideline. Selected individuals drafted the guideline which was then reviewed by all members of the writing group with experience in ARF and/or sore throat management and their suggestions were incorporated into a second draft.

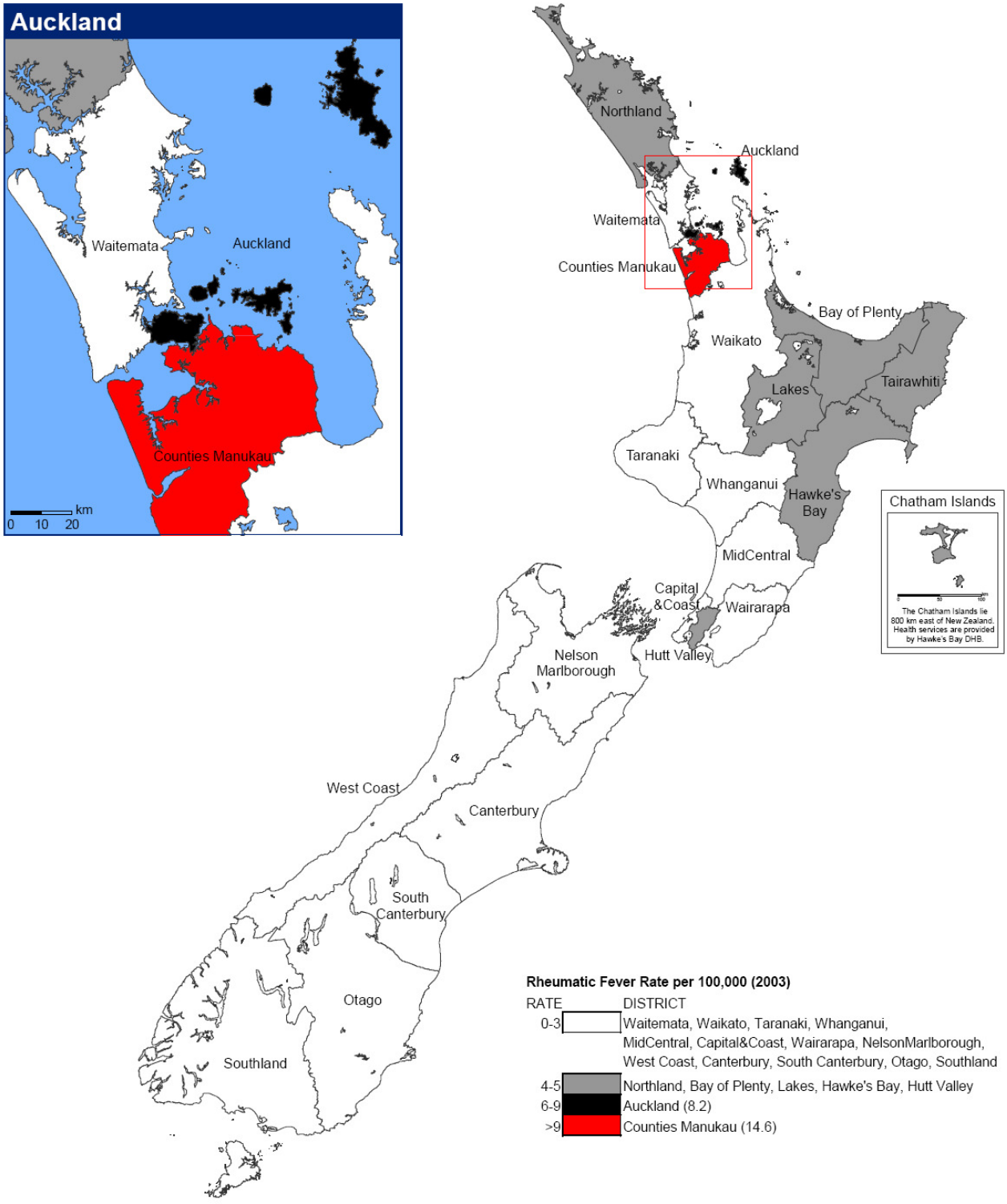
- The revised draft was widely distributed to a range of stakeholders who were then invited to comment.

- The stakeholders reviewed the draft and reached consensus on areas of disagreement.

- Comments were then incorporated to a final draft which was endorsed by the stakeholders.

A full description of the guideline search strategy is available to download from:
http://www.heartfoundation.org.nz

Appendix 2: Rheumatic fever incidence in New Zealand per District Health Board



Source: Public Health Intelligence, Ministry of Health. June 2007

Appendix 3: Areas of New Zealand with high incidences of rheumatic fever

Table 7. Areas of New Zealand with High Incidences of Rheumatic Fever

LOWER SOCIOECONOMIC REGIONS WITHIN:
Northland
Auckland
Waikato
Bay of Plenty/Rotorua
Gisborne
Hawke's Bay
Wellington area

Appendix 4: Incidence of ARF in children and adolescents in studies published since 1990

Table 8: Incidence of ARF in Children and Adolescents in Studies Published Since 1990 (after Carapetis)

STUDY	PLACE	YEAR	POPULATION SUB-GROUP	AGE (YEARS)	ARF INCIDENCE (PER 100 000 PER YEAR)
Cernay J et al. Incidence of rheumatic fever in Slovakia during the last 20 years. Cesk Pediatr. 1993; 48: 79-83	Slovenia	1990-91		0-14	0.7
Lopez R. RF/RHD: comprehensive programme for prevention. Pinar de Rio, Cuba, 1986-96 (primary and secondary prevention). Havana: University of Cuba, 2000	Cuba	1996		5-14	2.7
Noah PK. Trends in acute rheumatic fever: the Barbados experience. J Trop Pediatr. 1994; 40: 94-96	Barbados	1986-90		0-19	8
Lennon D. Rheumatic fever, a preventable disease? The New Zealand experience. In: Martin DR, Tagg JR, eds. Streptococci and streptococcal diseases; entering the new millennium. Porirua: Institute of Environmental Science and Research. 2000: 503-512	New Zealand	1982-97	European descent	5-15	<10
Kermani S, Berah H. La situation epidemiologique du RAA en Algerie depuis 1990. Algiers: Algerian Ministry of Health, Department of Epidemiology (National Program for the Prevention and Control of RF), 2001	Algeria	1997-2000		4-19	11.1 (1997) 6.2 (2000)
Eltohami EA et al. Acute rheumatic fever in an Arabian Gulf country: effect of climate, advantageous socioeconomic conditions, and access to medical care. Angiology. 1997; 48: 481-489	Qatar	1984-94		4-14	11.2
Eshel G et al. Chorea as a manifestation of rheumatic fever: a 30-year survey (1960-90). Eur J Pediatr. 1993; 152: 645-646	Israel	1980-90		5-15	15.5
Carp C. WHO/WHF/UNESCO joint consultation on RF/RHD prevention: A progress report of activities for Romania. Bucharest: Illescu Institute of Cardiology, 1999: 1-12	Romania	1999		5-15	16.5
Baker M et al. The comparative epidemiology of post streptococcal diseases in New Zealand: acute rheumatic fever and acute glomerulonephritis. In: Streptococci and streptococcal diseases: entering the new millennium. Porirua: Institute of Environmental Science and Research. 2000: 545-547	New Zealand	1988-97	All	5-14	16.7
Folomeeva OM, Benevolenskaia LI. Rheumatism in the Russian Federation: statistic and reality. Vesn Ross akad Med Nauk. 1996; 11: 21-24	Russia	1994		'children'	18
Omar A. Pattern of acute rheumatic fever in a local teaching hospital. Med J Malaysia. 1995; 50: 125-130	Kuala Lumpur	1981-90		'children'	21.2

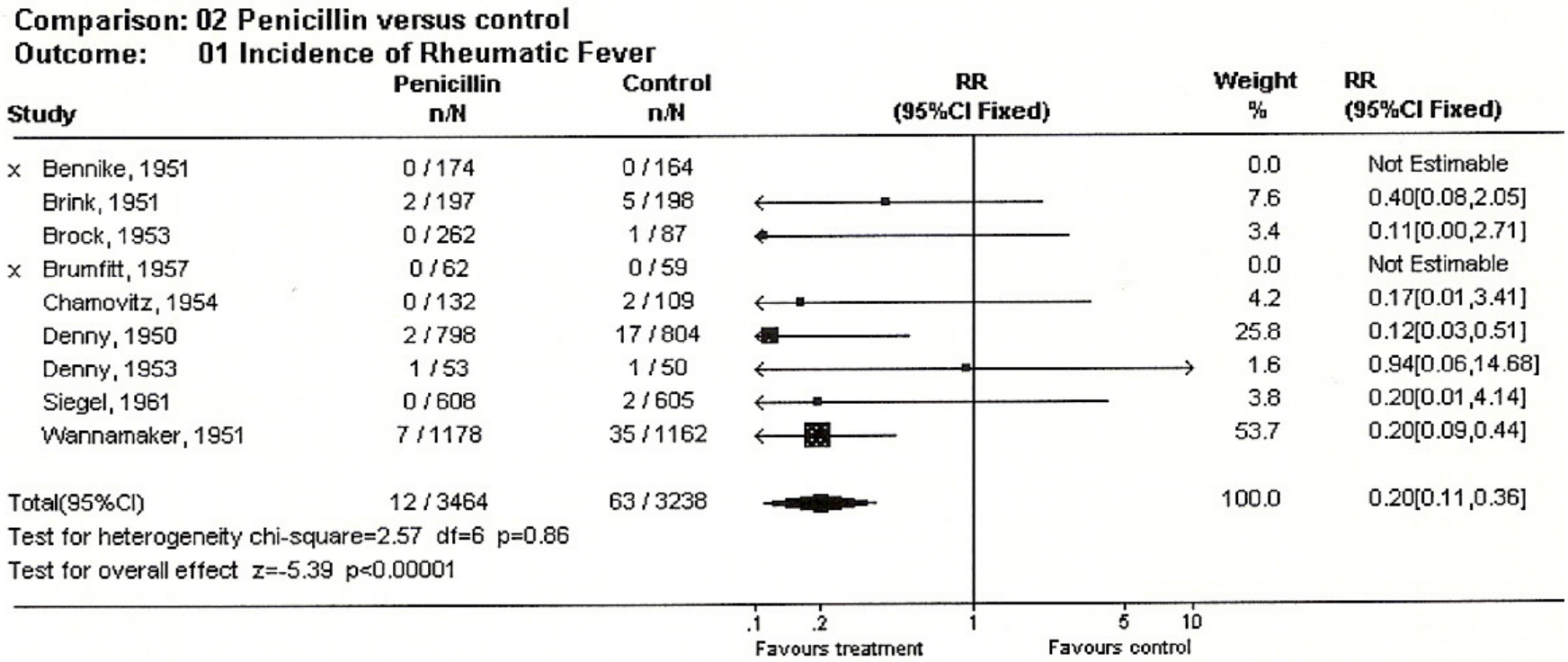
Kechrid A et al. Acute rheumatic fever in Tunisia: serotypes of group A streptococci associated with rheumatic fever. Adv Exp Med Biol. 1997; 418: 121-123	Tunisia	1990		4-14	30
Hasab AA et al. Rheumatic heart disease among Omani school children. Eastern Mediterranean Health J. 1997; 3: 17-23	Oman	1997		6-18	40
Lennon D. Rheumatic fever, a preventable disease? The New Zealand experience. In: Martin DR, Tagg JR, eds. Streptococci and streptococcal diseases; entering the new millennium. Porirua: Institute of Environmental Science and Research. 2000: 503-512	New Zealand	1982-97	Māori	5-15	40-80
Kayemba Kay's KS, Dupuis E. Acute rheumatic fever is still active in Martinique: epidemiological and clinical study of 34 cases observed during the 1987-1991 period. Pediatrie. 1993; 48 : 823-827	Martinique	1987-91		5-14	53
Padmavati S. Rheumatic fever and rheumatic heart disease in India at the turn of the century. Indian Heart J. 2001; 53: 35-37	India	1984-95		5-14	54
Lopez ESL. Fiebre rheumatica en el quinquenio 1994-1999 en dos hospitals en San luis potosi y en Mexico DF. Archivos Cardiologica Mexico. 2001; 71: 127-135	Mexico	1994-99		5-14	70
Lennon D. Rheumatic fever, a preventable disease? The New Zealand experience. In: Martin DR, Tagg JR, eds. Streptococci and streptococcal diseases; entering the new millennium. Porirua: Institute of Environmental Science and Research. 2000: 503-512	New Zealand	1982-97	Pacific Island peoples	5-15	80-100
Australian Institute of Health and Welfare: Field B. Rheumatic heart disease: all but forgotten in Australia except among Aboriginal and Torres Strait Islander peoples. Canberra: AIHW. 2004	Australia	1989-2002	Aboriginal	5-14	245-351
Meira ZMA. Prevalence of rheumatic fever in children from a public high school in Belo Horizonte, Brazil. Arch Brasilian Cardiol. 1995; 65: 331-334	Brazil	1992		10-20	360
Richmond P, Harris L. Rheumatic fever in the Kimberley region of Western Australia. J Trop Pediatr. 1998; 44: 148-152	Australia	1988-92	Aboriginal	5-14	375
Carapetis JR et al. Cumulative incidence of rheumatic fever in an endemic region: a guide to the susceptibility of the population? Epidemiol Infect. 2000; 124: 239-244			Aboriginal	5-14	508

Source: Adapted from Table 1. Reprinted from The Lancet. Vol 366. Carapetis JR et al. Acute Rheumatic Fever, 155-168. Copyright 2007, with permission from Elsevier.[89]

United States statistics: in the United States in 1977, the crude death rate from rheumatic fever was less than 1 per 100,000 of the population. (from figure 7[90])

Appendix 5: Forest plot of penicillin trial sizes

Figure 4. Forest Plot of Penicillin Trial Sizes



Source: Robertson KA et al. Antibiotics for the primary prevention of acute rheumatic fever: a meta-analysis. BMC Cardiovasc Disord. 2005 5: 1-9.[18]

Appendix 6: Randomised controlled trials of penicillin to prevent rheumatic fever

Table 9. Randomised Controlled Trials of Penicillin to Prevent Rheumatic Fever

STUDY	STUDY TYPE RANDOMISATION & CONCEALMENT OF TREATMENT ALLOCATION PROBLEMS	PARTICIPANTS & PLACE	INTERVENTION	EFFECT SIZE	% RANDOMISED
Bennike T. 1951[91]	Quasi-randomised. Inadequate concealment of treatment	349 admitted to hospital with ordinary acute tonsillitis, phlegmonous tonsillitis or ulcerative tonsillitis	1. Penicillin: IM 300,000 U/day for 6 days (adults) 2. Control: symptomatic treatment	Not estimable	88%
Brink WR et al. 1951[92]	Quasi-randomised. No concealment of treatment	475 males, aged 17-21, admitted to U.S. military hospital with respiratory symptoms or fever with exudate on tonsils or pharyngeal mucosa	1. Procaine penicillin G: IM 300,000 U/day for 4 days 2. Aureomycin: avg. 2g/day orally for 4 days 3. Control: no treatment	RR=0.29 (CI, 0.06-1.46)	Unknown
Brock L, Siegel AC. 1953[93]	Randomised. No concealment of treatment	349 males admitted to U.S. military hospital with exudative pharyngitis and laboratory-confirmed GAS	1. Procaine penicillin G: IM 600,000 U/day for 3 days	RR=0.11 (CI, 0.00-2.71)	Unknown
Brumfitt W, Slater JD. 1957[94]	Quasi-randomised. No concealment of treatment	121 males, aged 18-21, admitted to U.S. military hospital with sore throat, pyrexia and no clinical evidence of more generalised disease of which sore throat may have been coincident feature	1. Combination of procaine penicillin G: IM 600,000 U/day for 4 days and crystalline penicillin: IM 200,000 U/day for 4 days 2. Control: symptomatic treatment	Not estimable	Unknown
Chamovitz R et al. 1954[95]	Quasi-randomised. Unknown whether treatment allocation concealed	241 males admitted to U.S. military hospital with exudative tonsillitis or pharyngitis	1. DBED penicillin: IM 1,200,000 U 2. Control: IM placebo	RR=0.17 (CI, 0.01-3.41)	Unknown
Denny FW et al. 1950[17]	Quasi-randomised. No concealment of treatment	1,602 males admitted to U.S. military hospital with respiratory symptoms and observed exudate on the tonsils or pharyngeal wall	1. Penicillin G: IM 200,000 U/day for 3 days of 300,000 U/day for 4 days 2. Control: symptomatic treatment	RR=0.12 (CI, 0.03-0.50)	81.8%

Denny FW et al. 1953[96]	Randomised. Unknown whether treatment allocation concealed	207 males admitted to U.S. military hospital with suspected streptococcal infection based on presence of exudate on tonsils or pharynx and total leukocyte count exceeding 10,000	1. Crystalline procaine penicillin: IM 600,000 U/day for 5 days 2. Crystalline aureomycin avg. 2g/day for 5 days 3. Crystalline terramycin: avg. 2g/day for 5 days 4. Control: oral lactose placebo for 5 days	RR=0.63 (CI, 0.34-1.17)	Unknown
Houser HB et al. 1953[97]	Quasi-randomised. No concealment of treatment	2,044 males, ages 17-21, admitted to U.S. military hospital with exudative lesions on their tonsils or pharynx	1. Aureomycin: avg. 2g/day for avg. 5 days	RR=0.63 (CI, 0.34-1.17)	88%
Lennon D et al. 2008[24] submitted.	Group randomised. Schools randomised to intervention arm with sore throat clinics or no clinics. Under-powered, small numbers of cases of rheumatic fever. No concealment of treatment. High roll turnover at schools. Some had 100% student turnover in a single year. Does not take into account possible missed cases due to moving out of zone, truancy etc.	1998-2001. 24,000 school-attending children, in Auckland, New Zealand. 53 primary & secondary schools in South Auckland with a 70% or greater proportion of Māori and or Pacific Island students. Children's age 5-18 years. 27 schools (12,000 children) randomised to have clinics, 26 schools (12,000 children) were controls	Trained lay workers visited class rooms every day to encourage children with sore throats to report for a throat swab. Schools in treatment arm educated about importance of sore throats as precursor of ARF. GAS pharyngitis was treated with 250-500mg PO bd penicillin V (depending on weight). 24% reduction in rheumatic fever from the programme. Using 1992 Jones criteria: 26 definite cases in schools with sore throat clinics, 33 definite cases in control schools. Using 1965 Jones criteria, there were 29 cases of rheumatic fever in the control schools, per 31,531 person years and 24 cases of rheumatic fever in the programme schools (32,254 person years)	RR=0.67 (95% CI, 0.48-0.93), estimated by writing group, using the 1965 Jones criteria	Average of 83% (range 65-99%) of eligible students at each school consented to participate
Siegel A et al. 1961[98]	Quasi-randomised. No concealment of treatment	1,213 children, aged 3-16, with uncomplicated acute upper-respiratory tract disease and laboratory-confirmed GAS infection	1. Benzathine penicillin G: IM 600,000 U 2. Control: symptomatic treatment	RR=0.20 (CI, 0.01-4.14)	95%
Wanna-maker L et al. 1951[99]	Quasi-randomised. No concealment of treatment	2,340 males, aged 17-20, admitted to U.S. military hospital with respiratory symptoms and exudative lesions on the tonsils or oropharynx, or oral temp >100°F	1. Procaine penicillin G: IM various dosages (1,200,000 U over 4 days; 600,000 U over 3 days; 600,000 U single dose) 2. Control: no specific treatment	RR=0.21 (CI, 0.09-0.47)	83.3%

Source: Modified from Robertson KA et al. 2005,[18] with addition of Lennon data.

Appendix 7: Studies on seasonal prophylaxis for pharyngitis

Table 10. Studies on Seasonal Prophylaxis for Pharyngitis

STUDY	PATIENTS	INTERVENTION	OUTCOME IN CONTROLS	OUTCOME IN TREATMENT GROUP
Aksit S et al. 1998[100]	160 children aged 4-11 years, in Turkey, who had 2+ episodes of GAS pharyngitis during 4 month period in 1995	RCT. Treatment group: 80 patients given IM benzathine penicillin G every 3 weeks. 80 controls not given any medication. 4 month observation period for results	244 episodes of GAS pharyngitis. 5 control patients excluded for poor compliance	16 episodes of GAS pharyngitis. 2 patients excluded for poor compliance
Mora R et al. 2003[101]	180 children aged 4-14 years, who had 3+ episodes of tonsillitis in the previous year	RCT. Treatment group: 90 patients given cefpodoxime 100mg PO bd for 6 days a month for 6 months. 90 control patients given placebo medication at the same dosage and duration. Patients followed for 12 months	At 12 months: 86.4 episodes of tonsillopharyngitis and 86.4 episodes of non-complete eradication or re-infection with GAS (on pharyngeal swab)	At 12 months: 11.6 episodes of tonsillopharyngitis and 20 episodes of non-complete eradication or re-infection with GAS (on pharyngeal swab)

Appendix 8: Isolation of "pyodermal" GAS from throat in ARF

Table 11. Isolation of "Pyodermal" GAS from Throat in ARF

STUDY	TYPE	PLACE	INTERVEN-TION	OUTCOMES & CONCLUSIONS
Berrios X et al. 1986[11]	Observational study with control group	Santiago, Chile consecutive hospital-based series ARF n=104 APSGN n=84 Control n=71 (for ARF) Family contacts n=918	N/A	ARF and APSGN same seasonal trends (autumn peak). ARF cases, hospital controls and families had similar pharyngeal GAS. APSGN cases and families had higher GAS positivity in pharynx than ARF. No GAS pyoderma in ARF cases; rare in families of ARF cases. 10.7% of APSGN cases
Bisno AL et al. 1970[25]	Observational study	Tennessee, USA	N/A	Different seasons of ARF and APSGN mirrored by seasons of GAS pharyngitis and pyoderma respectively
Lennon D et al. 1988[8]	Observational study	Auckland, New Zealand	N/A	Different seasons of ARF and APSGN approx similar (autumn peak)
Lennon D et al. 2008[102]	Randomised controlled trial	Auckland, New Zealand	Sore throat clinics	Impetigo/cellulitis seen in 3/59 ARF cases in addition to pharyngitis
Martin DR et al. 1994[9]	Observational study	Auckland, New Zealand	N/A	ARF was associated with M6 (n=1), 53 (n=4), 55 (n=1), 66 (n=1), 89 (n=3). $p \leq 0.05$. These 'M' types were also commonly found in pyoderma in this study. Note: M12 ARF n=2 APSGN n=1 M4 ARF n=1 APSGN n=1
McDonald MI et al. 2006[22]	Observational study	Rural Australia	N/A	High rate of pyoderma, rare GAS pharyngitis (high rate of ARF in area). Infrequent data collection points
Popat K et al. 1976[103]	Descriptive	UK	N/A	Infected wound and ARF case (n=1). (T3/13/B3264: T pattern – usu pyodermal strain; has caused ARF also elsewhere)
Potter et al. 1977[23]	Observational study	Trinidad 1964-1970 1969-1970	N/A	Epidemic APSGN and endemic ARF occurring in parallel. Similarly endemic pyoderma and GAS pharyngitis. ARF cases, unlike APSGN cases, rarely have pyoderma
Tewodros et al. 2005[104]	Descriptive	Ethiopia	N/A	1/7 cases of ARF associated with GAS skin infection and not throat isolate. (ST2940) 6/7 cases of ARF found with GAS pharyngeal swab with or without skin isolates

Appendix 9: Studies which have shown associations between M/*emm* types and acute rheumatic fever

Table 12. Studies Which Have Shown Associations between M/*emm* types and Acute Rheumatic Fever

STUDY	TYPE	PLACE	INTERVENTION	OUTCOMES & CONCLUSIONS
Bisno AL et al. 1970[25]	Observational study	Tennessee, USA (PSAGN and ARF occur in same population)	N/A	Most GAS from throats non-typable (87%), i.e. antisera unavailable. No GAS from rheumatic fever cases (n=4)
Berrios X et al. 1986[11]	Observational study with control group	Santiago, Chile Consecutive hospital-based series ARF n=104 APSGN n=84 Control n=71 (for ARF) Family contacts n=918		ARF cases & M types: Cases M1 (n=2) in ARF cases; (n=6) in ARF family contacts M5 (n=3) in ARF cases; (n=1) in families M74 (n=1) in ARF cases; (n=4 pharyngeal, n=1 skin) in families M non-typable (n=2) in ARF cases In addition M types found in ARF families but not cases: M2, 4, 12, 53, 59 (n=1 of each) (M4 also found in APSGN n=1) Summary: M4, 12, 59 & 74 in ARF (and also APSGN patients) and/or families
Kechrid A et al. 1997[105]	Descriptive	Tunisia	N/A	M types, 2,9,11,33 and 49 from throats of ARF patients (M49 nephritogenic in other studies)
Lennon D et al. 1988[8]	Observational study	Auckland, New Zealand	N/A	ARF patients had M53 (n=2), M58 (n=1) serotypes cultured
Lennon D et al. 2008[24]	Randomised controlled trial	Auckland, New Zealand	Sore throat management	*emm*/M58, 74, 75: well supported with appropriate incubation period and raised streptococcal titres. Also *emm*/M76, 92,99 associated with ARF (1 case each) with raised antibody titres but preventable incubation periods
Majeed HA et al. 1986[106]	Descriptive	Kuwait	N/A	ARF and pharyngeal M types: 2 cases with M1, 1 case with M12, 1 case with M-non typable; in families of ARF cases M5 was found on one occasion; non-typable M strains on 4 occasions
Martin DR et al. 1994[9]	Observational study	Auckland, New Zealand	N/A	ARF was associated with M6 (n=1), 53 (n=4), 55 (n=1), 66 (n=1), 89 (n=3) ($p \leq 0.05$). These M types were also community founds in pyoderma in this study Note: M12; ARF n=2 APSGN n=1 M4; ARF n=1 APSGN n=1
Potter E et al. 1977[23]	Observational study	Trinidad	N/A	All throat (n=6) and skin (n=4) GAS isolates associated with ARF cases, non-typable with available anti-sera. M1 from APSGN cases (n=7)

Pruksakorn S et al. 2000[107]	Descriptive	Thailand	N/A	6 isolates from throats of ARF patients M22 (n=1) and M63 (n=2) and 3 new sequence types
Tewodros W, Kronvall G. 2005[104]	Descriptive	Ethiopia	N/A Isolates were pharyngeal (n=2), skin (n=2), both (n=1)	*emm*74 was associated with ARF (n=2) and PSAGN (n=1), also throat (n=6) and skin (n=4). *emm*114.2 was associated with ARF (n=1), throat (n=4), skin (n=1). *emm*18.8 ARF (n=1), throat (n=6) also 3 new sequence types associated with ARF cases (n=3)

Appendix 10: Studies on M/*emm* types associated with APSGN

Table 13. M/*emm* types associated with APSGN

STUDY	TYPE	PLACE	INTERVENTION	OUTCOMES & CONCLUSIONS
Berrios X et al. 1986[11]	Observation study with control group	Santiago, Chile Consecutive hospital-based series ARF n=104 APSGN n=84 Control n=71 (for ARF) Family contacts n=918	N/A	M1, M4, M12, M59, M74 seen in both ARF, APSGN and/or their families
Kechrid A et al. 1997[105]	Descriptive	Tunisia	N/A	M types, 2, 9, 11, 33 and 49 from throats of ARF patients (M49 nephritogenic in other studies)
Martin DR et al. 1994[9]	Observation study	Auckland, New Zealand	N/A	M1, M3, M4, M12, M53, M81 were seen in both APSGN and ARF cases
Potter E et al. 1978[10]	Observation study	Trinidad	N/A	Total absence of nephritogenic strains in ARF patients suggests these strains cannot cause ARF. The converse is less clear. "M41" may cause both APSGN and ARF
Tewodros et al. 2006[104]	Descriptive	Ethiopia	N/A	In 2 instances isolates of the same *emm* type were found in APSGN and ARF cases *emm*74: APSGN (n=1), ARF (n=2) and new sequence type *st*D62.0: ARF (n=1), APSGN (n=1)

Appendix 11: Comparison of studies relating D8/17 expression and rheumatic fever/rheumatic heart disease

Table 14. Comparison of Studies Relating D8/17 Expression and rheumatic fever/RHD.

STUDY	RHD OR RHEUMATIC FEVER/ CONTROLS (NUMBER)	METHOD	CUT OFF (% D8/17 POSITIVE B CELLS)	PATIENTS POSITIVE FOR D8/17 (%)	CONTROLS POSITIVE FOR D8/17 (%)
Feldman B et al. 1993[47] Canada	4**/-	PBMC's fluorescence microscopy	>20	100	-
Ganguly NK et al. 1992[109] India	90/50	B cells fluorescence microscopy	>40	66	14
Gibofsky A et al. 1991[110] Russia	82/78	Not described*	1SD above mean for controls	90-96	5
Gibofsky A et al. 1991[110] Mexico	39/72	Not described*	1SD above mean for controls	89	8
Gibofsky A et al. 1991[110] Chile	50/50	Not described*	1SD above mean for controls	90	16
Harel L et al. 2002[111] Israel	22/9	Whole blood flow cytometry	>7.55	90.2	0
Harrington Z et al. 2006[48] Australia	41/20/45****	Whole blood fluorescence microscopy	22.1	92.7	Relatives 50 Controls 6.6
Herdy GV et al. 1992[112] USA	10/14	Whole blood fluorescence	>12	90	0
Kaur S et al. 1998[113]	24/-	B cells flow cytometry	>10	71	-
India	140/50	Whole blood fluorescence microscopy	>10	65***	14
Khanna AK et al. 1989[46] USA and West Indies	84/76	PBMC's fluorescence microscopy	>12	99	14
Taneja V et al. 1989[114] India	54/32	B cells fluorescence microscopy	Not specified	63	13

Source: Modified from Harrington 2005.[108]

* These results described in Gibofsky are not referenced and presumably not published
** 2 patients with chorea and 2 past rheumatic fever (no details given)
*** Calculated as mean value between rheumatic fever and RHD patients
**** Rheumatic fever/RHD patients/first and second degree relatives/controls, percentages derived from published data

Appendix 12: Studies listing sore throat episodes and rheumatic fever

Table 15. Studies Listing Sore Throat Episodes and Rheumatic Fever

STUDY	PLACE	STUDY GROUP	NUMBER OF SORE THROATS	RESULTS	RR OF RHEUMATIC FEVER WITH THE FREQUENT SORE THROATS	P VALUE	CI
Adanja B et al. 1988[49]	Yugoslavia	Case-control. 148 patients with first attack of rheumatic fever, compared to 444 controls from the same neighbourhood	'Frequent' sore throat (not defined)	52.0% of rheumatic fever patients had a history of frequent sore throat, compared to 34.2% of controls	2.01	p=0.00018	1.41-2.89 (% CI un-stated)
Lennon D et al. 2008[24] submitted.	South Auckland, New Zealand	RCT. 24,000 school-children, half in treatment schools (with GAS pharyngitis clinics), half controls (no school clinics), followed for 4 years	In 1998, 50 throat swabs in children with pharyngitis were positive for GAS per 100 children per school year (in 24 schools). In children diagnosed with rheumatic fever, rate of sore throats was 1.13 per year. In children without rheumatic fever, rate of sore throats was 1.43 per year	Incidence of ARF using 1965 Jones criteria. In controls: 29 cases of rheumatic fever per 31,531 person years. In intervention schools, 24 cases of rheumatic fever per 32,254 person years	Not estimated	Not estimated	Not estimated
Vlajinac H et al. 1989[50]	Yugoslavia	Case control. Same study as Adanja above. 148 patients with first attack of rheumatic fever, diagnosed in 1982, compared to 444 controls matched for age/sex/place of residence	Frequent sore throats: 2 or more per year. Without sore throat meant a maximum of one sore throat per year	Exact numbers not given. Table 3 in the study gives combined results for frequent sore throat and other variables	RR=2.08	p<0.001	95% CI, 1.42-3.03
Vlajinac H et al. 1991[51]	Yugoslavia	Case-control. 148 cases with a first attack of rheumatic fever satisfying Jones criteria who were home at time of survey. Three healthy controls matched for each rheumatic fever patient	2 or more sore throats per year	Patients with 2 or more sore throats per year were 2.26 times more likely to get rheumatic fever than patients who had one or less	2.26	p=0.000	95% CI, 1.49-3.39

Appendix 13: Schools and community/school based sore throat intervention studies in meta-analysis

Table 16. School and Community/School Based Sore Throat Intervention Studies in Meta-analysis (n=6)

STUDY	TYPE	POPULATION AND TYPE OF INTERVENTION.	RF CRITERIA (IF STATED) & RF OUTCOME	ESTIMABLE EFFECT
Chun LJT et al. 1984[54]	Observational study. No blinding, no obvious randomisation	14-18 year old school children, Hawaii, 1976-80. Rheumatic fever clinic schools: 63,484 children, control schools: 48,740 children. Children with URTI's reported, and throats swabbed, if GAS positive, were referred to usual doctor	Modified Jones 1965. Rheumatic fever clinic schools: 36 cases of rheumatic fever in 63,484 children over 4 years, rate 14.2 annual incidences per 100,000 children enrolled. Control schools: 29 cases of rheumatic fever in 48,740 children over 4 years, rate 12.3 annual incidence per 100,000 (adjusted for the proportion of children receiving welfare, unclear how this was done). Program had little impact on rheumatic fever. Overall results, calculated by writing group: **Control group**: 29 cases of rheumatic fever per 1,949,690 person years. **Intervention:** 36 cases of rheumatic fever per 353,936 person years	RR=0.68 (95% CI, 0.42-1.12) calculated by writing group
Coulehan JL et al. 1982[55]	Observational study. No blinding or randomisation	1975-79, 51 months, on Navajo reservation in Arizona, Utah, New Mexico, involving school children aged 5-16 years. Throat cultures taken from symptomatic children, and in most schools throat swabs taken 1-9 times per year regardless of symptoms. Treated if GAS positive	1965 Jones criteria. 30 cases of ARF diagnosed, 25 initial, 5 recurrences. In 29 of those cases the school was determined: 7/29 attended intervention schools, 22/29 of other ARF patients were in uncovered schools. Less frequent ARF in participating schools	RR=0.39 (95% CI, 0.1-0.94) calculated by writing group
Lennon D et al. 2009[56] in press. Lennon D. 2002[115]	Randomised controlled trial. No blinding	1998-2001, South Auckland, New Zealand. 24,000 school children, attending primary and secondary schools (5-18 years), with 70% or greater proportion of Maori and/or Pacific students. Approx.12,000 in clinic schools, approx 12,000 in control schools. **Intervention:** children with sore throats swabbed in schools. If GAS positive, treatment po penicillin observed therapy	Statistics given using different rheumatic fever criteria. Using 1965 Jones criteria, RR, 29 cases of rheumatic fever in controls per 31,531 person years, and 24 cases of rheumatic fever in intervention schools, per 32,254 person years	RR=0.67 (95% CI, 0.48-0.93) estimated by writing group (using 1965 Jones)
Phibbs B.1975[53]	Before and after intervention	Wyoming USA, 1957-59 and Papago Indian Health Service, Arizona 1970-82. Classroom based intervention, teachers asked if sore	In 21 counties of Wyoming with control program: 1 case of rheumatic fever per 24,230 people. In 2 counties without	RR=0.41 (95% CI, 0.17-1.0) calculated by

	study. No mention of blinding or randomisation	throats then swabbed. Also inspected and cultured if throat inflammation once a week. GAS positive children sent home with note to commence treatment	program, 1 case of rheumatic fever per 6,250 people observed. Unclear which years. Before & after statistics for Papago Indian Health Service, Arizona (all ages). Cases of rheumatic fever verified by cardiologist: 29 cases of rheumatic fever in 31,200 person years (4 x 7,800 = 31,200) and after group: 6 cases of rheumatic fever in 15,600 person years (2 x 7,800 = 15,600: calculated by writing group)	writing group
Gordis L. 1973[19]	Before and after intervention study. No blinding or randomisation	Inner city Baltimore comprehensive care tracts. Community clinics for primary care. No mention of actual sore throat management	Diagnosis of ARF from medical record search (ICD 8th revision 390, 391, 392 1968-70) (ICD 7th revision 400, 401, 4092 1960-64) without a program 51/38,022 (26.8/100,000); with a program 11/34,609 (10.6/100,000)	RR=0.24 (95% CI, 0.12-0.45) calculated by writing group
Nordet P. 2008[57]	Before/after intervention (observational study). No blinding or randomisation	1986-96, Pinar del Rio province, Cuba. Total population 721,800 in 1996. Primary and secondary prevention program of RF/RHD. Involved training personnel, health education, dissemination of information, community involvement and epidemiological surveillance. Included RF/RHD registers, pamphlets, posters and special media broadcasts. Primary prevention emphasis was on the importance of early and correct treatment of sore throats/streptococcal pharyngitis. Cross-sectional studies on prevalence of RF/RHD were done at start and end, in 1985 and 1996. Cross-sectional studies of all schools using "multi-stratified random-sample method" and included all school children 5-15 years. After the program ended, viability assessed between 1997-2002	Not stated. Noted that echocardiography (no criteria stated) used for diagnosis. In 5-14 year olds, first attacks of rheumatic fever in 1986 28/119,600 (23.4/100,000). In 2002: 2/104375 (1.9/100,000). Rate of first attacks of RF/RHD in 5-25 year olds 34/279,400 (12.2/100,000). In 2002: 2/207,815 (1.0/100,000	RR=0.08 (95%CI,0.02, 0.34) calculated by writing group

Appendix 14: Schools and community/school based sore throat intervention studies in meta-analysis: studies not meeting criteria

Table 17. School and Community/School Based Sore Throat Intervention Studies in Meta-analysis (n=6)

STUDY	TYPE	POPULATION AND TYPEOF INTERVENTION	RF CRITERIA (IF STATED) & RF OUTCOME	ESTIMABLE EFFECT
Atha M et al. 1982[116]	Interventional before and after trial. No blinding or randomisation	13,000 Papago Indians, south Western Arizona, USA, 1972-78. Monthly swabs for GAS. Treatment in schools, homes and clinics. Also treatment asymptomatic patients. IM and PO penicillin (allergy: erythromycin)	Drop in rheumatic fever: 1970-71: 9.5 per 10,000 new cases. After study began 1980-81 was third consecutive year without a new case of rheumatic fever	Not estimable
Bender TR et al. 1972[117]	Interventional study with a control group. No blinding, no obvious randomisation	2 remote Eskimo villages in Alaska, Jan – May 1971. Nunaputchuk: 332 people (129 school-aged). Stebbins: 239 people (61 elementary school aged). GAS positive patients treatment with IM penicillin or erythromycin.	No cases of rheumatic fever in either village	Not estimable
Brant LJ et al. 1986[118]	Interventional study with a control group. No blinding, no obvious randomisation	Alaska 1972-76, USA. 2,500 people in intervention villages, 2,350 in control villages. Complex protocol. Patients with symptoms of GAS pharyngitis swabbed and treated, and in high-intensity groups, children were swabbed frequently regardless of symptoms. Treatment IM penicillin if GAS positive	Revised Jones. **Controls:** 4 cases of rheumatic fever/ 2,350 patients. **Intervention:** no cases of rheumatic fever /2,500 people	Not estimable
Chobin N et al. 1975[119]	Observational study. No obvious blinding or randomisation	3 year pilot project in 16 schools, then spread to over 450 schools in New Jersey USA. Years unclear. Study published 1975. Daily, students with URTI including sore throat reported for throat swab, referred to own doctor for treatment if GAS positive	No data on rheumatic outcomes given. (GAS isolation was reduced)	Not estimable
Cornfeld D et al. 1961[120]	Observational study. No blinding or randomisation. No controls	Oct 1955 – May 1959, 64 children followed, aged 6-12 yrs, attending school of 420 pupils. Throat cultures taken from school or home if a child in the study had symptoms of streptococcal illness	No cases of rheumatic fever	Not estimable
Davies AM et al. 1968[121]	Observational Study. No blinding or randomisation	821 Jerusalem school children aged 8-11 years, followed for the school year 1965-66. School selected to represent different economic levels. School nurse visited each class on alternate days and listed absentees. Homes were then visited and if the child had signs of sore throat or upper respiratory infection, a throat swab was taken. A further sub-group of 190 children was swabbed fortnightly, regardless of symptoms	No cases of rheumatic fever (rates of streptococcal pharyngitis and carriage recorded)	Not estimable

Davies AM et al. 1973[122]	Observational. No information regarding blinding or randomisation	7,500 school children, initially aged 7-11 years in Jerusalem, Israel. Followed through a school health service, prospectively for 3 years. Dates not given, would be before 1973 publication. 40% chosen as sample group. Throat swabs were taken by public health nurses for symptoms of upper respiratory infections (9,735 episodes). Sample group had sore throats treated by research team. Not stated. Remaining 60% were referred to their own family doctors with the laboratory report	Not stated. During the 3 years, 32 possible or probable cases of rheumatic fever (definite in 16). Not clear if this was in total or from just the control group alone	Not estimable
Jackson H. 1976[123]	Intervention, before and after study. No information about blinding or randomisation	Morgan county, Colorado, 1970-74. Difficult to interpret statistics. Four different school programs, involving throat swabs, some in symptomatic, and some in asymptomatic patients. Students with GAS were excluded from school until they began antibiotics	No mention of rheumatic fever cases. (Streptococcal prevalence was reduced)	Not estimable
Lin SM et al. 2008[124]	Interventional trial. Randomised. No blinding	Cluster sampling of school children in southern China. 201 treatment group, 193 controls, ages 9-12 years in 1992-93. Throat cultures taken from all monthly. Daily questionnaires on pharyngitis symptoms done by parents. Swabs taken when clinical findings. Random clinical checks on approx 50 patients per week. Pharyngitis with GAS positive throat swab: treatment group patients received IM benzathine penicillin G (or 10 days PO erythromycin if allergic); controls referred to own doctor	No rheumatic fever cases (result was fewer cases of GAS pharyngitis in controls)	Not estimable
Mooring PK.1966[125]	Observational	Douglas County, Nebraska, USA. Primary and secondary RF prevention program planned to be initiated. Throat swabs planned to be taken and result phoned to referring physician or dentist if positive for GAS	No rheumatic fever cases	Not estimable
Nicolle LE et al. 1990[126]	Intervention study. Some randomisation between antibiotics, but not an RCT	No numbers or time frame given. Two areas studied: (1): Rankin Inlet, school children 60% Inuit, 40% Caucasian. (2): St Therese Point: school children from a native Indian community. **Intervention:** children with pharyngitis or skin lesions swabbed and if GAS positive, were asked to consent to randomization of IM or PO penicillin treatment. Erythromycin if allergic. M and T typing determined if same GAS strain present: treatment failed	No mention of rheumatic fever (Pharyngitis numbers given)	Not estimable
Zimmerman R et al.1971[127]	Intervention trial. No blinding or randomisation	1969-70. **Intervention:** two schools of approx 250 children, in Mosca and Hooper, in Colorado, USA, **Control school:** Blanca, Colorado, with 275 students. **Intervention:** students asked daily if they had sore throat; if so, swabs were taken. Also, asymptomatic children had throat swabs periodically. Control schools: throat cultures taken from randomly selected students	Rheumatic fever cases not stated. (GAS positive swabs reduced in intervention group)	Not estimable

Appendix 15: Studies on other community/mixed community and school studies for rheumatic fever prevention

Table 18. Other Community/Mixed Community and School Studies for Rheumatic Fever Prevention

Note: for GATE study quality tool, see: http://www.health.auckland.ac.nz/population-health/epidemiology-biostats/epiq/ and click on the Intervention Studies CAT link. If there were only very few details, such as no details on rheumatic fever cases, the studies were not formally assessed through the GATE framework.
Effect size: where an effect size was not given, if there were no cases of rheumatic fever in either the control or programme group, the effect was not calculated by the writing group.

STUDY	STUDY TYPE & QUALITY (USING GATE), PROBLEMS	NO. OF PARTICIPANTS, WHERE & WHEN	INTERVENTION	RF DIAGNOSIS CRITERIA	OUTCOMES AND CONCLUSIONS	EFFECT SIZE
Atha M et al. 1982[116]	Intervention before and after trial. No blinding or randomisation. Not able to definitively diagnose streptococcal infection, as no serial bloods for anti streptococcal antibodies were taken. May have over-treated some patients, as asymptomatic patients with positive GAS throat cultures were treated. They could have had true GAS infection or been carriers, but were treated with antibiotics as they were in a high-rheumatic fever risk population. **Study quality:** mixed, major outcomes measured	13,000 Papago Indians, living in south western Arizona. Programme run 1972-78	18 Indian reservation schools had monthly surveillance, and all positive GAS throat culture patients were screened again after the initial culture. If re-culture was positive, staff went to the child's home and cultured the family and regular contacts. Children not at school were seen at the Indian Health Service clinic and cultures taken where indicated. Staff members arranged transport to the clinic if required. Tribe members were trained to take swabs, transport them and process and recognise streptococci. Results were reviewed monthly by a cardiac consultant. GAS was diagnosed presumptively where any signs and symptoms of pharyngitis and a GAS positive throat culture were present. There was a mass education campaign. Of those with GAS positive throat cultures, 72-91% were treated. Diagnoses were made in clinics, schools and homes. Treatment was with either: 1.2 IU of benzathine penicillin IM, or 250mg penicillin PO 3 times daily for 10 days, or if allergic to penicillin, erythromycin 250mg PO 3 times per day for 10 days	Not stated. Suspicious cases which might be rheumatic fever were hospitalised and reviewed by the cardiac consultant	A drop in rheumatic fever was found. Before the trial, in 1970-71 there were 9.5 per 10,000 new cases of rheumatic fever. After the study began, 1980-81 was the third consecutive year without a new case of rheumatic fever	Not estimable

Bender TR et al. 1972[117]	Interventional study, with a control group. One village had streptococcal throats treated, the other did not. No blinding. Treatment delays occurred from sending cultures away to the lab. Too short a time period to show any cases of rheumatic fever and a small population involved (under-powered study). No bloods were taken to identify carriers; asymptomatic patients with positive cultures were treated. Any adverse drug reactions were not documented. Antibiotic doses were not stated and may not have been standardised. No obvious randomisation. **Study quality:** mixed. Too short a timeframe and too few participants to give a meaningful result	2 remote Eskimo villages in Alaska, in Jan-May 1971. Nunapitchuk had 332 persons (129 school aged children); while the other village, Stebbins, had 239 persons (61 elementary school aged children)	**Intervention Village (Nuna-Pitchuk):** All patients positive for GAS were treated with either long-acting penicillin or erythromycin. **Control Village (Stebbins):** GAS positive patients were not treated. Throat cultures were taken from all age groups at the start and end of the study, from patients with sore throats presenting to the health aide and also a rotating sample of 25% of school children every week. In the intervention village, Nanapitchuk, there was an attempt to treat everyone in the village who was GAS positive and there were two epidemics of GAS in the 4 month period. Swabs were preserved in silica gel and sent to Colorado for testing, they were received there 3-15 days after being sent. **Bloods:** Group A and type specific antibodies (TSA) were taken in January and May from school children, as well as from as many adults as possible in January and in May from all adults who attended general clinics. **Urine:** Specimens were collected from children in the intervention village and dipsticked for blood or albumin, due to the possible epidemic situation. **Nasal washings:** Were taken from all school children in January and May for immunoglobins A and G and type specific antibodies	Not stated.	No cases of rheumatic fever were found in either village. One case of glomerulonephritis was found in one child of 96 tested in the intervention village (Nunapitchuk). The authors postulate that if rheumatic fever frequency is assumed to be 3% for a streptococcal epidemic, then treating the GAS positives, together with the mass prophylaxis campaign, may have prevented several cases of rheumatic fever. They found that patient reporting of pharyngitis was not helpful in detecting GAS-only. 10 patients in the intervention village and 6 in the control village were cultured by health aides because they had complained of sore throats. Higher levels of antibody to group A polysaccharides (reflecting previous GAS infections) were found than had been previously reported by others elsewhere	Not estimable. No cases of RF in either village

Brant L et al. 1986[118]	Interventional study, with control group. No obvious randomisation, no blinding. Patients divided into programme and control villages. **Study quality:** mixed	Alaska, 1972-76. 2,500 people in intervention villages. 2,350 in control villages	Community health aides collected swabs for throat culture in clinic, from patients with symptoms of streptococcal pharyngitis. Children in 9 villages were divided into 4 groups; specimens were collected from one group each week, regardless of symptoms (full intensity study). Extra villages were added in year 3 (12 in total), these were also divided into 4 groups and had a group swabbed every 2 weeks (reduced intensity). Also in the third year of the study, 3 villages changed from the full to the reduced intensity arm. Treated with benzathine penicillin if GAS positive throat swab	Revised Jones	**Intervention villages:** 0/2,500 cases of rheumatic fever between 1972-76. **Control villages:** 4/2,350 cases of rheumatic fever between 1972-76. Small numbers of cases of rheumatic fever and participants	Not estimable
Phibbs B. 1975[53]	Before and after intervention study. Mention is made of a control county without the scheme. Serial bloods not taken to identify true infection, instead a presumptive diagnosis of GAS pharyngitis was made on the basis of signs or symptoms of pharyngitis, accompanied by GAS positive throat swab. Antibiotic regime is not specified but in a previous article Phibbs[128] outlines the regime used then. No mention of blinding or randomisation. **Study quality:** mixed, difficult to interpret information from	Natrona county, then the scheme spread to 21 counties in Wyoming, 1954-69. The ages of children and exact years are unclear	Each morning in every classroom, teachers asked if children had any symptoms of a cold or a sore throat, those with symptoms were examined and swabbed. In addition, each child was inspected once a week for pharyngeal inflammation and was cultured if there was any sign of this. Children with GAS positive cultures were sent home with a note, stating that treatment must be implemented or a negative culture demonstrated, before the child could return to school. Volunteers were trained to inspect and swab throats	Not stated	Isolation of GAS from throat swabs fell from 10-20% at the beginning of each school year to below 5% before the end of the year. In the 21 counties of Wyoming using a streptococcal control programme, there was one case of rheumatic fever per 24,230 people observed, and in two counties without a streptococcal programme, there was one case of rheumatic fever per 6,250 people observed. Unclear over which years. Before: 29 cases of rheumatic fever in 31,200 person years (4 x 7,800 = 31,200) After: 6 cases of rheumatic fever in 15,600 person years (2 x 7,800 = 15,600) (calculated by writing group)	RR=0.41, 95% CI, 0.17-1.00 (calculated by writing group)

Appendix 16: School-based GAS pharyngitis/rheumatic fever prevention programmes

Table 19. School-based GAS Pharyngitis/Rheumatic Fever Prevention Programmes

Note: for GATE study quality tool, see: http://www.health.auckland.ac.nz/population-health/epidemiology-biostats/epig/ and click on the Intervention Studies CAT link. If there were only very few details, such as no details on rheumatic fever cases, the studies were not formally assessed through the GATE framework.
Effect size: where an effect size was not given, if there were no cases of rheumatic fever in either the control or programme group, the effect was not calculated by the writing group.

STUDY	STUDY TYPE & QUALITY (USING GATE), PROBLEMS	NO. OF PARTICIPANTS, WHERE & WHEN	INTERVENTION	RF DIAGNOSIS CRITERIA	OUTCOMES AND CONCLUSIONS	EFFECT SIZE
Chobin N et al. 1975[119]	Observational study. Unclear how many children were followed. Ages of children and follow up time frame unclear. Not stated whether any cases of rheumatic fever occurred or prevented, or whether this was a high-rheumatic fever risk population or not. No control group. No obvious blinding or randomisation. Culture plates read by school nurses, not laboratory staff. **Study quality:** very few study details, no notes on rheumatic fever cases, so not put through GATE	After a 3 year pilot project in 16 schools (public and parochial), the programme spread to over 450 schools in New Jersey. Dates of study unclear, but before article published in 1975	Each school day, students with symptoms of an upper respiratory tract infection including a sore throat and who had consented to be involved, reported to the school nurse for throat culture swab. Students returning to school after a sore throat or URTI were also cultured. Students with positive cultures were excused from school and referred to their own doctors for examination and treatment. Children were given forms to give their doctors, which had to be signed and brought back to the school nurses. It was recommended the child be on medication for at least 48 hours and be free of fever and feeling well before return to school. Three to five days after completing antibiotics, a repeat throat culture was taken by nurses and the same procedure followed. Other family members were also encouraged to obtain throat cultures from their family doctor, clinic or school nurse. School nurses were trained (7.5 hours total training time) to swab throats, plate, incubate and interpret cultures for GAS. Schools were supplied with incubators for the cultures	Not stated	No information on rheumatic fever cases given, unclear if any occurred. Isolation rate of GAS from symptomatic children was 7.7 in first year of project, 4.4 in second year, and 4.1 in third year. In the first year, 87% of children took part, at the end of the second year 95% of children were in the programme	Not estimable

Cornfeld D et al. 1961[120]	Observational study. Unclear whether 100 started the study and 46 dropped out. Data is given on 64 who completed the study, if so, no intention to treat analysis. No blinding or randomisation or controls. **Study quality:** poor, not formally put through GATE	From Oct 1955-May 1959, 64 children were followed. (?whether 100 started the study). Ages 6-12 from one elementary school, attending a school of approx 420 pupils. From low-middle income families	Throat cultures were taken in the school or home from children in whom signs or symptoms suggested the possibility of streptococcal illness (hyperaemic pharynx, with or without exudate, cervical adenopathy or ear ache). Cultures taken by trained technician employed throughout the course of the study. Blood taken for anti streptolysin O titre on all children in Sep 1958, before the routine throat culture for the school year. Other blood specimens were taken with illness	Not stated	No cases of rheumatic fever or acute glomerulonephritis. Positive cultures accompanying symptomatic illness occurred on average at the rate of 2 per 100 children per month, and 9 positive children with respiratory illness	Not estimable
Jackson H. 1976[123]	Intervention, before and after study. Morgan County, Colorado, 1970-74. Difficult to interpret statistics. Using table 3: Protocol (1) involved 3 schools and 1,359 children in 1970-71. Protocol (2) involved 2 schools and 1,030 children in 1971-72. Protocol (3) involved 3 schools and 907 children (155+752) in 1971-72. Protocol (4) involved 5 schools, 1,477 children in 1972-73. The same years are not compared directly. **Study quality:** no information about blinding or randomisation. No information on rheumatic fever statistics, so not put through GATE	See previous column	Four different school programmes. (1) Swabs taken daily from children with sore throats (2) Each week, all children inspected and throat cultures taken from those with signs of pharyngitis (3) Specimens from all students were cultured once per month (4) Specimens from all students were cultured once per month, but the students with GAS positive cultures were excluded from school until they began antibiotics	Not stated.	Schools using protocol (1) and (4) had a substantial reduction in streptococcal prevalence ($p<0.01$)	Not estimable

Nicolle LE et al. 1990[126]	Intervention study. Some randomisation between antibiotics but is not an RCT. No blinding. Time frame was not clear. Randomisation method not clear. Most common reason given for not wanting to be randomised was that the children did not want a needle, but details of how many children/parents gave this reason are not quantified. Many lost to follow up-11 of 48 children with pharyngitis in St Therese Pt. Unclear how many children were involved, or what percentage of those eligible participated. No intention to treat analysis used. Among the pharyngitis patients, 20 in Rankin and 11 in St Therese, were lost to follow up but excluded from the total percentages. **Study quality:** poor study with no mention of rheumatic fever cases-not put through GATE	No numbers or time frame given. Two areas were studied. Rankin Inlet: school children were 60% Inuit, 40% Caucasian. St Therese Point: school children from a native Indian community	Native community health workers visited the schools 3 times weekly to identify children with pharyngitis or skin lesions, and parents asked to consent to the randomisation of IM or PO penicillin. All children had repeat cultures at 10 days and 4 weeks. Swabs were transported to Winnipeg in Stuart's medium, within 24 hours of collection. M and T typing of streptococcal strains was performed. GAS pharyngitis was defined as the presence of subjective complaints of sore throat and pharyngeal isolation of GAS. Antibiotics were administered by nurses. Randomised medications were penicillin G 200,000-250,000 U PO 4 times per day for 10 days, or benzathine penicillin G 1.2 mU units IM if weight over 30kg, or 600,000 U IM if under 30kg. If penicillin allergy, then erythromycin was given at the dose 40mg/kg/day in four divided doses for 10 days. Failure of treatment was isolation of the same M and T type of streptococcal as the initial infecting strain	Not stated	No mention of whether there were any cases of rheumatic fever. **Rankin inlet**: 159 children had GAS pharyngitis, 20 of those lost to follow-up, 1 not given any therapy. Cure rate: 104 (given as 74%, 104/139-no intention to treat). Failure rate: 16 (12%-no intention to treat). **St Therese Pt:** 48 children had GAS pharyngitis, 11 were lost to follow up, 0 given no therapy. Cure rate: 30 (81% without intention to treat) and 2 (5%-no intention to treat) had a treatment failure	Not estimable

Zimmerman RA et al. 1971[127]	Intervention trial. No blinding or randomisation. No bloods taken to identify carriers. Exact numbers of patients with GAS positive pharyngitis difficult to read from graph. Both intervention schools analysed together. No mention of any rheumatic fever occurrences	1969-70. **Intervention:** Two schools totalling approximately 250 children, in the towns of Mosca (an elementary school) and Hooper (a junior-senior high school), in Colorado. **Control** school: a consolidated school in Blanca, Colorado with 275 students	**Intervention:** Teachers asked students if anyone had a sore throat at the start of the day. If they did, then throat cultures were taken by a school nurse at Mosca and a trained lay person at Hooper. Swabs were collected even without any signs of pharyngitis. Results were reported within 9 days of swab collection. At the end of the week, a randomly selected 10% of both school populations were cultured whether they had sore throats or not. Swabs were placed in silica gel and sent to Fort Collins, Colorado on Fridays. All children in attendance at the schools were also cultured at the start and end of the school year. Bloods were taken at least twice during the study, from over 92% of the students, for antibody titration (group A precipitating and type specific hem agglutinating antibodies). If a child was found to have a GAS positive throat swab, they were given a note to take home advising the parent to take the child to a doctor. **Control** school: throat cultures were obtained from a random selection of half of the student body, on each of two occasions in the spring of 1970	Not stated	No data on rheumatic fever statistics. 1,231 throat cultures taken, an average of five per child. At Mosca and Hooper, 25 children were GAS positive on throat swab, one treatment failure was noted. Rates of GAS positive throat swabs fell over time, as per Fig 1 in the study, but it is difficult to read the exact numbers from. **Control** school: rate of GAS positivity was 8.2% in the first round of culturing, and 12.3% in the second round of culturing	Not estimable

Appendix 17: Antimicrobial prophylaxis programmes for GAS in institutional settings

Table 20. Antimicrobial Prophylaxis Programmes for GAS in Institutional Settings

STUDY	STUDY TYPE	INTERVENTION AND RESULTS	EFFECT SIZE	CONCLUSION
Centre for Disease Control. 1988[129]	Intervention before and after study	Morbidity and mortality review article by the Center for Disease Control. Between December 15, 1986 and July 15, 1987, 10 cases of ARF were identified among recruits at the Naval Training Center in San Diego California, the first since the mid 1960s. The attack rate for ARF was 0.75 per 100,000 recruits from Jan 1 1982 to December 1 1986. In 1986 it was 80 per 100,000. Rapid tests were used to diagnose GAS pharyngitis in recruits with respiratory symptoms, 25% were positive (328/1298), and the emergency room took 149 throat cultures, 66 of which were positive (44%). For about 15 years, IM benzathine penicillin G was given to all incoming naval recruits as prophylaxis against streptococcal infection, until the practice was discontinued in 1980 because of perceived decreased risk of ARF. The adjacent Marine Corps recruit depot used benzathine penicillin G prophylaxis continuously since the mid 1960s, and had no cases of ARF at the time of this outbreak at the Naval centre. Mass prophylaxis of IM penicillin was reinstated, 1.2 MU IM	Not applicable	Mass prophylaxis of new recruits with IM penicillin needed to be reinstated in the face of an outbreak of ARF in a Naval training centre
Colling AL et al. 1980[130]	Case series study	1972-77 at a juvenile detention centre in Cleveland, United Kingdom, the boys were surveyed for streptococcal carriage, tonsillitis and rheumatic fever. Boys were aged 15-17 years. They were swabbed on entry, after 4 weeks and before discharge. They usually stayed 6-8 weeks. GAS was isolated from the throat swabs of 31% of boys during their stay, and there were 2 cases of rheumatic fever. Tonsillitis was treated with IM penicillin 0.6 IU bd until symptoms cleared, then PO penicillin 0.25g four times a day for 10 days. Carriers were treated with PO penicillin 0.25g four times a day for 10 days. Allergic patients were given erythromycin 0.25g four times a day instead, if required. From December 1974, penicillin prophylaxis was initiated. Penicillin PO (dose as above) was given to all boys on entry to the centre, before the throat swab results were known. The rate of tonsillitis fell gradually, reduced to 4.7% in Jan-June 1977. Boys complaining of sore throats fell from 67% to 3.2% during the two years of prophylaxis. 3,582 boys passed through the detention centre during the 5 years of the survey, 18% (648) had tonsillitis, and 4 (0.6%) had rheumatic fever (diagnosed by revised Jones criteria 1965). No cases of nephritis were found	Not estimated	Only full penicillin prophylaxis (PO) to all boys on admission effectively reduced the attack rate for tonsillitis to acceptable levels
Gray GC et al. 1991[131]	Prospective intervention study	Prospective study of rates of pharyngeal colonisation and infection by GAS among 736 male US marine recruits in 1989. From 38 states, Guam and Puerto Rico. Serum samples were obtained before and after training, and from acutely ill recruits. Recruits (93%) received prophylaxis with two IM injections of 1.2 MU of penicillin G benzathine (administered 30-39 days apart) and 42% had GAS infection (defined as a 2 dilution rise in anti-streptolysin O titre). 7% of recruits were allergic to penicillin and received no prophylaxis, they were more likely to be colonised with GAS. After the study was completed, the penicillin-allergic recruits were given courses of erythromycin 250mg bd for 60 days, and the average weekly rate of clinically evident GAS pharyngitis fell by more than 75%	Not estimated	For GAS pharyngitis prevention to be effective in closely confined populations such as the military, prophylactic antibiotics need to be given to all recruits. Penicillin-allergic recruits should not be exempted, as they may create a bacterial reservoir from which GAS infection can be transmitted

Heggie AD 1988[132]	Not a study, but a set of GAS pharyngitis prophylaxis guidelines from the military on prophylaxis	Summary of Navy and Marine Corps guidelines for control of GAS infections (NAVMEMDCOM instruction 6220.6). Weekly incidence of pharyngitis and skin and subcutaneous infections caused by GAS must be monitored year round at all Navy and Marine Corps recruit training centres. Benzathine penicillin prophylaxis (1.2 MU IM) should be given on the 14th day of training from October to April at all centres, except Orlando, Florida and women at Parris Island, SC (low GAS rates in those 2 centres). Training is 8 weeks, so a second penicillin injection (same dose) should be given on the 42nd day of training, if the incidence of GAS pharyngitis exceeds or equals 10 cases per 1,000 recruits per week, at or beyond the 42nd training day. Benzathine penicillin prophylaxis of incoming recruits must be implemented at any recruit training centre, regardless of location or time of year, whenever the incidence of GAS pharyngitis equals or exceeds 10 cases per 1,000 recruits per week	Not applicable	-
Heggie AD et al. 1992[133]	Intervention before and after study	1989, US Navy recruits involved in 8 week basic training, in two 12 day observation periods. Recruits routinely received benzathine penicillin prophylaxis. Penicillin-allergic Navy and Marine Corp patients were given erythromycin (has occurred since 1990). Throat cultures were taken from approximately 230 men before training and at 2, 4, and 7 weeks after prophylaxis and from men with pharyngitis diagnosed. The GAS pharyngitis rate was three to four times lower after prophylaxis. There were no cases of ARF diagnosed	Not estimated	Penicillin prophylaxis was effective in controlling GAS infections and ARF in Navy recruits
Peters JE et al. 1998[134]	Cross sectional study	The prevalence of GAS pharyngitis in 10,634 air force recruits at Lackland Air Force Base (Texas, US) was determined Nov 1993-March 1994, to give a baseline to compare with possible future protocol changes, including the possibility of mass prophylaxis of all trainees within the first week of training to prevent GAS outbreaks. The Air Force (unlike Navy and Army) did not use routine mass prophylaxis during basic training. Throat cultures were obtained on the second and last days of training (approximately 6 weeks later) and from trainees with pharyngitis. 9.4% received antibiotic prophylaxis as a result of monthly clinic positive cultures	Not applicable	Authors suggest further trials using control groups to better understand the optimal methods of prophylaxis for GAS

Appendix 18: Studies of access to healthcare and rheumatic fever

Table 21. Access to Healthcare and Rheumatic Fever

STUDY	STUDY TYPES	PARTICIPANTS, INTERVENTION & COMPARISON	OUTCOME	RESULTS/EFFECT SIZE	CONCLUSIONS
Eltohami EA et al. 1997[135]	Retrospective case series	Qatar, 1984-94. 11 year study of the incidence and consequences of ARF (86 children aged 4-14 years with ARF. Jones criteria for rheumatic fever used. Healthcare in Qatar is free of charge to all citizens, for nationals and expatriates. Medications are also free. There is one tertiary hospital with 1,000 beds. A physician to patient ratio of 1.4 per 1,000 was maintained throughout the decade studied	A declining incidence of rheumatic fever (average 11.2 per 100,000) was identified. The course of ARF was generally mild. No recurrences were identified	Not estimated	Reduction in incidence and reduction in sequelae of rheumatic fever may be due to an advantaged socioeconomic environment and accessibility to unlimited medical care in Qatar. This difference was striking when compared with nearby disadvantaged countries and was similar to countries of similar socioeconomic status
Walker K et al. 2005[136]	Retrospective case review	South Africa. 42 patients diagnosed with Sydenham's chorea*, aged 3-13 years, in a Cape Town, South African Hospital	All were poor, with poor access to medical care (not quantified)	Not estimated	All the patients with Sydenham's chorea had poor access to medical care

*Sydenham's chorea is a manifestation of acute rheumatic fever (refer to glossary)

Appendix 19: Barriers to access in New Zealand healthcare system

Table 22. Barriers to Access in New Zealand Healthcare System

General and cost-related access and medical bill problems, and overall quality and physician ratings, by country and income levels, 2001 unadjusted percentages.

ACCESS MEASURE	BELOW AVERAGE INCOME, % COMPLAINING OF PROBLEM IN NZ IN 2001 SURVEY	ABOVE AVERAGE INCOME, % COMPLAINING OF PROBLEM IN NZ IN 2001 SURVEY	p VALUE	CONCLUSIONS
Extremely or very difficult to see a specialist when needed	21%	6%	p<0.05	Significant link between low income and difficulty seeing a specialist
Did not do the following in the last year:				
Did not fill a prescription	20%	11%	p<0.05	Significant link between low income and not filling prescription
Did not get a recommended test, treatment, or follow-up	18%	11%	p<0.05	Significant link between low income and not getting test/treatment/follow up
Had medical problem but did not see doctor	24%	18%	p<0.05	Significant link between low income and not seeing doctor
Had problem paying medical bills	20%	7%	p<0.05	Significant link between low income and difficulty paying medical bills

Source: Adapted from table 3. Reprinted from Health Policy, 67, Schoen C, Doty MM, Inequalities in access to medical care in five countries: findings from the 2001 Commonwealth Fund International Health Policy survey, 309-322., Copyright (2004), with permission from Elsevier Health. [61]

Appendix 20: Socioeconomic indicators and Māori

Table 23. Socioeconomic Indicators and Māori

INDICATOR	% OF MĀORI	% OF NON-MĀORI	CONCLUSIONS
School completion (6th form certificate or higher),15+ years, 2001, %	32.5	50.8	Māori are less likely than non-Māori to have finished school, they are more likely to be unemployed, and be on a means-tested benefit. Māori less likely to have access to a telephone and less likely to have access to a car
Unemployed, 15+ years, 2001, %	11.4	4.0	
Receiving means tested benefit (including community wage (job seeker and sickness benefit), domestic purposes benefit, invalid's benefit and student allowance),15+ years, 2001, %	30.7	11.5	
Living in household without telephone access (household with no telephone access includes households stating no telephone access and households for which it was not stated) 15+ years, 2001, %	12.5	6.1	
Living in household without motor vehicle access,15+ years, 2001, %	11.9	5.6	

Source: Adapted from Table 6, Ministry of Health. 2006.[63] Copyrighted 2006.

Appendix 21: Studies of Māori and access to healthcare

Table 24. Māori and Access to Healthcare

STUDY	PARTICIPANTS, STUDY DESIGN/INTERVENTION	OUTCOME	RESULTS/EFFECT SIZE	CONCLUSIONS
Brabyn L et al. 2004[137]	Population/GP ratios, least cost path analysis (LCLPA) and an allocation model (considering the capacity constraint of general practitioners) were used to demonstrate differences in geographic accessibility to GPs. (n=38,336)	Travel time and distance to the closest GP was calculated for every census enumeration district in New Zealand. Population composition was analysed according to three criteria of need: Level of deprivation (NZdep2001), ethnicity (% Māori) and age (% <5 years, and % 65+ years old)	LCLPA analysis showed 1.9% (70,833) people resided more than 30 minutes from the closest GP	Many Māori had longer travel times on average, which could be explained by the rural nature of many Māori communities. Pacific peoples had lower travel times (on average) which could be explained by the large, urban Pacific population in Auckland
Davis P et al. 1997[138]	12,833 patient encounters, from a survey of Waikato general practices 1991-92 (Waikato Medical Care Survey, WaiMedCa)	Rates of Māori and non-Māori contact with GPs, annual rate per capita	• Age adjusted rate for Māori males: 3.6 visits to GP per year (for each person) • Non-Māori males: 4.1 visits to GP per year • Age-adjusted rate for Māori females: 4.6 visits to GP per year per year • Non-Māori females: 5.2 visits to GP per year Among 5-14 year olds (*age group with the most rheumatic fever*): • Māori males: 2.3 visits to GP per year • Non-Māori males: 3.4 visits to GP per year • Māori females: 2.6 visits to GP per year • Non-Māori females: 3.5 visits to GP per year	Māori are slightly less likely than non-Māori to see GPs, particularly in the 5-14 year old age group. This age group is where most of the cases of rheumatic fever occur
Malcolm L. 1996[139]	Data on GMS (general medical subsidy*) and laboratory expenditure obtained from Health Benefits Ltd, Christchurch. Pharmaceutical expenditure data from Health Benefits Ltd, Wanganui. Accident Compensation Corporation (ACC) figures for general practice consultations obtained from ACC. Eight health centres providing services to low income New Zealanders, in the North and South Islands, were surveyed between 1994-95. The proportion of Māori in the practices varied from 10-80%	Consultation rate (visits to GPs, not nurses). Annual rate per capita	NZ national rate: 4.46 visits to GP per year (for each person) 3 lowest yearly totals: • 1.67 visits per person to the GP per year in Te Waipareira practice (West Auckland) • 1.97 visits per person to the GP per year in the Otahuhu Union practice (South Auckland) • 2.01 visits per person per year to the GP in the Christchurch Union practice	Under-utilisation of and expenditure on medical care and related services, to Māori and New Zealanders in poor circumstances

Ministry of Health 1999[140]	Survey, Oct 1996-Oct 1997 by Statistics New Zealand. 7,862 adults 15+ years old surveyed	Proportion of people who felt they needed to see a GP in the last 12 months but did not (Adjusted rates for age and sex, 95% CI) (Adapted from Table 61 p.211)	European/Pakeha: 11.6% (CI, 10.4-12.8), population estimate 251,816	Māori are more likely to miss out on seeing the GP than Europeans
		Main reasons for unmet need relating to GPs (adjusted for age and sex, 95% CI) (Adapted from Table 62 p.212)	Māori 18.6% (CI, 15.5-21.7), population estimate 59,762	Cost and transport are barriers to Māori visiting GPs
		Cost: European/Pakeha Māori	 43.2% (CI, 37.3-49.1) 48.9% (CI, 39.9-57.9)	
		Had no transport: European/Pakeha Māori	 3.8% (CI, 2.2-5.4) 13.1% (CI, 7.0-19.2)	
Ministry of Health 2004A [67]	12,929 adults aged 15+ surveyed throughout New Zealand 2002-03	Highest unmet need for a general practitioner (age standardised), among all ethnic groups	Māori females approx 21%, exact numbers not stated (Read from bar graph, Fig 89 p.123)	Māori females are most likely to miss out on seeing the GP
		Most likely to not collect a prescription (age standardised)	Māori females approx 26%, exact numbers not stated (Read from bar graph, Fig 95 p.129)	Māori females are most likely to not collect their prescribed medications
Ministry of Health 2004B[141]	Summary of five health surveys and reports	**Foregone GP visits:** % Total NZ population Māori	 5.8 11.4	Māori are more likely to miss out on seeing the GP, and not pick up prescribed medications
		Foregone GP prescription items: % Total NZ population Māori	 4.6 13.0	

* GMS: subsidy paid to general practitioner, for each patient consultation

Appendix 22: Studies of healthcare access and Pacific peoples

Table 25. Healthcare Access and Pacific Peoples

STUDY	STUDY TYPE & PARTICIPANTS	OUTCOME	RESULTS/EFFECT SIZE	CONCLUSIONS
Ministry of Health 1999[139]	Survey of 7,862 adults by Statistics New Zealand, Oct 1996-Oct 1997	Proportion of people who felt they needed to see a GP in the last 12 months but did not (adjusted rates for age and sex, 95% CI) (Table 61, p.211)	European/Pakeha: 11.6% (CI, 10.4-12.8), population estimate 251,816. Pacific peoples 17.5% (CI, 12.8-22.2), population estimate 21,727	Pacific peoples are more likely than Europeans to miss out on seeing the GP
		Main reasons for unmet need relating to GPs (adjusted for age and sex, 95% CI) (Adapted from Table 62, p.212)		Cost and a lack of transport are barriers to Pacific peoples seeing the GP
		Cost: European/Pakeha Pacific peoples	 43.2% (CI, 37.3-49.1) 73.5% (CI, 63.7-83.3)	
		Had no transport: European/Pakeha Pacific peoples	 3.8% (CI, 2.2-5.4) 17.5% (CI, 1.8-33.2)	
Ministry of Health 2004A[67]	12,929 adults aged 15+ surveyed throughout New Zealand 2002-03	Highest unmet need for a GP (age standardised), among all ethnic groups	Highest unmet need was among Māori women (see section above), second highest unmet need for GP was among Pacific females, third highest was among Pacific males. Pacific females approx 18%, Pacific males approx 17% (Figure 89, p.123, no exact numbers stated)	There is a high unmet need for GPs among Pacific peoples. Pacific females and males are the second and third most likely groups in New Zealand to have an unmet need to see a GP
		Visits to dentists and dental therapists in last 12 months (age standardised)	Pacific men, followed by Pacific women, were the least likely of all people (by ethnic group) to have seen a dentist or dental therapist in the last 12 months. 18.8% of men and 22.3% of women, compared to 50% of European/other women (Tables 17-18, p.141-2)	Pacific peoples are the least likely ethnic group to have received dental care, eyecare

Ministry of Health 2004A[67]		Visits to opticians or optometrist in last 12 months (age standardised)	Pacific men, followed by Pacific women, were the least likely of all ethnic groups to have seen an optician/optometrist in the last 12 months. 5.5% of men and 7.6% of women, compared to 22.8% of European/other women (Tables 17-18, p.141-2)	
Ministry of Health 2004B[141]	Summary of five health surveys and reports	**Foregone GP visits:** % Total NZ population Pacific peoples	 5.8 8.0	Pacific peoples are more likely than Europeans to miss out on seeing the GP, and more likely to not pick up prescribed medications
		Foregone prescription items:% Total NZ population Pacific peoples	 4.6 8.4	

Appendix 23: Impact of Māori and Pacific healthcare providers

Table 26. Impact of Māori and Pacific Healthcare Providers

CULTURAL GROUP	OUTCOME OF INTEREST	REASON	EFFECT %	95 % CI
Māori	Visited health care worker from Māori health provider, in the last 12 months		13.7	11.3-16.0
	Very satisfied with visit to Māori healthcare provider		55.3	46.9-63.6
	Satisfied with visit to Māori healthcare provider		36.9	31.8-47.3
	Top 4 reasons for visiting Māori healthcare provider:	'I feel more comfortable talking to someone who understands my culture'	34.5	25.9-43.1
		'It was cheaper than going to another provider'	27.3	21.2-33.4
		Referred by friend or relative	25.9	19.3-32.5
		'They are interested in the impact that my health and its treatments has on my whanau or family'	25.5	17.5-33.4
	Adults who wanted or needed to see a Māori health provider in the last 12 months, but were unable to		5.9	4.3-7.3
Pacific peoples	Visited a healthcare worker at a Pacific health provider, in the last 12 months		9.4	5.8-13.0
	Very satisfied with visit to Pacific healthcare provider		43.6	25.8-61.3
	Satisfied with visit to Pacific healthcare provider		55.5	37.8-73.3
	Top 4 reasons for visiting Pacific healthcare provider:	'I feel more comfortable talking to someone who understands my culture'	74.4	57.9-90.9
		'It was cheaper than going to another provider'	37.7	18.2-57.3
		'I find they are willing to spend more time discussing my health'	31.8	15.0-48.5
		'They are interested in the impact that my health and its treatments has on my aiga or family'	25.9	15.5-36.3
	Adults who had wanted or needed to see a Pacific health provider in the last 12 months, but were unable to		3.1	1.3-4.9

Source: Data adapted from Ministry of Health 2004A.[67]

Appendix 24: Studies relating to the risk of GAS pharyngitis spread within a household

This topic and its search strategy are covered in more detail in the Group A Streptococal Sore Throat Management Guideline (available to download from: www.heartfoundation.org.nz).

There are four key studies in this area, which broadly agree on the rate of spread. After an initial index patient, there was about a 30% chance of another member of the household aquiring GAS pharyngitis in the following weeks. Transmission rates varied between 19.4 to 50%, and translated to about a five to six percent risk for each person per month.

There are no published trials (with intervention and control groups, regardless of randomisation) where the treatment or not of such households has been looked at.

The key studies are summarised below:

- Lindbaek et al found 27% (30 of 110) households had one or more new cases of GAS tonsillitis after an initial case (40 new infections). Lindbaek et al treated GAS pharyngitis with five days of penicillin.[69]

- Breese et al found half to quarter of sibling contacts developed a form of streptococcal infection during the study period and less than 1/20 parents did. He did not look solely at pharyngitis for those statistics: pharyngitis, tonsillitis, scarlet fever, otitis media and cervical adenitis were all counted. When he looked at streptococcal pharyngitis and tonsillitis alone, the attack rate in siblings was 96/496 (19.4%). Breese treated GAS pharyngitis with 600,000 U IM benzathine penicillin G.[70]

- Falck et al investigated 114 patients and their families, 305 possible exposed people, and found 95 (31%) were infected with GAS pharyngitis within a month. Falck treated GAS pharyngitis with five days phenoxymethyl penicillin. Falck et al proposed that most GAS treatment failures depended on ping-pong reinfection from family members with the same T and RFLP type as the index case and recommended further studies.[71]

- Poku estimated the probability of one person aged up to 16 contracting GAS, positive on throat swab, in one month was 0.05-0.06, i.e. in a household with five susceptible people, the risk of one person becoming infected with GAS is 1-0.94**5 (= 27%).[72]

From the above studies, the rate of spread seems to be about a 30% per household, or five to six percent chance per at-risk person in the household per month, although the numbers are small. It is not possible to draw significant conclusions about the likelihood of spread to any particular age group, but adults seemed to be at a lower risk of spread in general.

Appendix 25: Studies on crowding and rheumatic fever

Table 27. Crowding Studies and Rheumatic Fever

STUDY	STUDY TYPE	NO. OF PARTICIPANTS, WHERE & WHEN	RF DIAGNOSIS CRITERIA	OUTCOMES	EFFECT SIZE	CONCLUSIONS
Adanja B et al. 1988[49]	Case control	Yugoslavia. 148 patients with first attack of rheumatic fever, compared to 444 controls from the same neighbourhood	Revised Jones	Less than 5m^2 of living space per person	8.1% of rheumatic fever patients had this living circumstance, compared to 3.1% of controls, RR=2.83, (CI, 1.19-6.71) p=0.018	A link was found between a small amount of living space per person and rheumatic fever. Wide confidence intervals however. (CI% not stated)
				Crowding, defined as more than 2 persons per room	RR=1.72, (CI, 1.08-2.72) p=0.021	A link was found between crowding (2+ people per room) and rheumatic fever
				Sleeping in bed with another person	49.3% of rheumatic fever cases slept with one or more people in the bed, compared to 40.5 controls, RR=1.65, (CI, 1.02-2.66) p=0.040	A link was found between sleeping in bed with another person and rheumatic fever
Coggon D et al. 1993[142]	Retrospective cohort	Chesterfield, United Kingdom. 8,138 men and women born after 1900, whose houses were surveyed in 1936 and whose household size was known from the 1939 census. Subjects were followed through the National Health Service Central Register from 1951 to 1989. From 1951-89, 2,929 people died, 118 emigrated and 50 were lost to follow up	Not stated explicitly. Cause of death taken from codes in 9th revision of the International Classification of Diseases	Effect of housing in the 1930s on mortality from various diseases investigated. Risk in relation to crowding index was defined as: total persons resident in 1939, divided by persons allowed in 1936	Mortality from RHD according to crowding. Crowding index for all subjects: **<0.5:** 17 deaths in this group, RR 1. **Crowding index 0.5-0.99:** 24 deaths, RR=0.8, (95% CI, 0.4-1.5). **Crowding index 1.0+:** 10 deaths, RR=1.0, (CI, 0.4-2.3).	No effect between crowding at the time of the survey in the 1930s and death from RF in later life

Coggon D et al. 1993[142] (Cont'd)				Persons per bedroom was defined as: Total persons resident in 1939, divided by number of bedrooms in 1936	Mortality from RHD according to crowding. Persons per bedroom: **<1.50 persons:** 16 deaths in this group, RR=1. **1.5-2.49 persons:** 25 deaths, RR=0.9, (95% CI, 0.5-1.6). **2.50+ persons:** 10 deaths, RR=0.7 (95% CI, 0.3-1.6)	
Glover JA 1930[143]	Observational	United Kingdom. Review of rheumatic diseases in different settings. Mentions an epidemic of rheumatic fever in the winter of 1926-27 (in the Royal Air Force, location unclear). 2,000 boys entered at age 16 to undergo 9 month course of training. There was 'definite overcrowding'	Not stated	39 cases of rheumatic fever (reading from graph in figure 4) in total, between Oct-Aug 1926-27. First overcrowding peaked then 2-3 weeks later tonsillitis peaked. A further 2-3 weeks later, cases of rheumatism peaked	Not estimated	.
		Caterham Depot /Cateram Military Hospital records from 1916-18 showed an outbreak of cerebro-spinal fever and rheumatic fever		When the beds were spaced out (2.5 feet between them, between Oct-April 1917) and ventilation was improved, the rate of rheumatic fever dropped. A period of overcrowding led to a rise in the rate again	Not estimated	An association between crowding and rheumatic fever was found

Gordis L et al. 1969[144]	Cohort with concurrent controls	Medical records of Baltimore residents discharged from hospitals 1960-64 with the diagnosis of rheumatic fever. Patients aged 5-19 were analysed in census tracts	Not stated, hospital diagnosis of rheumatic fever	Population density per room, highest non-white socioeconomic fifth compared to lowest white socioeconomic fifth: **0.5 or less persons per room:** white: 47.0%, non-white 37.7% **Density 0.51-0.75 persons per room:** white 21.3%, non-white 26.3%. **Density 0.76-1.0 persons per room:** white 20.0%, non-white 23.0%. **Density 1.01 or more persons per room:** 11.8%, non-white 13.0%	Not estimated	Housing density similar in white and non-white groups
Gordis L et al. 1969[144]		Baltimore 1960-64		Range of crowding, % of housing units with 1.01 or more persons per room and rate of rheumatic fever: **White pop 1960-64**: 0.6-2.4 rheumatic fever rate:4.6 2.5-3.6 rheumatic fever: 4.2 3.7-5.2 rheumatic fever: 7.5 5.3-8.2 rheumatic fever: 9.8 8.3-25.3 rheumatic fever: 29.9 **Black pop 1960-64**: 0.6-2.4 rheumatic fever rate:19.1 2.5-3.6 rheumatic fever: 22.3 3.7-5.2 rheumatic fever: 24.5 5.3-8.2 rheumatic fever: 29.0 8.3-25.3 rheumatic fever: 19.7		Rate of rheumatic fever increases with the number of people per room

Gordis L et al. 1969[144]				Rate of rheumatic fever in whites and non-whites living in similar degrees of crowding. Crowding 1.01 or more persons per room, 11-20% of housing units crowded. In this population. Rheumatic fever incidence in white group: 27.0 per 100,000 population aged 5-19 years. Incidence of rheumatic fever in non-white group, 18.8 per 100,000 population aged 5-19 years		Non-white rate no higher than white rate of RF incidence, among groups living in similar degree of crowding
Gray F et al. 1952[145]	Case series with concurrent controls	776 people, from 40 rheumatic and 30 control (non-rheumatic) families. **Rheumatic families:** (122) selected from 1929-39 if one or more members had now or previously had rheumatic fever and were either on the paediatric or medical ward or enrolled in the dispensary of New Haven Hospital, Connecticut. Only 40 of the original 122 families were available for re-examination in 1947-49. **Control families:** 1930-33, selected on the basis that it was not known at the time of selection that any sibling of the control case had rheumatic fever (the contact having been a patient at the paediatric clinic of New Haven Hospital). Only 21 of the original 35 families could be found and were willing to be examined, so another 9 families were added (they had been followed for the same length of time for scarlet fever which was not followed by rheumatic fever or carditis). Both groups of families came from similar location. Visited at home by physician and social worker	Rheumatic fever as diagnosed by a physician **or** history of acute polyarthritis with fever, necessitating bed rest and leaving the patient without joint deformity. Patients with murmurs and heart sounds characteristic of rheumatic valvular disease were considered to have RHD, as per the criteria of the New York and American Heart Associations, (except that x-rays were not done to look for cardiac enlargement)	Crowding: defined as more than one person per room, more than two persons per bedroom, and more than two persons per bed. Abbreviations used: rheumatic families (RF), control families (CF) **1930-31:** **Crowding in home:** RF 85.9%, CF 76.6% **Crowding in bedroom:** RF 59.8%, CF 26.3 % **Crowding in bed:** RF 23.4%, CF 6.7% **1948-49:** **Crowding in home:** RF 30.5%, CF 24.7%. **Crowding in bedroom:** RF 19.8%, CF 17.6%. **Crowding in bed: RF** 1.5%, CF 2.3%	Not estimated	There was more crowding in rheumatic families, compared to controls

Grover A et al. 1993[146]		Northern India, Ambala district, 1988-91. A registry was set up for rheumatic fever /RHD. Health workers and school teachers were trained to identify suspected patients and medical specialists screened 31,200, 5-15 year olds. 102 cases of rheumatic fever/RHD were found, prevalence 0.09%. Of those, 48 were rheumatic fever, 22 recurrences of rheumatic fever, 32 had chronic RHD	Revised Jones	Rheumatic fever patients, those with rheumatic fever recurrences, and those with chronic RHD, lived in 2 room houses (mean) with an average of 4 siblings and shared a room with 3 others (room sharing with 3 others were taken to indicate overcrowding as defined by the Indian Council of Medical Research)	Not estimated	Not compared to control group, but patients with rheumatic fever/RHD shared rooms with 3 people, which was defined as crowding
Hewitt D, Stewart SA. 1952[147]		Oxford United Kingdom. Records of 593 cases of acute rheumatism notified between 1947-50 to the Institute of Social Medicine, Oxford (from surrounding areas)	Not stated, details of some diagnostic criteria given (in Table 3)	Larger proportion of cases were living in households with six or more members	Not estimated	Significant association with more household members and acute rheumatism
				Overcrowding and number of occupants of child's bedroom: slightly more among patients with rheumatism but overall not found to be significant	Not estimated	Not significant
Lennon D et al. 1988[8]	Case series	Auckland, New Zealand. Children with admissions to the Auckland branch of the New Zealand Rheumatic Fever register between 1980 and 1984 were studied. There were 104 with definite diagnoses of ARF and 104 with acute glomerulonephritis (APSGN)	Definite-revised Jones criteria 1965, or probable (modified Jones, 1956)	Household size for ARF patients was 5.6 persons per house (122 patients) in 1983-85. In 1983-84 for 130 APSGN patients, there were 6.2 patients per house. In comparison, the mean New Zealand household size was 3.0 in the 1981 census	Not estimated	Household size for ARF patients above the national average for NZ
Longo-Mbenza B et al. 1998[81]	Cross - sectional	Kinshasa, Zaire, 1996. 4,848 school children randomly selected from urban area & adjoining slums were screened for RHD. All examined, those suspected of RHD were seen by cardiologist. Prevalence of RHD: 59 definite cases, rate: 14.03 per 1,000 children	Not stated, diagnosis by cardiologist and echocardiography	Crowding: >8 people per household, versus <8 people per household	OR 4.10, (95% CI, 1.70-9.85), p=0.002	A link between crowding and rheumatic fever seen. Significant p value but wide confidence interval

Maddox K 1937[148]	Case series	Australia. Several rheumatic fever statistics compiled to obtain a New South Wales state rate: a) Admission rate for rheumatic fever and chorea to public hospitals of Sydney over years 1926-35 b) Admission rate for rheumatic valvular disease to the Royal Prince Alfred Hospital, Sydney, 1925-35 c) Incidence of rheumatic valvular disease in town and country, as found by the medical service of the Department of Education	Not stated	Findings for: a) Hospital incidence ranged from 0.27-0.735% of total admissions b) 0.47% of all admissions 424/88,865 c) 0.37% for small country schools, 0.45% for large country schools	Not estimated	The authors suggest that the small difference in rheumatic valvular disease rates between large and small country schools may be due to closer contact and urbanisation
McLaren MJ et al. 1975[149]	Cross sectional	Soweto, Johannesburg. 12,050 black children in crèches and primary schools were examined by cardiologists in 1972, looking for evidence of RHD	Not stated, diagnosed by cardiologists/trainees	Prevalence of RHD was found to be 6.9 per 1,000		There seemed to be an association between RHD and increasing family size
				Prevalence of RHD increased with 4 or more siblings	p<0.05	
				Number of people sharing child's bedroom: 4.3 for RHD patients, and 3.9 for control group	p=0.05	
Nandi S et al. 2001[77]	Cohort	Chandirgh, North India. 536 children aged 5-15 years from 261 families identified by systematic random selection were enrolled in the study. Episodes of sore throat were recorded and fortnightly home visits were made over one year. Date: prior to study publication in 2001	Not applicable. Looked for GAS sore throats, not rheumatic fever	Area per person (metres squared) of <2.32 was associated with 0.94 GAS sore throats per child year. This compared to area of >3.72, which was associated with 1.10 GAS sore throats per child year	Not significant	Area per person in the home was not associated with frequency of GAS sore throats

Oli K et al. 1999[150]	Cross-sectional survey	Addis Ababa, Ethiopia, 1995. School children attending ten randomly selected government and private schools were surveyed for the presence or absence of RHD. Children were aged 10-15 years, first screened by nurses and if they had a significant murmur, then by a cardiologist. 9,388 (93%) of the originally selected 10,053 were screened. Diagnosis of RHD was made in 60 children (prevalence 6.4 per 1,000)	Rheumatic heart disease diagnosed on clinical evaluation and confimed by echocardiography and doppler	**Class size** Results from multiple logistic regression with RHD as an outcome variable, adjusted for potential confounders including sex, class size, family size and persons per bedroom	OR=1.01 p=0.07, (95% CI, 0.99-1.02) .	Crowding conditions in the home, school and bedrooms were not associated with an increased risk of rheumatic heart disease
				Family size Family size and persons per bedroom were considered as continuous variable for this regression	OR=1.18 p=0.31, (95% CI, 0.94-1.15)	
				Number of persons per bedroom family size and persons per bedroom were considered as continuous variable for this regression	OR=1.00 p=0.99 (95% CI, 0.84-1.13)	

Perry C et al. 1937[151]	Case series	Two part study. Private practitioners and school medical officers in Wiltshire, Gloucestershire and Somerset were invited to notify RHD cases. As it had the highest RHD rate, 1.9 per 1,000, Bristol was studied in further detail, with a spot map for cases within the city	Criteria for RHD: 1. Heart disease arising in connection with rheumatism, chorea or scarlet fever in a child aged 5-14 years 2. Heart disease which, though not arising in connection with rheumatism, chorea or scarlet fever, is rheumatic in type with ventricular enlargement, mitral incompetence or acute pericarditis, in a child 5-14 years	Crowding more common in rheumatic families: Bristol 3.5% Bath 6.7% Gloucestershire 3.7% Somerset 0.1% Wiltshire 0% Swindon 21.1%. In the Bristol study, RHD per city ward rose in a linear manner as the density of persons per room increased	Not estimated	An association in the Bristol study was found between the incidence of rheumatic carditis and the density of population, expressed as persons per room
Potter E et al. 1977[23]	Case series	Trinidad, 1971. East Indian families of 21 patients with ARF (and 44 patients with APSGN) were examined in their homes. Blood was taken for serum, throats and skin infections were cultured for GAS and urinalysis were taken. ARF families: 155/184 were examined. APSGN families: 255/354 examined	Not stated	Family size in ARF families	Ranged from 3-16 members per household, average of 8.9 per household. (Compared to 4-16, average 8.0, for APSGN patients) When only persons 16 years and under were considered, the number of household members was 5.4 (4.7 in APSGN families)	Average of 8.9 house hold members in families of ARF patients. No information on number of bedrooms

Ransome OJ et al. 1983[152]	Cross sectional	South Africa, 1980. Asymptomatic school children, in the third grade of schooling, had throat swabs taken on 4 occasions, and were examined clinically. No attempt was made to look for evidence of streptococcal infection. Coloured children: mean age 8.2 years. Indian children: mean age 7.9 years. Parents were asked to fill in a questionnaire about how many people in the home and how many bedrooms. 120 coloured children, 126 Indian children surveyed	Not applicable	Not looking at rheumatic fever but at GAS positive throat swabs in asymptomatic children (carriage) Coloured children	Number of persons per bedroom, in the families of the 120 coloured children: mean 2.50, SD 1.03, max 5.00, min 0.75	No relationship was found between the number of people per bedroom and the GAS positivity rate within any of the racial groups or swab periods
Ransome OJ et al. 1983[152]	Cohort			Coloured children	Number of positive throat swabs from Coloured children: 0 positive swabs=72 children (61.5%) 1 positive swab=30 children (25.6%) 2 positive swabs=12 children (10.3%) 3 positive swabs=3 children (2.6%)	
Ransome OJ et al. 1983[152]	Cohort			Indian children	Number of persons per bedroom, in the families of the 126 Indian children: mean 1.99, SD 0.85, max 6.0, min 0.67	

Ransome OJ et al. 1983[152]				Indian children	Number of positive throat swabs from Indian children: 0 positive swabs=87 children (69.1%) 1 positive swab=34 children (26.9%) 2 positive swabs=5 children (3.9 %) 3 positive swabs=nil	
Ransome OJ et al. 1988[153]	Case series	South Africa. Paediatric patients (usual upper age limit for the ward was 12 years), admitted between 1981-84 to Coronation Hospital in South Africa with ARF. 45 children ages 4.5-12.4 years were found	Modified Jones 1956	46 children found, with a total of 50 attacks of rheumatic fever (4 were admitted twice), 3 died		Crowding levels similar to Ransome et al's earlier study above (1983)
				For 26 patients, crowding data available:	Mean number of children per classroom: 36 +/- 8.2 (range 20-54)	
				For 26 patients, crowding data available:	Mean number of people sleeping per room 2.7 +/- 1.8 (range 0.5-9)	
Rizvi SF et al. 2004[154]	Cross sectional	Pakistan 1993-94. In a rural setting, whole villages were randomly selected for RHD screening (9,430 people). 54 had RHD, prevalence of 5.7 in 1,000, (95% CI, 4.2-7.2)	1992 revised Jones	Given a crowding score based on number of household members and number of rooms, ranging from 1 (single room with 5 or more people) to 3 (3 rooms with fewer than 5 people, or more than 3 rooms). Households averaged 8 people living in 3 rooms. Patients with rheumatic fever: crowding score 1.42, controls 1.31	Not estimated	Slightly more crowding in the rheumatic fever patient households, but not enough to be significant. Problems: households all moderately crowded

Quinn RW et al. 1948[155]	Cross sectional study plus contemporary controls	Connecticut, prior to publication of article in 1948. Study looking for the prevalence of rheumatic fever and RHD, and for the effect of living conditions and crowding on RHD, among other variables. Children in the 7th and 8 the grades of Connecticut public schools, aged 11-13 years and a representative sample of rural children scattered throughout the state were included. There were 3,141 in total. The children underwent a cardiovascular examination by a physician. Crowding was defined as number of persons per room in each child's home. **Urban:** crowding was less than one room per person. **Rural:** crowding was defined as present when the number of rooms in the home was two less than the number of occupants	Complex (Detailed in article on p.1073-4)	Of children with rheumatic fever or RHD diagnosed: **Urban children:** 5.90% had crowding, 3.92% had no crowding. Chi square test 3.75 **Rural children:** 6.25% had crowding, 3.42% had no crowding, chi square 2.50 (Were compared to children from the area without rheumatic fever or RHD)	Overall the chi square was 6.25, and p=0.044 (significant)	The number of rheumatic (rheumatic fever or RHD) children was significantly higher in crowded homes, regardless of whether it was an urban or rural location

Quinn RW et al. 1950[156]	Cross sectional study	Connecticut, 1948. 7th and 8th grade children attending public and parochial schools (90-95% of available students examined), aged 10-18.9 years. In the areas of Derby and Shelton, Anstonia, and Milford. Looked at housing and crowding factors, and had cardiovascular exam looking for RHD. 1,229 children were examined. Crowding in the home was defined as more than one person per room. Crowding in the bedroom was when more than two people slept there. Crowding in bed was when more than two people slept in the bed	Complex (Detailed in article on p.1289)	The following data for 'rheumatic' children refers to rheumatic heart disease only. In Ansonia, Derby and Shelton combined, (ADS), 37.8% of rheumatic children lived in crowded homes, as did 39.38% of non rheumatic children. In Milford, 58.3% of rheumatic children lived in crowded homes, and 17.68% of non rheumatic children. In the bedroom: 31.1% of rheumatic children in ADS lived in crowded bedrooms, compared to 22.46% of non rheumatic children. In Milford, 8.3% of rheumatic children had crowding in the bedroom, as did 9.2% of non rheumatic children. In the bed, in ADS, 42.2% of rheumatic children had crowded beds, compared to 43.16% of non rheumatic children. In Milford, 25.0% of rheumatic children slept in crowded beds, as did 24.08% of non-rheumatic children		In Milford the homes of rheumatic children were consistently more crowded than in non rheumatic families

Vlajinac H et al. 1989[50]	Case control	Yugoslavia. 148 patients with first attack of rheumatic fever, compared to 444 controls from the same neighbourhood. (Same study as Adanja et al above & Vlajinac et al 1991 below)	Revised Jones	>2 persons per room, study group as a whole	p<0.05 RR=1.60 (95% CI, 1.05-2.44)	Some evidence of a link between crowding and rheumatic fever from this data. Frequent sore throat and the presence of any other factor such as flat dampness, crowding, low education of mother, family history of rheumatic fever or under-nourishment, all led to a significantly increased risk of rheumatic fever (see Table 1 in article for more details)
				Sleeping in bed with another person, study group as a whole	p<0.05 RR=1.43 (95% CI, 1.04-2.13)	
Vlajinac H et al. 1991[51]	Case control	Yugoslavia. 148 cases with a first attack of rheumatic fever satisfying Jones criteria, which were home at time of survey. Three healthy controls matched for each rheumatic fever patient	Revised Jones	Home crowding defined as more than 2 persons per room, having less than $5m^2$ of living space per capita and sleeping in bed with another person		No link between crowding and rheumatic fever
				Sleeping in bed with another person	Coefficient 0.043, adjusted relative risk 1.04, (CI, 0.99-1.09) p=0.060	
				Less than $5m^2$ of space per person	Coefficient 0.544, adjusted relative risk 1.72, 95% (CI, 0.69-4.25), p= 2.40	

Vlajinac H et al. 1991[51] (Cont'd)				More than 2 persons per room	Coefficient 0.303, adjusted relative risk 1.35, (CI, 0.61-3.00) p=0.460	
Wedum AG et al. 1944[157]	Case series	Cincinnati 1930-40. Hospital admissions for all ages were surveyed by the authors for rheumatic conditions. 583 patients had a diagnosis of rheumatic fever with or without RHD or chorea. Home addresses were found for 517	Not stated	Crowding was defined as persons per room. Density of population was defined as persons per acre. The 517 cases of rheumatic fever were distributed among census tracts, and related to crowding and density of population		An association was found between crowding and RHD and also between density of population and RHD
				Crowding of 11% or more:	found to have a significant chi squared test (n=1) X^2=45.0	
				Density, (persons per acre 23 or more)	significant chi squared test, of X^2=34.1	
Zaman M et al. 1997[158]	Case series and control group	Dhaka, Bangladesh, 1990-91. Medical records of patients presenting to the National Centre for Control of Rheumatic Fever and Heart Diseases (a hospital). 1,362 records were reviewed, 44 definite cases of rheumatic fever and 86 controls were found	Revised Jones 1992	Dwelling space (square feet per person), for rheumatic fever patients was median of 83 (range 17-333), for controls 138 (range 15-1500)	p<0.01	An association was found between less dwelling space per person and rheumatic fever
Zaman M et al. 1998B[75]	Case control	Dhaka, Bangladesh, 1994-45. Outpatients 5-20 yrs old with symptoms suggestive of ARF (348 patients), 60 cases met updated Jones criteria. Of the remaining patients, 104 were put into the control group	Revised Jones 1992	Persons per dwelling room: 3.1 for rheumatic fever cases, 3.0 for controls	2 p (t test for group means and chi square test for proportions) =0.58 (interpret as per p value)	No association found between persons per dwelling room and rheumatic fever

Appendix 26: Household crowding by DHB

Table 28. Ethnicity and Household Crowding in 2001, by Region

Ethnic Group		European Ethnic Group	Māori Ethnic Group	Pacific Peoples' Ethnic Group
Area	**Measures Crowding/Bedrms**	**2001**	**2001**	**2001**
Northland Region	No. of Bedrooms per Household	3.10	3.07	3.18
	No. of People per Bedroom	0.84	1.09	1.22
	Equivalised Crowding Index	0.57	0.78	0.86
Auckland Region	No. of Bedrooms per Household	3.04	3.10	3.17
	No. of People per Bedroom	0.88	1.15	1.41
	Equivalised Crowding Index	0.61	0.83	1.01
Waikato Region	No. of Bedrooms per Household	3.16	3.13	3.24
	No. of People per Bedroom	0.84	1.09	1.21
	Equivalised Crowding Index	0.57	0.79	0.86
Bay of Plenty Region	No. of Bedrooms per Household	3.09	3.07	3.18
	No. of People per Bedroom	0.83	1.10	1.20
	Equivalised Crowding Index	0.57	0.79	0.85
Gisborne Region	No. of Bedrooms per Household	3.18	3.09	3.21
	No. of People per Bedroom	0.84	1.07	1.26
	Equivalised Crowding Index	0.58	0.78	0.88
Hawke's Bay Region	No. of Bedrooms per Household	3.05	3.09	3.14
	No. of People per Bedroom	0.84	1.10	1.29
	Equivalised Crowding Index	0.58	0.80	0.92
Taranaki Region	No. of Bedrooms per Household	3.11	3.11	3.15
	No. of People per Bedroom	0.82	1.03	1.21
	Equivalised Crowding Index	0.56	0.74	0.87
Manawatu-Wanganui Region	No. of Bedrooms per Household	3.13	3.18	3.22
	No. of People per Bedroom	0.82	1.04	1.16
	Equivalised Crowding Index	0.57	0.75	0.83
Wellington Region	No. of Bedrooms per Household	2.99	3.02	3.11
	No. of People per Bedroom	0.85	1.09	1.26
	Equivalised Crowding Index	0.59	0.78	0.90
Tasman Region	No. of Bedrooms per Household	3.10	3.13	3.22
	No. of People per Bedroom	0.85	1.05	1.12
	Equivalised Crowding Index	0.57	0.72	0.80

Nelson Region	No. of Bedrooms per Household	2.95	2.96	3.01
	No. of People per Bedroom	0.84	1.09	1.22
	Equivalised Crowding Index	0.59	0.78	0.89
Marlborough Region	No. of Bedrooms per Household	3.09	3.16	3.17
	No. of People per Bedroom	0.81	1.02	1.13
	Equivalised Crowding Index	0.54	0.71	0.79
West Coast Region	No. of Bedrooms per Household	3.00	3.13	3.39
	No. of People per Bedroom	0.81	0.97	1.01
	Equivalised Crowding Index	0.55	0.67	0.73
Canterbury Region	No. of Bedrooms per Household	3.01	3.09	3.14
	No. of People per Bedroom	0.83	1.03	1.17
	Equivalised Crowding Index	0.57	0.74	0.84
Otago Region	No. of Bedrooms per Household	3.08	3.26	3.30
	No. of People per Bedroom	0.81	0.98	1.08
	Equivalised Crowding Index	0.56	0.72	0.81
Southland Region	No. of Bedrooms per Household	3.10	3.15	3.05
	No. of People per Bedroom	0.81	0.98	1.04
	Equivalised Crowding Index	0.56	0.69	0.76
Area Outside Region	No. of Bedrooms per Household	3.21	3.11	-

Source: Adapted from Statistics New Zealand's Table Builder: Crowding measures by ethnic group. Available online. URL: http://wdmzpub01.stats.govt.nz/wds/TableViewer/tableView.aspx?ReportId=484 Accessed September 2006.[73]

Appendix 27: Studies of ARF and quality of housing

Table 29. Studies of ARF and Quality of Housing

STUDY	STUDY TYPE	NO. OF PARTICIPANTS, WHERE & WHEN	RF DIAGNOSIS CRITERIA	OUTCOMES	EFFECT SIZE	CONCLUSIONS
Adanja B et al. 1988[49]	Case control	Yugoslavia. 148 patients with first attack of rheumatic fever, compared to 444 controls from the same neighbourhood	Revised Jones	**Inside toilet:** 35.1% of rheumatic fever patients and 39.9% of controls (RR=1.0) **Outside toilet:** rheumatic fever patients 64.9%, controls 60.1% (RR=1.68)	p not significant	No association between rheumatic fever and whether toilet inside or outside house
				Condition of dwellings: **Good:** 74.3% of rheumatic fever patients, 82.9% of controls (RR=1.0) **Deteriorated dwellings:** 25.7% of rheumatic fever patients and 17.1% of controls (RR=1.83)	p=0.01	Association found between deteriorated dwellings and rheumatic fever
				Damp home: "**No":** 84.5% of rheumatic fever patients, 92.8% of controls (RR=1.0) **"Yes":** 15.5% of rheumatic fever patients and 7.2% of controls (RR=2.48)	p=0.0042	Association found between damp home and rheumatic fever
				Home with water: **Inside:** rheumatic fever patients 54.7%, controls 61.0% (RR=1.0) **Outside:** rheumatic fever patients 45.3%, controls 39.0%, (RR=1.54)	p not significant	No association between rheumatic fever and whether water was inside or outside house

Coggon D et al. 1993[142]	Retrospective cohort	Chesterfield, United Kingdom. 8,138 men and women born after 1900, whose houses were surveyed in 1936 and whose household size was known from the 1939 census. Subjects were followed through the National Health Service Central Register from 1951-89. From 1951-89, 2,929 people died, 118 emigrated and 50 were lost to follow up	Not stated explicitly, cause of death taken from codes in 9th revision of the International Classification of Diseases	Effect of housing in the 1930s on mortality from various diseases investigated. **Presence of hot water tap:** Among those who did there were 1,240 deaths Among those who did not, there were 1,672 deaths	Hot tap: RR=1 No tap: RR=1.03, (95% CI, 0.98-11.14)	No significant difference between the presence of hot water tap, larder and gas cooker and overall mortality. (In those born 1925-39 there was a small trend to higher death rates for people with crowded homes and no hot water tap)
				Purpose built larder: Among those who did, there were 1,344 deaths Among those who did not, there were 1,569 deaths	Larder: RR=1. No larder: RR=1.01 (95% CI, 0.95-1.09)	
				Gas cooker: Among those who did not, there were 1,821 deaths Among those who did, there were 1,090 deaths	No gas cooker: RR=1. Gas cooker: RR=0.96 (95% CI, 0.89-1.03)	
Gordis L et al. 1969[144]	Case series and contemporary control group	Medical records of Baltimore residents discharged from hospitals 1960-1964 with the diagnosis of rheumatic fever. Patients aged 5-19 were analysed in census tracts	Not stated, hospital diagnosis of rheumatic fever	Highest non-white socioeconomic fifth compared to lowest white socioeconomic fifth: **Condition of housing:** White: 71.5% sound, 21.8% deteriorating, 6.7% dilapidated Non-white: 91.1% sound, 8.6% deteriorating, 0.3% dilapidated	Not estimated	Condition of house and age of house: superior quality in the non-white comparison group, in comparison of highest non-white socioeconomic fifth to lowest white socioeconomic fifth

				Age of housing: Built 1950-60: white 3.0%, non-white 11.6% Built 1940-49: white 2.4%, non-white 17.0% Built 1939 or earlier: white 94.6%, non-white 71.4%		
Gray F et al. 1952[145]	Case series and contemporary control group	776 people, from 40 rheumatic and 30 control (non-rheumatic) families. **Rheumatic families:** (122) selected from 1929-39 if one or more members had now or previously had, rheumatic fever and was either on the paediatric or medical ward or enrolled in the dispensary of New Haven Hospital, Connecticut. Only 40 of the original 122 families were available for re-examination in 1947-49. **Control families:** 1930-33, selected on the basis that it was not known at the time of selection that any sibling of the control case had rheumatic fever (the contact having been a patient at the paediatric clinic of New Haven Hospital). Only 21 of the original 35 families could be found and willing to be examined, so another 9 families were added (they had been followed for the same length of time for scarlet fever which was not followed by rheumatic fever or carditis). Both groups of families came from similar location. Visited at home by physician and social worker. Substandard homes were those without central heating, with shared toilet facilities and in need of major repair. Passable homes were mainly domiciles with central heating, private toilets and the need for major repairs met. Housing was good in respect to construction and repair	Rheumatic fever as diagnosed by a physician, **or** history of acute polyarthritis with fever, necessitating bed rest and leaving the patient without joint deformity. Patients with murmurs and heart sounds characteristic of rheumatic valvular disease were considered to have RHD as per the crieria of the New York and American Heart Associations, (except that x-rays were not done to look for cardiac enlargement)	In 1930-31, 93.4% of rheumatic families lived in substandard conditions, compared to 70.6% of controls. In 1948-49, 57.7% of rheumatic families lived in substandard conditions, compared to 50.4% of controls	Not estimated	Poorer living conditions were found in rheumatic families

Hewitt D, Stewart SA. 1952[147]	Cohort study	Records of 593 cases of acute rheumatism notified between 1947-50, to the Institute of Social Medicine, Oxford, United Kingdom (from surrounding areas)	Not stated, details of some diagnostic criteria given (in Table 3)	No differences in patients with rheumatism and controls when the following were assessed: Type of house (detached), dampness, light, ventilation, structure quality (good/fair/poor)	Not estimated	No association found
Nandi S et al. 2001[77]	Cohort study	Chandirgh, North India. Date: prior to study publication in 2001. 536 children aged 5-15 years from 261 families identified by systematic random selection were enrolled in the study. Episodes of sore throat were recorded and fortnightly home visits were made over one year	Not applicable. Looked for GAS sore throats, not rheumatic fever	Having a kitchen: 0.87 was associated with 0.87 GAS sore throats per child year, compared to not having a kitchen (0.99 GAS sore throats per child year)	$p<0.01$	Not having a kitchen was associated with more GAS sore throats (per child year)
Quinn RW et al. 1950[156]	Cross sectional study	Connecticut, 1947-48. 7th and 8th grade children attending public and parochial schools (90-95% of available students examined), aged 10-18. In the areas of Derby and Shelton, Ansonia and Milford. Looked at housing, crowding factors and had cardiovascular exam looking for RHD. 1,229 children were examined. Housing quality defined as: **Inadequate:** Without central heating, with shared toilet facilities and the need for major improvements. **Passable:** Central heating, private toilets and the need for major repairs met. **Adequate to good**: In respect to construction and repair	Complex (Detailed in article on p.1289)	Approximately 50% of rheumatic children in Ansonia, Derby and Shelton (combined) lived in poor housing, compared to approximately 40% of non-rheumatic children in those areas. In Milford about 18% of rheumatic children and 20% of non-rheumatic children, lived in poor housing. (Approximate figures from bar graph, in figure 4)	Not estimated	The number of rheumatic children in the poorest housing in all 4 cities was higher than in passable and good housing combined. Beyond that the correlation was not found to be consistent, as in Milford most rheumatic children lived in good houses. There is not enough evidence from this study for a causal relationship between poor housing and RHD

Rizvi SF et al. 2004[154]	Cross sectional	Pakistan 1993-94. In a rural setting, whole villages were randomly selected for rheumatic heart disease screening (9,430 people). 54 had RHD, prevalence of 5.7 in 1,000, (95% CI, 4.2-7.2)	1992 revised Jones	14% (7/50) RHD patient households had a latrine within the house, compared to 19.4% of those without RHD	Not estimated	Slightly more controls had toilets in the house compared to RHD patients
				House construction: No difference found (30% of those with RHD, compared to 32.1 T of controls). (House construction not defined further)	Not estimated	House construction not associated with RHD
Thakur JS et al. 1996[159]	Cross sectional	India, 1992-93. School children aged 5-16 years from Shimla town and adjoining rural area of Kasumpti-Suni block. 15,080 children were screened generally and specifically for evidence of RHD. After a case of rheumatic fever/RHD was diagnosed, home visit was made to study housing conditions	Revised Jones	Housing conditions: Poor conditions in 33/45, (73.3% of the rheumatic fever patients) (Good in 12/45=26.7%)	Not estimated	Most of the children diagnosed with rheumatic fever/RHD lived in poor conditions. 'Poor' is not defined further
Vlajinac H et al. 1989[50]	Case control	Yugoslavia. 148 patients with first attack of rheumatic fever, compared to 444 controls from the same neighbourhood	Revised Jones	Flat dampness (study group as a whole)	RR=2.37 (95% CI, 1.31-4.28) p<0.01	Some evidence of a link between home dampness and rheumatic fever
Vlajinac H et al. 1991[51]	Case control	Yugoslavia. 148 cases with a first attack of rheumatic fever satisfying Jones criteria, which were home at time of survey. Three healthy controls matched for each RF patient	Revised Jones	Home dampness	p=0.008, adjusted relative risk 2.40, (95% CI, 1.26-4.58)	An association between home dampness and rheumatic fever
				Deteriorated condition of dwelling	p=0.09, adjusted relative risk 1.02, (95% CI, 0.99-1.11)	No association between deteriorated condition of dwelling and rheumatic fever

Appendix 28: Studies on poverty in ARF

Table 30. Studies on Poverty in ARF

STUDY	STUDY TYPE	NO. OF PARTICIPANTS, WHERE & WHEN	RF DIAGNOSIS CRITERIA	OUTCOMES	EFFECT SIZE	CONCLUSIONS
Adanja B et al. 1988[49]	Case control	Yugoslavia, prior to study publication in 1988 148 patients with first attack of rheumatic fever, compared to 444 controls from the same neighbourhood	Revised Jones	**Both parents employed:** Of rheumatic fever patients, 134 (90.5%) had both parents employed, compared to 95.0% of controls	RR=1.0	No association between income and rheumatic fever
				High income: Rheumatic fever patients: 60.1% had a high income Controls: 66.2% had a high income	RR=1.0	
				Family income: Among rheumatic fever patients, 39.9% had a low income, of the controls, 33.8% had a low income	RR=1.38 p not significant	
				The incomes were further broken into per capita income in dinars: **Family income per capita in dinars:** **<3000:** 1 (1.2%) of rheumatic fever patients, 9 (3.7%) of controls **3001-5999:** 12 (14.8%) of rheumatic fever patients, 41 (16.9%) of controls **6000-8999:** 38 (46.9%) of rheumatic fever patients, 117 (48.1%) of controls **9000+:** 30 (37%) of rheumatic fever patients, 76 (31.3%) of controls	for incomes under 9000, RR=0.0 and p values not significant RR=1 for income 9000+	

Al-Sekait MA et al. 1990[160]	Cohort	Western Desert, Saudi Arabia, 1987. 9,418 asymptomatic school children aged 6-15 years were screened by random sampling. Screened by team including doctor for rheumatic fever	Revised Jones, (1984 Circulation)	Income level: **Low:** 3,407 children. Prevalence of RHD: 3.1 per 1,000 **Middle:** 4,463 children. Prevalence of RHD: 2.0 per 1,000 **High:** 1,748 children Prevalence of RHD: 1.1 per 1,000	-	RHD is more common in lower socioeconomic levels in Saudi Arabia
Bhave SY et al. 1991[161]	Case series and contemporary controls study	Bombay, India, prior to study publication in 1991 (exact years unclear). Children aged 1 month to12 years attending a general hospital for non-infective conditions were selected to represent normal children (unclear exactly how many patients, 787 in one table) and 522 patients considered to have active rheumatic fever	Page1504 of article, referred to criteria elsewhere. Radiological and electrocardio-graphical grounds	Point prevalence of rheumatic heart disease for ages 5-15 years (n=51,992) was estimated. 68/39,868 (0.17%) of the low income group had RHD. This compared to 6/12,124 (0.05%) of the high income group	Not estimated	More RHD patients were estimated to be from a low income background
Gordis L et al. 1969[144]	Case series and contemporary controls study	Baltimore. Medical records of Baltimore residents discharged from hospitals 1960-64 with the diagnosis of rheumatic fever. Patients aged 5-19 were analysed in census tracts	Not stated, hospital diagnosis of rheumatic fever	In the socioeconomic fifths, the average annual incidence rate of rheumatic fever for 1960-64: **1st lowest:** whites 15.8%, non-whites 26.6%. **2nd fifth:** whites 14.2%, non-whites 27.6%. **3rd fifth:** whites 11.6 %, non-whites 17.8%. **4th fifth:** whites 8.0%, non-whites 21.8%. **5th highest:** whites 3.4% and non-whites 29.0%	Not estimated	Rheumatic fever rates for non-whites are consistently higher than for whites in each socioeconomic fifth in Baltimore and the lowest non-white rate is as high or higher than the highest white rate

Gray F et al. 1952[145]	Case series and contemporary controls study	776 people, from 40 rheumatic and 30 control (non-rheumatic) families. **Rheumatic families:** (122) selected from 1929-39 if one or more members had now or previously had, rheumatic fever, and was either on the paediatric or medical ward or enrolled in the dispensary of New Haven Hospital, Connecticut. Only 40 of the original 122 families were available for re-examination in 1947-49. **Control families:** 1930-33, selected on the basis that it was not known at the time of selection that any sibling of the control case had rheumatic fever (the contact having been a patient at the paediatric clinic of New Haven Hospital). Only 21 of the original 35 families could be found and willing to be examined, so another 9 families were added (they had been followed for the same length of time for scarlet fever which was not followed by rheumatic fever or carditis). Both groups of families came from similar location. Visited at home by physician and social worker. Low income homes were judged too meagre to cover adequate nutrition, proper clothing and other basic essentials of family life	Rheumatic fever as diagnosed by a physician **or** history of acute polyarthritis with fever, necessitating bed rest and leaving the patient without joint deformity. Patients with murmurs and heart sounds characteristic of rheumatic valvular disease were considered to have RHD, as per the criteria of the New York and American Heart Associations, (except that x-rays were not done to look for cardiac enlargement)	In 1930-31: 93.7% of the rheumatic families had low income levels, compared to 85.9% of controls. In 1948-49: 36.7% of rheumatic families were low income, compared to 33.2% of controls	-	In 1948-49 about the same percentage of rheumatic families and controls were living in poverty

Grover A et al. 1993[147]	Cross sectional study	Northern India, Ambala district, 1988-91. A registry was set up for rheumatic fever /RHD. Health workers and school teachers were trained to identify suspected patients and medical specialists screened 31,200, 5-15 year olds. 102 cases of rheumatic fever/RHD were found, prevalence 0.09%. Of those, 48 were rheumatic fever, 22 recurrences of rheumatic fever, 32 had chronic RHD	Revised Jones	Socioeconomic status: **Very poor:** 6/48 rheumatic fever patients, 2/22 of recurrence patients and 4/32 of chronic RHD patients. **Poor:** 16/48 of rheumatic fever patients, 10/22 of recurrence patients and 15/32 of chronic RHD patients. **Middle:** 26/48 rheumatic fever patients, 10/22 recurrence patients and 13/32 of chronic RHD patients	Not estimated	Not compared to controls. More of the recurrence and chronic RHD patients were poor or very poor, but more of the rheumatic fever patients were middle income
Holmes MC, Rubbo SD. 1953[162]	Case series study	Melbourne, Australia, 1938-48. 1,469 children treated in Melbourne hospitals	Not stated	Of 1,469 cases of rheumatic fever detected, 942 lived in low rental areas (cheaper areas), compared to 202 in high rental areas. 325 were living in medium rental areas	Not estimated	Most rheumatic fever patients lived in cheaper rental areas
Longo-Mbenza B et al. 1998[81]	Cross sectional study	Kinshasa, Zaire, 1996. 4,848 school children randomly selected from urban area and adjoining slums were screened for RHD. All examined, those suspected of RHD were seen by cardiologist. Prevalence of RHD: 59 definite cases, rate: 14.03 per 1,000 children	Not stated, diagnosis by cardiologist and echocardiography	Lower versus higher socioeconomic status	OR=2.68 (95% CI, 1.43-5.01) p=0.002	lower socioeconomic status was a prognostic factor for rheumatic heart disease occurrence, in the Kinshasa slums
				RHD in slum schools: 22.2 per 1,000 vs urban schools: 4 per 1,000	not estimated	Rheumatic fever was more common in slum schools than in urban schools
McLaren MJ et al. 1975[149]	Cross sectional study	Soweto, Johannesburg, 1972. 12,050 black children in crèches and primary schools were examined by cardiologists looking for evidence of RHD	Not stated, diagnosed by cardiologists/trainees	Prevalence of RHD was found to be 6.9 per 1,000. No association was found between socioeconomic status and RHD, when RHD children were compared to controls	Not estimated	No association between poverty and RHD found, but it is unclear who the control group were (? The children without RHD in the survey). It may be there is little significant difference in income between households in the area

Meira ZM et al. 2005[76]	Case series study	Brazil, 1983-98. Patients prospectively followed up with their first attack of ARF. 258 children and adolescents, diagnosed between 1983-98	Revised Jones	Family income of less than 3 x the minimum wage in Brazil (US $240): as a risk factor for progression severe valvular disease	p=0.26, RR=1.52, (95% CI, 0.74-3.12)	Income not significant predictor for progress from ARF to severe valvular disease
Nandi S et al. 2001[77]	Cohort study	Chandirgh, North India. Date: prior to study publication in 2001. 536 children aged 5-15 years from 261 families identified by systematic random selection were enrolled in the study. Episodes of sore throat were recorded and fortnightly home visits were made over one year	Not applicable. Looked for GAS sore throats, not rheumatic fever	Socioeconomic status: **Lower:** 0.98 GAS sore throats per child year **Lower middle:** 0.91 **Upper middle:** 0.97 GAS sore throats per child year	Not significant	No association found between socioeconomic status and number of GAS sore throats
Oli K et al. 1999[150]	Cross sectional survey	Addis Ababa, Ethiopia, 1995. School children attending ten randomly selected government and private schools were surveyed for the presence or absence of RHD. Children were aged 10-15 years, first screened by nurses and if they had a significant murmur, then by a cardiologist. 9,388 (93%) of the originally selected 10,053 were screened. Diagnosis of RHD was made in 60 children (prevalence 6.4 per 1000)	RHD diagnosed on clinical evaluation and confirmed by echocardiography and doppler	Prevalence of RHD in low socioeconomic groups (government schools): 7.1 per 1,000 RHD in high socioeconomic groups (private schools): 1 per 1,000 .	RHD and low socioeconomic status as an outcome variable: OR=6.7 p=0.07, (95% CI, 0.84-44.32) Results from multiple logistic regression with RHD as an outcome variable, adjusted for potential confounders including sex, class size, family size and persons per bedroom	There was no significant association between lower socio economic status and RHD in these Ethiopian school children

Thakur JS et al. 1996[159]	Cross sectional	India, 1992-93. School children aged 5-16 years from Shimla town and adjoining rural area of Kasumpti-Suni block, India, in 1992-93. 15,080 children were screened generally and specifically for evidence of RHD. 45 children had rheumatic fever/RHD. After a case of rheumatic fever/RHD was diagnosed a home visit was made to study housing conditions	Revised Jones	Rheumatic fever/ RHD prevalence per thousand, per social classes (ranked I-V). Class I: 0 Class II: 2.49 Class III: 2.71 Class IV: 3.97 Class V: 4.59 (Rheumatic fever/RHD total prevalence per 1,000 for study sample: 2.98)	p>0.05	Prevalence of rheumatic fever /RHD was higher among lower social classes, but these differences were not statistically significant
Wedum AG et al. 1944[157]	Case series study	Cincinnati 1930-40. Hospital admissions for all ages were surveyed by the authors, for rheumatic conditions. 583 patients had a diagnosis of rheumatic fever with or without RHD or chorea. Home addresses were found for 517	Not stated	In relation to cases of rheumatic fever by census tract, the cheaper rental properties (less than $21.65 monthly) were associated with the most significant chi square test (n=1) X^2 61.8	(n=1) X^2 61.8	In terms of rheumatic fever cases and their distribution by census tract, cheap rental property had the most significant association. The authors found poverty to be an important factor in the genesis of rheumatic fever
Zaman M et al. 1997[158]	Case series and contemporary controls study	Dhaka, Bangladesh, 1990-91. Medical records of patients presenting 1990-91 to National Centre for Control of Rheumatic Fever and Heart Diseases (a hospital). 1,362 records were reviewed, 44 definite cases of rheumatic fever and 86 controls were found	Revised Jones 1992	Income (taka/month/person) in the rheumatic fever group was a median of 600 (range 122-7,143), compared to controls: income median 750 (range 100-4,000)	p=0.02	Rheumatic fever patients had a lower income per person in their homes than controls. An association was found

Appendix 29: Studies addressing the role of nutrition and ARF

Table 31. Studies Addressing the Role of Nutrition and ARF

STUDY	STUDY TYPE	NO. OF PARTICIPANTS, WHERE, WHEN & INTERVENTION	RF DIAGNOSIS CRITERIA	OUTCOMES	EFFECT SIZE	CONCLUSIONS
Coburn A. 1960[79]	Two interventions: 1. Survey – food diary	Chicago. Surveyed 7-15 year old children in Chicago, from 1947. Nutritionist and nurse took dietary histories, food recall for prior 24 hours. Patients were given 7 day food diaries to take home. Selection criteria of patients not stated	Not stated	Rheumatic children in poverty had a mean egg consumption of 2.8 per week (SD +/- 2.7), compared to non-rheumatic children living in prosperity 4.3 eggs per week, (SD +/- 3.2)	p<0.01	Families who had escaped poverty had a higher consumption of egg yolk and other foods, compared to rheumatic and non-rheumatic families in poverty
	2. Literature review	Overview of literature surrounding egg yolks, eggs and rheumatic fever. Five studies discussed (not all named). Interventions included giving patients eggs, egg yolks, egg yolk powder or egg yolk alcohol-soluble material (ASM). No mention of control or comparison groups	Not stated	These studies showed that if egg yolk or its alcohol soluble fraction were given, rheumatic recurrences fell below the "expected" number. Low consumption of eggs seemed to be associated with higher incidence of rheumatic recurrences	Not estimated	Coburn suggests these studies show a link between egg consumption and a lower risk of rheumatic fever recurrence, but points out that the study designs are 'not ideal'
Longo-Mbenza B et al. 1998[81]	Cross sectional study	Kinshasa, Zaire, 1996. 4,848 school children randomly selected from urban area and adjoining slums were screened for RHD. All examined and those suspected of RHD were seen by a cardiologist. Prevalence of RHD: 59 definite cases, rate 14.03 per 1,000 children	Not stated	BMI 13.41 +/- 5.78 kg/m < mean - 1 SD versus > mean -1 SD	OR=2.64, (95% CI, 1.48-4.70) p=0.001	Low BMI was a prognostic factor for rheumatic heart disease in the Kinshasa slums
				Low birth weight	OR=1.81, (95% CI, 1.04-3.15) p=0.03	Low birth weight was associated with rheumatic fever
				BMI <7.63 kg/m^2	RR=2.64	A lower BMI was associated with a greater risk of rheumatic fever

Vlajinac H et al. 1989[50]	Case control	Yugoslavia. 148 cases with a first attack of rheumatic fever, satisfying Jones criteria, who were at home at time of survey. Three healthy controls matched for each rheumatic fever patient	Revised Jones	Under-nourishment in the study group as a whole	RR=2.18, (95% CI, 1.33-3.58), p<0.01	Some association between under-nourishment and rheumatic fever
				Frequent sore throats and under-nourishment together	RR=5.53, (95% CI, 2.70-11.34), p<0.001	An association between frequent sore throats and under-nourishment was found
Vlajinac H et al. 1991[51]	Case control	148 cases with a first attack of rheumatic fever satisfying Jones criteria, which were home at time of survey. Three healthy controls matched for each rheumatic fever patient	Revised Jones	Body weight below normal (more than 10% below Baldwin-Wood's table weights)	Coefficient 0.348, adjusted relative risk 1.42, (95% CI, 1.08-1.86), p=0.010	An association between below – normal body weight and rheumatic fever was seen
Zaman M et al. 1998A[80]	Case series with controls	Dhaka, Bangladesh. 218 consecutive patients aged 5-20 with group A beta haemolytic streptococcal infections from an outpatient clinic were screened. 60 had rheumatic fever and 44 of those had fasting convalescent blood samples taken 3-4 weeks after first contact. The remaining 139 patients did not have rheumatic fever. Rheumatic fever cases were matched with controls matched for sex and for age within one year. Blood levels of albumin, cholesterol, triglycerides, haemoglobin, PCV, iron, total iron binding capacity and transferring saturation were analysed. (Only significant results discussed in outcome column)	Updated Jones 1992	Albumin levels(g/ l): rheumatic fever patients had a mean level of 44 (SD +/- 4), controls had mean levels of 48 (SD +/- 3)	Adjusted for location of residence, parental schooling, number of siblings and CRP. Adjusted OR: 0.75, (95% CI, 0.60-0.95), p=0.02	Significant link between low albumin and rheumatic fever found
				Iron levels (µm/l): rheumatic fever patients had a mean level of 9 (SD+/-5), compared to controls, who had a mean iron level of 14 (SD+ /-6)	OR=0.82, (95% CI, 0.68-0.97) p=0.02	A link between low iron stores and rheumatic fever was found
Zaman M et al. 1998B[75]	Case series with controls	Same study as above. 60 cases of rheumatic fever and 104 patients put in control group. Socioeconomic indicators, various body measurements and intake of 13 foodstuffs were assessed. (Only significant foodstuffs and body measurements discussed in outcomes column)	Updated Jones 1992	'Low' was defined as less than median intakes in controls. Low intake of eggs: If less than the median intake of controls (amount not specified for eggs)	Adjusted for age, sex, location of residence, parental schooling, log income, and parental schooling. Adjusted OR=2.29, (95% CI, 1.01-5.27), p=0.05	An association between low intake of egg and thin upper arms for age, was observed
				Upper arm circumference for age <80%	Adjusted OR=2.40, (95% CI, 1.04-5.77), p<0.05	

Appendix 30: Role of fomites in spread of GAS

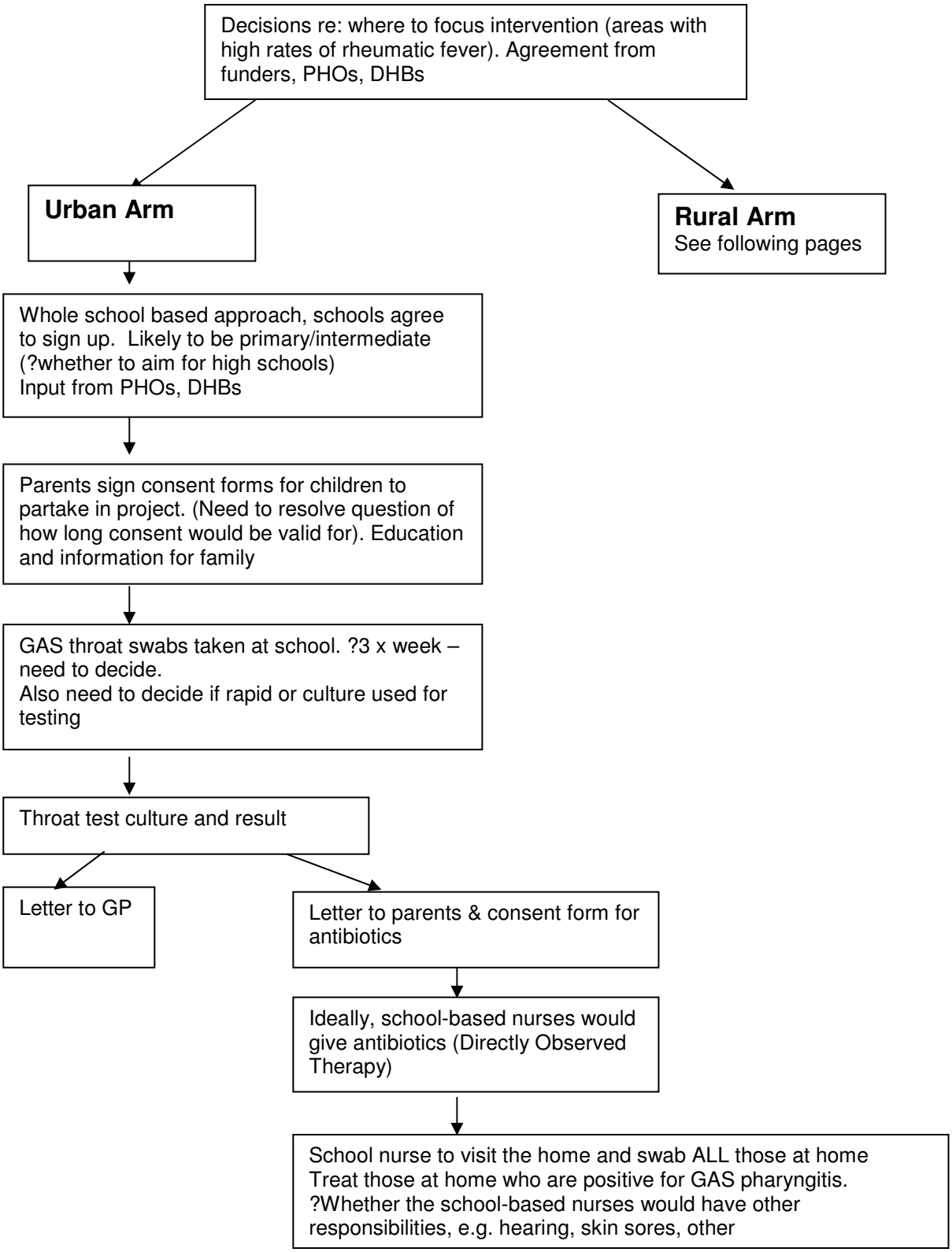
Table 32. Role of fomites in spread of GAS

STUDY	PATIENTS	INTERVENTION	RESULT
Falck G et al. 1998[72]	114 patients with GAS pharyngitis and 289 family members	Experimental study with control group. 54 patients and their families were instructed to change their toothbrush, bed linen and wash children's toys. At 6-10 days, household members had nose throat swabs taken and samples were taken from pillowcases, floors, toothbrushes, children's dummies and toys. T typing was done. Followed for 28-35 days	Recurrence with the same T type was designated treatment failure, and assessed after 35 days. **Intervention group:** 17/46=37% had treatment failure. **Control group:** 10/39=26% had treatment failure
Perry WD et al. 1957A[84]	Wyoming, USA. 37 airmen, 8 volunteers (laboratory staff and jail inmates), all involved in the intervention.	Experimental study. 2 volunteers (staff): Repeatedly exposed to dust contaminated with GAS in confined space. 6 volunteers (staff and jail inmates) directly inoculated by sprinkling dust on posterior oropharynx or forcibly blowing the sample into the posterior nasopharynx. 37 airmen: Lived in GAS dust-contaminated barracks. Nasal and oropharangeal cultures were taken regularly, for up to 10 days. M typing was done	No infections resulted
Perry WD et al. 1957B[85]	Wyoming, USA. 85 airmen (intervention group), 177 airmen as controls.	Experimental study with control group. **Intervention group:** 85 airmen given blankets 'naturally contaminated' with during the winter of 1952. **Control group:** 177 airmen. Oropharyngeal and nasal cultures were taken and a record of respiratory symptoms was kept. They were observed for 17-23 days. M typing was done	**Intervention group:** 6 GAS oropharyngeal infections (in 8,688 days exposed). 4 of those were of a different serotype from the GAS on the blankets, 2 were the same. **Control group:** 16 GAS oropharyngeal infections (in 16,021 days exposed). 14 of those were a different serotype from the GAS on the blankets, 2 were the same

Appendix 31: Proposed school clinic sore throat project

Figure 5. School Clinic Sore Throat Model (Urban & Rural)

Firstly, need to increase the profile of rheumatic fever to raise the awareness of the importance of treating sore throats.

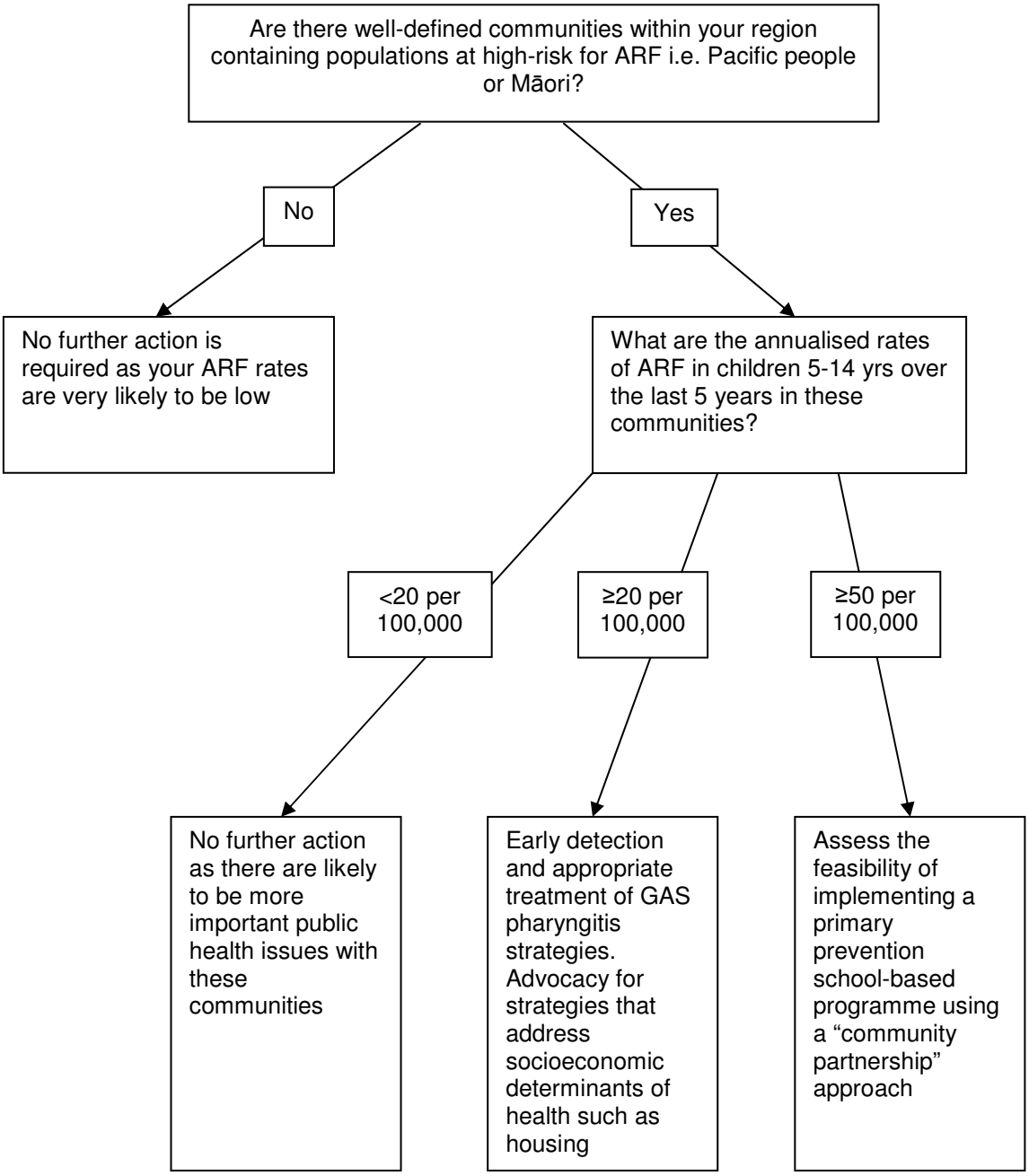


Source: Rheumatic Fever Primary Prevention in small town and rural settings (by J. Jarman)

Appendix 32: Algorithm Guide for Public Health Units

Figure 6: Algorithm Guide for Public Health Units

Selection of appropriate strategies for primary prevention of acute rheumatic fever in small town and rural settings in New Zealand.



Feasibility Assessment of Community Partnership Approach

Whangaroa in Northland implemented a school-based rheumatic fever prevention programme in 2002. Prior to the intervention the rates of disease were the highest in New Zealand and all cases were Māori. The last case from this area occurred 8 days after the programme started in 2002.

Factors that were associated with the successful Whangaroa programme:

- Preceding community concern
- Concern by local health care workers about the level of disease in the community
- Support of the programme by the community paediatrician
- Well-defined area with single iwi provider and primary health provider
- Schools mainly take children from the high incidence area
- Partnership, participation, protection and "passion" – the iwi provider and primary health provider are both committed to the programme; the iwi provider acts as the local "champion" for the programme; there is joint decision making shared between the iwi provider; the primary health provider and the regional public health provider; the community and schools are very supportive; and local people are employed to do the throat swabbing in the schools
- Awareness of the scale of the disease and willingness by the District Health Board and Ministry of Health to tackle a serious childhood disease with major inequalities

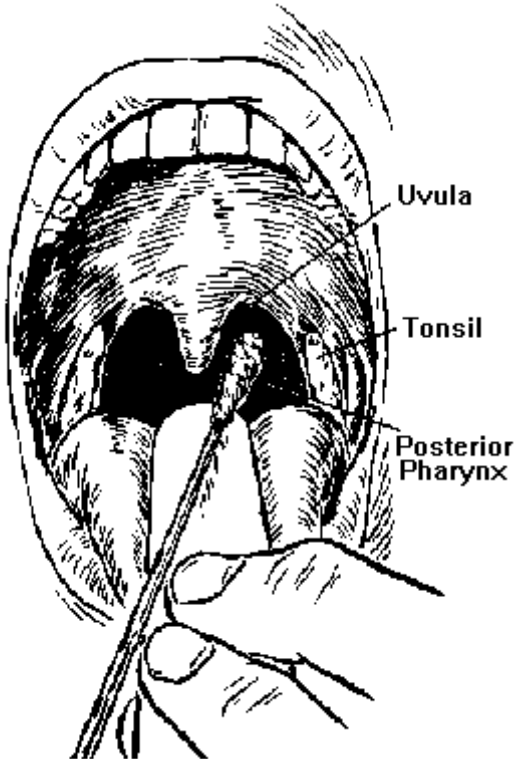
Table 33: Feasibility Assessment

1.	Is the epidemiology of the disease well described? • What are the numbers of cases and annualised rates for children aged 5-14 years over the last 10 years? • Are the numbers and/or rates increasing, decreasing or stable? • Are there ethnic disparities? • How do the rates compare with national rates? • Are there "hotspots" based on attendance at certain schools? • Is there a high level of population mobility?
2.	Is there community concern about rheumatic fever especially in the populations with the highest level of risk?
3.	Is there concern by local health care workers (PHOs, iwi health providers, Pacific health providers and others) about the level of disease in the community and are they knowledgeable about its preventability?
4.	Do the local paediatricians support a rheumatic fever prevention programme in this community?
5.	Is the area well defined? Do schools mainly take children from the high incidence area?
6.	Is there a community agency that can act as the local "champion"?
7.	Can the local health providers, iwi providers and regional public health provider work together in partnership with the community on this issue?
8.	Are the local schools knowledgeable about rheumatic fever and supportive of a school-based prevention programme?
9.	Are the District Health Board and the Ministry of Health aware of the level of disease in the area and know about: • The evidence supporting a school-based initiative from the meta-analysis of community intervention trials (including the New Zealand trial)? • The effectiveness of the Whangaroa rheumatic fever prevention programme which has eradicated rheumatic fever?

RECOMMENDATIONS
Public Health Units with communities containing populations that are at high-risk for ARF (i.e. Māori and Pacific peoples) should regularly calculate rheumatic fever rates for children aged 5-14 years in those specific communities
If annualised age-specific rheumatic fever rates over the last 5 years are 20 per 100,000 and over in communities then it is recommended that Public Health Units should implement strategies that: • target the early detection and appropriate treatment of GAS pharyngitis • address socio-economic determinants of health such as housing
If annualised age-specific rheumatic fever rates over the last 5 years are 50 per 100,000 and over in communities then it is recommended that Public Health Units should assess the feasibility of implementing a primary prevention school-based programme using a “community action” approach

Appendix 33: Throat swab technique

Figure 7. Throat Swab Technique



Technique:

Ask the culturee to open the mouth widely and say a long "ah". The tongue should be gently depressed with a sterile tongue blade. The swab is then gently passed over the tongue and into the posterior pharynx. The mucosa behind the uvula and between the tonsils should then be gently swabbed with a back-and-forth motion. (Downloaded 26/09/06 from: http://web.indstate.edu/thcme/micro/samp-lab.html

The tongue should be depressed and the throat adequately exposed and illuminated. Routinely the swab should be rubbed over each tonsillar area and the posterior pharynx. Any area exhibiting exudate should also be touched. Care should be taken to avoid contaminating the swab by touching the tongue and lips.[163]

Source: Diagram and related text reprinted with permission from Johnson 2007.[164]
http://web.indstate.edu/thcme/micro/samp-lab.html

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14. Key Definitions

Group A streptococcus (GAS): Also known as *Streptococcus pyogenes*: Gram positive cocci producing beta haemolysis on blood agar.

Pharyngitis: Acute pharyngitis is an inflammatory syndrome of the pharynx caused by a variety of micro organisms. Most cases are of viral aetiology and occur as part of common colds and influenza syndromes. The most important cause of bacterial pharyngitis is that due to group A beta haemolytic streptococci (*Streptococcus pyogenes)*.[165]

Rheumatic fever: Acute rheumatic fever (ARF) is a disease characterised by non-suppurative inflammatory lesions involving primarily the heart, joints, central nervous system, and skin and subcutaneous tissues. Permanent sequelae may result from cardiac involvement. Current opinion holds that all cases of ARF follow a group A streptococcal (GAS) upper respiratory tract infection, although the exact mechanism is unclear. ARF is diagnosed using the Jones Criteria[166] and adapted in New Zealand (and also Australia) to permit echocardiography as a diagnostic criteria (see www.nhf.org.nz , New Zealand Guidelines for Rheumatic Fever: 1. Diagnosis, Management and Secondary Prevention, table 3: Major manifestations of ARF).

Sydenham's chorea: Jerky, unco-ordinated movements, especially affecting hands, feet, tongue and face. Can be a manifestation of ARF. (for a more detailed explanation of Sydenham's chorea see www.nhf.org.nz, New Zealand Guidelines for Rheumatic Fever: 1. Diagnosis, Management and Secondary Prevention, table 3: Major manifestations of ARF).

Case control study: A study which involves identifying with the outcome of interest (cases) and control patients who do not have the same outcome, and looking back to see if they had an exposure of interest.[167]

Confidence interval (CI): Quantifies uncertainty in measurement, usually uses 95% or 99%. A 95% CI is the range of values within which we can be 95% certain that the true value for the whole population lies.[167]

Meta analysis: A systematic review that uses quantitative methods to synthesize and summarise the results.[167]

Odds ratio (OR): The odds of having the target disorder in the experimental group, compared to the odds in favour of having the target disorder in the control group (in cohort studies or systematic reviews) OR the odds in favour of being exposed in participants with the target disorder divided by the odds in favour of being exposed in control participants (without the target disorder).[167]

p value: The probability a result could have occurred by chance. It is usually set at 0.05 by convention, which means there is a 5% probability that the effect occurred by chance. A p value of $p > 0.05$ means the effect may have been due to chance, a P value of $P < 0.05$ means the association between the exposure and the disease is considered statistically significant.[168]

Randomised controlled clinical trial (RCT): Clinical trial in which participants are randomly allocated into an experimental or into a control group, and followed over time for the outcomes of interest.[167]

Risk ratio (RR): The ratio of risk in the treated group compared to the risk in the control group.[167]

Sensitivity: The proportion of people with the target disorder who have a positive test result.[167]

Specificity: The proportion of people without the target disorder who have a negative test result.[167]

Systematic review: A summary of medical literature that uses explicit methods to perform a comprehensive literature search and critical appraisal of individual studies, and that uses appropriate statistical techniques to combine the valid studies.[167]

15. Glossary

APSGN..... acute post streptococcal glomerulonephritis
ARF..... acute rheumatic fever
ASO..... antistreptolysin O
BD..... twice a day
DHB..... District Health Board
GAS..... group A streptococcal
IDSA..... Infectious Diseases Society of America
IM..... intramuscular
MU..... million units
OD..... once a day
PO..... orally
QID..... four times a day
RCT..... randomised control trial
TDS..... three times a day
U..... units
URTI..... upper respiratory tract infection

Cardiovascular disease is the leading cause of death in New Zealand, accounting for 40 percent of all deaths annually (approx. 10,500 people).

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- Working with Pacific people through Pacific Islands Heartbeat (PIHB).

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