



Evidence synthesis

Group A *Streptococcus* and acute rheumatic fever in Aotearoa New Zealand

A summary of current knowledge in Aotearoa New Zealand

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Office of the Prime Minister's Chief Science Advisor
Kaitohutohu Mātanga Pūtaiao Matua ki te Pirimia
Private Bag 92019
Victoria Street West
Auckland 1140
New Zealand

Phone: +64 9 923 6318
Website: www.pmcsa.ac.nz
Email: info@pmcsa.ac.nz

Overview

This review aims to summarise what we know about the processes that lead to group A streptococcus (GAS) infection, acute rheumatic fever (RF) and rheumatic heart disease (RHD) in Aotearoa New Zealand. It has been produced by the OPMCSA, supported by an expert panel, and has been provided to the Ministry of Health to inform their rheumatic fever workstream. It has a primary focus on the Aotearoa New Zealand knowledge base and lessons learned from previous initiatives, but places this in an international context where appropriate. It does not contain recommendations.

The areas covered in the full report are:

- How GAS infection leads to RF and RHD, including emerging evidence of the possible role of skin infections.
- The global context for RF and RHD, including Aotearoa New Zealand's position within this context.
- How GAS infection, RF and RHD are monitored in Aotearoa New Zealand.
- Current rates and trends of GAS infection, RF and RHD in Aotearoa New Zealand.
- Data on the uneven burden of RF and RHD affecting Māori and Pacific peoples, including evidence for the drivers of these inequities.
- Indirect risk factors associated with RF.
- Lived experience of people with RF and RHD and their whānau.
- The financial and social costs of the high disease burden.
- The range of interventions that have been tried and whether there is evidence of effectiveness.
- Future developments in this area, including vaccines, new diagnostic tools and drug development/reformulation.
- Research priorities to fill in knowledge gaps.
- AMR considerations associated with treatment and prevention of these diseases.

Note that the review is largely focused on local studies and evidence, both published and gleaned from conversations with experts within the research and medical community, so most information is from Aotearoa New Zealand. Where evidence is from overseas, this is explicitly stated.

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Our panel

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- Dr Matire Harwood (Ngāpuhi) (co-chair), University of Auckland and Papakura Marae Health Clinic
- Dr Anneka Anderson (Kāi Tahu, Kāti Māmoe), University of Auckland
- Professor David Murdoch, University of Otago
- Dr Dianne Sika-Paotonu, University of Otago
- Professor Jack Heinemann, University of Canterbury
- Dr Kristin Dyet, ESR
- Associate Professor Mark Thomas, University of Auckland and Auckland DHB
- Distinguished Professor Nigel French, Massey University
- Dr Sharon Gardiner, Canterbury DHB
- Associate Professor Siouxsie Wiles, University of Auckland



The Kotahitanga panel and OPMCSA staff. From left to right: Kristin Dyet, Ellen Rykers, Siouxsie Wiles, Rachel Chiaroni-Clarke, Mark Thomas, Dianne Sika-Paotonu, Nigel French, Juliet Gerrard, Jack Heinemann, Matire Harwood, Sharon Gardiner, George Slim, Anneka Anderson, David Murdoch.

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- Rachel Pearce – Capital and Coast DHB
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- Iain Diamond – Hauora Tairāwhiti DHB
- Aaron Randall – Hutt Valley DHB
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- Dr Catherine Jackson and Joanne Rivers – Northland DHB
- Adam Wardle, Dr Richard Vipond, Kelly Reddington and Savaira Delaibatiki – Waikato DHB
- Kim MacRae – Waitematā DHB
- Dr Teuila Percival – KidzFirst Hospital
- Associate Professor Nigel Wilson – Starship Hospital and Auckland DHB
- Dr Elizabeth Wilson – Starship Hospital
- Mary McLean and Dr Alastair McLean – Western Heights Health Centre
- Associate Professor Arindam Basu – University of Canterbury
- Dr Julie Bennett – University of Otago
- Professor John Fraser – University of Auckland
- Dr Jacelyn Loh – University of Auckland
- Associate Professor Nikki Moreland – University of Auckland
- Dr Rachel Brown – National Hauora Coalition
- Mark Cox – Health IT consulting
- Dr Eric Hillerton – Independent consultant
- Patrick Cummeskey – St John
- Carla White – Health Literacy NZ
- Dr Willy-John Martin – Ministry of Business, Innovation and Employment

Abbreviations

Abbreviation	Definition
AMR	Antimicrobial resistance
ARPHS	Auckland Regional Public Health Service
BPG	Benzathine Penicillin G
CANVAS	Coalition to Advance New Vaccines for Group A <i>Streptococcus</i>
CI	confidence interval
DALY	Disability-adjusted life year
DHB	District Health Board
GAS	Group A <i>Streptococcus</i>
HCP	Healthcare professional
HRC	Health Research Council
ICD	International Classification of Diseases
IGH	immunoglobulin heavy chain
LAMP	loop-mediated isothermal amplification
NHMRC	National Health and Medical Research Council
QALY	Quality-adjusted life year
RF	Acute rheumatic fever
RFPP	Rheumatic fever prevention programme
RHD	Rheumatic heart disease

Executive summary

Despite Aotearoa New Zealand's government previously setting reduction targets and establishing multi-agency approaches to reduce the incidence of acute rheumatic fever (RF), rates of this disease have remained stubbornly high. Certain subgroups of the population – namely, young Māori and Pacific peoples – are burdened with rates otherwise only seen in low-income nations or within Indigenous populations. The evidence that previous interventions have not resulted in sustained decreases in RF rates highlights the need to re-evaluate the evidence base and redouble efforts in areas that may make a difference.

There are four points of intervention for tackling problems associated with RF in Māori and Pacific people aged 3–30 years:

- **Preventing Group A *Streptococcus* (GAS) exposure.** This is also referred to as primordial prevention, which reduces GAS infections caused by social and environmental determinants and may also include biomedical interventions. Reducing the risk of GAS transmission and infection will be the most significant way to prevent more adverse health outcomes.
- **Preventing RF.** This is also referred to as primary prevention which attempts to diagnose, manage and treat GAS infection. We know that for some people the more times a person has GAS infection, the more likely they develop RF, so early effective diagnosis and treatment of GAS infection in high-risk groups is critical.¹
- **Preventing RHD.** This is also referred to as secondary prevention, a strategy to prevent reinfection by GAS, at least until they have passed the age group who are at risk, therefore preventing another episode of RF. Each episode of RF damages the heart so those who have had RF once need to be targeted to prevent another episode.
- **Minimising complications of RHD.** This is also referred to as tertiary intervention, which relates to medical management and interventions that optimise the outcomes for a person with RHD.

Within this context, this review highlights the following:

1. How RF triggers lead to disease is not fully understood

- How RF is triggered is not fully understood, which provides barriers to implementing effective primary prevention approaches. The evidence to date suggests a substantial focus on treating GAS sore throats hasn't made a sustained significant difference to RF rates, although there are significant regional successes.
- Observed associations between RF and GAS skin infections suggests a role in development of RF which may be significant. Further work is required to determine whether treating GAS skin infections with antibiotics will lead to a reduction in RF.
- Changes to rates of RF need to be interpreted in the context of some key risk factors changing for high-risk groups (e.g. housing conditions, access to primary healthcare and poverty) which may change the baseline against which the intervention is measured.

2. Risk factors for RF are complex but can guide interventions

- Evidence supports a more targeted intervention approach based on family history of RF, ethnicity, level of socio-economic deprivation and age.
- There is evidence to suggest that improving socio-economic and living conditions would reduce RF risk, and this would have broader positive impacts on health for the individual and their whānau. There is significantly more work to be done to reduce the RF risks associated with housing and poverty, especially household crowding.
- Other risk factors relating to health and nutrition, and compromised skin integrity, have weaker evidence and the mechanisms are not understood well enough to inform interventions yet.

¹ Lorenz, N., Ho, T.K., McGregor, R., *et al.* (2021). Serological profiling of group A *Streptococcus* infections in acute rheumatic fever. *Clinical Infectious Diseases*. <https://doi.org/10.1093/cid/ciab180>

- The 2021 fall in RF rates for Pacific populations needs evaluation – whether this is explained by reduced travel between Aotearoa New Zealand and the South Pacific should be investigated in order to understand whether this travel is a significant risk factor.

3. It's not only overrepresentation for other risk factors that leads to higher RF rates for Māori and Pacific peoples

- The evidence demonstrates that irrespective of deprivation level, the risk for RF is higher for Māori and Pacific peoples. Complex factors, which may include racism in the healthcare sector that causes barriers to access and inequity in quality of treatment, are understood to contribute to the burden of disease experienced by Māori and Pacific peoples.
- Evidence of the lived experience of Māori and Pacific peoples navigating the healthcare system to deal with GAS infection, RF or RHD provides important insights to guide interventions and reduce some of these barriers to accessing care and healthcare delivery.

4. A greater focus on active case finding for latent RHD may improve disease outcomes

- Evidence shows that 80% of patients presenting with RHD never presented with RF and that around 2% of people in cohorts at high risk of RF might have latent RHD.²
- Emerging evidence indicates that giving antibiotics to prevent relapse of RF (secondary prophylaxis) improves outcomes for people with latent RHD. This suggests that active case finding using echocardiography and effective secondary prevention services could be an effective way to reduce the poor health outcomes associated with RF and RHD (subject to resourcing requirements and meeting Ministry of Health screening criteria).
- It would be useful to audit a sample of initial RHD patients not previously hospitalised for RF to see if diagnostic opportunities had been missed with prior health encounters.

5. Going forward, the approach to RF/RHD prevention and control should be holistic, collaborative, Māori- and Pacific-led and underpinned by a national strategy which includes local context in its application

- One intervention alone is unlikely to significantly reduce the incidence of GAS and RF and it is likely that a coordinated suite of interventions is needed.
- Features of multipronged approaches where significant reductions in RF rates were achieved in Costa Rica, Cuba, the French Caribbean and Tunisia, included:
 - Improving living and socio-economic conditions.
 - Free and easy access to healthcare to remove barriers to receiving primary care.
 - The use of a one-off benzathine benzylpenicillin injection instead of a 10-day course of oral antibiotics to treat GAS throat infection to improve antibiotic adherence.
 - A centralised RF patient register and patient management system to coordinate a robust secondary prophylaxis service.
- Barring the roll-out of a vaccine, RF remains a complex disease which will not be eliminated until poverty, household crowding, racism and barriers to accessing health services are tackled.³ Inequities need to be addressed and framing should not just be that individuals are responsible for their own health outcomes when structural issues are at play.⁴
- Australia has the Endgame Strategy, which is the blueprint to eliminate RHD in Australia by 2031. The Endgame Strategy includes resourcing an Aboriginal and Torres Strait Islander national

² Oliver, J., Robertson, O., Zhang, J., *et al.* (2021). Ethnically disparate disease progression and outcomes among acute rheumatic fever patients in New Zealand, 1989–2015. *Emerging Infectious Diseases*, 27(7), 1893-1902. <https://doi.org/10.3201/eid2707.203045>

³ Shaio, M.-F. (2021). The impact of racism on rheumatic fever rates. *Kai Tiaki: Nursing New Zealand*, 27(1), 36-37.

⁴ Anderson, A. and Spray, J. (2020). Beyond awareness: Towards a critically conscious health promotion for rheumatic fever in Aotearoa, New Zealand. *Social Science & Medicine*, 247, 112798. <https://doi.org/10.1016/j.socscimed.2020.112798>

implementation unit to coordinate work, deliver resources, and link communities and researchers.⁵ Successes and failures of this strategy could inform equivalent initiatives in Aotearoa New Zealand.

- A nationally coherent strategy could be adapted to local contexts; research into this is well-advanced.

6. Monitoring and surveillance of RF and RHD rates and outcomes is inadequate

- Evidence highlighted in this report shows that monitoring and surveillance of GAS infection, RF and RHD needs to be significantly improved.
- This is of particular importance to determine the effectiveness of interventions on RF rates and outcomes.
- Interventions require better design to enable robust monitoring of impact, and future interventions require robust monitoring and evaluation from the outset.
- A national RF register would be a key step in improving data related to RF rates and outcomes, and enabling robust monitoring of the effectiveness of interventions.
- Experts have been calling for a national register for many years.⁶ This was announced as part of the 'Healthy Homes and Hearts Rheumatic Fever Initiative' but has not yet been implemented.⁷ Work is currently underway to explore what such a patient management system might look like.
- A series of recommendations were made in a Ministry of Health-commissioned surveillance sector review by Oliver *et al.* 2014, though most have not yet been implemented.⁸ This provides detailed advice on how to utilise existing datasets to establish a national register.
- Using innovative IT solutions to de-silo data, share records with patients and whānau, integrate lab results for a fast response and support patient follow-up could support better outcomes

7. Biomedical research offers medium term potential for prevention and treatment

- Research into a vaccine offers a promising avenue for prevention of GAS infections.
- Research into new methods of formulation and delivery of antibiotics offers hope for improved compliance with long-term treatment regimens.

⁵ Wyber, R., Noonan, K., Halkon, C., *et al.* (2020). Ending rheumatic heart disease in Australia: The evidence for a new approach. *Medical Journal of Australia*, 213, S3-S31. <https://doi.org/10.5694/mja2.50853>; *ibid.*

⁶ Oliver, J., Pierse, N. and Baker, M.G. (2014). Improving rheumatic fever surveillance in New Zealand: Results of a surveillance sector review. *BMC Public Health*, 14(1), 528. <https://doi.org/10.1186/1471-2458-14-528>; Bennett, J., Anderson, A., Malakai'Ofanoa, P.A., *et al.* (2021). Acute rheumatic fever—a preventable, inequitable disease: A call for action. *The New Zealand Medical Journal*, 134(1535), 93-95. ; Bennett, J., Zhang, J., Leung, W., *et al.* (2021). Rising ethnic inequalities in acute rheumatic fever and rheumatic heart disease, New Zealand, 2000–2018. *Emerging Infectious Diseases*, 27(1), 36. <https://doi.org/10.3201/eid2701.191791>

⁷ New Zealand Labour Party. (2020, 4 October 2020). *Healthy homes and hearts in rheumatic fever initiative* [Press release]. Retrieved from <https://www.scoop.co.nz/stories/PO2010/S00043/healthy-homes-and-hearts-in-rheumatic-fever-initiative.htm>

⁸ Oliver, J., Pierse, N. and Baker, M.G. (2014). Improving rheumatic fever surveillance in New Zealand: Results of a surveillance sector review. *BMC Public Health*, 14(1), 528. <https://doi.org/10.1186/1471-2458-14-528>

1 Introduction: Group A *Streptococcus* infection can lead to serious heart disease

Streptococcus pyogenes (referred to here as GAS⁹) is one of the most pervasive human pathogens. GAS spreads exclusively from person to person, through large airborne droplets and skin-to-skin contact. This bacterium can cause different types of disease, including throat infections (commonly referred to as strep throat or GAS pharyngitis).¹⁰ A course of an oral antibiotic (usually 10 days of amoxicillin), or a single injection of a long-acting intramuscular penicillin antibiotic (benzathine benzylpenicillin, BPG) every 28 days, can usually cure GAS throat infections. It can also self-resolve without the need for antibiotic treatment, therefore only children at risk require a prescription. In practice, this requires doctors and other healthcare professionals to recognise when it is necessary to treat a sore throat with antibiotics, bearing in mind that most sore throats will be caused by a viral infection and not by GAS infection, and the need to limit inappropriate use of antibiotics to reduce the risk of antimicrobial resistance (AMR).

... only children at risk require a prescription

Left untreated during acute infection, some GAS throat infections can trigger an autoimmune response in a small percentage of susceptible children and young people. In these patients, repeated exposure to GAS primes the immune system to attack its own cells.¹¹ An autoimmune response can cause RF and the person's symptoms may include fever, joint pain, tiredness, breathlessness, and in some cases, skin rash and involuntary movements. All suspected cases of RF are recommended to be assessed in hospital, though recent evidence suggests that many people with RF do not seek medical attention.¹² However, many people with RHD have no prior symptoms, or vague symptoms that are not picked up in primary care.

In Aotearoa New Zealand, RF diagnosis is made clinically using the Heart Foundation Guidelines which are based on the Jones Criteria, or by using a throat swab and by excluding other differential diagnoses, the latter leading to probable cases. Evidence of earlier infection with GAS must be shown, which is usually done by demonstrating raised concentrations of antibody to GAS in the patient's blood and/or pharyngeal culture of group A *Streptococcus*.¹³ Early and accurate diagnosis of RF is important because it enables doctors to start treatment (secondary prophylaxis) immediately and support young patients and their family/whānau to understand their need for long-term care.¹⁴

It is estimated that less than 3% of people who have an untreated GAS throat infection will develop a subsequent autoimmune response.¹⁵ We don't know yet exactly why GAS throat infection leads to RF in some children and young people but not others. Those who have previously developed RF and then end up with another GAS throat infection are more likely to have another RF episode and with that damage, or worsening damage, to the heart. This means preventing subsequent GAS infections in those who have already suffered from RF is a top priority. Without a GAS vaccine (see section 10.1), the most effective recommended preventative measure for children and young people involves adherence to a long-term, painful regimen of

⁹ *Streptococcus pyogenes* is also referred to as *S. pyogenes*, group A *Streptococcus*, group A strep or GAS.

¹⁰ Bisno, A.L. (1991). Group A streptococcal infections and acute rheumatic fever. *New England Journal of Medicine*, 325(11), 783-793. <https://doi.org/10.1056/NEJM199109123251106>

¹¹ Raynes, J.M., Frost, H.R.C., Williamson, D.A., et al. (2016). Serological evidence of immune priming by group A streptococci in patients with acute rheumatic fever. *Frontiers in Microbiology*, 7(1119). <https://doi.org/10.3389/fmicb.2016.01119>; Lorenz, N., Ho, T.K., McGregor, R., et al. (2021). Serological profiling of group A *Streptococcus* infections in acute rheumatic fever. *Clinical Infectious Diseases*. <https://doi.org/10.1093/cid/ciab180>

¹² Oliver, J., Robertson, O., Zhang, J., et al. (2021). Ethnically disparate disease progression and outcomes among acute rheumatic fever patients in New Zealand, 1989–2015. *Emerging Infectious Diseases*, 27(7), 1893-1902. <https://doi.org/10.3201/eid2707.203045>

¹³ Cannon, J.W., Zhung, J., Bennett, J., et al. (2021). The economic and health burdens of diseases caused by group A *Streptococcus* in New Zealand. *International Journal of Infectious Diseases*, 103, 176-181. <https://doi.org/10.1016/j.ijid.2020.11.193>; Jack, S., Moreland, N.J., Meagher, J., et al. (2019). Streptococcal serology in acute rheumatic fever patients: Findings from 2 high-income, high-burden settings. *The Pediatric Infectious Disease Journal*, 38(1), e1-e6. <https://doi.org/10.1097/INF.0000000000002190>

¹⁴ Wyber, R., Noonan, K., Halkon, C., et al. (2020). Ending rheumatic heart disease in Australia: The evidence for a new approach. *Medical Journal of Australia*, 213, S3-S31. <https://doi.org/10.5694/mja2.50853>

¹⁵ Bennett, J., Zhang, J., Leung, W., et al. (2021). Rising ethnic inequalities in acute rheumatic fever and rheumatic heart disease, New Zealand, 2000–2018. *Emerging Infectious Diseases*, 27(1), 36. <https://doi.org/10.3201/eid2701.191791>

monthly intramuscular BPG injections (known as secondary prophylaxis) for at least ten years or more. For most people this requires them to attend clinics every four weeks for a minimum of ten years, although home and school treatment is available in some District Health Boards (DHBs).

High adherence to this treatment regimen is associated with reduced recurrence of RF and improved long-term cardiac outcomes.¹⁶ Issues with long-term adherence to the current BPG injections persist, with a new formulation better suited for RF/RHD prevention urgently needed – research work is currently underway in Aotearoa New Zealand to develop a less painful and longer lasting alternative.

Preventing one or more episodes of RF is important because each autoimmune attack causes inflammation in many body tissues, including the heart. When the inflammation and other symptoms resolve, the heart damage remains. Approximately 60% of those with RF will move on to develop RHD.¹⁷ RHD commonly leads to damage to the heart valves and subsequently can lead to damage to the heart muscle causing heart failure (less effective pumping of the blood through the body), arrhythmia (abnormal heartbeat), increased risk of infective endocarditis (bacterial infection of the valves of the heart), stroke or other embolic complications, bleeding in those taking anticoagulation, pregnancy complications, and early death. RHD can be caused by a single severe episode or multiple recurrent episodes of RF and each episode can worsen the damage to the heart.¹⁸ RHD severity is caused by the host immune response and is associated with the degree of carditis during the initial RF episodes and repeated immunological insults caused by recurrent GAS infections and RF attacks.¹⁹ In those with severe RHD, surgery may be needed to repair or replace a damaged heart valve. All patients with RHD need to be recognised and monitored to try to prevent serious outcomes and death.

In brief:

- GAS infection (throat, or perhaps skin) is a requirement for developing RF.
- The more times a child or young person has an RF episode, the more likely they will develop RHD.
- Antibiotic prophylaxis (where people without evidence of infection are given antibiotics to prevent infection) is given to patients who have previously had RF to prevent them having repeated episodes of GAS infection that might predispose them to recurrent episodes of RF. This takes the form of BPG injections every 28 days for ten years or more.
- Prevention of RF helps prevent development of RHD and reduces its severity.
- The downside is that the widespread use of an antibiotic provides a haven for development of AMR infections of other kinds. It is important to ensure that antibiotic treatment is reserved for those who benefit and that they are not prescribed for viral sore throats.

¹⁶ de Dassel, J.L., de Klerk, N., Carapetis, J.R., *et al.* (2018). How many doses make a difference? An analysis of secondary prevention of rheumatic fever and rheumatic heart disease. *Journal of the American Heart Association*, 7(24), e010223. <https://doi.org/10.1161/JAHA.118.010223>

¹⁷ Lawrence, J.G., Carapetis, J.R., Griffiths, K., *et al.* (2013). Acute Rheumatic Fever and Rheumatic Heart Disease. *Circulation*, 128(5), 492-501. <https://doi.org/doi:10.1161/CIRCULATIONAHA.113.001477>

¹⁸ Karthikeyan, G. and Guilherme, L. (2018). Acute rheumatic fever. *The Lancet*, 392(10142), 161-174. [https://doi.org/10.1016/S0140-6736\(18\)30999-1](https://doi.org/10.1016/S0140-6736(18)30999-1)

¹⁹ Sika-Paotonu, D., Beaton, A. and Carapetis, J. (2018). Epidemiology and global burden of rheumatic heart disease *ESC CardioMed*: Oxford University Press.

GAS disease pathway

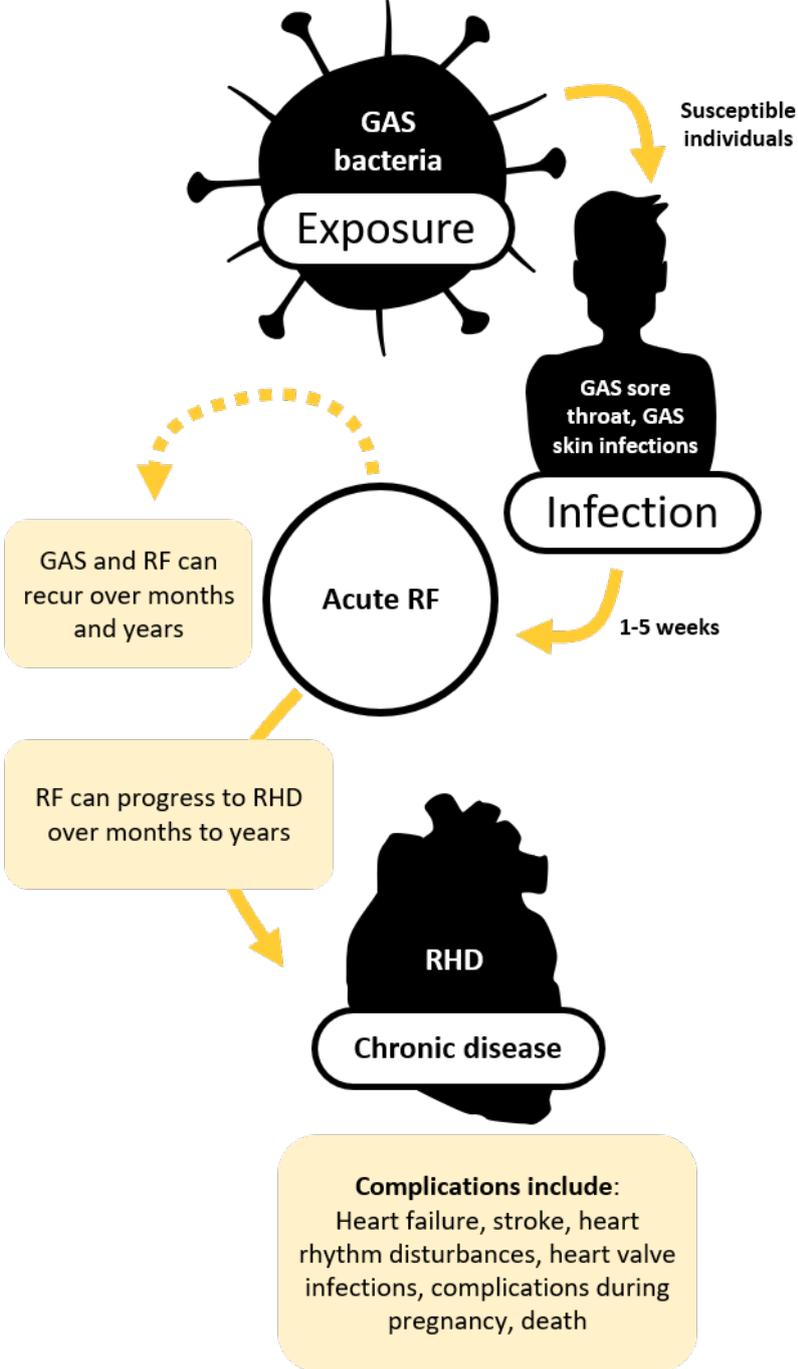


Figure 1: The process from being exposed to GAS bacteria through to the chronic heart condition of RHD.

1.1 Emerging evidence suggests GAS skin infections may be associated with rheumatic fever

The evidence for what triggers RF is evolving. Previously, the autoimmune responses that cause RF have been thought to be exclusively a consequence of GAS throat infections, but we know that not every child or young person has a sore throat before getting RF.²⁰ Estimates suggest up to 50% of cases do not recall having a sore throat in the weeks prior to an RF episode.²¹

Not every child has a sore throat before getting RF.

Investigations into the possible role of GAS skin infections in the development of RF have been undertaken for some time.²² Accumulating recent evidence, detailed below, explores the association between GAS skin infections and RF:

- A recent study found that 12.8% of skin swabs taken in Tāmaki Makaurau Auckland and sent to Labtests between 2010 and 2018 were positive for GAS, with much higher rates for Pacific and Māori people under 20 years (4.0 times and 6.8 times higher risk than other ethnicities, respectively).²³ Fifty percent of skin infections in Pacific children and 30% in Māori children were found to be due to GAS.
- A case-control study found that people with RF were 2.5 times more likely to report having had any skin infection recently.²⁴ The same study found a significantly elevated risk (16 times) of developing RF where the case had had both skin and throat infections recently, but the risk was not increased when looking at skin infections without throat infection. This is consistent with GAS throat infections being the primary driver of RF but a concurrent GAS skin infection increasing the risk markedly.
- Monthly, prospective surveillance of households in three remote Aboriginal communities in Australia found lower rates of GAS throat infection compared to GAS skin infections. For throats, the median point prevalence for GAS throat carriage was 3.7%, with 19.5% of children having GAS-positive throat swabs at some time during the two-year study, though none reported symptoms of a sore throat. For skin, the median point prevalence for GAS skin carriage was between 11.9–20.0%, while 37.7% of children had at least one skin infection during the study with 93% confirmed to be due to GAS.²⁵ There was a very high incidence of RF, with seven people diagnosed during the study period, with an incidence of 350 cases per 100,000 population per year.
- Recent testing of rapid molecular diagnostics for GAS found slightly higher rates of detectable GAS in the throat at the time of ARF diagnosis – but still a minority of all ARF cases.²⁶ Such rapid molecular diagnostics will help answer many questions on GAS carriage in throat and skin.

²⁰ O'Sullivan, L., Moreland, N.J., Webb, R.H., *et al.* (2017). Acute rheumatic fever after group A *Streptococcus* pyoderma and group G *Streptococcus* pharyngitis. *The Pediatric Infectious Disease Journal*, 36(7). <https://doi.org/10.1097/INF.0000000000001558>; Oliver, J.R., Pierse, N., Stefanogiannis, N., *et al.* (2017). Acute rheumatic fever and exposure to poor housing conditions in New Zealand: A descriptive study. *Journal of Paediatrics and Child Health*, 53(4), 358-364. <https://doi.org/10.1111/jpc.13421>

²¹ Baker, M.G., Gurney, J., Oliver, J., *et al.* (2019). *The New Zealand rheumatic fever risk factors study (RF RISK): Draft report on study findings*. Wellington, New Zealand: Rheumatic Fever Risk Factors Study.

²² Murphy, G.E. and Swift, H.F. (1949). Induction of cardiac lesions, closely resembling those of rheumatic fever, in rabbits following repeated skin infections with group A streptococci. *Journal of Experimental Medicine*, 89(6), 687. <https://doi.org/10.1084/jem.89.6.687>; Kerdemelidis, M., Lennon, D.R., Arroll, B., *et al.* (2010). The primary prevention of rheumatic fever. *Journal of Paediatrics and Child Health*, 46(9), 534-548. <https://doi.org/10.1111/j.1440-1754.2010.01854.x>

²³ Thomas, S., Bennett, J., Jack, S., *et al.* (2021). Descriptive analysis of group A *Streptococcus* in skin swabs and acute rheumatic fever, Auckland, New Zealand, 2010–2016. *The Lancet Regional Health - Western Pacific*, 8, 100101. <https://doi.org/10.1016/j.lanwpc.2021.100101>

²⁴ Baker, M.G., Gurney, J., Oliver, J., *et al.* (2019). *The New Zealand rheumatic fever risk factors study (RF RISK): Draft report on study findings*. Wellington, New Zealand: Rheumatic Fever Risk Factors Study.

²⁵ McDonald, M.I., Towers, R.J., Andrews, R.M., *et al.* (2006). Low rates of streptococcal pharyngitis and high rates of pyoderma in Australian aboriginal communities where acute rheumatic fever is hyperendemic. *Clinical Infectious Diseases*, 43(6), 683-689. <https://doi.org/10.1086/506938>

²⁶ Ralph, A.P., Holt, D.C., Islam, S., *et al.* (2019). Potential for Molecular Testing for Group A *Streptococcus* to Improve Diagnosis and Management in a High-Risk Population: A Prospective Study. *Open Forum Infectious Diseases*, 6(4). <https://doi.org/10.1093/ofid/ofz097>

- In an Aboriginal community in Australia that had a cluster of RF, only 4% of contacts tested had throat swabs positive for GAS compared to 46% of skin swabs from those with clinical evidence of impetigo being positive.²⁷
- In a prospective study of children in Australia, 93% of whom were Aboriginal from both urban, rural or remote settings, 19% reported skin sores prior to their RF diagnosis.²⁸ This needs to be interpreted in the context of the background population of skin sores.²⁹
- A review of rates of GAS skin infection and RF in tropical developing countries found a ‘striking epidemiologic association’ between the two and suggested it was time to reassess the dogma that only sore throats could lead to RF.³⁰

If GAS skin infections are associated with an increased risk in the development of RF for those with a GAS sore throat, this provides new opportunities for intervention – indeed, many school sore throat clinics include skin screening and are treating skin infections already (see table 7). However, whether treating GAS skin infections leads to a reduction in RF rates has not been shown and how they are treated is also important: antiseptics and coverings may not be enough. So far, the studies described above have demonstrated an association between skin infections and RF but not causation. Further research to understand the role of skin infections in the development of RF, and whether treating skin infections prevents RF, is essential and urgent to inform new interventions to reduce rates of RF.

1.2 Possible role for other *Streptococcus* groups

It has been proposed that the trigger for RF may, in some instances, be different beta hemolytic *Streptococci* bacteria – groups A, C and G. GAS are the main type of bacteria involved in the development of RF, but there is suggestive evidence that strep C and G may also play a role. These types of strep are less common than GAS.

Studies demonstrating a possible role for strep C or G in triggering RF include:

- Local case reports have identified people who developed RF that had recently had group C or G strep throat, but not a recent GAS throat infection. However, one person who developed RF after group G strep throat had also had GAS skin infection, so that may have been the trigger.³¹
- In remote Aboriginal communities in Australia, researchers found much higher loads of group C and G strep throat in the population, compared to GAS.³²

Confirming whether these other types of streptococcal infection prime the immune system for RF and understanding the proportion of RF cases that these infections may account for, is important to inform approaches to disease prevention and diagnosis. Again, to date these studies have only found an association and there is not yet evidence of causation. The role of group C and G strep throat infections in RF should be explored further.

²⁷ Francis, J.R., Gargan, C., Remenyi, B., *et al.* (2019). A cluster of acute rheumatic fever cases among Aboriginal Australians in a remote community with high baseline incidence. *Australian and New Zealand Journal of Public Health*, 43(3), 288-293. <https://doi.org/10.1111/1753-6405.12893>

²⁸ Noonan, S., Zurynski, Y.A., Currie, B.J., *et al.* (2013). A national prospective surveillance study of acute rheumatic fever in Australian children. *The Pediatric Infectious Disease Journal*, 32(1). <https://doi.org/10.1097/INF.0b013e31826faeb3>

²⁹ Bowen, A.C., Mahé, A., Hay, R.J., *et al.* (2015). The global epidemiology of impetigo: A systematic review of the population prevalence of impetigo and pyoderma. *PLOS ONE*, 10(8), e0136789. <https://doi.org/10.1371/journal.pone.0136789>

³⁰ Parks, T., Smeesters, P.R. and Steer, A.C. (2012). Streptococcal skin infection and rheumatic heart disease. *Current Opinion in Infectious Diseases*, 25(2). <https://doi.org/10.1097/QCO.0b013e3283511d27>

³¹ Lennon, D. (2018). A clear-cut case of acute rheumatic fever after group G streptococcal pharyngitis in New Zealand. *The Pediatric Infectious Disease Journal*, 37(4). <https://doi.org/10.1097/INF.0000000000001834>; O’Sullivan, L., Moreland, N.J., Webb, R.H., *et al.* (2017). Acute rheumatic fever after group A *Streptococcus* pyoderma and group G *Streptococcus* pharyngitis. *The Pediatric Infectious Disease Journal*, 36(7). <https://doi.org/10.1097/INF.0000000000001558>

³² Haidan, A., Talay, S.R., Rohde, M., *et al.* (2000). Pharyngeal carriage of group C and group G streptococci and acute rheumatic fever in an Aboriginal population. *The Lancet*, 356(9236), 1167-1169. [https://doi.org/10.1016/S0140-6736\(00\)02765-3](https://doi.org/10.1016/S0140-6736(00)02765-3)

The role of group C and G strep throat infections in RF should be explored further.

1.3 Understanding the role of different GAS serotypes

Researchers have also studied serotypes for GAS to understand the relationship with RF risk. Serotypes are distinguishable groups within a single microbial species. They are classified based on the differences in their surface structures (antigens). The serotypes for GAS are based on the on the cell surface 'M protein' – so are referred to as 'emm types' – and over 220 variants have been described.³³ Serotype analyses are complex and have limitations.³⁴ Whole genome sequencing approaches could also be deployed as a complementary approach.

The particular serotype causing infection may influence the site of infection or whether a specific vaccination or treatment works against it. For GAS, different serotypes can typically be associated with throat infections, skin infections or be generalist, and not all are known to trigger RF. Some serotypes are referred to as 'rheumatogenic' after being associated with RF, but RF is not restricted to those serotypes.³⁵

The different serotypes of GAS that cause RF have important implications for infection prevention, including vaccine development.³⁶ The differences can also be used to trace transmission and outbreaks.

Some local studies have examined the serotypes in circulation in Aotearoa New Zealand and how these are associated with RF risk:

- A local study evaluated whether GAS serotypes differed in places with high or low rates of RF found diverse serotypes with no clear pattern of distribution to explain differences in RF rates.³⁷
- Another study found that children at high risk of RF were more likely to have the skin serotype (*emm*-pattern D) and more diverse serotypes were circulating in those populations than in low-risk settings.³⁸
- The finding that serotypes associated with RF in Aotearoa New Zealand were those associated with skin, not the serotypes associated with RF in overseas studies, was also shown in another study.³⁹

³³ Sanderson-Smith, M., De Oliveira, D.M., Guglielmini, J., *et al.* (2014). A systematic and functional classification of *Streptococcus pyogenes* that serves as a new tool for molecular typing and vaccine development. *The Journal of Infectious Diseases*, 210(8), 1325-1338. <https://doi.org/10.1093/infdis/jiu260>

³⁴ Campbell, P.T., Tong, S.Y.C., Geard, N., *et al.* (2019). Longitudinal analysis of group A *Streptococcus emm* types and *emm* clusters in a high-prevalence setting: Relationship between past and future infections. *The Journal of Infectious Diseases*, 221(9), 1429-1437. <https://doi.org/10.1093/infdis/jiz615>; de Crombrugge, G., Baroux, N., Botteaux, A., *et al.* (2019). The limitations of the rheumatogenic concept for group A *Streptococcus*: Systematic review and genetic analysis. *Clinical Infectious Diseases*, 70(7), 1453-1460. <https://doi.org/10.1093/cid/ciz425>; Frost, H.R., Davies, M.R., Velusamy, S., *et al.* (2020). Updated *emm*-typing protocol for *Streptococcus pyogenes*. *Clinical Microbiology and Infection*, 26(7), 946.e945-946.e948. <https://doi.org/10.1016/j.cmi.2020.02.026>

³⁵ Williamson, D.A., Smeesters, P.R., Steer, A.C., *et al.* (2015). M-protein analysis of *Streptococcus pyogenes* isolates associated with acute rheumatic fever in New Zealand. *Journal of Clinical Microbiology*, 53(11), 3618-3620. <https://doi.org/10.1128/JCM.02129-15>; de Crombrugge, G., Baroux, N., Botteaux, A., *et al.* (2020). The limitations of the rheumatogenic concept for group A *Streptococcus*: Systematic review and genetic analysis. *Clinical Infectious Diseases*, 70(7), 1453-1460. <https://doi.org/10.1093/cid/ciz425>

³⁶ Williamson, D.A., Smeesters, P.R., Steer, A.C., *et al.* (2016). Comparative M-protein analysis of *Streptococcus pyogenes* from pharyngitis and skin infections in New Zealand: Implications for vaccine development. *BMC Infectious Diseases*, 16(1), 561. <https://doi.org/10.1186/s12879-016-1891-6>

³⁷ Mhlanga, N., Sharp, G. and Nulsen, M. (2017). *Emm* type distribution of group A *Streptococcus* isolates from the throat swabs of children living in areas with a high (Northland and Gisborne) or low (Palmerston North) incidence of acute rheumatic fever. *The New Zealand Medical Journal*, 130(1460), 13-20.

³⁸ Williamson, D.A., Smeesters, P.R., Steer, A.C., *et al.* (2016). Comparative M-protein analysis of *Streptococcus pyogenes* from pharyngitis and skin infections in New Zealand: Implications for vaccine development. *BMC Infectious Diseases*, 16(1), 561. <https://doi.org/10.1186/s12879-016-1891-6>

³⁹ Williamson, D.A., Smeesters, P.R., Steer, A.C., *et al.* (2015). M-protein analysis of *Streptococcus pyogenes* isolates associated with acute rheumatic fever in New Zealand. *Journal of Clinical Microbiology*, 53(11), 3618-3620. <https://doi.org/10.1128/JCM.02129-15>

Serotypes associated with RF in Aotearoa New Zealand have been associated with skin, not the serotypes associated with RF in overseas studies.

Further studies that assess serotypes in children who develop RF compared to those that do not are underway. There is also a current opportunity to get a baseline measure of circulating strains while the borders are closed due to the COVID-19 pandemic, to establish how these change upon reopening. Research is planned to compare GAS serotypes in Aotearoa New Zealand with those in Samoa and Tonga.⁴⁰ This research should be Pacific led.

1.4 GAS carriage in the throat

Not everyone who has GAS in their throat has a true GAS pharyngitis (defined as an infection that causes a two-fold increase in the streptococcal antibody titre). Sometimes the bacteria can colonise the throat without causing symptoms. It is not yet known whether it is the throat infection or the presence of bacteria without an infection that triggers RF or whether carriers infect others. However, the traditional way of testing for GAS throat infection is by testing for the presence of bacteria, not whether it has triggered an infection. Infection can be detected through serology testing, but it is not usually performed due to the requirement for a blood test, and time and cost constraints associated with repeat blood tests.

Estimates vary somewhat, but typically, in high income countries, one in five children with a sore throat will have GAS infection in their throat, but in only one in ten will the GAS infection be the cause of their sore throat. The other one in ten will have GAS carriage and an intercurrent virus infection that is the cause of the sore throat. A meta-analysis⁴¹ of studies provides more detail.

These findings suggest that treating all sore throats with antibiotics may only reduce the risk of RF for around 10% of patients with a true GAS sore throat. If treatment is narrowed down to those with a positive test for GAS, it may still only reduce risk for 50-60% of patients who have an active GAS throat infection. Using antibiotics on the remainder serves no benefit and has a wider cost of contributing to antimicrobial resistance issues.

These findings suggest that treating all sore throats with antibiotics may only reduce the risk of RF for around 10% of patients with a true GAS sore throat. If treatment is narrowed down to those with a positive test for GAS, it may still only reduce risk for 50-60% of patients who have an active GAS throat infection.

An even higher rate of carriage of around 30% was estimated for school children in Aotearoa New Zealand in the 1970s.⁴² A study from 2017 found GAS pharyngeal prevalence of 22.4% in Auckland children prior to the commencement of a school sore throat clinic programme.⁴³

Accurate diagnosis of an active GAS throat infection remains a major barrier to effective RF prevention, especially because over-use of antibiotics creates challenges for the long term effectiveness of those antibiotic treatments.

⁴⁰ Wilson, N. (2021). Personal communication.

⁴¹ Oliver, J., Malliya Wadu, E., Pierse, N., et al. (2018). Group A *Streptococcus* pharyngitis and pharyngeal carriage: A meta-analysis. *PLOS Neglected Tropical Diseases*, 12(3), e0006335. <https://doi.org/10.1371/journal.pntd.0006335>

⁴² Wallace, M.R., Leng, R., Gordon, H., et al. (1978). The throat carriage rate of group A beta-haemolytic streptococci among Waikato primary school children. *The New Zealand Medical Journal*, 87(608), 207-208. ; Dierksen, K.P., Inglis, M. and Tagg, J.R. (2000). High pharyngeal carriage rates of *Streptococcus pyogenes* in Dunedin school children with a low incidence of rheumatic fever. *The New Zealand Medical Journal*, 113(1122), 496-499.

⁴³ Lennon, D., Anderson, P., Kerdemilidis, M., et al. (2017). First presentation acute rheumatic fever is preventable in a community setting: A school-based intervention. *The Pediatric Infectious Disease Journal*, 36(12). <https://doi.org/10.1097/INF.0000000000001581>

1.5 Looking beyond GAS throat infections to prevent RF is warranted

Targeting sore throats alone may miss some at-risk children and young people. Many children do not have a sore throat before developing RF, so targeting sore throats would not have been able to prevent RF for those cases. Skin is likely to play a role, based on evidence of GAS skin infections prior to RF episodes and the circulation of skin-associated serotypes in children who develop RF in Aotearoa New Zealand.

Targeting sore throats alone may miss at-risk children and young people.

It is worth noting that current interventions are largely focused on identifying and treating those with sore throats, therefore those children and young people who didn't have a sore throat may be the ones slipping through. Equivalent interventions for skin infections may be important. Many programmes throughout Aotearoa New Zealand have already expanded to include skin infections, but this needs rigorous evaluation. For example, a fuller picture of the extent to which antibiotics are prescribed to treat skin infections, and whether this treatment is connected to better outcomes, would be useful. It is also important to consider the AMR implications of scaling up antibiotics to treat skin infections. A current research project, the Treatment of Impetigo with Antiseptics – Replacing Antibiotics (TIARA) trial, is assessing the effectiveness of antiseptic creams in treating skin sores as a possible alternative to antibiotic creams.⁴⁴

The current way sore throats are targeted may also be contributing to unnecessary antibiotic use, which may account in part for the increase in amoxicillin dispensing. It is estimated that only half of the GAS-positive throat swabs from symptomatic children are active GAS throat infections. Serological tests may be an important addition to the diagnostic process to ensure appropriate targeted treatment and to minimise unnecessary antibiotic use. However, this needs to be mindful of practical considerations, including the need for a blood test (not available in some primary care or school settings), resourcing implications, and a several-day delay in results running the risk of an immune response being activated ahead of treatment.

There are still many unknowns about what triggers RF. Further research is needed (and some is underway) to better understand:

- The extent of the role of GAS skin infections in the development of RF in the Aotearoa New Zealand context.
- Whether treating GAS skin infections with antibiotics may reduce RF rates (which is challenging to demonstrate as RF is a rare outcome).
- The extent of strep C or G infections in the development of RF.
- Whether different GAS serotypes are related to RF risk.
- The role of GAS carriage in RF risk.
- The prevalence of true GAS pharyngitis (not GAS carriage or carriage and a viral infection).

These unknowns also provide reason to target upstream preventative methods such as vaccines (see section 10.1) and upstream risk factors that can reduce the overall burden of GAS infections and have wider positive implications for health outcomes, beyond preventing RF (see section 6.2).

⁴⁴ HRC New Zealand. (2021). Treatment of Impetigo with Antiseptics - Replacing Antibiotics (TIARA) Trial. Retrieved 28 September, 2021, from <https://www.hrc.govt.nz/resources/research-repository/treatment-impetigo-antiseptics-replacing-antibiotics-tiara-trial>

2 Aotearoa New Zealand is one of few high-income nations that still has high rates of rheumatic fever

RF and RHD are potentially preventable (see section 2.1). Treating GAS throat infections can prevent RF and preventing RF can prevent RHD. These diseases are now essentially non-existent in most high-income countries. The decline in high-income countries is often attributed to improved living standards, though this has not been proven directly.⁴⁵ Other preventative interventions have been shown to be effective in certain settings (see section 2.1).

However, Aotearoa New Zealand remains an outlier, along with Australia and Canada, as high-income countries with very high rates of disease in certain population subgroups. It is primarily the Indigenous populations within these countries that experience RF – specifically Māori in Aotearoa New Zealand, Aboriginal and Torres Strait Islanders in Australia, and First Nations peoples in Canada. Pacific peoples (referring to people from a diverse group of Pacific Island populations) living in Aotearoa New Zealand also experience very high rates of disease.

Rates in Indigenous populations within these high-income countries can surpass rates seen in low-income countries and sit in contrast to high-income countries with marked inequities between non-Indigenous rich and poor.⁴⁶ However, RHD rates can be high even when RF rates are low – particularly in resource-limited settings.⁴⁷ Though scarce, other data suggests that Indigenous peoples have higher rates of this disease across all countries, but this is not studied in as much detail as in Aotearoa New Zealand, Australia and Canada.⁴⁸

Essentially, the rates of RF dropped for NZ Europeans, but have remained unchanged for Māori and Pacific children. Other countries in the Pacific also experience high rates of RF and RHD.⁴⁹ This warrants attention as prior to the COVID-19 pandemic, there were high rates of movement between the Pacific Islands and Aotearoa New Zealand, with Pacific peoples currently experiencing the highest disease burden in Aotearoa New Zealand (see section 4).

It is difficult to determine the global burden of RF and RHD due to data limitations from developing countries where the prevalence is the highest, but systematic estimates have been published. A 2005 systematic review (which took a conservative approach) estimated that there were approximately 471,000 cases of RF each year globally, with the highest prevalence in children aged 5–14 years at 336,000 cases.⁵⁰ Estimates from the more recent Global Burden of Disease study suggest that the number of people with RHD in 2019 was around 40 million, and that more than 300,000 deaths were due to RHD – mostly occurring in low-income and middle-income countries.⁵¹ The Global Burden of Disease study reported that the health-related burden of RHD has declined worldwide by nearly 50% from 1990 to 2015, with regional differences.⁵² The reduction in RHD

⁴⁵ Steer, A.C. (2015). Historical aspects of rheumatic fever. *Journal of Paediatrics and Child Health*, 51(1), 21-27. <https://doi.org/10.1111/jpc.12808>

⁴⁶ Carapetis, J.R., Steer, A.C., Mulholland, E.K., et al. (2005). The global burden of group A streptococcal diseases. *The Lancet Infectious Diseases*, 5(11), 685-694. [https://doi.org/10.1016/S1473-3099\(05\)70267-X](https://doi.org/10.1016/S1473-3099(05)70267-X); Wyber, R., Wade, V., Anderson, A., et al. (2021). Rheumatic heart disease in Indigenous young peoples. *The Lancet Child & Adolescent Health*, 5(6), 437-446. [https://doi.org/10.1016/S2352-4642\(20\)30308-4](https://doi.org/10.1016/S2352-4642(20)30308-4)

⁴⁷ Okello, E., Ndagire, E., Muhamed, B., et al. (2021). Incidence of acute rheumatic fever in northern and western Uganda: a prospective, population-based study. *The Lancet Global Health*, 9(10), e1423-e1430. [https://doi.org/10.1016/S2214-109X\(21\)00288-6](https://doi.org/10.1016/S2214-109X(21)00288-6)

⁴⁸ Wyber, R., Wade, V., Anderson, A., et al. (2021). Rheumatic heart disease in Indigenous young peoples. *The Lancet Child & Adolescent Health*, 5(6), 437-446. [https://doi.org/10.1016/S2352-4642\(20\)30308-4](https://doi.org/10.1016/S2352-4642(20)30308-4)

⁴⁹ Viali, S., Saena, P. and Futi, V. (2011). Rheumatic fever programme in Samoa. *The New Zealand Medical Journal*, 124(1329), 26-35. ;

Carapetis, J.R., Hardy, M., Fakakovikaetau, T., et al. (2008). Evaluation of a screening protocol using auscultation and portable echocardiography to detect asymptomatic rheumatic heart disease in Tongan schoolchildren. *Nature Clinical Practice Cardiovascular Medicine*, 5(7), 411-417. <https://doi.org/10.1038/ncpcardio1185>; Watkins, D.A., Johnson, C.O., Colquhoun, S.M., et al. (2017). Global, regional, and national burden of rheumatic heart disease, 1990–2015. *New England Journal of Medicine*, 377(8), 713-722. <https://doi.org/10.1056/NEJMoa1603693>

⁵⁰ Carapetis, J.R., Steer, A.C., Mulholland, E.K., et al. (2005). The global burden of group A streptococcal diseases. *The Lancet Infectious Diseases*, 5(11), 685-694. [https://doi.org/10.1016/S1473-3099\(05\)70267-X](https://doi.org/10.1016/S1473-3099(05)70267-X)

⁵¹ Coffey, S., Roberts-Thomson, R., Brown, A., et al. (2021). Global epidemiology of valvular heart disease. *Nature Reviews Cardiology*. <https://doi.org/10.1038/s41569-021-00570-z>

⁵² Watkins, D.A., Johnson, C.O., Colquhoun, S.M., et al. (2017). Global, regional, and national burden of rheumatic heart disease, 1990–2015. *New England Journal of Medicine*, 377(8), 713-722. <https://doi.org/10.1056/NEJMoa1603693>

burden is due to reduction in RF rates and effective prevention strategies in some countries. However, limitations in these methods have been pointed out, including that it neglects other related heart complications and that study criteria could lead to an underestimation of how endemic RHD is in different countries.⁵³

Reducing RHD is a global priority. In 2018, the World Health Assembly called on Member States to improve prevention and management of RHD, asking them to report on progress at the 74th World Health Assembly in 2021.⁵⁴ Aotearoa New Zealand delivered a statement on rheumatic heart disease under the Global Strategy for Women's, Children's, and Adolescents' Health item at this year's 74th World Health Assembly. At the time of writing, we await the report from this assembly.⁵⁵

Globally the prevalence of RHD is somewhere between 30 and 40 million cases per year, and the number of annual deaths is more than 300,000. In Aotearoa New Zealand, on average around 140 people die from RHD each year.

In response to the high RF rates experienced by Aboriginal and Torres Strait Islanders in Australia, Australia has developed a strategy to eliminate RHD in Australia by 2031. The basis of the Endgame strategy is that it is evidence-based, feasible, equitable, acceptable, and impactful. The strategy includes resourcing an Aboriginal and Torres Strait Islander national implementation unit to coordinate work, deliver resources, and link communities and researchers.⁵⁶ Monitoring the success of this strategy, or otherwise, may inform interventions on this side of the Tasman. Aotearoa New Zealand does not currently have an equivalent national strategy to address its high rates of RF and RHD; it does have active programmes, and an Endgame project running out of the University of Otago.⁵⁷

2.1 We can learn from countries that dramatically reduced rates of RF and RHD

Since around the 1940s, the rates of RF and RHD decreased in developed countries worldwide.⁵⁸ The rapid decrease in RF is widely attributed to improved living and societal conditions, as most decreases occurred before antibiotics were routinely used to treat GAS throat infections. The near elimination of RF in non-Indigenous Australians and stubbornly high RF rates in Indigenous Australians shows that these improvements haven't been afforded equitably across Australia.⁵⁹ Similar inequities in socio-economic improvements are likely to have influenced RF rates in Aotearoa New Zealand, and crowded living conditions and poverty remain an ongoing issue for many, although inequities remain between ethnicities after socio-economic status has been allowed for in the analysis (see section 4). Significant reductions have also been achieved in developing countries with fewer resources when a multipronged approach was taken. The approaches taken in Aotearoa New Zealand have benefited from these experiences which inform the delivery of the rheumatic fever prevention programme.

⁵³ Sohrabi, B., Ranjbar, A., Johannsen, R.A., *et al.* (2018). Global burden of rheumatic heart disease. *New England Journal of Medicine*, 378(1), e2. <https://doi.org/10.1056/NEJMc1714503>

⁵⁴ World Health Assembly. (2018, 26 May 2018). *Seventy-first World Health Assembly Agenda item 12.8: Rheumatic fever and rheumatic heart disease*.

⁵⁵ World Health Organization. (2021). *Committing to implementation of the Global Strategy for Women's, Children's and Adolescents' Health (2016–2030)*. Retrieved from https://apps.who.int/gb/ebwha/pdf_files/WHA74/A74_14-en.pdf; World Health Organization. (2021).

Updates and future reporting: Rheumatic fever and rheumatic heart disease. Retrieved from https://apps.who.int/gb/ebwha/pdf_files/WHA74/A74_40-en.pdf

⁵⁶ Wyber, R., Noonan, K., Halkon, C., *et al.* (2020). Ending rheumatic heart disease in Australia: The evidence for a new approach. *Medical Journal of Australia*, 213, S3-S31. <https://doi.org/10.5694/mja2.50853>; *ibid.*

⁵⁷ University of Otago. (n.d.). Developing an optimal strategy for the rheumatic fever endgame. Retrieved 28 September, 2021, from <https://www.otago.ac.nz/wellington/departments/publichealth/research/heiru/research/otago701137.html>

⁵⁸ Carapetis, J.R., Beaton, A., Cunningham, M.W., *et al.* (2016). Acute rheumatic fever and rheumatic heart disease. *Nature Reviews Disease Primers*, 2(1), 15084. <https://doi.org/10.1038/nrdp.2015.84>; Steer, A.C. (2015). Historical aspects of rheumatic fever. *Journal of Paediatrics and Child Health*, 51(1), 21-27. <https://doi.org/10.1111/jpc.12808>

⁵⁹ Steer, A.C. (2015). Historical aspects of rheumatic fever. *Journal of Paediatrics and Child Health*, 51(1), 21-27. <https://doi.org/10.1111/jpc.12808>

The rapid decrease in RF is widely attributed to improved living and societal conditions, as most decreases occurred before antibiotics were routinely used to treat GAS throat infections.

Here we highlight the similarities in the approaches taken in four places that achieved significant reductions in rates of RF:

- **Cuba:** In 1986, the Pinar del Rio province in Cuba had high rates of RF and RHD, but both decreased significantly after a comprehensive 10-year prevention programme was implemented. Rates of RF per 100,000 5–25-year-olds dropped from 18.6 (1986) to 2.5 (1996), and rates of recurrence decreased from 6.4 (1986) to 0.4 (1996).⁶⁰
- **Costa Rica:** A wider plan to reduce infectious diseases implemented in the 1970s included specific actions for RF. It mainly focused on improving primary prevention. Rates decreased from around 90 cases per 100,000 people in the 1970s to around 8 in the mid-1980s and around 1 in 1990.⁶¹
- **French Caribbean:** High rates of RF and RHD were reported in the two French Caribbean islands of Martinique and Guadeloupe up until 1980 triggered an eradication programme. Rates decreased by 78% in Martinique and 74% in Guadeloupe. The persisting cases at the end of the programme were from the areas of highest deprivation, though declines had been seen in these areas.⁶²
- **Tunisia:** A strategy to reduce RF led to a reduction in cases from 8.7/100,000 people in 1980 to 0.08/100,000 people in 2015. Significant population growth occurred during this period along with significant economic development.⁶³

⁶⁰ Nordet, P., Lopez, R., Duenas, A., *et al.* (2008). Prevention and control of rheumatic fever and rheumatic heart disease: The Cuban experience (1986–1996–2002). *Cardiovascular Journal of Africa*, 19(3), 135–140. <https://doi.org/10.10520/EJC23128>; Watkins, D.A., Mvundura, M., Nordet, P., *et al.* (2015). A cost-effectiveness analysis of a program to control rheumatic fever and rheumatic heart disease in Pinar del Rio, Cuba. *PLoS One*, 10(3), e0121363. <https://doi.org/10.1371/journal.pone.0121363>

⁶¹ Arguedas, A. and Mohs, E. (1992). Prevention of rheumatic fever in Costa Rica. *The Journal of Pediatrics*, 121(4), 569–572. [https://doi.org/10.1016/S0022-3476\(05\)81146-1](https://doi.org/10.1016/S0022-3476(05)81146-1)

⁶² Bach, J., Chalons, S., Forier, E., *et al.* (1996). 10-year educational programme aimed at rheumatic fever in two French Caribbean islands. *The Lancet*, 347. [https://doi.org/10.1016/s0140-6736\(96\)91202-7](https://doi.org/10.1016/s0140-6736(96)91202-7)

⁶³ Yusuf, S., Narula, J. and Gamra, H. (2017). Can we eliminate rheumatic fever and premature deaths from RHD? *Global Heart*, 12, 3–4. <https://doi.org/10.1016/j.gheart.2017.05.001>

Table 1: Comparison of overseas approaches in different settings that achieved significant reductions in RF rates.

	Cuba ⁶⁴	Costa Rica ⁶⁵	French Caribbean ⁶⁶	Tunisia ⁶⁷
Programme timing	1986–1996	Approximately 1970–1990	1981–1991	1978 start
Access to healthcare	Free Easy access	Timing aligned with broader efforts to make primary care more accessible	Well-structured medical system with free access	Not reported
Economic development and socioeconomic variables over time	No improvement, possibly a decline	Significant improvement	No significant improvement	Significant improvement
Target	Throat	Throat	Throat and skin	Throat
Primary prevention	Healthcare professional education Raising public awareness via schools and media; community involvement	Healthcare professional education Shifted from 10 days amoxicillin to one-off BPG for GAS throat infection to improve adherence No longer required diagnostic proof of GAS throat infections to dispense antibiotics; ensured sufficient antibiotic at all clinics	Healthcare professional education Raising public awareness via schools, media and public meetings; education for social and educational professionals	Healthcare professional education Education of patients, families, and wider public Shifted from 10 days amoxicillin to one-off BPG for GAS throat infection to improve adherence
Secondary prevention	Register Case finding, referral, registration, surveillance, follow-up and regular secondary prophylaxis	No changes made as part of programme	Register	Made RF a notifiable disease Secondary prophylaxis service
Tertiary prevention	None reported	None reported	None reported	Screening for RHD and referral for specialised care
Other			Local research	Continual evaluation of programme effectiveness

⁶⁴ Nordet, P., Lopez, R., Duenas, A., *et al.* (2008). Prevention and control of rheumatic fever and rheumatic heart disease: The Cuban experience (1986–1996–2002). *Cardiovascular Journal of Africa*, 19(3), 135–140. <https://doi.org/10.10520/EJC23128>; Watkins, D.A., Mvundura, M., Nordet, P., *et al.* (2015). A cost-effectiveness analysis of a program to control rheumatic fever and rheumatic heart disease in Pinar del Rio, Cuba. *PLoS One*, 10(3), e0121363. <https://doi.org/10.1371/journal.pone.0121363>

⁶⁵ Arguedas, A. and Mohs, E. (1992). Prevention of rheumatic fever in Costa Rica. *The Journal of Pediatrics*, 121(4), 569–572. [https://doi.org/10.1016/S0022-3476\(05\)81146-1](https://doi.org/10.1016/S0022-3476(05)81146-1)

⁶⁶ Bach, J., Chalons, S., Forier, E., *et al.* (1996). 10-year educational programme aimed at rheumatic fever in two French Caribbean islands. *The Lancet*, 347. [https://doi.org/10.1016/s0140-6736\(96\)91202-7](https://doi.org/10.1016/s0140-6736(96)91202-7)

⁶⁷ Yusuf, S., Narula, J. and Gamra, H. (2017). Can we eliminate rheumatic fever and premature deaths from RHD? *Global Heart*, 12, 3–4. <https://doi.org/10.1016/j.gheart.2017.05.001>

The historical reductions in high-income countries and more recent improvements in countries with fewer resources suggest the following aspects are integral parts of a multipronged approach to reduce RF:

- Improving living and socio-economic conditions,
- Free and easy access to healthcare to remove barriers to receiving primary care,
- The use of a one-off BPG injection instead of a 10-day course of oral antibiotics to treat GAS throat infections,
- A centralised RF patient register/control programme to coordinate a robust secondary prophylaxis service.

3 There's room to improve data and surveillance of GAS, acute rheumatic fever and acute rheumatic heart disease

At a high level, the current data on rates of RF and RHD are sufficient to inform action and monitor overall trends in disease incidence. However, the sources of data currently relied on have limitations, and improved monitoring and surveillance of these conditions could provide better data to inform more targeted prevention and management.

Accurate data on disease rates is crucial so that the true burden of disease is captured, and the effectiveness of interventions can be accurately measured. Accuracy across each stage of progression is critical to ascertain how many cases are falling through the cracks and not being diagnosed.

There are three stages of this disease and outcomes that need to be monitored: 1) throat and skin infection with GAS, 2) RF, and 3) RHD. Table 2 summarises the current monitoring and surveillance at each stage.

Table 2: Summary of monitoring of GAS infection through to RHD in Aotearoa New Zealand.

	GAS throat infection	GAS skin infection	Rheumatic fever	Rheumatic heart disease
Notifiable	No	No	Yes	No
Ad hoc active case finding	Some schools and clinics	Some schools and clinics	No	No – only for research studies
National active case finding	No	No	No	No
National data available	No	No	Yes	In development and close to completion

Monitoring and surveillance of GAS infection

Knowledge of the incidence of GAS throat and skin infections is important to better understand and prevent development of RF. The infections themselves are common and not notifiable. Therefore, epidemiological studies are relied on to understand how common they are in different populations and what other factors are at play that lead to RF. Selection bias in studies to date, due to samples being from those who have sought medical attention, mean that the information we hold is not necessarily representative. The true incidence of GAS infections is very hard to measure, because only those who present and have a throat swab are counted, with all those who don't seek medical support, or who do but are not swabbed, being missing from the data set.

Various approaches to address this issue have been considered, each with their own challenges. Notification of GAS infections to public health units is hard to implement as there is no follow-up that is needed in response from the public health unit, so it is seen as a waste of time. Primary care codes around sore throats could in theory provide an idea of how on how common they are, but they are currently coded in different ways by different practitioners, which presents challenges. It is also important to note that sore throats are very common and that not all present to primary care, and when they do, the majority are viral. All these factors add up to make implementation of surveillance for GAS very hard.

However, ESR undertakes surveillance of invasive GAS infections – that is, infections where GAS has invaded parts of the body where it is not normally found, such as blood, cerebrospinal fluid, pleural fluid, synovial fluid, and deep tissue. This form of GAS infection is severe and life-threatening, resulting in disease such as toxic shock syndrome or necrotising fasciitis. ESR's laboratory-based surveillance relies on individual laboratories sending in clinically relevant GAS isolates for further typing. The most recent report, published in 2017 and covering data from 2016, records a rate of 9.0 per 100,000 population – an increase from the 2015 rate of 7.5, and similar to the peak of 9.3 observed in 2011 prior to a decrease.⁶⁸ As seen in other types of GAS infection, the burden is inequitable: the rate among Pacific peoples is 17 times higher than the rate among European and

⁶⁸ Hambling, T., Galloway, Y., Jack, S., et al. (2017). *Invasive group A streptococcal infection in New Zealand, 2016*. Porirua, NZ: ESR. Retrieved from https://surv.esr.cri.nz/PDF_surveillance/InvasiveGAS/InvGASinfectioninNewZealand2016.pdf

other non-Māori ethnicities (73.9 per 100,000 vs 4.3 per 100,000). The rate among Māori was 23.5 per 100,000, five times higher than European and other ethnicities. The report also notes that the leading candidate GAS 30-valent vaccine, could have provided protection for 48% of the 421 cases in 2016.

Monitoring and surveillance of RF

There are three main sources of data on rates of RF in Aotearoa New Zealand. Each has limitations and captures some different cases – as a result there is not a single source of truth, but all show the same trends.⁶⁹

- **Disease notification data**

- Initial episodes and recurrence of RF in Aotearoa New Zealand are notifiable to the Medical Officer of Health under the Health Act 1956.
- The Ministry of Health's Annual Surveillance Report of notifiable diseases publishes the rates of RF via ESR each year. However, the most recent report available is from 2019. This data relies on 'report' date not 'onset' date so is not accurate on the timing of infections, as some reporting may be delayed.
- Historically many cases were not notified or were notified in batches over six months after cases were diagnosed. This means that notification data may not be reliable for longer-term trends.⁷⁰ This has been highlighted in a study of RF rates in the Bay of Plenty which showed that improvements post any intervention are masked by increasing completeness of notification data over the same period. When multi-source data was used it showed a decline in rates which was otherwise not seen when looking at notification data alone. This may have affected interpretation of the data for school-based sore throat clinic assessments (see section 9.3).⁷¹ This varies across Aotearoa New Zealand – for example, the Auckland Regional Public Health Service (ARPHS) publishes RF data every quarter and triangulates with hospital discharge data locally.

Improvements post-intervention are masked by increasing completeness of notification data over the same period.

- **National hospitalisation data**

- Specific medical classification codes (International Classification of Diseases or ICD codes) are used for this reporting. They include initial and subsequent hospitalisations for RF and those which match Ministry of Health criteria for reporting are collected.
- This is used by the Ministry of Health for annual reporting.
- Hospitalisation data should be comprehensive for symptomatic cases as in Aotearoa New Zealand it is recommended that people are hospitalised when they have an episode of RF, and the majority are. A study in Auckland confirmed Ministry of Health understanding that hospitalisation data may over-count cases due to miscoding and misdiagnoses.⁷² Over-counting occurs because rheumatic fever is prioritised in the coding algorithm. For example, if the differential diagnosis includes 'suspected' rheumatic fever, this diagnosis is prioritised as the primary code even if further assessment in outpatient clinics deem that this is not a

⁶⁹ Oliver, J., Pierse, N. and Baker, M.G. (2015). Estimating rheumatic fever incidence in New Zealand using multiple data sources. *Epidemiology and Infection*, 143(1), 167-177. <https://doi.org/10.1017/S0950268814000296>

⁷⁰ Lennon, D., Te Aro Moxon, P.A., Leversha, A., et al. (2017). Is a rheumatic fever register the best surveillance tool to evaluate rheumatic fever control in the Auckland region? *The New Zealand Medical Journal*, 130(1460), 48. ; Wauchop, K., Shetty, A. and Bremner, C. (2019). The epidemiology of acute rheumatic fever in Northland, 2012-2017. *The New Zealand Medical Journal*, 132(1498), 32-40.

⁷¹ Walsh, L., Innes-Smith, S., Wright, J., et al. (2021). *Bay of Plenty Rheumatic fever epidemiology 2000-18; Baywide ARF rates in Māori reduce substantially utilizing multi-sourced data. Notification data leads to underestimation of programme effectiveness - Unpublished manuscript.*

⁷² Lennon, D., Te Aro Moxon, P.A., Leversha, A., et al. (2017). Is a rheumatic fever register the best surveillance tool to evaluate rheumatic fever control in the Auckland region? *The New Zealand Medical Journal*, 130(1460), 48.

case. This is a manifestation of the fact that RF is not easy to diagnose and is confirmed by comparison to the audited ESR data.⁷³

- **Regional patient registers**
 - Most regions with high rates of RF in Aotearoa New Zealand have established their own registers, primarily for BPG secondary prophylaxis delivery, but there is currently no national register (see section 9.10) or coordinated and funded programme.
 - Despite some underreporting in registers, they are more accurate than disease notification data.⁷⁴ Although there is variation by region and overtime – e.g. ARPHS data has apparently improved since this study was published.
 - Accuracy is especially improved when the register integrates hospitalisation and disease notification data and adds a process of individual case-notification scrutiny, as happens in Auckland with the EpiSurv data.
- **Epidemiological studies**
 - In addition to the main three data sources, other studies done on an ad hoc basis can provide more insight into disease incidence in specific populations and may show trends over time.

Monitoring and surveillance of RHD

Unlike RF, RHD is not currently a notifiable disease in Aotearoa New Zealand. Some experts have argued it should be.⁷⁵ The Ministry of Health reviewed whether RHD should become a notifiable disease and undertook consultation, including with the Medical Officers of Health. They concluded that RHD does not need to be made a notifiable, taking into account the purpose of notification, and that there was no clear action for public health following notification of RHD.

A New Zealand Rheumatic Heart Disease Registry was established in 2018.⁷⁶ The patient register is still in development but is close to completion. It is populated using surgical, echocardiographic and outpatient databases, and cross-referenced with RF registries, ICD hospital discharge codes and national mortality data. Addition of data from GP patient management systems could strengthen this resource. The aim is to be able to analyse the outcomes of the people on the RHD register through the national minimum dataset to better understand disease progression and outcomes for people in the Aotearoa New Zealand context. This is discussed further in section 9.10.

ICD codes for RHD have been shown to over-estimate cases significantly (by up to 70%), particularly in high-income countries, limiting their use.⁷⁷ Any database using hospitalisation data will not include patients who have either had their diagnosis missed or who were not admitted to hospital. This places a caveat around interpretation of data. This could be overcome in part by wider education of healthcare professionals on specific criteria for diagnosis.

ICD codes for RHD have been shown to over-estimate cases significantly (by up to 70%), particularly in high income countries, limiting their use.

Using innovative IT solutions to de-silo data, share records with patients and whānau, integrate lab results for a fast response and support patient follow-up could support better outcomes.

⁷³ Institute of Environmental Science & Research Limited. (n.d.). Rheumatic fever reports. Retrieved 28 September, 2021, from <https://surv.esr.cri.nz/surveillance/RheumaticFever.php>

⁷⁴ Lennon, D., Te Aro Moxon, P.A., Leversha, A., *et al.* (2017). Is a rheumatic fever register the best surveillance tool to evaluate rheumatic fever control in the Auckland region? *The New Zealand Medical Journal*, 130(1460), 48.

⁷⁵ Wilson, N. (2010). Rheumatic heart disease in Indigenous populations – New Zealand experience. *Heart, Lung and Circulation*, 19(5), 282-288. <https://doi.org/10.1016/j.hlc.2010.02.021>

⁷⁶ Wilson, N., Mitchelson, B., Peat, B., *et al.* (2018). The New Zealand rheumatic heart disease registry. *Heart, Lung and Circulation*, 27, S19. <https://doi.org/10.1016/j.hlc.2018.05.141>

⁷⁷ Oliver, J., Robertson, O., Zhang, J., *et al.* (2021). Ethnically disparate disease progression and outcomes among acute rheumatic fever patients in New Zealand, 1989–2015. *Emerging Infectious Diseases*, 27(7), 1893-1902. <https://doi.org/10.3201/eid2707.203045>

4 Current rates of rheumatic fever and rheumatic heart disease demand attention

4.1 There are significant inequities in the incidence of GAS infections, RF and RHD

Differences in the burden of GAS infections by ethnicity are more pronounced for skin than throat.

- Pacific peoples are 1.7 times more likely and Māori 1.3 times more likely than other ethnicities to suffer a sore throat from which GAS is cultured.⁷⁸
- For people under 20 years old, Pacific peoples are 6.8 times more likely and Māori are 4 times more likely than other ethnicities to have a skin swab positive for GAS.⁷⁹

The increased risk of initial hospitalisation for RF for Māori and Pacific peoples is much higher than the higher burden of GAS.

- This suggests that it is not that Māori and Pacific peoples simply have higher carriage or infection rates of GAS, but that other factors influence risk of developing RF.
- Looking at the rate of RF nationwide masks the huge disease burden in certain population groups. The national rates represent an average, but the difference in risk for different ethnicities is huge in areas of high incidence, compared to the areas of the country with low incidence.
- The differences in disease risk always show higher rates for Māori and Pacific peoples.
- Looking at differences in rates across the whole country, the increased risk of initial hospitalisation for Pacific peoples is 24 times and for Māori it is 12 times.⁸⁰ That is because areas where there is lower disease risk, including for Māori and Pacific peoples, are included.
- However, in an area with the highest rates of disease in the country, these differences in risk are much more pronounced. The risk of initial hospitalisation for RF in Auckland is increased 240 times for Pacific peoples and 87 times for Māori compared to non-Māori and non-Pacific peoples from Auckland.⁸¹ (Noting that hospitalisation data does over-estimate cases, see section 3.)

In an area with the highest rates of disease in the country, these differences in risk are much more pronounced. The risk of initial hospitalisation for RF in Auckland is increased 240 times for Pacific peoples and 87 times for Māori compared to non-Māori and non-Pacific peoples from Auckland.

The increases in RF risk compound so that in the high-risk group of Pacific boys aged 5–14 years in Counties Manukau DHB the annual incidence accounts for 0.1% of the population.

- Differences in rates are seen with sex, age, ethnicity and region, and the cumulative increased risk compounds – so, for people that fall into the highest risk group across age, sex, ethnicity and region, the rate of RF per 100,000 reaches up to 112.8 compared to 3 for the overall country rate (see figure 3).⁸²

⁷⁸ Oliver, J., Upton, A., Jack, S.J., *et al.* (2020). Distribution of streptococcal pharyngitis and acute rheumatic fever, Auckland, New Zealand, 2010–2016. *Emerging Infectious Diseases*, 26(6), 1113. <https://doi.org/10.3201/eid2606.181462>

⁷⁹ Thomas, S., Bennett, J., Jack, S., *et al.* (2021). Descriptive analysis of group A *Streptococcus* in skin swabs and acute rheumatic fever, Auckland, New Zealand, 2010–2016. *The Lancet Regional Health - Western Pacific*, 8, 100101. <https://doi.org/10.1016/j.lanwpc.2021.100101>

⁸⁰ Bennett, J., Zhang, J., Leung, W., *et al.* (2021). Rising ethnic inequalities in acute rheumatic fever and rheumatic heart disease, New Zealand, 2000–2018. *Emerging Infectious Diseases*, 27(1), 36. <https://doi.org/10.3201/eid2701.191791>

⁸¹ Oliver, J., Upton, A., Jack, S.J., *et al.* (2020). Distribution of streptococcal pharyngitis and acute rheumatic fever, Auckland, New Zealand, 2010–2016. *Emerging Infectious Diseases*, 26(6), 1113. <https://doi.org/10.3201/eid2606.181462>

⁸² RF hospitalisation data provided by the Ministry of Health

Annual rate of rheumatic fever hospitalisations in 2020 in different population groups

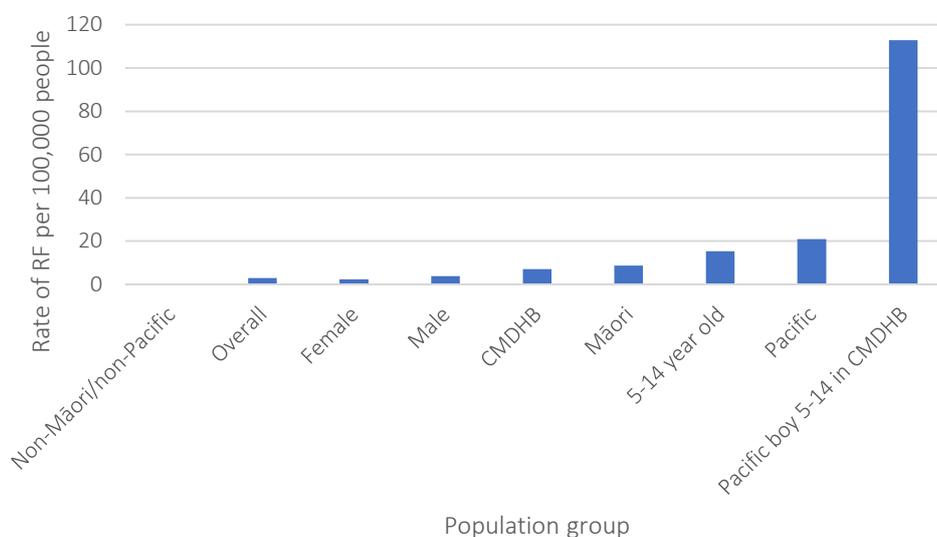


Figure 2: Rates of rheumatic fever in different population groups in Aotearoa New Zealand in 2020; data provided by the Ministry of Health.

Significantly more people are diagnosed with RHD each year than RF – with around 270 RHD diagnoses compared to 150 RF diagnoses (subject to the caveats above in section 3 around ICD codes).

- Approximately 150 people in Aotearoa New Zealand have a first episode of RF each year.⁸³
- Each year, around 270 people in Aotearoa New Zealand are diagnosed with RHD, around 630 are admitted to hospital, and on average 143 people die of RHD.⁸⁴
- Even with secondary prophylaxis, the chance of RF developing into recurrent RF or RHD is around 7–14%, but for Māori and Pacific peoples disease progression is about two times more likely, and likely to be quicker. The risk increases with age.⁸⁵
- Recurrence of RF is strongly associated with RHD progression.⁸⁶
- There is evidence that people fall through the cracks for secondary prophylaxis and echocardiography with specialist follow-up within and between DHBs, and between services within DHBs, particularly during adolescence, which contributes to rates of disease progression.⁸⁷ Reasons include complex lives with barriers to accessing care (see section 7).

⁸³ Institute of Environmental Science and Research Limited (ESR). (2021). Annual Notifiable Disease Tables. Retrieved 28 July 2021, from https://surv.esr.cri.nz/surveillance/annual_diseasetables.php; RF hospitalisation data provided by the Ministry of Health

⁸⁴ Bennett, J., Zhang, J., Leung, W., *et al.* (2021). Rising ethnic inequalities in acute rheumatic fever and rheumatic heart disease, New Zealand, 2000–2018. *Emerging Infectious Diseases*, 27(1), 36. <https://doi.org/10.3201/eid2701.191791>

⁸⁵ Oliver, J., Robertson, O., Zhang, J., *et al.* (2019). Progression of acute rheumatic fever to recurrence, rheumatic heart disease, and death in New Zealand children and youth: A cohort study. *Heart, Lung and Circulation*, 28, S4. <https://doi.org/10.1016/j.hlc.2019.05.013>; Dennison, A., Peat, B., Wilson, E., *et al.* (2020). Rheumatic fever recurrences in New Zealand 2010–14. *The New Zealand Medical Journal*, 133(1516), 47–46.

⁸⁶ Dennison, A., Peat, B., Wilson, E., *et al.* (2020). Rheumatic fever recurrences in New Zealand 2010–14. *The New Zealand Medical Journal*, 133(1516), 47–46.

⁸⁷ *Ibid.* Oetzel, J.G., Lao, C., Morley, M., *et al.* (2019). Efficacy of an incentive intervention on secondary prophylaxis for young people with rheumatic fever: A multiple baseline study. *BMC Public Health*, 19(1), 385. <https://doi.org/10.1186/s12889-019-6695-3>

There are significant inequities in the burden of RHD, with Māori and Pacific peoples both more likely to develop RHD and for the disease to be fatal.

- Māori are three times and Pacific peoples around five times more likely than other ethnicities to develop RHD (based on initial hospitalisations), and both are around 11 times more likely to die from RHD.⁸⁸

The rates of RHD are likely to be significantly underestimated due to undetected community cases.

- Over 80% of patients who developed RHD did not receive antibiotic treatment at the RF stage, with higher rates for non-Māori and non-Pacific peoples (>90%) and females (>85%).⁸⁹
- Echocardiographic screening done prior to the Rheumatic Fever Prevention Programme (RFPP) found around 1 in 50 Pacific young adults in South Auckland may be living with RHD.⁹⁰ Repeating this study to determine the impact of the RFPP on unrecognised RHD would be beneficial and inform potential future screening programmes.
- These high proportions of patients presenting to hospital with RHD without prior hospitalisation for RF are concerning as it highlights missed opportunities for secondary prevention. This is likely due to a complex combination of factors including barriers to healthcare access, leading to patients missing out on necessary secondary prophylactic prevention injections. It is possible that some patients might have migrated to Aotearoa New Zealand after an episode of RF elsewhere but before hospitalisation for RHD, but this wouldn't account for all patients missed.

⁸⁸ Bennett, J., Zhang, J., Leung, W., *et al.* (2021). Rising ethnic inequalities in acute rheumatic fever and rheumatic heart disease, New Zealand, 2000–2018. *Emerging Infectious Diseases*, 27(1), 36. <https://doi.org/10.3201/eid2701.191791>

⁸⁹ Oliver, J., Robertson, O., Zhang, J., *et al.* (2021). Ethnically disparate disease progression and outcomes among acute rheumatic fever patients in New Zealand, 1989–2015. *Emerging Infectious Diseases*, 27(7), 1893-1902. <https://doi.org/10.3201/eid2707.203045>

⁹⁰ Webb, R. (2020). *Rheumatic heart disease in New Zealand children: Echocardiographic disease burden and clinical outcomes*. ResearchSpace@Auckland, Auckland, New Zealand. Retrieved from <https://onlinelibrary.wiley.com/doi/10.1111/j.1440-1754.2011.02218.x>

High proportions of patients presenting to hospital with RHD without prior hospitalisation for RF are concerning as this highlights lost opportunities for secondary prevention.

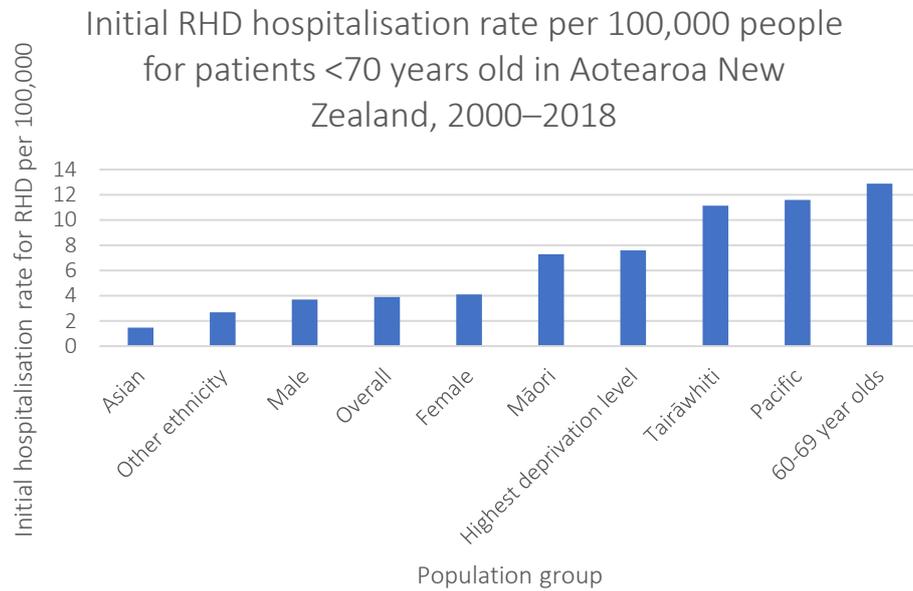


Figure 3: Differences in rates of initial hospitalisation for RHD by population group in Aotearoa New Zealand. Data from Bennett et al. 2021

Risk of **GROUP A STREP INFECTION** is higher for Māori and Pacific people than other ethnicities

EXPLORING DISEASE RATES



Skin GAS infection risk:
Māori 4x more likely
Pacific 7x more likely
than other ethnicities



Throat GAS infection risk:
Māori 1.3x more likely
Pacific 1.7x more likely
than other ethnicities

Rates of **RHEUMATIC FEVER** differ by ethnicity and age

Across all locations, the increased risk of initial hospitalisation is higher for Māori and Pacific people than other ethnicities.

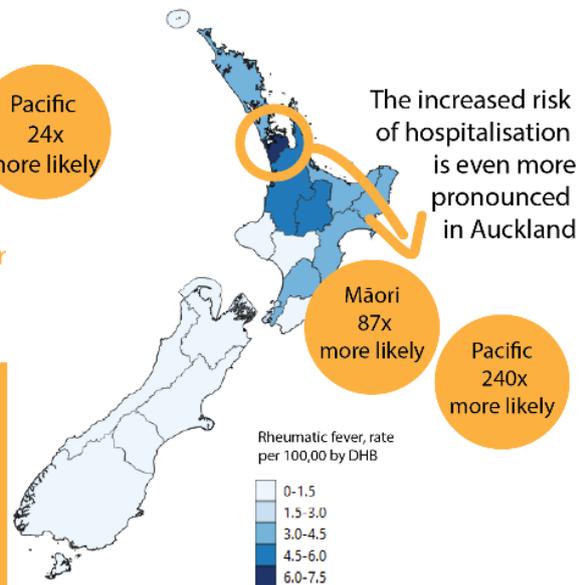
Māori
12x
more likely

Pacific
24x
more likely

Rates in 5 - 14 year olds are at least 3x higher than any other age group

RISKS COMPOUND

Pacific boys aged 5-14 years old in Counties Manukau DHB have one of the highest rates of rheumatic fever at 112.8/100,000 (0.1% of this population).



Rheumatic fever can progress to **RHEUMATIC HEART DISEASE**

Rates are highest for those aged over 60

Each year there are around 270 new RHD diagnoses and around 630 people admitted to hospital.

For Māori and Pacific people, progression from RF to RHD is more likely and faster, and dying from RHD is more likely.

Figure 4: Rates of GAS infection, RF and RHD highlight the inequitable burden of these diseases on Māori and Pacific peoples in Aotearoa New Zealand.

4.2 Our understanding of the incidence of GAS infections is limited

The studies referred to above that showed higher rates of GAS infection in Māori and Pacific peoples are the key studies from which we can understand more about the incidence of GAS. Further detail from each study is included below in Table 3.

The comparison of these studies shows similar patterns in terms of increased risk for children, Māori and Pacific peoples, and those from the most socio-economically deprived areas. The magnitude of increased risk of GAS infections is generally higher for skin than for throat. However, sampling bias might influence these rates as the samples are not representative of the general population and instead reflect healthcare service use. Treatment of sore throat in a school setting, in particular, targets high risk groups, so has been excluded from table 3.

The evidence that the proportion of GAS-positive throat swabs does not substantially differ by ethnicity indicates that it is not simply a higher rate of GAS throat infections in Māori and Pacific peoples that leads to higher RF risk. Similar proportions of GAS-positive throat swabs between Māori and non-Māori 3–20-year-olds have also been shown in a Northland study, with around 19% of throat swabs returning a GAS-positive result.⁹¹ In contrast, GAS skin infections show more marked differences by ethnicity (see table 3) which may be relevant given the suggestion that concurrent throat and skin infections may be a factor. Note that treatment of ‘Auckland’ as a single population in this study is a limitation, and it would be interesting to further analyse by DHB.

Overall, differences in the risk of GAS-positive swabs across ethnicity and socio-economic group are insufficient to explain the differences in risk seen for RF (see section 4.1).

Table 3: Comparison of GAS incidence for throat and skin infections from two Auckland studies.

	GAS throat infections ⁹²	GAS skin infections ⁹³	Comparison
Study details	Auckland 2010–2016, but used 2014–2016 data for risk comparisons	Auckland 2010–2016	Same location and years
Swab source	1,257,058 throat swabs from people presenting with sore throats at primary care, including school sore throat clinics, sent to the pathology lab service Data included here is only for primary care, not schools	377,410 skin swabs from people presenting with skin infection at primary care, sent to the pathology lab service	Both sampled symptomatic people
% of swabs positive for GAS	15%	12.8%	Similar rates
% of swabs positive for GAS by ethnicity	Māori – 20.1% Pacific – 20.7% Asian – 15.0% European/other – 22.3%	Māori – 24.5% Pacific – 46.2% Asian – 4.2% European/other – 25.2%	Little or no difference between ethnicities for throat, greater differences for skin
Peak age for GAS positive swab	5–9 years (see figure 6)	0–9 years (see figure 7)	Similar ages
Difference in risk of GAS positive swab by ethnicity	Māori – 1.3x Pacific – 1.7x Asian – 0.5x European/other – ref	Māori – 4x Pacific – 6.8x Asian – 0.5x European/other – ref	Similar – highest risk for Pacific peoples, followed by Māori, more pronounced for skin

⁹¹ Shetty, A., Mills, C. and Eggleton, K. (2018). A repeat audit of primary care management of group A streptococcal pharyngitis in Northland, New Zealand 2016. *Journal of Primary Health Care*, 10(1), 18. <https://doi.org/10.1071/hc17056>

⁹² Oliver, J., Upton, A., Jack, S.J., et al. (2020). Distribution of streptococcal pharyngitis and acute rheumatic fever, Auckland, New Zealand, 2010–2016. *Emerging Infectious Diseases*, 26(6), 1113. <https://doi.org/10.3201/eid2606.181462>

⁹³ Thomas, S., Bennett, J., Jack, S., et al. (2021). Descriptive analysis of group A *Streptococcus* in skin swabs and acute rheumatic fever, Auckland, New Zealand, 2010–2016. *The Lancet Regional Health - Western Pacific*, 8, 100101. <https://doi.org/10.1016/j.lanwpc.2021.100101>

Difference in risk of GAS positive swab by deprivation index	Quintile 1 – ref Quintile 2 – 0.9x Quintile 3 – 1.1x Quintile 4 – 1.9x Quintile 5 – 2.3x	Quintile 1 – ref Quintile 2 – 1.3x Quintile 3 – 1.6x Quintile 4 – 2.6x Quintile 5 – 7.0x	Similar – increasing risk with increasing level of deprivation. The risk is a lot higher in the GAS-positive skin groups in quintile 5.
Seasonal peak	Winter	Autumn	Different seasonal peaks
Trend	Increasing number of positive swabs – 5842 (2010) to 46,760 (2016)	Increasing number of positive swabs – 32% increase from 2010 to 2016 (<20 year olds)	Similar – both increasing

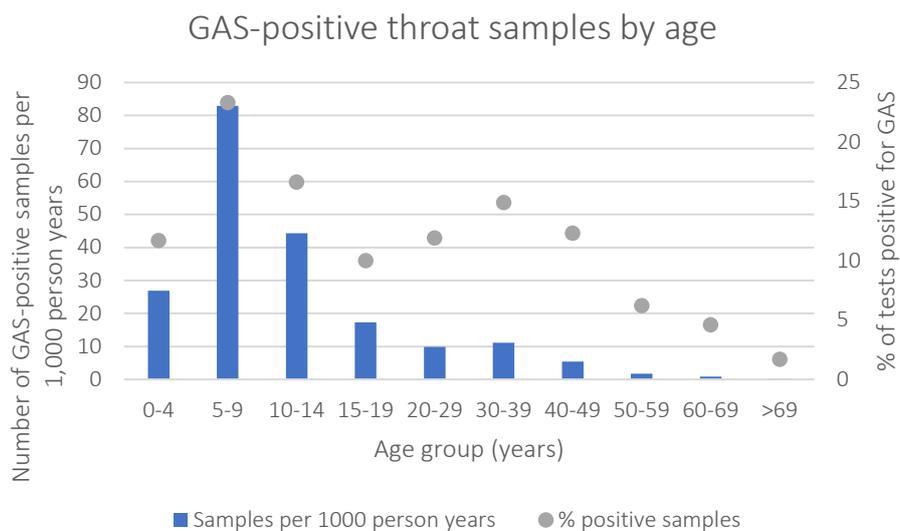


Figure 5: The rate of throat swab samples that were positive for GAS by age group. Data from Oliver et al. 2020.

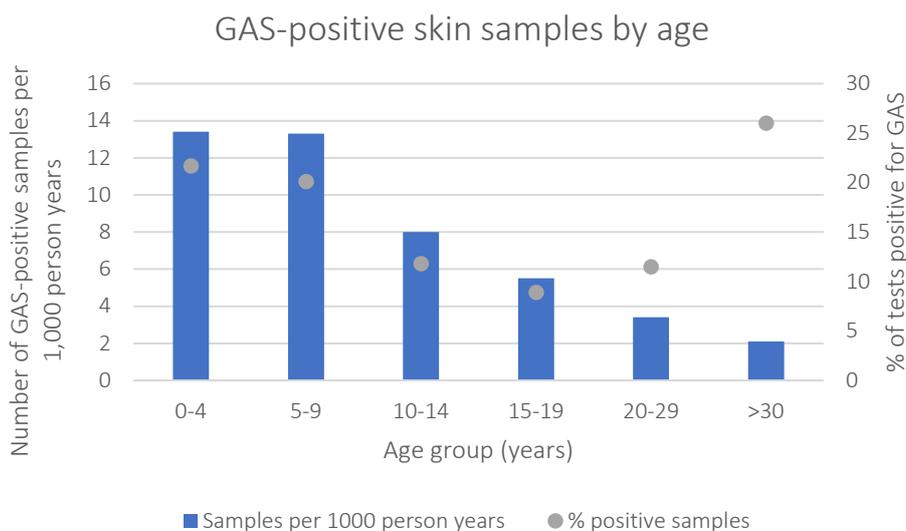


Figure 6: The rate of skin swab samples that were positive for group A strep by age group. Data from Thomas et al 2021.

4.3 We are yet to see a lasting downward trend for rates of rheumatic fever in Aotearoa New Zealand

Rates of RF in Aotearoa New Zealand have shown significant variation in incidence over time (see figure 8).

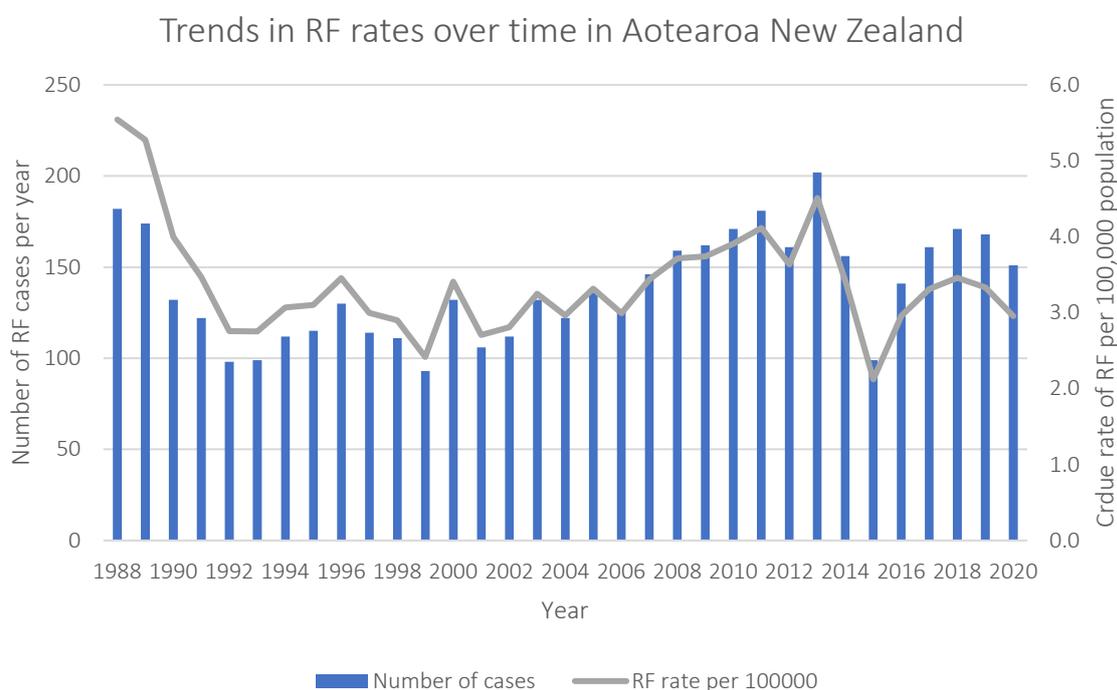


Figure 7: Annual number of RF cases and rate of RF per 100,000 people by RF hospitalisations over time in Aotearoa New Zealand. Data from the Ministry of Health.

In 2020, 154 cases of RF were notified, of which 60% were male and 40% female. Only 5% of these notified cases were not of Māori or Pacific ethnicity.⁹⁴ According to national hospitalisation data, RF rates were lower in 2020 (see figure 9)⁹⁵ and there is predicted to be an even more dramatic drop in 2021 with a marked decrease in Pacific cases.⁹⁶ The rate per 100,000 people differed significantly by ethnicity – the rate for Pacific peoples was the highest at 20.9 and for Māori it was 8.7, compared to other ethnicities at 0.3 per 100,000 (see figure 9). A decrease in the number of cases from 2019 was seen for Pacific peoples but not for Māori. According to the MOH’s most recent reporting, in the second quarter of 2021, only six confirmed or probable cases of acute RF were notified to ARPMS – the smallest number of cases since regular reporting commenced in 2010. Of these cases, four identified as Māori and two as Pasifika.

The possible impacts of COVID-19 on this year’s data should be noted. One study has found that during the COVID-19 alert levels 2–4 in 2020, the mean weekly rates of hospital discharge with RF per 100,000 people did not differ significantly from previous years.⁹⁷ However, the impacts of the COVID-19 pandemic over 2020 and 2021 may have caused potential delays in presentation and diagnosis, which may limit the accuracy of this data. This will be an important consideration when continuing to analyse data from 2021. Another potential

⁹⁴ Institute of Environmental Science and Research Limited (ESR). (2021). Annual Notifiable Disease Tables. Retrieved 28 July 2021, from https://surv.esr.cri.nz/surveillance/annual_diseasetables.php

⁹⁵ RF hospitalisation data provided by the Ministry of Health.

⁹⁶ Anderson, P. (2021). Personal communication.

⁹⁷ Duffy, E., Thomas, M., Hills, T., *et al.* (2021). The impacts of New Zealand’s COVID-19 epidemic response on community antibiotic use and hospitalisation for pneumonia, peritonsillar abscess and rheumatic fever. *The Lancet Regional Health - Western Pacific*, 12, 100162. <https://doi.org/10.1016/j.lanwpc.2021.100162>

impact is due to the closure of borders, which has stopped movement between Aotearoa New Zealand and other countries, including the Pacific Region.

Another potential impact is due to the closure of borders, which has stopped movement between Aotearoa New Zealand and other countries, including the Pacific Islands.

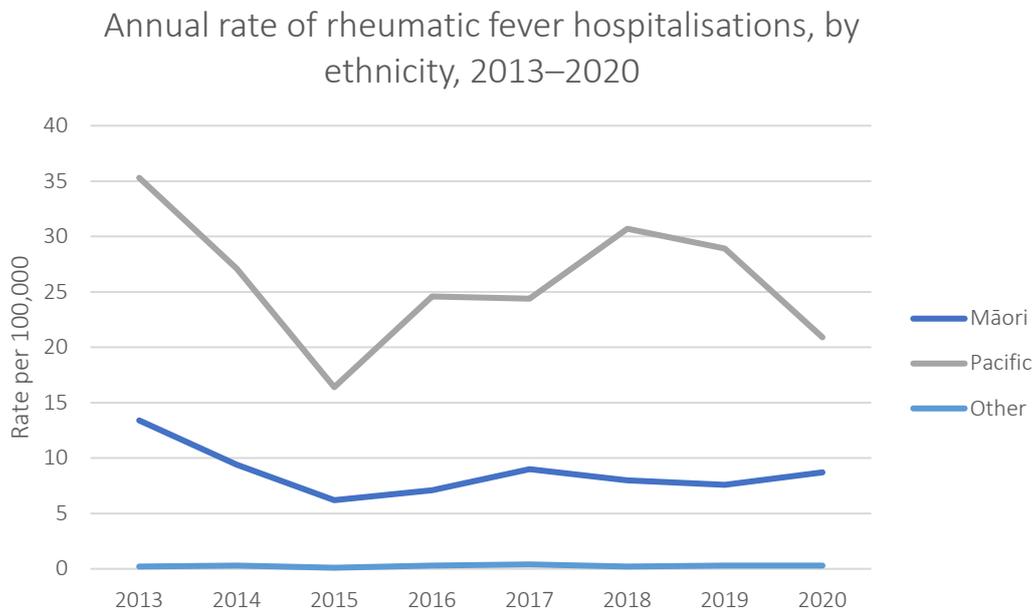


Figure 8: Annual rate of rheumatic fever hospitalisations over time in Aotearoa New Zealand by ethnicity. Data from the Ministry of Health.

As mentioned in section 1.3, there is a huge opportunity to understand how and why Pacific RF rates are lower than pre-COVID-19 rates, in order to inform interventions for sustained reduction in RF rates. That RF rates have fallen for Pacific people in this window but not for Māori is striking and coincides with restricted travel to and from Samoa, Tonga, Fiji and other South Pacific countries. Pacific Islands have very high rates of RF and RHD (multiple studies), supporting a hypothesis that the reduction in Pacific rates of RF in Aotearoa is due to fewer GAS strains entering from the Pacific Islands.⁹⁸

In the highest-risk cohort – boys aged 4–15 years – the differences in disease rates by ethnicity are even more disparate. The rate of initial RF hospitalisations per 100,000 people in that population group was 78.5 for Pacific boys, 41.8 for Māori boys and 0.9 for other boys of other ethnicities (see figure 10).

⁹⁸ Wilson, N., Wilson, E. and Percival, T. (2021). Personal communication.

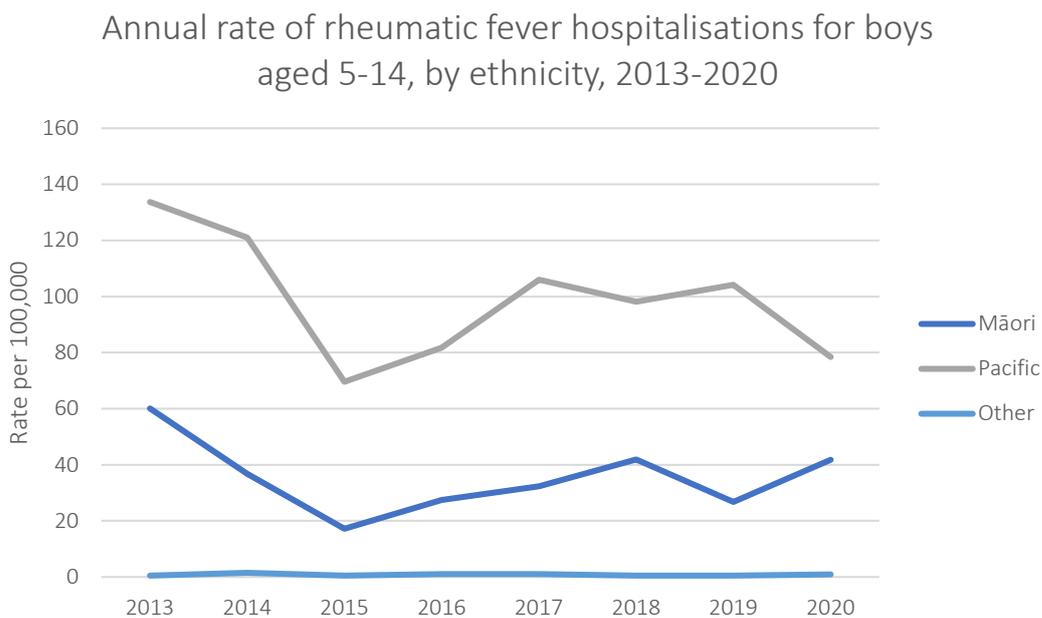


Figure 9: Annual rate of rheumatic fever hospitalisations in boys aged 5 to 14 over time in Aotearoa New Zealand. Data from the Ministry of Health.

Regional differences in rates are evident in the national data (see figure 11). However, the small population sizes and low number of cases in some regions may mean that rates per 100,000 people or trends may be misleading.

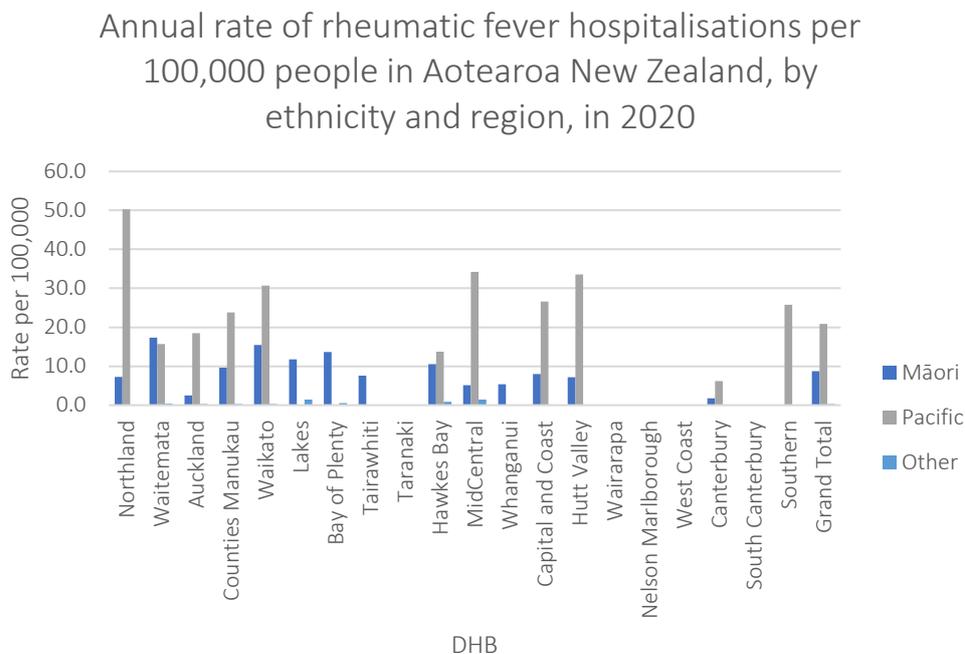


Figure 10: Annual rate of rheumatic fever hospitalisations in 2020 Aotearoa New Zealand. Data from the Ministry of Health.

Region-specific studies may provide more accurate disease rates and trends over time due to some inherent limitations in how cases are counted for hospitalisation data and the increasing completeness of disease notification data over time (see section 3).

Individual studies that have combined data from multiple sources (notification data, a local RF register and hospitalisation data), as opposed to relying on a single data source, have found higher rates of RF than what is reported by the Ministry of Health (either the national notification data or national hospitalisation data). In Counties Manukau, the numbers recorded by ARPHS are lower than those recorded at the Ministry.⁹⁹

For example, a study in Northland found the RF incidence rate in 2017 to be double the hospitalisation data rate reported by the Ministry of Health (7 per 100,000 compared to 3.5 per 100,000). The researchers explained that this is likely to be because only the hospitalised cases of first episodes of RF/RHD are reported in the Ministry of Health's data while any cases diagnosed in primary care and emergency departments are not. In the Northland dataset, Māori and Pacific children aged 5–14 had very high rates per 100,000 people at 64.5 for Māori and 54.6 for Pacific peoples.¹⁰⁰

Only the hospitalised cases of first episodes of RF/RHD are reported in the Ministry of Health's data while any cases diagnosed in primary care and emergency departments are not.

The Bay of Plenty study mentioned above in section 3 also found differences in the trend of RF rates when combining data from multiple sources. The multi-sourced data showed RF rates declined by 22% after interventions were implemented (2000–2010 vs 2011–2018), with even higher rates of decline for children and young people aged 5–14 (32%) and Māori 5–14-year-olds (31%).¹⁰¹

These findings suggest that multi-sourced data should be used to determine the RF trends throughout Aotearoa New Zealand to ensure accuracy in reported disease rates and robustness in measures of the impact of interventions.

Multi-sourced data should be used to determine the RF trends throughout Aotearoa New Zealand to ensure accuracy in reported disease rates and robustness in measures of the impact of interventions.

⁹⁹ Anderson, P. (2021). Personal communication.

¹⁰⁰ Wauchop, K., Shetty, A. and Bremner, C. (2019). The epidemiology of acute rheumatic fever in Northland, 2012–2017. *The New Zealand Medical Journal*, 132(1498), 32–40.

¹⁰¹ Walsh, L., Innes-Smith, S., Wright, J., et al. (2021). *Bay of Plenty Rheumatic fever epidemiology 2000–18; Baywide ARF rates in Māori reduce substantially utilizing multi-sourced data. Notification data leads to underestimation of programme effectiveness - Unpublished manuscript.*

4.4 The rates of rheumatic heart disease show an increasing trend

A study of RHD hospitalisation data from 2000–2018 found an increasing rate of initial RHD hospitalisation over time (see figure 12). Subject to the caveats above section 3 around ICD code, the mean age of initial RHD hospitalisation was 60 years and risk for RHD was associated with increasing age, Māori and Pacific ethnicity, and socio-economic deprivation.¹⁰²

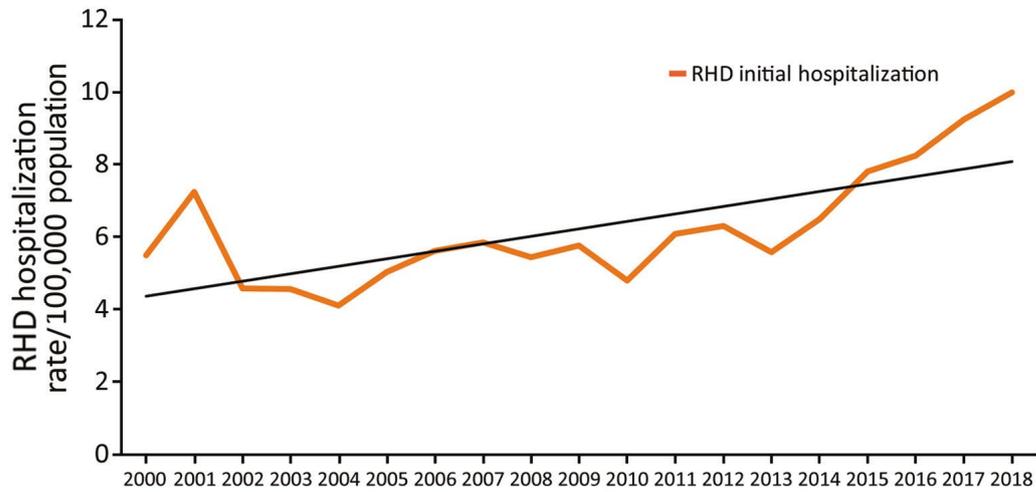


Figure 11: Annual incidence rates of initial RHD hospitalisations, all ages, 2000–2018 in Aotearoa New Zealand from Bennett et al. 2021.

¹⁰² Bennett, J., Zhang, J., Leung, W., et al. (2021). Rising ethnic inequalities in acute rheumatic fever and rheumatic heart disease, New Zealand, 2000–2018. *Emerging Infectious Diseases*, 27(1), 36. <https://doi.org/10.3201/eid2701.191791>

5 The burden of disease falls on Māori and Pacific peoples

RF occurs almost exclusively within Māori and Pacific population groups living in Aotearoa New Zealand – it is at the extreme end of the health inequities that we see in this country – and these ethnic inequities are reportedly rising.¹⁰³

That Māori and Pacific peoples have higher rates of RF and RHD is undisputed. However, the exact reasons for the increased risk among these ethnicities are likely to be complex and multifaceted.

That Māori and Pacific have higher rates of RF and RHD is undisputed. However, the exact reasons for the increased risk among these ethnicities are likely to be complex and multifaceted.

It is not that Māori and Pacific peoples are simply over-represented in other areas that increase disease risk (detailed in section 6). One study showed that when adjusted for age, sex and socio-economic deprivation, hospitalisation rates for RF are 23.6 times higher for Pacific peoples and 11.8 times higher for Māori compared to European and other ethnicities. For hospitalisation for RHD, the rates were 4.6 times and 3.2 times higher, respectively.¹⁰⁴

Another study showed similar rates of increased hospitalisation risk by ethnicity and demonstrated that ethnicity alone had a higher magnitude of risk associated with it than socio-economic deprivation alone. When age and deprivation were adjusted for, the increased risk associated with ethnicity was 14 times higher for Māori and 21 times higher for Pacific peoples.¹⁰⁵ In comparison, when age and ethnicity were adjusted for, the increased risk for the most and next most deprived groups were 9 and 4 times higher, respectively. That same study clearly demonstrated that Māori and Pacific peoples from the least deprived areas still had higher risk than European, Asian or other ethnicities from the most deprived regions (see table 4).

When adjusted for age, sex and socio-economic deprivation, hospitalisation rates for RF are 23.6 times higher for Pacific Peoples and 11.8 times higher for Māori compared to European and other ethnicities.

Table 4: RF rate per 1000 people by age, ethnicity and deprivation status taken from Gurney *et al.*¹⁰⁶

	Deprivation index Least deprived → Most deprived				
	1-2	3-4	5-6	7-8	9-10
5–9 years					
Pacific peoples	0.4	0.9	1.1	1.6	3.6
Māori	0.3	0.7	0.8	1.1	2.5
European/other	0	0	0.1	0.1	0.2
Asian	0	0	0	0.1	0.2
10–14 years					
Pacific peoples	0.7	1.6	1.9	2.7	6.2
Māori	0.5	1.1	1.3	1.9	4.4
European/other	0	0.1	0.1	0.1	0.3
Asian	0	0.1	0.1	0.1	0.3

¹⁰³ Ibid.

¹⁰⁴ Ibid.

¹⁰⁵ Gurney, J., Stanley, J., Baker, M., *et al.* (2016). Estimating the risk of acute rheumatic fever in New Zealand by age, ethnicity and deprivation. *Epidemiology and Infection*, 144(14), 3058-3067. <https://doi.org/10.1017/S0950268816001291>

¹⁰⁶ Ibid.

Studies have identified that the ethnic disparities for development of RF are greater than occur with GAS throat and skin infections alone, implying that there are factors beyond GAS infection driving the disparity in RF occurrence.¹⁰⁷ There are also concerns concerning ethnic inequities in the progression from a first episode of RF to recurrent episodes of RF or RHD.¹⁰⁸

Closing these gaps and achieving health equity for Māori across the life course is also required to meet the obligations of Te Tiriti o Waitangi.

The complex drivers of these inequities likely include:

- **Racial discrimination.** There is evidence that racial discrimination is associated with a range of poorer health outcomes and reduced access to and quality of healthcare, making racism in the healthcare sector a determinant of health in Aotearoa New Zealand.¹⁰⁹ It has previously been shown that maternal experience of racism from a healthcare professional is an independent predictor of infant infectious disease hospitalisation.¹¹⁰
- **Inequity in access.** Systemic barriers to accessing healthcare affect Māori and Pacific peoples more.¹¹¹ For example, in the 2019 New Zealand Health Survey, the percentage of people not accessing a prescription due to cost¹¹² was around double for Māori and Pacific peoples, including children, when compared to other ethnicities.¹¹³
- **Inequity in quality.** Even when Māori and Pacific peoples can access care, the quality of care received may be poorer than that received by non-Māori and non-Pacific peoples. This relates to services, treatment and communications.¹¹⁴

There is evidence that systemic racism and discrimination experienced in the healthcare system, as well as the inequities in being able to access care and the quality of care received, contribute to the high rates of RF and RHD experienced by Māori and Pacific peoples in Aotearoa New Zealand (discussed further in section 7).¹¹⁵ These inequities can influence risk of disease progression at a number of stages, from whether people receive

¹⁰⁷ Oliver, J., Upton, A., Jack, S.J., et al. (2020). Distribution of streptococcal pharyngitis and acute rheumatic fever, Auckland, New Zealand, 2010–2016. *Emerging Infectious Diseases*, 26(6), 1113. <https://doi.org/10.3201/eid2606.181462> Thomas, S., Bennett, J., Jack, S., et al. (2021). Descriptive analysis of group A *Streptococcus* in skin swabs and acute rheumatic fever, Auckland, New Zealand, 2010–2016. *The Lancet Regional Health - Western Pacific*, 8, 100101. <https://doi.org/10.1016/j.lanwpc.2021.100101>

¹⁰⁸ Oliver, J., Robertson, O., Zhang, J., et al. (2021). Ethnically disparate disease progression and outcomes among acute rheumatic fever patients in New Zealand, 1989–2015. *Emerging Infectious Diseases*, 27(7), 1893–1902. <https://doi.org/10.3201/eid2707.203045>

¹⁰⁹ Talamaivao, N., Harris, R., Cormack, D., et al. (2020). Racism and health in Aotearoa New Zealand: A systematic review of quantitative studies. *The New Zealand Medical Journal*, 133(1521), 55–55.

¹¹⁰ Hobbs, M.R., Morton, S.M., Atatoa-Carr, P., et al. (2017). Ethnic disparities in infectious disease hospitalisations in the first year of life in New Zealand. *Journal of Paediatrics and Child Health*, 53(3), 223–231. <https://doi.org/10.1111/jpc.13377>

¹¹¹ Health Quality & Safety Commission. (2019). *A window on the quality of Aotearoa New Zealand's health care 2019 – A view on Māori health equity*. Wellington, New Zealand: Health Quality & Safety Commission. Retrieved from <https://www.hqsc.govt.nz/our-programmes/health-quality-evaluation/publications-and-resources/publication/3721/>; Ryan, D., Grey, C. and Mischewski, B. (2019). *Tofa Saili: A review of evidence about health equity for Pacific Peoples in New Zealand*. Wellington, New Zealand: Pacific Perspectives Ltd. Retrieved from <https://www.pacificperspectives.co.nz/publications>

¹¹² There is no prescription fee for children aged 13 and under. For others, \$5 is the standard fee for the first 20 new prescription items in a year, unless there is access to a provider who waives this fee, e.g. Chemist Warehouse.

¹¹³ Ministry of Health. (2019). New Zealand Health Survey Annual Data Explorer. Retrieved 15 July 2021, from <https://minhealthnz.shinyapps.io/nz-health-survey-2018-19-annual-data-explorer>

¹¹⁴ Health Quality & Safety Commission. (2019). *A window on the quality of Aotearoa New Zealand's health care 2019 – A view on Māori health equity*. Wellington, New Zealand: Health Quality & Safety Commission. Retrieved from <https://www.hqsc.govt.nz/our-programmes/health-quality-evaluation/publications-and-resources/publication/3721/>; Ryan, D., Grey, C. and Mischewski, B. (2019). *Tofa Saili: A review of evidence about health equity for Pacific Peoples in New Zealand*. Wellington, New Zealand: Pacific Perspectives Ltd. Retrieved from <https://www.pacificperspectives.co.nz/publications>

¹¹⁵ Anderson, A., Leversha, A., Ofanoa, M., et al. (2018). *Māori and Pacific whānau experiences of recurrent rheumatic fever and unexpected rheumatic heart disease in New Zealand*. Auckland, New Zealand: University of Auckland. Retrieved from <https://tomaioira-research-group.blogs.auckland.ac.nz/tomaioira-our-mahi/research-project-1/>; Anderson, A., Mills, C. and Eggleton, K. (2017). Whānau perceptions and experiences of acute rheumatic fever diagnosis for Māori in Northland, New Zealand. *The New Zealand Medical Journal*, 130(1465), 80–89. ; The National Hauora Coalition, Anderson, A., Brown, R., et al. (2020). Pacific Fono: a community-based initiative to improve rheumatic fever service delivery for Pacific Peoples in South Auckland. *Journal of Primary Health Care*, 12(4), 384–390. <https://doi.org/10.1071/HC20022>; Shaio, M.-F. (2021). The impact of racism on rheumatic fever rates. *Kai Tiaki: Nursing New Zealand*, 27(1), 36–37. ; Burgess, H. (2016). *Māori Whānau experiences of rheumatic fever: Reflections of social and structural inequity*. ResearchSpace@Auckland, Auckland, New Zealand. Retrieved from <https://researchspace.auckland.ac.nz/bitstream/handle/2292/30703/whole.pdf?sequence=2>

antibiotics for GAS infection, through to timely diagnosis of RF, and appropriate management and treatment of RF and RHD.

An audit of treatment of GAS throat infection by GPs in Northland found differences in the management of care for Māori and non-Māori patients, with young Māori people being significantly less likely than non-Māori to receive antibiotics according to all criteria in the national guidelines, suggesting that implicit biases in prescribing practices contribute to the inequities in outcomes.¹¹⁶

This highlights that broader approaches to address systemic racism and inequities and healthcare access and quality are an essential part of an approach to reduce rates of RF. In addition to being a disease of concern itself, RF is a symptom of broader health inequities. A holistic and preventative approach to reduce these health inequities will have broader positive implications and help to close the health gaps we currently see in Aotearoa New Zealand.

6 A complex range of risk factors increase a person's risk of developing rheumatic fever

After GAS infection, other risk factors may contribute to development of RF and RHD. Having robust evidence about the role of different risk factors is important to inform public health interventions to reduce rates of disease.

In this section we summarise the evidence for different risk factors for RF, with a particular focus on evidence from our local setting and where these findings have been replicated overseas. The strength of evidence for different risk factors varies and some remain understudied. A summary of the findings is included in table 5 and further detail is included below.

¹¹⁶ Shetty, A., Mills, C. and Eggleton, K. (2018). A repeat audit of primary care management of group A streptococcal pharyngitis in Northland, New Zealand 2016. *Journal of Primary Health Care*, 10(1), 18. <https://doi.org/10.1071/hc17056>

Table 5: Summary of evidence for risk factors for rheumatic fever, references are provided in the text following text.

Factor	Evidence of association with RF	Finding	Influence on approach
Demographic factors			
Family history of RF	✓✓✓	Strong increased risk up to 6x	These risk factors can guide who to target for interventions, specifically family history and young age which increase risk significantly
Young age	✓✓✓	Most cases are in 5–14-year olds	
Male sex	✓	Higher risk for males in local context	
Genetic predisposition	✓	Some variants increase risk by a small amount, but it is complex No evidence of genetic variants unique to Māori and Pacific peoples that increase risk	
Living and socioeconomic conditions			
Inadequate housing	✓✓✓	Strong increased risk with different factors Crowded housing (either due to not having enough rooms or needing to share rooms to keep warm) Poor housing conditions which make houses cold, damp and mouldy Unstable housing forcing people to move often	These risk factors can be addressed by targeted improvements and would have a broader impact on health outcomes
Socio-economic deprivation	✓✓✓	Strong association where RF risk increases as deprivation level increases	
Poor healthcare access	✓	Evidence this increases risk but not well studied quantitatively	
Other health determinants			
Excess body weight	✓✓	Increased risk up to 3x for overweight and obese people	These risk factors suggest could guide a general intervention around health and nutrition, which would have broader impacts on health outcomes
High sugary drink intake	✓✓	Increased risk 1.6x with more sugary drinks consumed, but whether a proxy for something else and how it increases risk unclear	
Exposure to smoke	✓	Some evidence this increases risk but it might be a proxy for some other risk factors	Unclear which risk factors play a potential role in causing RF and which are proxies
Low vitamin D	✓	Some evidence of lower vitamin D levels being associated with increased risk but possible confounding due to sick children not going outside as much	
Poor nutrition	~	Mixed evidence – not a clear risk factor for significant increases	
Dental caries	~	Mixed evidence – likely a proxy related to other factors	
Skin infection and other impacts			
Scabies infection	✓✓	One study found increased risk for the small proportion of people who have this infection; further study warranted, especially to probe secondary GAS infection	These risk factors could guide interventions to support better skin hygiene practices and treatment of other types of skin infections
Poor skin hygiene	✓	Some evidence that not having access to enough hot water for showers increases risk but no differences in laundry practices	
Skin damage	X	No evidence that insect bites, cuts or grazes increase the risk of RF	
Having pets	X	No evidence that pets are a pathway for disease transmission	
Health awareness			
Health knowledge and literacy	X	No evidence that knowledge about RF or healthcare seeking for throat and skin infections decreases the risk of RF	Suggests targeting this will not decrease RF risk

6.1 Demographic factors

There is evidence of some demographic factors increasing the risk of RF. These risk factors can guide who to target for interventions – specifically considering family history and young age which increase risk significantly – but it’s likely that 50% of cases will still be missed.

People with a family/whānau history of RF are at higher risk

The increased risk of developing RF for people whose family/whānau have had the condition is well established. Overseas studies dating back many decades have shown this link and high rates of positive family history have been reported in surveys in Aotearoa New Zealand as well.¹¹⁷

In a robust case-control study in Aotearoa New Zealand, a family history of RF was associated with a six times greater risk of developing the disease. This same analysis estimated that 44.8% of the disease could be reduced if family history was not a risk factor.¹¹⁸

A family history of RF was associated with a six times greater risk of developing the disease.

Whether this is due to genetics, to shared environmental factors (e.g. inadequate housing conditions, systemic societal racism), or shared gene-environment interaction is not fully resolved.

Family history of disease provides a good way to prioritise people at increased risk of developing RF with more targeted disease interventions. However, local research is needed to understand how this knowledge about increased risk for those with a positive family history can be applied without stigmatising whānau.

School-aged children are most affected by RF

The highest risk of RF is for children aged 5–14 (see figure 13).¹¹⁹ The next highest risk is for those over 15, but children younger than five can still be affected. Māori and Pacific populations are younger and have a higher proportion of their population within these younger age brackets, but that does not explain the differences in disease rates and these groups remain disproportionately impacted.

¹¹⁷ Cheadle, W.B. (1889). *The various manifestations of the rheumatic state as exemplified in childhood and early life*. London, UK: Smith, Elder and Co; Diamond, E.F. (1957). Hereditary and environmental factors in the pathogenesis of rheumatic fever. *Pediatrics*, 19(5), 908-915. ; Institute of Environmental Science and Research Limited (ESR). (2017). *Rheumatic fever in New Zealand annual report July 2014 to June 2015*. Porirua, New Zealand: Institute of Environmental Science and Research Limited (ESR). Retrieved from https://surv.esr.cri.nz/PDF_surveillance/RheumaticFever/Rheumaticfeverannualreport2014-15.pdf

¹¹⁸ Baker, M.G., Gurney, J., Oliver, J., et al. (2019). *The New Zealand rheumatic fever risk factors study (RF RISK): Draft report on study findings*. Wellington, New Zealand: Rheumatic Fever Risk Factors Study.

¹¹⁹ Bennett, J., Rentta, N., Leung, W., et al. (2021). Structured review of primary interventions to reduce group A streptococcal infections, acute rheumatic fever and rheumatic heart disease. *Journal of Paediatrics and Child Health*. <https://doi.org/10.1111/jpc.15514>; Baker, M.G., Gurney, J., Oliver, J., et al. (2019). Risk factors for acute rheumatic fever: Literature review and protocol for a case-control study in New Zealand. *International Journal of Environmental Research and Public Health*, 16(22), 4515. <https://doi.org/10.3390/ijerph16224515>

Annual rate of rheumatic fever hospitalisations by age and ethnicity in 2020

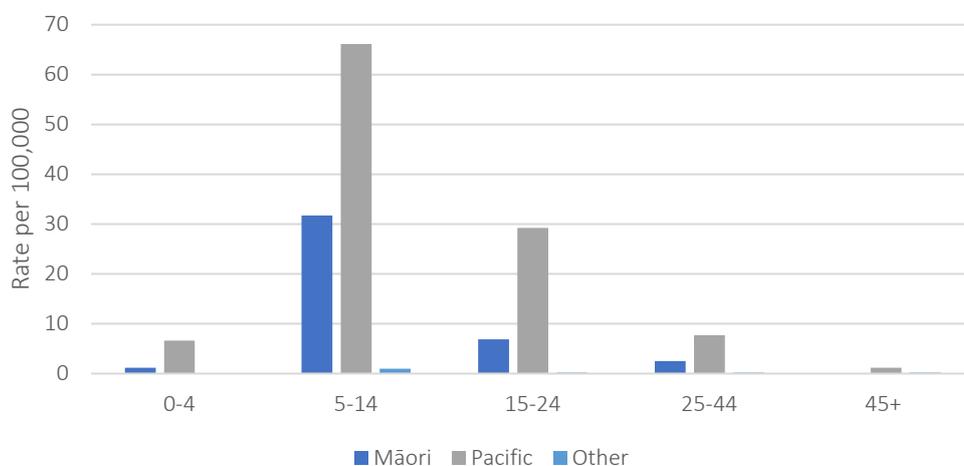


Figure 12: Differences in the rate of rheumatic fever in Aotearoa New Zealand by age. Data from Bennett et al. (2021).

Boys are at higher risk of developing RF

In Aotearoa New Zealand males are at increased risk of developing RF.¹²⁰ This is different to overseas contexts where the evidence is for increased risk in females.¹²¹ The specific reasons for increased risk for females overseas are not clear, but some of the proposed reasons may not be relevant here (i.e. reduced access to prophylaxis of RF) though other reasons would be relevant here (i.e. innate immune differences, closer involvement in child rearing, worsening pre-existing disease during pregnancy).

The role, if any, of genetics in increasing risk of RF for Māori and Pacific peoples isn't clear

There is evidence that genetics play a role in predisposing people to developing RF and RHD.¹²² Studies that have looked at family inheritance (including when the same environment is not shared between genetically related people), disease risk in twins, and the association between millions of genetic variations and disease in thousands of individuals, have all suggested that genetics is a contributor to the risk of developing RF, but in a complex way.

Studies that have looked at family inheritance, disease risk in twins, and the association between millions of genetic variations and disease in thousands of individuals, have all suggested that genetics is a contributor to the risk of developing RF, but in a complex way.

The specific role of genetic predisposition in Māori and Pacific population groups is less well understood. One study focused on Pacific populations and found an association between genes that coded for the immunoglobulin heavy chain (IGH) and risk of RF. Each copy of a specific gene in IGH increased risk by 1.4

¹²⁰ Bennett, J., Rentta, N., Leung, W., et al. (2021). Structured review of primary interventions to reduce group A streptococcal infections, acute rheumatic fever and rheumatic heart disease. *Journal of Paediatrics and Child Health*. <https://doi.org/10.1111/jpc.15514>; Baker, M.G., Gurney, J., Oliver, J., et al. (2019). Risk factors for acute rheumatic fever: Literature review and protocol for a case-control study in New Zealand. *International Journal of Environmental Research and Public Health*, 16(22), 4515. <https://doi.org/10.3390/ijerph16224515>

¹²¹ Carapetis, J.R., Beaton, A., Cunningham, M.W., et al. (2016). Acute rheumatic fever and rheumatic heart disease. *Nature Reviews Disease Primers*, 2(1), 15084. <https://doi.org/10.1038/nrdp.2015.84>

¹²² Ibid.; Muhamed, B., Parks, T. and Sliwa, K. (2020). Genetics of rheumatic fever and rheumatic heart disease. *Nature Reviews Cardiology*, 17(3), 145-154. <https://doi.org/10.1038/s41569-019-0258-2>

times and for Samoan ethnicity alone it was over two times.¹²³ Another study of Māori and Pacific peoples found an association between a specific variant in the IL-6 gene and risk of RF, and this has been replicated with other ethnic groups in some but not all overseas studies.

While these studies highlight a potential genetic influence amongst Māori and Pacific populations, it is not known whether other ethnicities also carry these genetic variants. There is currently no evidence that Māori and Pacific populations have unique genetic variants that increase their risk of RF (in contrast to other studies that have undertaken analogous assessments overseas¹²⁴). The fact that non-Māori and Pacific peoples in Aotearoa New Zealand previously experienced high rates of RF also suggests that the increased risk would not only be driven by genetics. Aotearoa New Zealand did not share the dramatic decline in RF seen in countries such as the US and Denmark which began in the 1940s; instead, our rates have remained stable.¹²⁵

There is currently no evidence that Māori and Pacific populations have unique genetic variants that increase their risk of RF.

6.2 Living and socioeconomic conditions

There is strong evidence that poor housing conditions, socio-economic deprivation and poor healthcare access all increase the risk of RF. These risk factors could all be targeted and would have significant impacts on overall health outcomes. Work such as the Healthy Homes Initiative¹²⁶ seeks to address this but is beyond the scope of this review.

Living in inadequate housing increases the risk of developing RF

The way GAS spreads means that exposure, transmission and infection are closely tied to how people live and interact in households. There is strong evidence internationally and in Aotearoa New Zealand that crowded housing, other poor housing conditions such as under-insulation and inadequate heating, and transient living situations are associated with RF, though not every individual study has found a link.¹²⁷

The different housing factors that have been associated with RF in Aotearoa New Zealand include:

¹²³ Parks, T., Mirabel, M.M., Kado, J., *et al.* (2017). Association between a common immunoglobulin heavy chain allele and rheumatic heart disease risk in Oceania. *Nature Communications*, 8(1), 14946. <https://doi.org/10.1038/ncomms14946>

¹²⁴ Machipisa, T., Chong, M., Muhamed, B., *et al.* (2021). Association of novel locus with rheumatic heart disease in black African individuals. *JAMA Cardiology*. <https://doi.org/10.1001/jamacardio.2021.1627>

¹²⁵ Lennon, D. (1999). *Rheumatic fever, a preventable disease? The New Zealand experience*. Paper presented at the XIV Lancefield International Symposium on Streptococci and Streptococcal Diseases, Auckland, New Zealand.

¹²⁶ Ministry of Health. (n.d., 29 June 2021). Healthy Homes Initiative. Retrieved 28 September, 2021, from <https://www.health.govt.nz/our-work/preventative-health-wellness/healthy-homes-initiative>

¹²⁷ Jaine, R., Baker, M. and Venugopal, K. (2011). Acute rheumatic fever associated with household crowding in a developed country. *The Pediatric Infectious Disease Journal*, 30(4). <https://doi.org/10.1097/INF.0b013e3181fbd85b>; Oliver, J.R., Piers, N., Stefanogiannis, N., *et al.* (2017). Acute rheumatic fever and exposure to poor housing conditions in New Zealand: A descriptive study. *Journal of Paediatrics and Child Health*, 53(4), 358-364. <https://doi.org/10.1111/jpc.13421> Baker, M.G., Gurney, J., Oliver, J., *et al.* (2019). Risk factors for acute rheumatic fever: Literature review and protocol for a case-control study in New Zealand. *International Journal of Environmental Research and Public Health*, 16(22), 4515. <https://doi.org/10.3390/ijerph16224515>; Adanja, B., Vlajinac, H. and Jarebinski, M. (1988). Socioeconomic factors in the etiology of rheumatic fever. *Journal of Hygiene, Epidemiology, Microbiology, and Immunology*, 32(3), 329-335. ; Baker, M., McDonald, A., Zhang, J., *et al.* (2013). *Infectious diseases attributable to household crowding in New Zealand: A systematic review and burden of disease estimate*. Wellington, New Zealand: He Kainga Oranga/Housing and Health Research. Retrieved from <http://www.healthyhousing.org.nz/wp-content/uploads/2010/01/HH-Crowding-ID-Burden-25-May-2013.pdf>; Cannon, J.W., Abouzeid, M., de Klerk, N., *et al.* (2019). Environmental and social determinants of acute rheumatic fever: A longitudinal cohort study. *Epidemiology and Infection*, 147, e79-e79. <https://doi.org/10.1017/S0950268818003527>; Tartof, S.Y., Reis, J.N., Andrade, A.N., *et al.* (2010). Factors associated with group A *Streptococcus emm* type diversification in a large urban setting in Brazil: A cross-sectional study. *BMC Infectious Diseases*, 10(1), 327. <https://doi.org/10.1186/1471-2334-10-327>; Gordis, L., Lilienfeld, A. and Rodriguez, R. (1969). Studies in the epidemiology and preventability of rheumatic fever—II: Socio-economic factors and the incidence of acute attacks. *Journal of Chronic Diseases*, 21(9), 655-666. [https://doi.org/10.1016/0021-9681\(69\)90037-X](https://doi.org/10.1016/0021-9681(69)90037-X); Coffey, P.M., Ralph, A.P. and Krause, V.L. (2018). The role of social determinants of health in the risk and prevention of group A streptococcal infection, acute rheumatic fever and rheumatic heart disease: A systematic review. *PLOS Neglected Tropical Diseases*, 12(6), e0006577. <https://doi.org/10.1371/journal.pntd.0006577>

- **Crowding**
 - An Aotearoa New Zealand study found that for every 1% increase in the average crowding level of an area there would be a 6.5% increase in the expected incidence of RF in that area. The definition of crowding was based on a measure that took into account the number, age, sex and relationship of people within a household, and the size of the house by number of bedrooms. The association between crowding and RF persisted when adjusted for possible confounding risk factors such as ethnicity and household income.¹²⁸
 - Fifty-eight percent of people who had been recently diagnosed with RF reported household crowding, with 35% living in severe crowding (short at least two bedrooms), and 49% sharing a bed.¹²⁹ The study design means that a causal association is not proven but it adds to the wider body of evidence.
 - A case-control study found consistent strong associations with all forms of housing crowding and RF.¹³⁰ The crowding included structural (situations where there is insufficient living space for the occupants of a dwelling to maintain health and wellbeing based on established norms for the size and composition of that household and the size and characteristics of the dwelling) and functional (situations where levels of household crowding are increased by how the house is used) crowding, and bed sharing. Around 20% of incidents of RF were attributable to household crowding.
- **Dampness, mould and cold**
 - Nearly four in five people who had been recently diagnosed with RF reported dampness and mould in their house, and living in a cold house, which often meant having to share rooms to keep warm.¹³¹
 - In the case-control study mentioned above, around 28% of incidents of RF were attributable to cold and/or damp housing.¹³²

“My house was so cold, I hated it, we would just stay in the room and watch TV, oh it was so cold. We had no carpet, I couldn’t believe that housing...”¹³³

- **Transient housing**
 - A high proportion of people who have had RF in Aotearoa New Zealand live in rental or state housing.¹³⁴
 - The case-control study mentioned above found that RF risk was associated with shorter duration of living in a house, with living in a house for less than a year increasing risk by over three times.¹³⁵

This evidence demonstrates that a significant proportion of RF occurrences are due to poor housing and highlights the need for improving housing conditions to be a substantial part of the public health intervention to reduce rates of this disease.

¹²⁸ Jaine, R., Baker, M. and Venugopal, K. (2011). Acute rheumatic fever associated with household crowding in a developed country. *The Pediatric Infectious Disease Journal*, 30(4). <https://doi.org/10.1097/INF.0b013e3181fbd85b>

¹²⁹ Oliver, J.R., Pierse, N., Stefanogiannis, N., et al. (2017). Acute rheumatic fever and exposure to poor housing conditions in New Zealand: A descriptive study. *Journal of Paediatrics and Child Health*, 53(4), 358-364. <https://doi.org/10.1111/jpc.13421>

¹³⁰ Baker, M.G., Gurney, J., Oliver, J., et al. (2019). *The New Zealand rheumatic fever risk factors study (RF RISK): Draft report on study findings*. Wellington, New Zealand: Rheumatic Fever Risk Factors Study.

¹³¹ Oliver, J.R., Pierse, N., Stefanogiannis, N., et al. (2017). Acute rheumatic fever and exposure to poor housing conditions in New Zealand: A descriptive study. *Journal of Paediatrics and Child Health*, 53(4), 358-364. <https://doi.org/10.1111/jpc.13421>

¹³² Baker, M.G., Gurney, J., Oliver, J., et al. (2019). *The New Zealand rheumatic fever risk factors study (RF RISK): Draft report on study findings*. Wellington, New Zealand: Rheumatic Fever Risk Factors Study.

¹³³ Burgess, H. (2016). *Māori Whānau experiences of rheumatic fever: Reflections of social and structural inequity*.

ResearchSpace@Auckland, Auckland, New Zealand. Retrieved from <https://researchspace.auckland.ac.nz/bitstream/handle/2292/30703/whole.pdf?sequence=2>

¹³⁴ Oliver, J.R., Pierse, N., Stefanogiannis, N., et al. (2017). Acute rheumatic fever and exposure to poor housing conditions in New Zealand: A descriptive study. *Journal of Paediatrics and Child Health*, 53(4), 358-364. <https://doi.org/10.1111/jpc.13421>

¹³⁵ Baker, M.G., Gurney, J., Oliver, J., et al. (2019). *The New Zealand rheumatic fever risk factors study (RF RISK): Draft report on study findings*. Wellington, New Zealand: Rheumatic Fever Risk Factors Study.

Socio-economic deprivation increases risk of infection and disease progression

People living in the most deprived regions are around five times more likely to be hospitalised with RF than those living in the least-deprived regions, when adjusted for age, sex and ethnicity.¹³⁶ Access to primary care is critical in the prevention of RF. People living in more deprived areas may have insufficient access to effective healthcare, which could result in people missing diagnosis and treatment for GAS infections and RF. Cost barriers of prescriptions affect people aged over 13 in the most deprived areas around four times as much as those living in the least deprived areas.¹³⁷

Māori and Pacific peoples are still more likely to suffer from RF, no matter where they live, suggesting it is not only deprivation that is responsible for health disparities (see section 5).¹³⁸

In a survey of people recently diagnosed with RF there were high rates of financial deprivation (nearly 85%), such as not being able to pay power bills on time, having power cut off, and not using heating to save money.¹³⁹

Lower caregiver education level has been associated with RF in a robust case-control study of children in Aotearoa New Zealand, but this association did not remain when adjusted for other deprivation factors suggesting it is a marker of deprivation overall.¹⁴⁰

Associations with socio-economic status, educational level and employment of the caregiver have also been shown in overseas studies.¹⁴¹

Interventions that target populations based on deprivation will include the highest risk groups, but will miss some that are high risk (e.g. Māori and Pacific individuals living outside high deprivation areas) and include some that are low risk (i.e. non-Māori/non-Pacific peoples in high deprivation settings).¹⁴²

Not being able to access healthcare for a sore throat increases the risk of RF

RF risk has been associated with reported barriers to primary care access within the 12 months prior to the RF occurrence. Of these barriers, problems with accessing childcare for other children (which prohibited taking the sick child to the doctor) was the most important and the only one that showed a significant association with RF risk on its own. Approximately 40% of cases and controls did not seek healthcare for their most recent

¹³⁶ Bennett, J., Rentta, N., Leung, W., et al. (2021). Structured review of primary interventions to reduce group A streptococcal infections, acute rheumatic fever and rheumatic heart disease. *Journal of Paediatrics and Child Health*. <https://doi.org/10.1111/jpc.15514>

¹³⁷ Ministry of Health. (2019). New Zealand Health Survey Annual Data Explorer. Retrieved 15 July 2021, from <https://minhealthnz.shinyapps.io/nz-health-survey-2018-19-annual-data-explorer>

¹³⁸ Bennett, J., Rentta, N., Leung, W., et al. (2021). Structured review of primary interventions to reduce group A streptococcal infections, acute rheumatic fever and rheumatic heart disease. *Journal of Paediatrics and Child Health*. <https://doi.org/10.1111/jpc.15514>; Bennett, J., Zhang, J., Leung, W., et al. (2021). Rising ethnic inequalities in acute rheumatic fever and rheumatic heart disease, New Zealand, 2000–2018. *Emerging Infectious Diseases*, 27(1), 36. <https://doi.org/10.3201/eid2701.191791>

¹³⁹ Oliver, J.R., Pierse, N., Stefanogiannis, N., et al. (2017). Acute rheumatic fever and exposure to poor housing conditions in New Zealand: A descriptive study. *Journal of Paediatrics and Child Health*, 53(4), 358-364. <https://doi.org/10.1111/jpc.13421>

¹⁴⁰ Baker, M.G., Gurney, J., Oliver, J., et al. (2019). *The New Zealand rheumatic fever risk factors study (RF RISK): Draft report on study findings*. Wellington, New Zealand: Rheumatic Fever Risk Factors Study.

¹⁴¹ Cannon, J.W., Abouzeid, M., de Klerk, N., et al. (2019). Environmental and social determinants of acute rheumatic fever: A longitudinal cohort study. *Epidemiology and Infection*, 147, e79-e79. <https://doi.org/10.1017/S0950268818003527>; Tartof, S.Y., Reis, J.N., Andrade, A.N., et al. (2010). Factors associated with group A *Streptococcus emm* type diversification in a large urban setting in Brazil: A cross-sectional study. *BMC Infectious Diseases*, 10(1), 327. <https://doi.org/10.1186/1471-2334-10-327>; Zaman, M.M., Yoshiike, N., Chowdhury, A.H., et al. (1997). Socio-economic deprivation associated with acute rheumatic fever: A hospital-based case-control study in Bangladesh. *Paediatric and Perinatal Epidemiology*, 11(3), 322-332. <https://doi.org/10.1111/j.1365-3016.1997.tb00011.x>; Coffey, P.M., Ralph, A.P. and Krause, V.L. (2018). The role of social determinants of health in the risk and prevention of group A streptococcal infection, acute rheumatic fever and rheumatic heart disease: A systematic review. *PLOS Neglected Tropical Diseases*, 12(6), e0006577. <https://doi.org/10.1371/journal.pntd.0006577>

¹⁴² Gurney, J., Stanley, J., Baker, M., et al. (2016). Estimating the risk of acute rheumatic fever in New Zealand by age, ethnicity and deprivation. *Epidemiology and Infection*, 144(14), 3058-3067. <https://doi.org/10.1017/S0950268816001291>

sore throat, suggesting potential for improved primary healthcare uptake.¹⁴³ Barriers to accessing healthcare are covered in more detail in section 7.

6.3 Other health determinants

Evidence for the role of a range of other health and nutrition factors in RF risk is not clear. There seems to be an association between certain variables (body weight, nutrition, sugar intake, dental health) though it remains unknown which factors play a role in disease risk and which are proxies for other risks. General interventions relating to improved health and nutrition would have broader positive impacts on a range of health outcomes beyond RF.

Exposure to smoke may increase the risk of RF

There is some evidence from a local case-control study that people who lived in the same house as smokers had around two times higher risk of RF, although this effect did not hold up when other risk factors were controlled for and so further study is needed.¹⁴⁴ Another study that interviewed people recently diagnosed with RF found 71% lived with smokers.¹⁴⁵

Vitamin D may play a role in RF but further study is needed

There is evidence from a study in Aotearoa New Zealand that children who have RF had lower levels of vitamin D. However, it is possible that their behaviour in the weeks before hospitalisation (e.g. staying indoors because they are sick) may have driven this.¹⁴⁶ Similar studies overseas have found an association, but none have measured vitamin D levels prior to illness onset.¹⁴⁷

Being overweight may increase a person's risk of RF

The case-control study that found an association with sugary drinks also found a higher risk of RF of around three times for children who were overweight and obese.¹⁴⁸ An increased risk of RF for children who were overweight or obese was also found in a study from Israel.¹⁴⁹

Sugary drinks may be an important risk factor for RF

There is emerging evidence that there may be dietary associations with RF. Drinking more sugary drinks each day increased risk by around 1.6 times – nearly 60% of children with RF in one study had one or more sugary drinks per day, compared to around 40% of children without the disease.¹⁵⁰ Around 32% of incidents of RF were associated with sugary drink intake. The role of sugary drinks in causing this disease is not clear, but it could enhance conditions in the throat that promote GAS pharyngitis. Alternatively, this factor could be a proxy for body mass, poor nutrition or tooth decay, although in the same study that found an association there wasn't evidence for it being through these mechanisms.

¹⁴³ Baker, M.G., Gurney, J., Oliver, J., et al. (2019). *The New Zealand rheumatic fever risk factors study (RF RISK): Draft report on study findings*. Wellington, New Zealand: Rheumatic Fever Risk Factors Study.

¹⁴⁴ Ibid.

¹⁴⁵ Oliver, J.R., Pierse, N., Stefanogiannis, N., et al. (2017). Acute rheumatic fever and exposure to poor housing conditions in New Zealand: A descriptive study. *Journal of Paediatrics and Child Health*, 53(4), 358-364. <https://doi.org/10.1111/jpc.13421>

¹⁴⁶ Baker, M.G., Gurney, J., Oliver, J., et al. (2019). *The New Zealand rheumatic fever risk factors study (RF RISK): Draft report on study findings*. Wellington, New Zealand: Rheumatic Fever Risk Factors Study.

¹⁴⁷ Thorup, L., Hamann, S.A., Tripathee, A., et al. (2020). Evaluating vitamin D levels in rheumatic heart disease patients and matched controls: A case-control study from Nepal. *PLOS One*, 15(8), e0237924. <https://doi.org/10.1371/journal.pone.0237924>

¹⁴⁸ Baker, M.G., Gurney, J., Oliver, J., et al. (2019). *The New Zealand rheumatic fever risk factors study (RF RISK): Draft report on study findings*. Wellington, New Zealand: Rheumatic Fever Risk Factors Study.

¹⁴⁹ Machluf, Y., Chaïter, Y., Farkash, R., et al. (2020). Rheumatic fever in large cohort of adolescents in Israel. *Frontiers in Medicine*, 6(328). <https://doi.org/10.3389/fmed.2019.00328>

¹⁵⁰ Baker, M.G., Gurney, J., Oliver, J., et al. (2019). *The New Zealand rheumatic fever risk factors study (RF RISK): Draft report on study findings*. Wellington, New Zealand: Rheumatic Fever Risk Factors Study.

The role of poor nutrition in RF requires further study

Evidence of poor nutrition increasing risk of RF has been found since as early as the 1940s in overseas studies.¹⁵¹ However, overall the results of studies looking for an association have been mixed and a strong association has not been consistently found.¹⁵² In an Aotearoa New Zealand case-control study an association was found but it did not remain when confounding factors were controlled for.¹⁵³ Nutrition was measured by asking participants about fruit and vegetable intake and eating from fast food places.

Poor dental health may increase risk of RF

There is mixed evidence about the association between dental health and RF.

A cohort study of Māori and Pacific children in Auckland found that those who had five or more primary teeth affected by caries were 57% more likely to develop RF or RHD during follow-up, compared to children whose primary teeth were caries free. The study estimated that 22% of the incidents of RF in that cohort were attributable to dental caries.¹⁵⁴

A case-control study that looked at dental health history and linked dental records found no significant differences between children who developed RF and children who didn't.¹⁵⁵

These findings suggest that it is not dental health itself that is a risk factor for RF but rather it might be a proxy for sugar intake, other nutritional factors or more general factors including access to healthcare.

6.4 Skin impacts

There is some evidence that factors that impact skin health could increase the risk of RF. This knowledge could guide interventions to support improved skin hygiene practices and treatment of other types of skin infections; however, a better understanding of the mechanisms through which this increases RF risk is needed.

Other skin infections may provide a pathway for GAS skin infection

Because breaking the skin barrier may lead to GAS skin infections, researchers have looked to see if there are associations with other skin issues and RF.

Scabies is caused by a mite, not GAS, but scratching itchy skin may lead to super infection with GAS which could lead to RF.¹⁵⁶ Evidence of an association between scabies and RF has been found in Aotearoa New Zealand.¹⁵⁷ In a case-control study, the risk of developing RF was nearly six times higher if a person had

¹⁵¹ Coburn, A.F. and Moore, L.V. (1943). Nutrition as a conditioning factor in the rheumatic state. *American Journal of Diseases of Children*, 65(5), 744-756. <https://doi.org/10.1001/archpedi.1943.02010170066008>; Rinehart, J.F. (1943). Rheumatic fever and nutrition. *Annals of the Rheumatic Diseases*, 3(3), 154. <https://doi.org/10.1136/ard.3.3.154>

¹⁵² Coffey, P.M., Ralph, A.P. and Krause, V.L. (2018). The role of social determinants of health in the risk and prevention of group A streptococcal infection, acute rheumatic fever and rheumatic heart disease: A systematic review. *PLOS Neglected Tropical Diseases*, 12(6), e0006577. <https://doi.org/10.1371/journal.pntd.0006577>

¹⁵³ Baker, M.G., Gurney, J., Oliver, J., et al. (2019). *The New Zealand rheumatic fever risk factors study (RF RISK): Draft report on study findings*. Wellington, New Zealand: Rheumatic Fever Risk Factors Study.

¹⁵⁴ Thornley, S., Marshall, R.J., Bach, K., et al. (2017). Sugar, dental caries and the incidence of acute rheumatic fever: A cohort study of Māori and Pacific children. *Journal of Epidemiology and Community Health*, 71(4), 364-370. <https://doi.org/10.1136/jech-2016-208219>

¹⁵⁵ Baker, M.G., Gurney, J., Oliver, J., et al. (2019). *The New Zealand rheumatic fever risk factors study (RF RISK): Draft report on study findings*. Wellington, New Zealand: Rheumatic Fever Risk Factors Study.

¹⁵⁶ Thornley, S., King, R., Marshall, R., et al. (2020). How strong is the relationship between scabies and acute rheumatic fever? An analysis of neighbourhood factors. *Journal of Paediatrics and Child Health*, 56(4), 600-606. <https://doi.org/10.1111/jpc.14697>; Thornley, S., Marshall, R., Jarrett, P., et al. (2018). Scabies is strongly associated with acute rheumatic fever in a cohort study of Auckland children. *Journal of Paediatrics and Child Health*, 54(6), 625-632. <https://doi.org/10.1111/jpc.13851>; Middleton, K. and Bowen, A.C. (2021). Addressing normalization using culturally relevant approaches: An important adjunct to reducing the burden of impetigo and scabies. *The Lancet Regional Health - Western Pacific*, 7, 100102. <https://doi.org/10.1016/j.lanwpc.2021.100102>

¹⁵⁷ Thornley et al., "How strong is the relationship between scabies and acute rheumatic fever? An analysis of neighbourhood factors," *Journal of Paediatrics and Child Health* 56, no. 4 (2020); Thornley et al., "Scabies is strongly associated with acute rheumatic fever in a cohort study of Auckland children," *Journal of Paediatrics and Child Health* 54, no. 6 (2018)

experienced scabies in the past four weeks and around two times higher if they had had scabies in the past year. However, this is unlikely to be a big driver of RF as only around 6% of cases had scabies.¹⁵⁸

In contrast with what has been seen with scabies, there is no evidence that bites, grazes or cuts increase risk of RF via skin infections. In a case-control study from Aotearoa New Zealand there was no evidence that having any skin cuts, grazes or wounds, or insect bites, in last four weeks led to a higher risk of developing RF.¹⁵⁹

Skin hygiene may play an important role in the risk of RF

Researchers in Aotearoa New Zealand have found that people who develop RF may have had less access to hot water for showers and baths, but did not have a difference in access to working baths and showers, use of soap, and access to their own towel, or differences in methods or frequency of washing household laundry.¹⁶⁰ There was a 1.6 times increased risk of developing RF for those without sufficient hot water for washing themselves, and it was estimated that around 14% of RF incidents were attributable to this. GAS infections could possibly be transmitted to skin via surfaces or clothing – however, a study that looked to see if different methods or frequencies of washing laundry was associated with RF did not find an association.¹⁶¹

Pets are not known to be a risk factor for RF

Companion animals are not known to transmit GAS infection to humans, though some studies have found the same isolates in humans and animals in the same household.¹⁶² In the local case-control study mentioned above, there was no association between having a family pet and the risk of RF.¹⁶³

6.5 RF awareness

There's no link between health awareness and developing RF

The risk of developing RF was not associated with knowledge of RF or health-seeking behaviour when a child had a sore throat or skin infection. Almost all cases and controls were aware that a sore throat can cause RF and that RF can damage the heart, and as a result would always or often see the doctor or nurse when a child had a sore throat or skin infection.¹⁶⁴

6.6 The complexity demands a systems approach

The risk factors associated with increased risk of RF, such as inadequate housing, socio-economic deprivation, and barriers to healthcare access, are concentrated inequitably among communities in Aotearoa New Zealand. The challenge in addressing these in a holistic way lies in the fact that the issues are fragmented across a range of societal factors including health, housing, education, and as such managed by several different government departments. Therefore, a coordinated approach to boost services, local capacity and infrastructure is needed across government to improve health outcomes for RF and many other health conditions. Targeting these upstream health determinants or developing a GAS vaccine will have the most significant and lasting impacts on RF rates.

Australia's experience is similar to ours, with a high burden of infection and disease in Aboriginal and Torres Strait Islanders, and negligible rates outside this group. A claim from Australian researchers and clinicians that

¹⁵⁸ Baker, M.G., Gurney, J., Oliver, J., *et al.* (2019). *The New Zealand rheumatic fever risk factors study (RF RISK): Draft report on study findings*. Wellington, New Zealand: Rheumatic Fever Risk Factors Study.

¹⁵⁹ *Ibid.*

¹⁶⁰ *Ibid.*

¹⁶¹ *Ibid.*

¹⁶² Baker, M.G., Gurney, J., Oliver, J., *et al.* (2019). Risk factors for acute rheumatic fever: Literature review and protocol for a case-control study in New Zealand. *International Journal of Environmental Research and Public Health*, 16(22), 4515. <https://doi.org/10.3390/ijerph16224515>

¹⁶³ Baker, M.G., Gurney, J., Oliver, J., *et al.* (2019). *The New Zealand rheumatic fever risk factors study (RF RISK): Draft report on study findings*. Wellington, New Zealand: Rheumatic Fever Risk Factors Study.

¹⁶⁴ *Ibid.*

RHD is “too often addressed as a biomedical diagnosis rather than a symptom of pervasive social injustice”¹⁶⁵ has relevance to the inequitable situation in Aotearoa New Zealand.

¹⁶⁵ Wyber, R., Noonan, K., Halkon, C., *et al.* (2020). Ending rheumatic heart disease in Australia: The evidence for a new approach. *Medical Journal of Australia*, 213, S3-S31. <https://doi.org/10.5694/mja2.50853>

7 Lived experience suggests the system needs to change to improve health outcomes

A number of studies have been undertaken in Aotearoa New Zealand to understand the lived experience for people navigating health and other support systems for RF and RHD and workshops convened by the Ministry of Health in 2018 surfaced several of the themes summarised in this section, which informed some of the interventions currently being trialled. As almost all of the patients who develop these conditions are Māori and Pacific peoples, the studies have focused on experiences in these population groups. Understanding lived experience is critical to inform prevention and management approaches for RF and RHD.

In this section we collate and synthesise the key themes arising from these studies of lived experience.¹⁶⁶

7.1 Experiences of patients highlight barriers to accessing quality care

People have varied understanding of sore throats, RF and RHD

- Although knowledge of RF and behaviour relating to sore throats is not associated with RF risk (see section 6.5), understanding of sore throats, RF and RHD can still have an impact on the experience of an individual and their whānau when a diagnosis occurs.
- Children and parents/caregivers both need to understand each stage of disease progression, but studies show that peoples' understanding about what these conditions are and how they are caused varies widely.
- For some, a child's diagnosis is their first encounter with RF and they have no or limited understanding of the condition. In these cases, parents/caregivers did not take their children to the doctor when they had an episode of RF because they did not understand the severity of their disease (e.g. thought the symptoms were growing pains).
- People who understood what RF was still did not understand what caused it and how it could have been prevented, and many families wanted more information solely about RF, presented in a way that wasn't stigmatising.
- A study of Pacific peoples found that the few participants who knew about RF had learnt about it in their home countries not in Aotearoa New Zealand, including from family members.¹⁶⁷
- Not understanding the significance of sore throats led to people using home remedies rather than seeking healthcare for antibiotics.

¹⁶⁶ Anderson, A., Leversha, A., Ofanoa, M., et al. (2018). *Māori and Pacific whānau experiences of recurrent rheumatic fever and unexpected rheumatic heart disease in New Zealand*. Auckland, New Zealand: University of Auckland. Retrieved from <https://tomaioira-research-group.blogs.auckland.ac.nz/tomaioira-our-mahi/research-project-1/>; Anderson, A., Mills, C. and Eggleton, K. (2017). Whānau perceptions and experiences of acute rheumatic fever diagnosis for Māori in Northland, New Zealand. *The New Zealand Medical Journal*, 130(1465), 80-89. ; Anderson, A., Mills, C., Eggleton, K.S., et al. (2015). *Northland District Health Board research report: Whānau experiences of the diagnosis and management of acute rheumatic fever for tamariki in Te Tai Tokerau, Aotearoa*. Auckland, New Zealand: University of Auckland. ; Anderson, A., Peat, B., Ryland, J., et al. (2019). Mismatches between health service delivery and community expectations in the provision of secondary prophylaxis for rheumatic fever in New Zealand. *Australian and New Zealand Journal of Public Health*, 43(3), 294-299. <https://doi.org/10.1111/1753-6405.12890>; Anderson, A. and Spray, J. (2020). Beyond awareness: Towards a critically conscious health promotion for rheumatic fever in Aotearoa, New Zealand. *Social Science & Medicine*, 247, 112798. <https://doi.org/10.1016/j.socscimed.2020.112798>; Burgess, H. (2016). *Māori Whānau experiences of rheumatic fever: Reflections of social and structural inequity*. ResearchSpace@Auckland, Auckland, New Zealand. Retrieved from <https://researchspace.auckland.ac.nz/bitstream/handle/2292/30703/whole.pdf?sequence=2>; Barker, H., Oetzel, J.G., Scott, N., et al. (2017). Enablers and barriers to secondary prophylaxis for rheumatic fever among Māori aged 14–21 in New Zealand: A framework method study. *International Journal for Equity in Health*, 16(1), 201. <https://doi.org/10.1186/s12939-017-0700-1>; Naea, N., Dobson, A., Leversha, A., et al. (2016). Awareness and understanding of rheumatic fever among Pacific people in Auckland. *Neonatal, Paediatric & Child Health Nursing*, 19(1), 7-12. ; Spray, J. (2018). The value of anthropology in child health policy. *Anthropology in Action*, 25(1), 29-40. <https://doi.org/10.3167/aia.2018.250104>; Ryan, D. (2015). *Health care experiences of Pacific families who have children with rheumatic fever*. Wellington, NZ: Pacific Perspectives Ltd. Retrieved from https://2ad85816-c406-4fbd-96af-68d86f851586.filesusr.com/ugd/840a69_3f5dc99e07f14c5790c3d9e2fb11bcdc.pdf; The Heart Foundation. (2018). *Ngā Kokonga Ngākau: Perceptions and experiences of Māori Heart Health in Te Tai Tokerau*. The Heart Foundation. Retrieved from <https://www.innovationunit.org/thoughts/nga-kokonga-ngakau-perceptions-and-experiences-of-maori-heart-health-in-te-tai-tokerau/>; Anderson, P., King, J., Moss, M., et al. (2016). Nurse-led school-based clinics for rheumatic fever prevention and skin infection management: Evaluation of Mana Kidz programme in Counties Manukau. *The New Zealand Medical Journal*, 129(1428), 36-45.

¹⁶⁷ Naea, N., Dobson, A., Leversha, A., et al. (2016). Awareness and understanding of rheumatic fever among Pacific people in Auckland. *Neonatal, Paediatric & Child Health Nursing*, 19(1), 7-12.

- Children also have an understanding of sore throats and the potential for progression. Most had a clear idea that if their sore throat was not checked it could get worse and progress to RF then heart damage, which they linked to death. However, there is confusion between children about what a sore throat actually is, and some thought they had RF when their sore throat was being treated.

Child asked to define a sore throat: “‘What is a sore throat?’ ‘Like the fever, you know? Coughs and that, sneezing and that, cold and that.’”¹⁶⁸

- Even after hospitalisation and treatment, many families had poor understanding of RF. Understanding may have improved in recent years but, to our knowledge, this has not been published. Studies are apparently underway in the Auckland region.¹⁶⁹

People have had negative experiences with health communications about RF and RHD

- The way information about RF and RHD is communicated impacts individuals and whānau.
- People learnt about RF from health promotion campaigns, media coverage and discussions with healthcare professionals.
- There was a feeling that the communications implied that being Māori or Pacific was the problem and reason for getting RF. These messages were internalised individually and collectively, even by those who had not experienced the disease.
- The messaging caused anxiety, internalised blame, whakamā (shame), guilt and stigma for those whose children became sick. It implied that families did something wrong if their child developed RF and reinforced stereotypes of the irresponsible “brown” parents/caregivers.

“I was like ‘oh my God’ that was my fault because I knew that it [RF] comes from a sore throat. They [medical professionals] said, ‘well you just didn’t pick it up that they had a sore throat’ and I was like ‘Oh my God’ you feel like a terrible parent cause you just missed all this stuff”.¹⁷⁰

- Even people who did not have a sick child felt fear and burdened with responsibility to monitor their children for a sore throat, which can be a subjective symptom and difficult to always catch.
- Children also constructed their understanding of the disease from health promotion campaigns, though it was targeted at parents/caregivers.
- People felt conflict between their cultural way of living and what might increase risk of the disease – for example, thinking of Māori ways of living or sleeping on a marae as ‘crowded’.
- Pacific peoples in particular struggled with the way that information was presented, preferring translated material but emphasising that the translations needed to be accurate and of good quality. Some Māori also struggled with the English language medium default. For Kura Kaupapa students having to be taught in English at hospital schools was especially challenging.¹⁷¹
- There was high awareness of RF sore throat campaigns, but many families wanted more information solely about RF.
- Upon diagnosis, some people reported being overwhelmed by information initially while others experienced a lack of information. Written and verbal health information was overwhelming for some who preferred videos.
- Pacific communities experienced possible confusion amongst families with RF health promotion messages and other health messages targeted specifically at their communities.

¹⁶⁸ Spray, J. (2018). The value of anthropology in child health policy. *Anthropology in Action*, 25(1), 29-40. <https://doi.org/10.3167/aia.2018.250104>

¹⁶⁹ Anderson, P. and Stefanogiannis, N. (2021). Personal communication.

¹⁷⁰ Anderson, A., Mills, C., Eggleton, K.S., et al. (2015). *Northland District Health Board research report: Whānau experiences of the diagnosis and management of acute rheumatic fever for tamariki in Te Tai Tokerau, Aotearoa*. Auckland, New Zealand: University of Auckland.

¹⁷¹ Ibid.

Many barriers get in the way of accessing healthcare for these conditions, even when the importance of doing so is understood

- Whānau were living in situations that limited their access to health services, such as having lack of income to meet the costs of healthcare, not having a car or enough petrol to get to appointments, inadequate childcare, other social obligations, and work commitments that lacked flexibility.

“I have no car half the time, so I have to wait for somebody to come along and drop me off at the hospital, and the buses, there’s a bus station over here, but on certain days, I had no money to get over there, but I had food.”¹⁷²

“When they [nurses] stopped coming around I had to go to the medical centre, it [bicillin] cost \$15 dollars so I had to stop.”¹⁷³

“Money was very tight ... so we couldn’t afford [to visit the doctor] and my parents would just say a prayer”.¹⁷⁴

- People also moved around a lot which meant that accessing healthcare was more difficult as they could get lost to follow up or not build a strong a relationship with their healthcare professional. This was a particular issue for those moving between DHBs or to and from other Pacific nations, who are risk of becoming ‘unenrolled’.

“I had my injections regularly, every month; I don’t want to miss it, until 2014, when I started missing them because we moved. I was getting my home visits, the nurse would come and do my injections at home, but, because we moved out here, I didn’t know where to go. I’ll go to my GP, but they said I would have to go to another place to get them done. So, I didn’t know any information on how I can get the home visits.”¹⁷⁵

- At GP clinics, the waiting times, brief consultations and limited opening hours were a barrier to accessing care.
- Long wait lists led to delays in receiving treatment, which was exacerbated by patients missing appointments due to other barriers.
- At school clinics, children choose whether to get tested and they report being influenced by much more than whether their throat is sore. This includes feeling shame about going, determining whether to go based on peers, using clinics to get out of class when symptoms weren’t present, and going when they did not have symptoms due to anxiety.

Some people reported not being happy with the standard of care they received, but few complained

- A common experience for parents/caregivers was having to pressure GPs to take throat swabs or prescribe antibiotics when their child had a sore throat. This wasn’t always successful, and some children did not get antibiotics when needed. The need for primary care upskilling is a concerning piece of the RF puzzle and one that should be more quickly and simply solvable than housing conditions or income inadequacy.

¹⁷² Anderson, A., Peat, B., Ryland, J., *et al.* (2019). Mismatches between health service delivery and community expectations in the provision of secondary prophylaxis for rheumatic fever in New Zealand. *Australian and New Zealand Journal of Public Health*, 43(3), 294-299. <https://doi.org/10.1111/1753-6405.12890>

¹⁷³ Ibid.

¹⁷⁴ Naea, N., Dobson, A., Leversha, A., *et al.* (2016). Awareness and understanding of rheumatic fever among Pacific people in Auckland. *Neonatal, Paediatric & Child Health Nursing*, 19(1), 7-12.

¹⁷⁵ Anderson, A., Peat, B., Ryland, J., *et al.* (2019). Mismatches between health service delivery and community expectations in the provision of secondary prophylaxis for rheumatic fever in New Zealand. *Australian and New Zealand Journal of Public Health*, 43(3), 294-299. <https://doi.org/10.1111/1753-6405.12890>

- For RF, people experienced missed diagnoses due to a lack of knowledge and awareness from GPs. Even when families raised concerns about RF they reported dismissal of concerns and delayed diagnosis and referral for specialist RF testing or treatment.

“I think it’s the brushing off like, ‘you’ve just got the flu’ you know? It’s like you’re made to feel you’re a bit bloody second class citizen, like that sort of sort attitude, like we don’t count....I would say to him [GP] questions like ‘ah doctor X do you think she needs to see a specialist?’ [He’ll reply] ‘who is the qualified doctor here?’ that sort of crap”.¹⁷⁶

- Some people went straight to ED to avoid the cost and time associated with primary healthcare when a child had RF.
- People receiving prophylactic injections had experiences of having their injections given the wrong way which caused pain for up to a week.

“There was one nurse that I didn’t really like because she had done it too rough and fast. I actually stopped getting them because I was frustrated... I just hate how they were just like, ‘Think about your future’ and all that.”¹⁷⁷

- Children who were hospitalised found it very stressful being separated from parents/caregivers (when parents/caregivers couldn’t stay because they had to look after other children or work).

“Some of the nurses were happy that I was there, because some of them would come in, and they would talk to me about it. You know “it’s nice to have a mother here, with her child, because some parents don’t come in, and they don’t care about their children, whereas we know you care about your child, and it’s good that you’re here, so you know exactly what’s going on with your daughter”.”¹⁷⁸

- There were experiences of people receiving disrespectful treatment during care and feeling dehumanised – e.g. given injections while sleeping in hospital.
- Poor communication and rapport from healthcare professionals was an important element that determined whānau experiences of healthcare.
- Pacific families explained that they respected the clinical skills and expertise of health professionals, but wanted greater input and involvement during consultations and treatment.

Experiencing racism and discrimination in healthcare system was common

- Racism was experienced by whānau at institutional and individual levels within primary and secondary healthcare contexts and this created a barrier to improving RF outcomes.

“Through my work dealing with the doctors, I’ve seen a lack of Māori understanding; no effort to try and pronounce names, and a lack of empathy for their circumstances.”¹⁷⁹

- The clinical experience was poor due to a lack of cultural safety. The service was not suited to those it served – the Westernised biomedical approach did not align with Pacific and Māori holistic

¹⁷⁶ Anderson, A., Mills, C., Eggleton, K.S., et al. (2015). *Northland District Health Board research report: Whānau experiences of the diagnosis and management of acute rheumatic fever for tamariki in Te Tai Tokerau, Aotearoa*. Auckland, New Zealand: University of Auckland.

¹⁷⁷ Barker, H., Oetzel, J.G., Scott, N., et al. (2017). Enablers and barriers to secondary prophylaxis for rheumatic fever among Māori aged 14–21 in New Zealand: A framework method study. *International Journal for Equity in Health*, 16(1), 201. <https://doi.org/10.1186/s12939-017-0700-1>

¹⁷⁸ Burgess, H. (2016). *Māori Whānau experiences of rheumatic fever: Reflections of social and structural inequity*. ResearchSpace@Auckland, Auckland, New Zealand. Retrieved from <https://researchspace.auckland.ac.nz/bitstream/handle/2292/30703/whole.pdf?sequence=2>

¹⁷⁹ The Heart Foundation. (2018). *Ngā Kokonga Ngākau: Perceptions and experiences of Māori Heart Health in Te Tai Tokerau*. The Heart Foundation. Retrieved from <https://www.innovationunit.org/thoughts/nga-kokonga-ngakau-perceptions-and-experiences-of-maori-heart-health-in-te-tai-tokerau/>

approaches to health, and treatment was not always culturally safe. For example, Māori patients had experienced their head (which is considered sacred) being touched without asking first.

*Caden, a hospital-based paediatrician: "The institutionalised racism that is served up in many health services in and around NZ still. I think you have to be deaf, daft and blind not to spot it on a regular basis in our hospitals. It's all around us I'm afraid; it's rather endemic."*¹⁸⁰

- People did not like the dynamic between themselves as patients and the healthcare professionals. They reported feeling that their doctors did not look them in the eye, were more interested in typing on the computer than paying them attention, did not listen to them, and were dismissive of their experiences and questions. Pacific peoples reported wanting to work in partnership with health services.
- Some issues related to limitations in communication and language, which was contributed to by healthcare professionals being of different ethnicity to the patient.
- Experiencing racism and discrimination resulted in some people avoiding going to the doctor unless absolutely necessary.

People who had to have secondary prophylactic antibiotic injections every 28 days reported many barriers to adherence

- Not everyone had a solid understanding of why this treatment needed to happen and why for so long.

*"Oh I just couldn't be bothered. Being so constant and every single month, for however long I had to do it; I was just over it and I couldn't be bothered anymore."*¹⁸¹

- Upon learning that they would need to have injections for up to 10 years, people felt shock and disappointment.
- Most patients experienced significant pain with injections, and so feared having them.
- Some patients felt that they might prefer taking a pill daily than receive painful injections every 28 days.
- Scheduling the appointments at a suitable time and location was difficult.
- For younger patients still at school, the flexibility of receiving these at home or school was perceived as good for most, but some people were worried about having their injections at school as they might seem different to their peers. One study reported a child who felt shame about receiving injections, instead of explaining what would happen he would tell his class he was in trouble with the principal when he was called to the office to meet the district health nurse.
- For older patients or those not at school, the location of the injection administration depended on DHB. Some services were either clinic-based or delivered at homes or work (but this was not offered everywhere).
- Peoples' complex lives meant that the different service locations didn't always work for people. For example, home visits assumed that people had stable living situations, but some moved often or were homeless.

¹⁸⁰ Anderson, A., Peat, B., Ryland, J., *et al.* (2019). Mismatches between health service delivery and community expectations in the provision of secondary prophylaxis for rheumatic fever in New Zealand. *Australian and New Zealand Journal of Public Health*, 43(3), 294-299. <https://doi.org/10.1111/1753-6405.12890>

¹⁸¹ Barker, H., Oetzel, J.G., Scott, N., *et al.* (2017). Enablers and barriers to secondary prophylaxis for rheumatic fever among Māori aged 14–21 in New Zealand: A framework method study. *International Journal for Equity in Health*, 16(1), 201. <https://doi.org/10.1186/s12939-017-0700-1>

“I wasn’t taking [the injections], because I was like in and out, I was in foster homes and stuff. So I wasn’t really stable, and I didn’t want anything to do with stuff like that. And then, once I got back into a stable place, then I went back onto it.”¹⁸²

- Moving or travelling meant some people fell through the gaps and were lost to follow up.

Care was not well suited to adolescents

- Both families and healthcare professionals recognised a gap in age-appropriate care for adolescents and a lack of formal transitions from paediatric-to-adult services, with a particular risk of losing people who had left school. Some DHBs had better systems than others.
- Young patients described how the adolescent life stage was difficult and this influenced their perceptions of the diseases and treatment. During this stage, some people rebelled against injections, their families, and healthcare professionals.
- Healthcare professionals reported that they felt ill-equipped to cope with young people who were struggling with the life changes and demands of adolescence.

Not everyone accessed the assistance or social services they were entitled to¹⁸³

- Very few Pacific families were referred to a social housing provider during their child’s illness.
- Despite being aware of social support most families could not or did not access it.

7.2 Both individuals and their whānau are impacted by these experiences

RF significantly impacts the lives of whānau by causing emotional, health, social and economic stress.

Going through RF and/or RHD affects a person’s emotional and social wellbeing. Parents/caregivers reported feeling worried, stressed, sad, angry, guilty and confused.

- Their health outcomes were also significantly impacted by these experiences. For example, having barriers to accessing healthcare led to delayed diagnoses or difficulty accessing prophylactic treatment which led to poorer health outcomes.
- People who had RF and/or RHD had difficulties accessing employment and education. School was disrupted for the individual and their siblings for up to six months and students found it hard to concentrate.
- Whānau members experienced significant financial costs. Some parents/caregivers, particularly mothers, had to leave their job for up to a year. Healthcare and prescriptions costs for those over 13 years old are significant.

“Yeah, [I had to quit] netball... I put on a lot of weight, which made me depressed too. That was another thing... being on bed rest, and not being able to be physical, and I put on a lot of weight, and so when I went back to school here, I just had a hard time settling in again, and repeating all over again...”¹⁸⁴

“[The Doctors] just, basically just told me that I have a heart disease, and that I need to drop basically everything I am doing in my life, and start fresh. Because everything I was doing was all physical, and sports and all of that... ...I was doing good as [at school]. I was doing well with [rugby] league, getting up there with my sports, everything, school. I was

¹⁸² Burgess, H. (2016). *Māori Whānau experiences of rheumatic fever: Reflections of social and structural inequity*. ResearchSpace@Auckland, Auckland, New Zealand. Retrieved from <https://researchspace.auckland.ac.nz/bitstream/handle/2292/30703/whole.pdf?sequence=2>

¹⁸³ Ryan, D. (2015). *Health care experiences of Pacific families who have children with rheumatic fever*. Wellington, NZ: Pacific Perspectives Ltd. Retrieved from https://2ad85816-c406-4fbd-96af-68d86f851586.filesusr.com/ugd/840a69_3f5dc99e07f14c5790c3d9e2fb11bcdc.pdf

¹⁸⁴ Burgess, H. (2016). *Māori Whānau experiences of rheumatic fever: Reflections of social and structural inequity*. ResearchSpace@Auckland, Auckland, New Zealand. Retrieved from <https://researchspace.auckland.ac.nz/bitstream/handle/2292/30703/whole.pdf?sequence=2>

alright in intermediate. I was naughty but I always you know, got through, what I was asked to do and all that. And once I found out I had rheumatic fever and it would affect my life, and I just didn't want to know anybody, didn't want to do anything. Just didn't wanna listen, anything like that. It just changed my whole, my whole life around really.”¹⁸⁵

7.3 Wraparound support can make experiences for individuals and whānau more positive

- **Good rapport, communication and continuity of care** with healthcare professionals had a very positive impact on patients and whānau. This was true for GPs in primary care and for district nurses involved with secondary prophylaxis. Good information sharing and referral pathways for the transition from paediatric-to-adult services also had a positive impact.

About the GP: “She’s really approachable, and very, the good thing about, we go to appointments and she obviously read up her notes before and you know, she’s totally up with the play when you go in there, so, she asks relevant questions and it’s not like, starting from scratch like it has been with some other doctors.”¹⁸⁶

- **Community-based models of care** where district nurses came to patients for their secondary prophylaxis, and were flexible with timing and location, were positive for patients.
- When children were hospitalised, being able to have whānau stay with them, participate in ‘fun’ activities, and have similar aged children in the same ward led to a more positive experience of hospital.
- **Efforts to reduce pain with their monthly injections** improved patient’s experiences. These included the use of numbing cream, freezer buzzy bees (a handheld vibrating device with removable ice wings that can be used as a method of pain relief and distraction) and massage. Patients had reduced pain with experienced nurses delivering their injections, and this was improved when nurses would listen to feedback from children and their whānau about administration.
- People with RF who did their own research online to understand their illness felt this was a positive experience.
- The Pacific focus groups used in one study were viewed positively and participants suggested that participating in **small group discussions, particularly through the churches**, might be a good way of making their people more aware of RF and its prevention.
- Families who had been involved with the Mana Kidz programme in Counties Manukau reported positive experiences, seeing the school clinic services as worthwhile. They reported that the teams were **culturally competent**, had positive, trusting relationships with children, families and schools, and were effective in engaging with children, parents/caregivers/whānau.

7.4 Things that could improve the lived experience for people and whānau impacted by rheumatic fever

Suggestions of ways to improve the lived experience from GAS throat infection management through to prophylactic antibiotic treatment were made in the reports by both study participants and authors of one study.¹⁸⁷ These are summarised below.

- Improving **information services** about prevention and care. This might include online support and information groups, and would be centred on youth and whānau. Information might also be shared in person at Pacific community-based venues (e.g. churches) and through using a Talanoa process (open,

¹⁸⁵ Ibid.

¹⁸⁶ Ibid.

¹⁸⁷ Anderson, A., Peat, B., Ryland, J., et al. (2019). Mismatches between health service delivery and community expectations in the provision of secondary prophylaxis for rheumatic fever in New Zealand. *Australian and New Zealand Journal of Public Health*, 43(3), 294-299. <https://doi.org/10.1111/1753-6405.12890>

informal conversations). A long-term healthcare plan, especially for parents/caregivers of children with RHD, would improve understanding of the process and ease worry.

“It’s important to come to the people, see them, face to face, and listen to the stories so that they know it’s real.”¹⁸⁸

- Delivering **health information in different formats** (e.g. video as well as written) and different languages. Ensuring nurses and community workers are equipped to provide appropriate information to patients in their preferred format would also help, with clear and consistent messaging across different media.
- Having **culturally safe health promotion campaigns** that are developed in consultation with Māori and Pacific people, focusing not just on how the campaign will affect awareness and behaviour but also how they will experience the public health messages (e.g. victim-blaming messages). Channels of communication could also include Pacific media to ensure the target audience is reached.
- A **multi-pronged intervention approach to reduce access barriers**. This could include flexible appointment times and locations, free rapid response throat swabbing for high-risk populations, and reduced cost barriers associated with transport, childcare and loss of income. Reducing these barriers could enable whānau to better support those with the condition. The use of technology (e.g. mobile phones and apps) to connect patients undergoing secondary prophylaxis with their district nurse might help determine preferred pain management and other related strategies.
- A **RF register** and patient management system to reduce the number of patients lost to follow up care when moving between DHBs or transitioning from paediatric to adult care.
- Raising **adherence to the sore throat guidelines** in primary care and **awareness of the symptoms of RF** in primary and secondary care to avoid missed diagnoses and treatment opportunities. Raising adherence can happen via two methods: improving GP/nurse adherence and having more people using the guidelines. The issue with GAS throat infections is not that they require GP expertise to manage, but rather they need to be easily and quickly identified and treated to reduce RF risk. The pool of people who can test and confirm GAS throat infections could be extended to include more accessible health professionals such as pharmacists.¹⁸⁹
- **Cultural safety training** and evaluation for healthcare professionals and greater emphasis on building rapport and continuity of care.
- Creating a more **adolescent-centred system** for diagnosing and treating RF and RHD.

¹⁸⁸ Naea, N., Dobson, A., Leversha, A., et al. (2016). Awareness and understanding of rheumatic fever among Pacific people in Auckland. *Neonatal, Paediatric & Child Health Nursing*, 19(1), 7-12.

¹⁸⁹ White, C. (2021). Personal communication.

8 There is a high cost to our high disease burden

The high rates of RF and RHD in Aotearoa New Zealand have significant societal and financial costs. Failure to prevent RF now means RHD will be a burden for decades to come for the health services and society, and this will particularly impact Māori and Pacific communities.¹⁹⁰ Addressing child health inequities and primary care access inequities will have longer-term economic and social benefits, even if short-term healthcare expenditure is not decreased.¹⁹¹

Some studies have estimated the current costs on the healthcare system of treating these preventable diseases:

- \$12 million per year for hospitalising people with RF and RHD, though this may now be an underestimate as the data was from 2000–2009.¹⁹²
- \$30 million per year for the direct costs associated with GAS infections.¹⁹³
- \$141 million per year of public sector costs directly attributable to substandard housing conditions, that cause diseases, including RF. Around 230 deaths per year attributable to adverse housing with an estimated cost of \$1 billion.¹⁹⁴

\$141 million per year of public sector costs directly attributable to substandard housing conditions, that cause diseases, including RF.

Due to the high costs of managing RF and RHD we would expect that investing in interventions to prevent disease would be financially beneficial in the long term.

This has been shown in Cuba, where a comprehensive programme to control RF and RHD was undertaken from 1986 to 1996 (see section 2.1). Compared to doing nothing, the Cuban program averted 5051 disability-adjusted life years (DALYs) (1844 per 100,000 school-aged children) and saved \$7,848,590 (2010 USD) despite a total program cost of \$202,890 over 10 years.¹⁹⁵

Compared to doing nothing, the Cuban program averted 5051 disability-adjusted life years (DALYs) and saved \$USD7,848,590 despite a total program cost of \$202,890 over 10 years.

¹⁹⁰ Wilson, N. (2010). Rheumatic heart disease in Indigenous populations – New Zealand experience. *Heart, Lung and Circulation*, 19(5), 282-288. <https://doi.org/10.1016/j.hlc.2010.02.021>

¹⁹¹ Mills, C., Reid, P. and Vaithianathan, R. (2012). The cost of child health inequalities in Aotearoa New Zealand: A preliminary scoping study. *BMC Public Health*, 12(1), 384. <https://doi.org/10.1186/1471-2458-12-384>

¹⁹² Milne, R.J., Lennon, D., Stewart, J.M., et al. (2012). Mortality and hospitalisation costs of rheumatic fever and rheumatic heart disease in New Zealand. *Journal of Paediatrics and Child Health*, 48(8), 692-697. <https://doi.org/10.1111/j.1440-1754.2012.02446.x>

¹⁹³ Cannon, J.W., Zhung, J., Bennett, J., et al. (2021). The economic and health burdens of diseases caused by group A *Streptococcus* in New Zealand. *International Journal of Infectious Diseases*, 103, 176-181. <https://doi.org/10.1016/j.ijid.2020.11.193>

¹⁹⁴ Riggs, L., Keall, M., Howden-Chapman, P., et al. (2021). Environmental burden of disease from unsafe and substandard housing, New Zealand, 2010–2017. *Bulletin of the World Health Organization*, 99, 259-270. <https://doi.org/10.2471/BLT.20.263285>

¹⁹⁵ Watkins, D.A., Mvundura, M., Nordet, P., et al. (2015). A cost-effectiveness analysis of a program to control rheumatic fever and rheumatic heart disease in Pinar del Rio, Cuba. *PLOS One*, 10(3), e0121363. <https://doi.org/10.1371/journal.pone.0121363>

9 Intervention stocktake: Is there evidence of success?

Many interventions have been tried to reduce the stubbornly high rates of RF in Aotearoa New Zealand. Despite these efforts the rates of disease remain high as shown in section 4. Specific challenges that may have contributed to the limited success of efforts to date include:

- **There has been no national long-term evidence-informed strategy.** This has meant that some interventions have been tried on an ad hoc basis and have not always been adequately monitored for their effectiveness to reduce rates of RF.
- **Interventions have not addressed broad structural determinants of health.** Despite recognition that determinants of health such as racism, poverty and housing are key drivers of RF, interventions have not tackled these in a systematic way.
- **Some of these determinants have actually been getting worse.** Any improvements resulting from interventions (for example, the Healthy Homes Initiative) may be less evident when some of the risk factors for RF, such as poverty and poor housing conditions, have been worsening over the same period, negating progress.
- **We have relied heavily on the work of a few dedicated individuals to drive change.** Champions of programmes are important, but where their efforts aren't supported by an effective system and there is no contingency for continued success of programmes, it can lead to a drop-off in success when the champion of an initiative leaves. An example is the Pū Manawa network, which is a non-funded voluntary group to address RF and RHD.¹⁹⁶
- **There was initially a lack of flexibility to account for unique community needs.** The initial approaches in the government's prevention programme were top-down and prescriptive, though this improved over time.¹⁹⁷ A new approach was needed to achieve evidence-informed policies implemented through culturally responsive processes. Work in this space is underway with the Rheumatic Fever Co-design Initiative focusing on equity, innovation and partnership with Māori, Samaon and Tongan communities.¹⁹⁸
- **The evidence base was initially largely limited to biomedical science.** The evidence informing early efforts to date was primarily from biomedical science and peer-reviewed literature. However, there is Māori- and Pacific-led research incorporating Indigenous methodologies that isn't published in peer-reviewed literature and which may be beneficial to include in evidence-based decision-making processes, for example work by Pacific Perspectives and other Māori- and Pacific-led frameworks and approaches. The RFPP included this evidence in a co-designed approach.
- **The public are receiving mixed messages.** For RF prevention, the key message has been to seek antibiotics for a sore throat. However, for AMR, messages relate to avoiding unnecessary use of antibiotics to prolong effectiveness of antibiotics. This mixed messaging may lead to some healthcare professionals and patients avoiding antibiotics for GAS throat infections. Further confusion has arisen during COVID-19 where nasopharyngeal swabbing was prioritised for PCR testing.¹⁹⁹
- **The lack of age-specific care.** Models of care haven't been designed to target the children and adolescents who are the age group burdened with GAS infections and RF.

A new approach needs to achieve evidence-informed policies implemented through culturally responsive processes.

¹⁹⁶ Pū Manawa. (2021). Rheumatic fever. Retrieved 29 September, 2021, from <https://www.pumanawa.org.nz/rheumatic-fever>

¹⁹⁷ Burgess, H. (2016). *Māori Whānau experiences of rheumatic fever: Reflections of social and structural inequity*. ResearchSpace@Auckland, Auckland, New Zealand. Retrieved from

<https://researchspace.auckland.ac.nz/bitstream/handle/2292/30703/whole.pdf?sequence=2>

¹⁹⁸ Ministry of Health. (2020). Co-design process for the prevention of rheumatic fever - Auckland. Retrieved 29 September, 2021, from <https://www.gets.govt.nz/MOH/ExternalTenderDetails.htm?id=23561392>

¹⁹⁹ Town, I. (2021). Personal communication.

There are four points of intervention for tackling problems associated with RF in Māori and Pacific people aged 3–30 years:

- **Preventing Group A streptococcus (GAS) exposure.** This is also referred to as primordial prevention, which reduces GAS infections caused by social and environmental determinants and may also include biomedical interventions. Reducing the risk of GAS transmission and infection will be the most significant way to prevent more adverse health outcomes.
- **Preventing RF.** This is also referred to as primary prevention which attempts to diagnose, manage and treat GAS infection. We know that for some people the more times a person has GAS infection, the more likely they develop RF, so early effective diagnosis and treatment of GAS infection in high-risk groups is critical.²⁰⁰
- **Preventing RHD.** This is also referred to as secondary prevention, a strategy to prevent reinfection by GAS, at least until they have passed the age group who are at risk, therefore preventing another episode of RF. Each episode of RF damages the heart so those who have had RF once need to be targeted to prevent another episode.
- **Minimising complications of RHD.** This is also referred to as tertiary intervention, which relates to medical management and interventions that optimise the outcomes for a person with RHD.

The interventions tried to date are summarised in table 6, and further detail is provided thereafter.

²⁰⁰ Lorenz, N., Ho, T.K., McGregor, R., *et al.* (2021). Serological profiling of group A *Streptococcus* infections in acute rheumatic fever. *Clinical Infectious Diseases*. <https://doi.org/10.1093/cid/ciab180>

Table 6: Intervention stock take for RF and RHD prevention. Further detail with references is included in the following text.

Stage of prevention	Intervention	Status	Details
Preventing GAS exposure <i>Primordial prevention</i>	Improving housing conditions (Healthy Homes Initiative and regional initiatives)	Implemented and ongoing	Effectiveness on RF rates not measured Programme led to fewer hospitalisations, fewer GP visits, fewer medicines dispensed by pharmacists, and shorter and cheaper hospitalisations, with second evaluation report due out in early 2022 Includes assessment of housing needs, and relies, in part, on partnerships/philanthropic funding and some seed funding to provide interventions to improve housing conditions Requires significant expansion which is being addressed in Budget 21
	Improving socioeconomic conditions	Various government initiatives but none specific to RF	Known to be a significant risk factor for RF
	Explore in more depth the role of skin integrity and skin infections	Research only	More research needed to discount the role of eczema, scabies, impetigo and boils
Preventing RF <i>Primary prevention</i>	Sore throat management targeted by age risk (School-based sore throat management clinics and rapid response clinics and improved access to primary care)	Implemented and ongoing in some DHBs in primary care – including guidelines, regular reminders to primary care about sore throat management, and an e-learning resource ²⁰¹	Schools Tried in all but one high-incidence DHB targeting the 4–19 year age group and their whānau Effective in some but not all settings Features of contexts where service is effective included concentrated high-risk students, active case-finding, whānau swabbing and skin included Rapid response Effectiveness on RF rates not well measured
	Antibiotic treatment of skin infections targeted by age risk	Partially implemented	Included in some school-based services but not universally, will enable impact of swabbing and treating GAS skin infections in relation to RF risk to be better understood

²⁰¹ LearnOnline. (n.d.). Rheumatic fever. Retrieved 29 September, 2021, from https://learnonline.health.nz/totara/catalog/index.php?catalog_fts=rheumatic+fever

Stage of prevention	Intervention	Status	Details
	(School-based sore throat clinics and rapid response clinics)		
	Improving antibiotic adherence for GAS infection	Trialled, some implementation e.g. BPG injection	Nurses administering antibiotics shown to be effective, while daily text reminders and use of blister packs for medication adherence not shown to be effective Use of one-off injection not shown to be effective at reducing number of children with a GAS-positive swab post-treatment but further study needed
	Public health communications	Implemented but discontinued	National campaigns run in 2014 and 2015 found to be effective at messaging and recall; local campaigns continue, e.g. campaign in Auckland targeted at Samoan, Tongan and Māori communities in 2016. Other evidence suggests knowledge doesn't always improve outcomes. Issues around messaging causing anxiety and stigma raised
	Decision support for health care professionals including pharmacies	Implemented and ongoing	Guidelines available, limited available evidence suggests adherence may vary by ethnicity – likely needs more focus on healthcare provider awareness of and access to guidelines Prediction rules not effective in local context
	Rapid diagnostics	Trialled	None shown to be as effective as culture technique in local setting A US National Institute of Health review found insufficient evidence to meaningfully compare or rank available tests and highlighted importance of trialling in local context
	Identifying at-risk children through hospitalisation	Trialled	Active case finding amongst hospitalised children based on other housing-related illnesses was not shown to be effective at picking up later RF cases
	Reducing barriers to healthcare access	Free prescriptions under 13 policy supports the RFPP. Other policies targeting non-cost barriers in development	Work underway in some DHBs to make services more culturally safe and age-appropriate School-based and rapid response clinics partly addressed this Some DHBs e.g. Tairāwhiti deliver a holistic primary care approach

Stage of prevention	Intervention	Status	Details
	Throat swabs targeted by family history risk	Not fully addressed	Some school-based sore throat clinics included family swabbing, partly addressing this, but broader and systematic approach not implemented
	<i>Reducing sugar intake or improving nutrition</i>	<i>Not addressed</i>	<i>Significant knowledge gaps remain about how this increases risk and what interventions may be effective</i>
	Probiotics (BLIS trial)	Trialled	Mixed evidence, with limited effectiveness in Aotearoa New Zealand setting Requires further trials
	Vaccine	In development	Research underway
Preventing or minimising RHD <i>Secondary prevention</i>	RF patient register	Implemented regionally	Currently there are only regional registers not a national register Local evidence that data is more accurate from regional registers than national datasets Overseas evidence that registers improve disease outcomes Strong call for fully resourced national register to coordinate secondary prophylaxis delivery from many experts and stakeholders
	Improving adherence to prophylactic antibiotics	Trialled in some DHBs, some successful implementation	Giving patients a mobile phone and monthly top-up was effective at improving adherence for some patients, but effectiveness declined after a while Methods to reduce pain decreased fear of injections and are widely used, but whether this improved adherence was not assessed
	Less stringent diagnostic criteria	Implemented	Overseas evaluations found this prevents underdiagnosis Implemented but not specifically evaluated in Aotearoa New Zealand
	Diagnostic tool for RF	In development	Research underway to improve serology and find a biomarker
	Development of a new penicillin for RF/RHD prevention	In development	Research is currently underway to investigate the pharmacokinetics of BPG for RF/RHD prevention within predominantly Pacific and Māori children and young people in Aotearoa New Zealand with a previous diagnosis of RF

Stage of prevention	Intervention	Status	Details
			<p>Research undertaken to investigate the BPG preferences and experiences of children and youth currently receiving BPG injections for RF/RHD prevention in Aotearoa New Zealand</p> <p>Research also undertaken to investigate the BPG preferences and experiences of families with children and youth currently receiving BPG injections for RF/RHD prevention in Aotearoa New Zealand</p> <p>Research has been undertaken to investigate the BPG preferences and experiences of health professionals currently delivering BPG injections for RF/RHD prevention in Aotearoa New Zealand</p> <p>Research initiated to begin development of new formulations of penicillin for RF/RHD prevention</p> <p>There is an opportunity to build on new sustained release technologies via surgical implants²⁰²</p>
Minimising complications of RHD	Treatments to reduce severity of heart disease	Trialled	Some suggestion that hydroxychloroquine could be an effective treatment for RF, with a research trial underway funded by Cure Kids
<i>Tertiary prevention</i>	Active case finding	Trialled	Evidence that latent cases likely to be found via screening in high-risk groups in Aotearoa New Zealand and emerging evidence that prophylaxis will improve outcomes for these patients

²⁰² Montagnat, O.D., Webster, G.R., Bulitta, J.B., *et al.* (2018). Lessons learned in the development of sustained release penicillin drug delivery systems for the prophylactic treatment of rheumatic heart disease (RHD). *Drug Delivery and Translational Research*, 8(3), 729-739. <https://doi.org/10.1007/s13346-018-0482-z>

GAS disease pathway

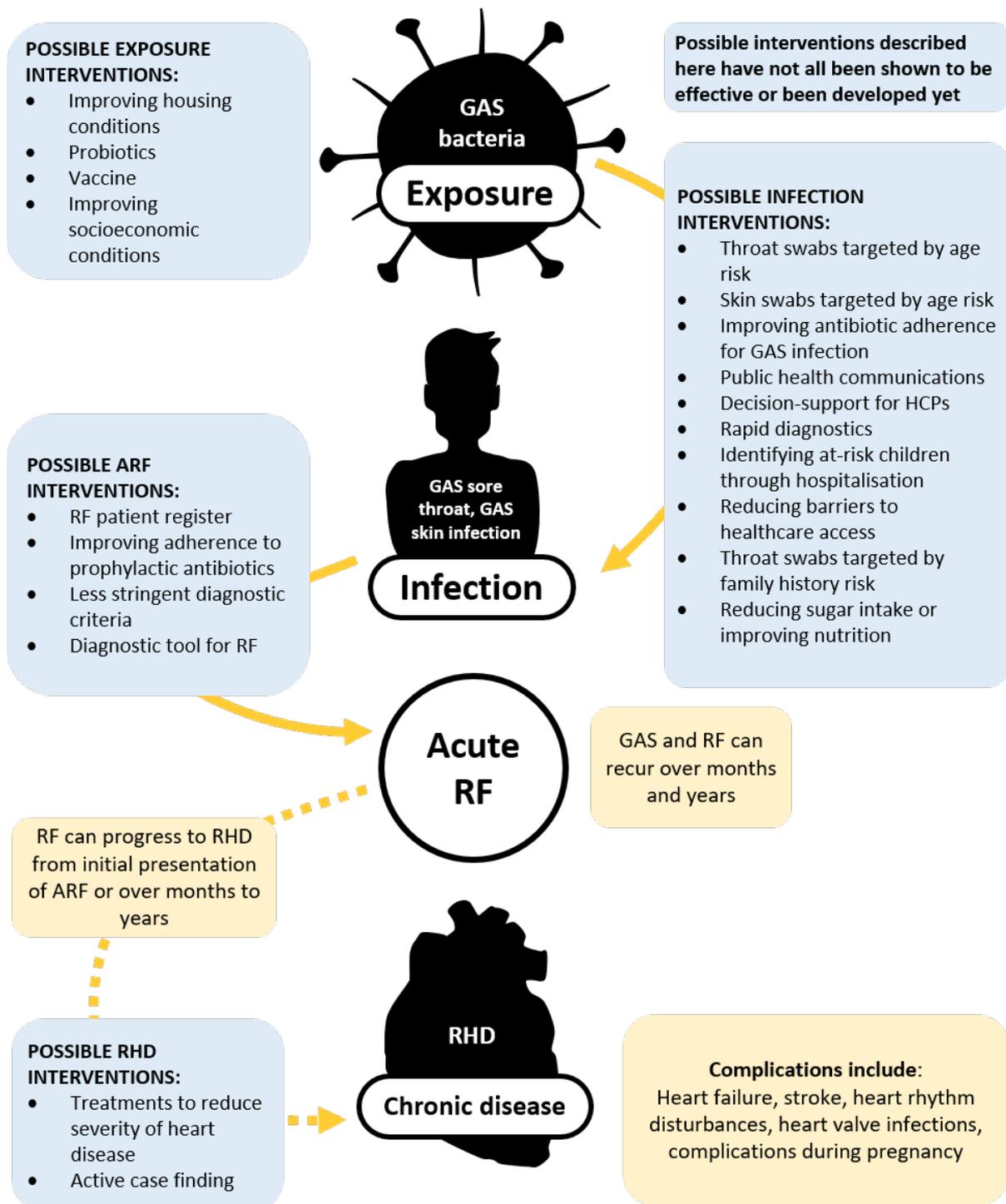


Figure 13: Interventions targeted at preventing different stages of progression from GAS infection to RHD. Interventions include those trialled, implemented or proposed. HCPs: healthcare professionals.

9.1 Improving housing conditions

Stage of intervention: Preventing GAS exposure

There is work underway related to improving housing conditions. A detailed analysis is beyond the scope of this review and is challenging in this context because RF is a comparatively rare outcome, making significantly significant shifts hard to observe. The Healthy Homes Initiative is the key housing intervention to reduce RF rates tried on a national scale; led by the Ministry of Health, implementation has been at a regional level by different organisations. The initiative includes assessment of the warmth envelope of the home. As of the 1 July 2021, funding has been provided to build the supply of interventions including a small percentage to direct purchase interventions. Charities and other organisations, including regional councils, work in partnership with the HHI providers to supply some interventions and establish services such as curtain banks. The programme is whānau-centred and focuses on the warmth envelope of a home, improving insulation, heating and has a large education component focusing on how to live in a warm, dry and healthy home. The HHI providers especially discuss crowding (functional and structural). The success of the programme has been recognised and additional Government funding announced to expand the reach and impact of the programme to the whole country from 1 July 2022.²⁰³

An assessment of the Healthy Homes Initiative up to December 2018 found that the programme led to fewer hospitalisations for a range of conditions, fewer GP visits, fewer medicines dispensed by pharmacists, and hospitalisations that did occur were shorter and cost less due to reduced severity of the condition. The specific estimates for the Healthy Homes Initiative's impact on healthcare events in the year immediately after the intervention was received were:²⁰⁴

- 1,533 fewer hospitalisations, saving \$6.3 million
- 0.69 nights shorter for hospital stays
- \$541 cheaper hospital visits, saving \$3.3 million
- 9,443 prevented GP visits, saving \$755,440
- 8,784 fewer medicines dispensed, saving \$74,225.

The extrapolated total costs for three years following the intervention was estimated at nearly \$30 million but impacts outside the direct health impacts on the child who was referred for the programme were not included. It is expected that the impacts would extend to the family and also have wider social benefits (e.g. missing school less, parents/caregivers missing work less).

Other assessments have been done, but these relate to improving service delivery.²⁰⁵ Recent evaluations of Wellington's specific Well Homes initiative found that:

- Visiting the homes, having health and energy organisations work together, and having an integrated approach that includes interventions as well as education and advocacy were key to the success of the programme. One key challenge to the programme's aim of improving health outcomes for children were landlords' reluctance to implement improvements. However, with the adoption of the Healthy Homes Standard under the Healthy Homes Guarantee Act, which has a primary focus of addressing a lack of heating, and dampness within homes, there has been a notable shift, with landlords become compliant. Other challenges include, homeowners' inability to afford

²⁰³ Ministry of Health. (2021, 29 June 2021). Healthy Homes Initiative. Retrieved 28 July 2021, 2021, from <https://www.health.govt.nz/our-work/preventative-health-wellness/healthy-homes-initiative>

²⁰⁴ Pierse, N., White, M. and Riggs, L. (2019). *Healthy Homes Initiative outcomes evaluation service: Initial analysis of health outcomes*. Wellington, New Zealand: Retrieved from <https://www.health.govt.nz/publication/healthy-homes-initiative-outcomes-evaluation-service-initial-analysis-health-outcomes-interim-report>

²⁰⁵ Allen + Clarke. (2018). *Healthy Homes Initiative evaluation - final report*. Wellington, New Zealand: Allen + Clarke. Retrieved from <https://www.health.govt.nz/system/files/documents/publications/healthy-homes-initiative-evaluation-apr-2018.pdf>

improvements, limitations to staff resources, and client stress and income constraints, which meant that some interventions did not necessarily lead to housing improvements.²⁰⁶

The specific impact of the Healthy Homes Initiative on the rates of RF in individuals or family that have received this service has not been assessed, and to do so will be challenging.

Sustained improvement in housing quality, and ability to pay for heating and adequate insulation to reduce dampness and mould is likely to reduce RF rates. Warmer and drier houses would also help to reduce crowding and co-sleeping where it is being done as a source of warmth. To further address crowding in houses, affordable housing, with designs appropriate to different cultures and ways of living, is likely to reduce RF risk. This is because housing built under European norms creates crowding for larger and multigenerational families. Public health communications that highlight that sharing a bed when sick may spread infections might also influence RF risk.

9.2 Probiotics

Stage of intervention: Preventing GAS exposure

A probiotic developed in Aotearoa New Zealand, marketed as BLIS, aims to colonise 'good' bacteria in the mouth to crowd out 'bad' bacteria (the bacteria that cause GAS throat infections). It is taken orally e.g. as a lozenge or powder.

There is mixed evidence of effectiveness of probiotics in the prevention of sore throat in overseas settings.²⁰⁷ An Aotearoa New Zealand trial found a non-significant reduction in in GAS-positive throat swabs in a high-risk population (children enrolled in the RFPP), when the product was used intermittently at school.²⁰⁸ Study limitations that may have led to the non-significant reduction have been highlighted by others: administration was limited to school days; active cases were counted as those with a positive GAS culture but they may not have had true clinical infection; and the study group had previously had intensive antibiotics as an intervention so there were overall low rates of GAS.²⁰⁹ Further trials are needed to determine if BLIS is effective at reducing GAS throat infection.

Other issues that might limit application of BLIS in populations at high risk of developing RF include:

- It may be cost prohibitive
- It requires continued use, so there may be possible adherence issues
- The likely practical way of administering the intervention (at school) was not shown to be effective.

Currently, probiotics are used as part of the approach in Bay of Plenty DHB's RF programme for select children with recurrent GAS infection.

There is mixed evidence of effectiveness of BLIS probiotics in the prevention of sore throat.

²⁰⁶ Allen + Clarke. (2018). *Healthy Homes Initiative evaluation - final report*. Wellington, New Zealand: Allen + Clarke. Retrieved from <https://www.health.govt.nz/system/files/documents/publications/healthy-homes-initiative-evaluation-apr-2018.pdf>

²⁰⁷ Wilcox, C.R., Stuart, B., Leaver, H., et al. (2019). Effectiveness of the probiotic *Streptococcus salivarius* K12 for the treatment and/or prevention of sore throat: A systematic review. *Clinical Microbiology and Infection*, 25(6), 673-680. <https://doi.org/10.1016/j.cmi.2018.12.031>

²⁰⁸ Doyle, H., Pierse, N., Tiatia, R., et al. (2018). Effect of oral probiotic *Streptococcus salivarius* K12 on group A *Streptococcus* pharyngitis: A pragmatic trial in schools. *The Pediatric Infectious Disease Journal*, 37(7). <https://doi.org/10.1097/INF.0000000000001847>

²⁰⁹ Di Pierro, F. (2019). Assessment of efficacy of BLIS-producing probiotic K12 for the prevention of group A *Streptococcus* pharyngitis: A short communication. *Probiotics and Antimicrobial Proteins*, 11(1), 332-334. <https://doi.org/10.1007/s12602-018-9398-7>

9.3 School-based sore throat clinics

Stage of intervention: Preventing RF

In order to target the high-risk age group and reduce barriers to primary care access, school-based sore throat clinics have been run in various high-risk settings around the country. The RFPP was the main driver for wider uptake among DHBs, but some DHBs had already established these services prior to that programme and others didn't include this intervention (see table 7).²¹⁰ Some DHBs took a broader approach and included the assessment and management of uncomplicated skin infections.

Evidence of the potential effectiveness of school-based interventions was drawn on to inform this approach in the RFPP. A randomised control trial involving around 22,000 students showed a non-significant reduction of 28% in the school-based sore throat clinic programs compared to GP-based care.²¹¹ A meta-analysis which drew on six very different studies, including the pilot intervention, estimated that RF cases would decrease by about 60% using a school or community clinic to treat GAS throat infections.²¹²

²¹⁰ Jack, S., Williamson D, Galloway Y, *et al.* (2015). *Interim evaluation of the sore throat component of the rheumatic fever prevention programme – quantitative findings*. Porirua, New Zealand: The Institute of Environmental Science and Research Ltd (ESR). Retrieved from <https://www.health.govt.nz/publication/interim-evaluation-sore-throat-management-component-new-zealand-rheumatic-fever-prevention-programme>

²¹¹ Lennon, D., Stewart, J., Farrell, E., *et al.* (2009). School-based prevention of acute rheumatic fever: A group randomized trial in New Zealand. *The Pediatric Infectious Disease Journal*, 28(9). <https://doi.org/10.1097/INF.0b013e3181a282be>

²¹² Lennon, D., Kerdemelidis, M. and Arroll, B. (2009). Meta-analysis of trials of streptococcal throat treatment programs to prevent rheumatic fever. *The Pediatric Infectious Disease Journal*, 28(7). <https://doi.org/10.1097/INF.0b013e3181a8e12a>

Table 7: Differences in school sore-throat clinics by DHB

DHB	Programme timing	Effectiveness shown in setting?	Swabbing days per week	Skin included	Antibiotic compliance checks	Whānau swabbing	Coverage	Swabs/child/year	Swab to result (days)	Cost/child/year	Cost/QALY ²¹³ gained	Comments
Northland ²¹⁴	2002–ongoing	?	3	?	?	?	?	2.2 (1.7–3.7)	5+	?	\$250,000–300,000	
Auckland ²¹⁵	2012–ongoing	No	3	Yes	Yes	Yes	16 schools	Unknown	1–3	\$200	\$80,000–\$100,000 ²¹⁶	
Waitemata ²¹⁷	2012–ongoing	No	3	Yes	Yes	Yes	5 schools	Unknown	1–3	\$200	\$125,000 ²¹⁸	
Counties Manukau ²¹⁹	2011–ongoing	Yes	5	Yes	Yes (day 5 and 10)	Yes	91% of at risk population (2013 assessment)	4–5	2–3	\$200	\$12,000–24,000	Much broader programme than just sore throat management. Led by the National Hauora Coalition, a Māori health NGO/PHO. Provides clinical leadership and co-ordinates a network of providers to deliver the programme
Waikato	2011–2015	Delivered in three schools before being discontinued										

²¹³ QALY: quality-adjusted life year.

²¹⁴ Northland District Health Board. (2013). *Rheumatic Fever prevention plan*. Northland, New Zealand: Retrieved from <https://www.northlanddhb.org.nz/assets/Buttons/Communications/Publications/NDHB-Rheumatic-Fever-Prevention-Plan-V1-0.pdf>

²¹⁵ Auckland District Health Board. (2016). *Rheumatic Fever prevention programme*. Auckland, New Zealand: Auckland District Health Board. Retrieved from <https://www.adhb.health.nz/assets/Documents/About-Us/Planning-documents/ADHB-Refreshed-Rheumatic-Fever-Plan-2016-17.pdf>

²¹⁶ Auckland District Health Board. (2021). *Community and Public Health Advisory Committee – Commissioning Health Equity Advisory Meeting*. Auckland. Retrieved from <https://www.adhb.health.nz/assets/Documents/About-Us/Board-agendas-and-minutes/2021/Open-CPHAC-Meeting-Pack-16-June-2021.pdf>

²¹⁷ Waitemata District Health Board. (2016). *Rheumatic Fever prevention programme*. Auckland, New Zealand: Waitemata District Health Board. Retrieved from <https://www.waitemataadhb.govt.nz/assets/Documents/health-plans/WaitemataDHB-RhFPlan.pdf>

²¹⁸ Auckland District Health Board. (2021). *Community and Public Health Advisory Committee – Commissioning Health Equity Advisory Meeting*. Auckland. Retrieved from <https://www.adhb.health.nz/assets/Documents/About-Us/Board-agendas-and-minutes/2021/Open-CPHAC-Meeting-Pack-16-June-2021.pdf>

²¹⁹ Counties Manukau Health. (2013). *Rheumatic Fever prevention plan*. Auckland, New Zealand: Counties Manukau Health. Retrieved from <https://countiesmanukau.health.nz/assets/About-CMH/Reports-and-planning/5683dfdbba/2013-2017-Rheumatic-fever-prevention-plan.pdf>

DHB	Programme timing	Effectiveness shown in setting?	Swabbing days per week	Skin included	Antibiotic compliance checks	Whānau swabbing	Coverage	Swabs/child/year	Swab to result (days)	Cost/child/year	Cost/QALY ²¹³ gained	Comments
Bay of Plenty ²²⁰	2009–ongoing	Yes	Most places 2, Whakatāne area 1	Yes	Yes	Yes	37 schools	Unknown	1–3, commonly 2	\$165	\$13,488	Iwi-led collaborative approach; strong community approach; give out toothbrushes
Lakes ²²¹	2015–ongoing	Not studied	5	Yes	Yes	Yes – if criteria met	Unclear and difficult to study	0.3 but 1.7 for children presenting to school clinic	1–3 days	Difficult to determine as contract also includes rapid response clinics	Has not been calculated	Service run out of community-based GP clinic with wider professional support. Allows easy referral for other issues. Good relationships with schools and whānau
Tairāwhiti	2011–2014											Discontinued as not able to be delivered in local context
Hawke's Bay ²²²	2010–ongoing	Yes	2 or 3	Not formally but done ad hoc	Yes	Yes	96% of eligible children consented	?	2 days	\$300	\$60,000	Run in partnership with Te Taiwhenua o Heretaunga (a kaupapa Māori primary health care provider)
Capital & Coast ²²³	2011–?											Discontinued after evaluation of school-based programmes found not to be cost effective
Hutt Valley ²²⁴	NA – no school clinics											

²²⁰ Bay of Plenty District Health Board. (2015). *Bay of Plenty and Lakes Rheumatic Fever Prevention Plan: Summary Version*. Bay of Plenty, New Zealand: Bay of Plenty District Health Board. Retrieved from <https://www.ttophs.govt.nz/vdb/document/1509>

²²¹ Lakes District Health Board. (2015). *Refreshed Rheumatic Fever Prevention Plan 2016-2018*. Rotorua, New Zealand: Retrieved from <https://www.ttophs.govt.nz/vdb/document/1496>

²²² Hawke's Bay District Health Board. (2016). *Refreshed rheumatic fever prevention plan*. Hawke's Bay, New Zealand: Retrieved from <http://www.ourhealthhb.nz/assets/Publications/HBDHB-Rheumatic-Fever-Prevention-Plan.pdf>

²²³ Greater Wellington sub-region Wairarapa Hutt Valley and Capital & Coast DHBs. (2015). *Rheumatic Fever prevention plan*. Wellington, New Zealand: Retrieved from <http://www.huttvalleydhb.org.nz/content/23ea0b72-12b3-46e6-a002-41b96215970d.cmr>

²²⁴ Ibid.

There has been mixed evidence of effectiveness of school-based sore-throat clinics

There have been few robust studies of the effectiveness of school-based sore throat clinics, and none have been published that include data from after 2018.

The process of designing and implementing the school-based services in a real-world context as opposed to a research setting made analysis complex:

- The school-based service of the RFPP was not adequately designed to be systematically and comprehensively evaluated. In particular, the lack of control sites is a limitation.
- Data limitations on the rates of RF can limit the analysis of the effectiveness of interventions (see section 3). Specifically, where data relied on disease notifications, the increase in notification reporting may have masked effectiveness.²²⁵
- The studies were unable to account for other possible confounding effects that may have impacted trends of RF over the period studied, including other interventions or increases in exposure to certain risk factors (e.g. inadequate housing).
- With the available data, it is unclear whether no evidence of effectiveness is the result of limitations in intervention design or delivery.
- Because RF is uncommon, a change in incidence will need to be large to be statistically significant, so relying on statistical significance to prove that a service is working may have limitations.
- Due to these limitations, determining effectiveness might rely on trends of RF following discontinuation of services.

Table 8 is a summary of the assessments of effectiveness of school-based sore throat clinics at reducing RF rates. A national evaluation would be useful.

- A blanket assessment across all DHBs might be misleading because each had variations in delivery and occurred in different contexts (see table 7 above).
- The most recent and longest studies (Counties Manukau²²⁶ and Bay of Plenty²²⁷) have both indicated that the school-based sore throat clinic led to a reduction in the rate of RF in those contexts. These positive results were found in DHBs where treatment of skin infection was included, but whether including skin conditions in RFPPs reduces risk of RF is yet to be determined. Skin infection was included as a general health intervention, not specific to a possible association with RF. As such, an examination of the data with respect to treatment type (e.g. antibiotic vs not) might be instructive.
- Findings suggest that a school-based approach may be beneficial under certain conditions, including targeting a densely populated area of high-risk children with a well-run service that possibly includes active case-finding and includes both sore throat and skin identification and treatment.²²⁸

²²⁵ Walsh, L., Innes-Smith, S., Wright, J., et al. (2021). *Bay of Plenty Rheumatic fever epidemiology 2000-18; Baywide ARF rates in Māori reduce substantially utilizing multi-sourced data. Notification data leads to underestimation of programme effectiveness - Unpublished manuscript.*

²²⁶ Lennon, D., Anderson, P., Kerdemilidis, M., et al. (2017). First presentation acute rheumatic fever is preventable in a community setting: A school-based intervention. *The Pediatric Infectious Disease Journal*, 36(12). <https://doi.org/10.1097/INF.0000000000001581>

²²⁷ Walsh, L., Innes-Smith, S., Wright, J., et al. (2020). School-based streptococcal A sore-throat treatment programs and acute rheumatic fever amongst Indigenous Māori: A retrospective cohort study. *The Pediatric Infectious Disease Journal*, 39(11), 995-1001. <https://doi.org/10.1097/INF.0000000000002770>

²²⁸ Jack, S.J., Williamson, D.A., Galloway, Y., et al. (2018). Primary prevention of rheumatic fever in the 21st century: Evaluation of a national programme. *International Journal of Epidemiology*, 47(5), 1585-1593. <https://doi.org/10.1093/ije/dyy150>

Table 8: Summary of assessments of effectiveness of school-based sore throat clinics

DHB	Evaluation details	Positive effect?	Detailed findings	Comments
National (10 DHBs)	Interim evaluation – comparing ‘before’ (2009–2011) to ‘after’ (2012–2014) ²²⁹	~	17% reduction in RF cases among children aged 5–12 years attending decile 1–3 schools – but this was not statistically significant (95% CI: -17% to 42%)	Notification data was used and increasing completeness of notifications over time may have masked a stronger result
National (10 DHBs)	Cohort study, children 5–12 at schools with service, 2012–2016 ²³⁰	✓ ✓ X	All schools = 23% effectiveness Counties Manukau only = 46% effectiveness Other 9 DHBs = -7% effectiveness	Used hospitalisation data, which only accounts for first episode of RF
Northland	No evaluation			
Auckland	No evaluation			
Waitemata	No evaluation			
Counties Manukau	RF rate changes before and after staggered introduction of clinics 2010–2016 ²³¹	✓	58% reduction in RF in two years (pre-clinic 88/100,000, 95% CI ²³² 79–111; post-clinic 37/100,000, 95% CI 15–83). This was compared to projected rates rather than baseline rates	Used regional RF register data
Counties Manukau	Interim evaluation – comparing ‘before’ (2009–2011) with ‘after’ (2012–2014) ²³³	✓	31% reduction in RF cases among children aged 5–12 years attending decile 1–3 schools – but this was not statistically significant (95% CI: -13% to 58%)	Notification data was used and increasing completeness of notifications over time may have masked a stronger result
Counties Manukau	All of CMDHB before the programme was implemented (May 2013) compared with a year later (May 2014) ²³⁴	✓	Higher risk of a GAS positive throat swab before implementation (2013) vs after (2014) (relative risk 1.8, 95% CI 1.3–2.3, p=0.01)	Short assessment time and early in timing of programme to evaluate outcomes

²²⁹ Jack, S., Williamson D, Galloway Y, *et al.* (2015). *Interim evaluation of the sore throat component of the rheumatic fever prevention programme – quantitative findings*. Porirua, New Zealand: The Institute of Environmental Science and Research Ltd (ESR). Retrieved from <https://www.health.govt.nz/publication/interim-evaluation-sore-throat-management-component-new-zealand-rheumatic-fever-prevention-programme>

²³⁰ Jack, S.J., Williamson, D.A., Galloway, Y., *et al.* (2018). Primary prevention of rheumatic fever in the 21st century: Evaluation of a national programme. *International Journal of Epidemiology*, 47(5), 1585–1593. <https://doi.org/10.1093/ije/dyy150>

²³¹ Lennon, D., Anderson, P., Kerdemilidis, M., *et al.* (2017). First presentation acute rheumatic fever is preventable in a community setting: A school-based intervention. *The Pediatric Infectious Disease Journal*, 36(12). <https://doi.org/10.1097/INF.0000000000001581>

²³² CI: Confidence interval.

²³³ Jack, S., Williamson D, Galloway Y, *et al.* (2015). *Interim evaluation of the sore throat component of the rheumatic fever prevention programme – quantitative findings*. Porirua, New Zealand: The Institute of Environmental Science and Research Ltd (ESR). Retrieved from <https://www.health.govt.nz/publication/interim-evaluation-sore-throat-management-component-new-zealand-rheumatic-fever-prevention-programme>

²³⁴ Anderson, P., King, J., Moss, M., *et al.* (2016). Nurse-led school-based clinics for rheumatic fever prevention and skin infection management: Evaluation of Mana Kidz programme in Counties Manukau. *The New Zealand Medical Journal*, 129(1428), 36–45. ; King, J., Moss, M. and McKegg, K. (2014). *School based primary health care programme evaluation: Final report*. Auckland, New Zealand: Counties Manukau District Health Board. Retrieved from <https://countiesmanukau.health.nz/assets/About-CMH/Performance-and-planning/health-status/c956de4a74/2014-school-based-phc-programme-evaluation-Mana-report.pdf>

DHB	Evaluation details	Positive effect?	Detailed findings	Comments
			<p>No significant difference in rates of skin infection between 2013 and 2014 (relative risk 1.4, 95% CI 0.7–2.7, p=0.4)</p> <p>The percentage of parents/caregivers who had heard of RF or RHD increased from 71% in 2013 to 89% in 2014</p> <p>Focus group feedback suggested that the programme had increased access to social support services, as nurses refer family/whānau for further assistance</p>	
Counties Manukau	Updating above assessments: commissioning for independent evaluation late 2021			
Waikato	No evaluation			
Bay of Plenty	Retrospective assessment of outcomes from 3 cohorts – 1 school, 1 GP, 1 both, from 2000–2010 to 2011–2018 ²³⁵	✓	<p>School-based programmes with Māori health workers, sore-throat swabbing, and GP/nurse support reduced first-presentation RF incidence in Māori students in highest-risk settings. The opposite occurred in GP-only care</p> <p>The school program cohort saw a post-intervention (2011–18) reduction of RF incidence of 60%, 148 to 59/100,000/year, rate ratio (RR)=0.40 (95% CI 0.22–0.73) p=0.002</p> <p>The cohort with both GP care and the school programme for only highest risk schools found RF incidence decreased 48%, 50 to 26/100,000/year RR=0.52 (95% CI 0.27–0.99) p=0.044</p> <p>RF doubled in GP-only care cohort, increasing 30 to 69/100,000/year RR=2.28 (95% CI 0.99–5.27) p=0.047</p>	Used multi-sourced data, so data more robust than hospitalisation or notification data and not impacted by increasing completeness of notification data
Bay of Plenty	Local audit and evaluation on preliminary data 2000–2010 vs 2011–2014; Māori children aged 5–14 ²³⁶	✓	<p>RF rate pre-intervention = 128.7/100,000 (95% CI 60.6–177.4)</p> <p>RF rate post-intervention = 50.7/100,000 (95%CI 16.3–118.3)</p>	

²³⁵ Walsh, L., Innes-Smith, S., Wright, J., *et al.* (2020). School-based streptococcal A sore-throat treatment programs and acute rheumatic fever amongst Indigenous Māori: A retrospective cohort study. *The Pediatric Infectious Disease Journal*, 39(11), 995-1001. <https://doi.org/10.1097/INF.0000000000002770>

²³⁶ Bay of Plenty District Health Board. (2015). *Bay of Plenty and Lakes Rheumatic Fever Prevention Plan: Summary Version*. Bay of Plenty, New Zealand: Bay of Plenty District Health Board. Retrieved from <https://www.ttophs.govt.nz/vdb/document/1509>

DHB	Evaluation details	Positive effect?	Detailed findings	Comments
<i>The above study expands on these findings</i>				
Lakes	No evaluation			
Tairāwhiti	No evaluation			
Hawke's Bay	Comparing annual RF incidence in five years before (2005–2010) to four years after (2011–2014) in children aged 5–14 years. ²³⁷	✓	66% decrease in annual RF incidence from before implementation (221.1/100,000) to after (76.2/100,000) p=0.0249 Estimated that ~700 children would need to participate for one year to prevent one case of RF The programme was judged as “somewhat effective” for improving equity of access to throat swabbing	Included both notification and hospitalisation data Assessment of whole programme, not just school-based sore throat clinics ²³⁸
Hawke's Bay	Update on above study to include five years further data		Not yet published	
Capital & Coast	No evaluation			
National study	Case-control study of RF cases within 11 high-incidence DHBs ²³⁹	X	Being at a school with a sore-throat programme was associated with 2.6 times higher RF risk	Finding likely due to confounding from school programmes targeting high-risk schools

²³⁷ Stevens, J. (2015). *Say Ahh rheumatic fever prevention programme evaluation report*. Hawke's Bay DHB.

²³⁸ A comprehensive review of the evidence for RF prevention in the Hawke's Bay with recommendations to the Hawke's Bay District Health Board is being finalised at the time of writing.

²³⁹ Baker, M.G., Gurney, J., Oliver, J., et al. (2019). *The New Zealand rheumatic fever risk factors study (RF RISK): Draft report on study findings*. Wellington, New Zealand: Rheumatic Fever Risk Factors Study.

There are important considerations to take into account when interpreting these findings.

- **Effectiveness may differ depending on what is being measured.**
 - Assessments to date have largely been focused on costs-benefit analysis rather than an equity analysis. Changing the outcome to focus on equitable access to healthcare should be considered given that RF and RHD almost exclusively effect Māori and Pacific peoples.
- **There are broader benefits beyond reducing the rate of RF.**
 - There are anecdotal reports of additional health benefits (beyond RF reduction) from operating school-based health services such as improved skin health. These have not been captured in assessments to date but robust assessment of the impacts on health outcomes should inform decisions around reducing or scaling-up programmes.
 - Some programmes reported improved health literacy as a result of the school-based clinics.
- **Impacts on antimicrobial stewardship are unclear.**
 - On the one hand, there are positive antimicrobial stewardship implications. For example, there was high compliance with the protocol for antimicrobial administration for school-based clinics in Counties Manukau DHB.²⁴⁰ Services that have checks for antibiotic compliance also support antimicrobial stewardship.
 - While compliance to guidelines is high in school-based programmes, the impact of this is limited given the use of broad-spectrum antibiotics as first-line therapy. These clinics also lead to more detection of GAS colonisation and more unnecessary antibiotic use, when antibiotics are given to children who are not at risk of RF.
- **School-based clinics have some limitations.**
 - Monitoring children for a sore throat is easier said than done, as it requires children to identify their sore throat and tell a caregiver. Children’s interpretation of what a ‘sore throat’ is does not necessarily align with what the programme wants to capture.²⁴¹

Child asked to define a sore throat: “What is a sore throat?’ ‘Like the fever, you know? Coughs and that, sneezing and that, cold and that.”²⁴²

- The nature of being available at school means these services are limited to school days and the school term, which may lead to loss of accessibility benefits for some, but improve access for others.

9.4 Rapid response clinics

Stage of intervention: Preventing RF

Towards the end of 2013, the Ministry of Health expanded the sore throat management component to set up rapid response sore throat management clinics which are free, drop-in clinics for people aged 4–19 years who identify as Māori and Pacific and/or live in the areas with the most deprivation. The specific places rapid response clinics are offered differ by DHB (see table 9). They can include:

- Pharmacies
- Afterhours access to GP clinics
- Community clinics
- High-need secondary schools
- Youth health services.

²⁴⁰ Tsai, J.-Y.C., Anderson, P., Broome, L., *et al.* (2016). Antimicrobial stewardship using pharmacy data for the nurse-led school-based clinics in Counties Manukau District Health Board for management of group A streptococcal pharyngitis and skin infection. *The New Zealand Medical Journal*, 129(1435), 29-38.

²⁴¹ Anderson, A. and Spray, J. (2020). Beyond awareness: Towards a critically conscious health promotion for rheumatic fever in Aotearoa, New Zealand. *Social Science & Medicine*, 247, 112798. <https://doi.org/10.1016/j.socscimed.2020.112798>

²⁴² Spray, J. (2018). The value of anthropology in child health policy. *Anthropology in Action*, 25(1), 29-40. <https://doi.org/10.3167/aia.2018.250104>

Table 9: Differences in school sore-throat clinics by DHB

DHB	Approximate programme timing	Settings for rapid response clinics	Skin infection treatment included	Other features
Northland	2014–ongoing	Pharmacies	No	Shifting to empirical treatment for high-risk people due to swab result delays
Auckland	2014–2017	GP clinics but discontinued	No	Required practices to use the advanced form for visibility of numbers of people treated
Waitemata	2014–2017	GP clinics but discontinued	No	Required practices to use the advanced form for visibility of numbers of people treated
Counties Manukau	2013–2017	GP clinics and decile 1–4 secondary schools	No	Required practices to use the advanced form for visibility of numbers of people treated
Waikato	2015–ongoing	Pharmacies and some GP clinics	No	
Bay of Plenty	2017–ongoing	Pharmacies	Yes	Standing orders to supply antibiotics at the time of swabbing to at risk populations (Māori/Pacific), living in over-crowded housing, or a personal or family history of RF
Lakes	2015–ongoing	GP clinics	Yes (about half the work now)	Dedicated space in clinic, which demonstrates priority and establishes familiarity for whānau
Tairāwhiti	2015	Discontinued		
Hawke's Bay	2014	Trialled in GP clinics but discontinued. Currently planning a pilot in pharmacies		
Capital & Coast	2014–ongoing	Pharmacies and GP clinics		
Hutt Valley	2014–ongoing	Pharmacies and GP clinics		

There has not been an assessment of the impact of rapid response clinics on reducing RF rates in the Aotearoa New Zealand context. An evaluation done for the Ministry of Health in 2015, intended to inform service improvement, found variable awareness of the presence of services by DHB, mixed awareness about who the services were free for, and limited awareness of pharmacies as a service.²⁴³ The assessment was done early on in the programme and over five years ago so may no longer be relevant to how these services are received today.

There has not been an assessment of the impact of rapid response clinics on reducing RF rates in the Aotearoa New Zealand context.

²⁴³ Litmus, Kaipuke and Integrity Professionals. (2015). *Formative evaluation of sore throat clinics, report prepared for Ministry of Health*. Wellington, New Zealand: Retrieved from <https://www.health.govt.nz/system/files/documents/publications/formative-evaluation-sore-throat-clinics-mar16.pdf>

9.5 Improving antibiotic adherence for sore throats

Stage of intervention: Preventing RF

There are different approaches to antibiotic treatment of GAS throat infections. Oral penicillin for 10 days has been the main treatment, with a move to twice daily dosing likely improving adherence over the alternative three times daily dosing. The direct alternative of amoxicillin once a day for 10 days may be easier for some patients to take, but has the disadvantage of promoting AMR. The Australian guidelines do not include amoxicillin at all for this reason. Liquid formulations of penicillin and amoxicillin both require refrigeration which may be a barrier for some. An alternative option is one-off injection of BPG – this is the same treatment as the secondary prophylaxis (see section 1) and has guaranteed adherence. Barriers to the one-off injection include that it is painful, not all nurses are confident administering it, and it requires a health professional/nurse appointment with associated travel and longer appointment times. The use of oral antibiotics versus the injection is variable and is largely driven by DHB policy and clinical expertise and patient preferences. The Heart Foundation have guidelines for the treatment of sore throats for RF prevention.²⁴⁴

There is limited evidence about the levels of adherence to antibiotics prescribed for GAS throat infection. A study in Northland of patients who presented to ED with presumed GAS throat infection found that 48 of the 65 patients completed their full course of antibiotics.²⁴⁵

There is limited evidence about the levels of adherence to antibiotics prescribed for GAS throat infection.

Interventions have been tried to improve adherence to antibiotics to treat GAS throat infections. A trial undertaken in South Auckland in 2014 studied four interventions to test their effectiveness in improving adherence to antibiotics prescribed for GAS throat infection.²⁴⁶

- **Nurses administering antibiotics** at school was significantly more effective than self-administration ($p=0.01$). Twenty-one percent of the children who were responsible for their own adherence had a positive swab after their course of antibiotics should have been finished, compared to 4.6% of those who had been administered theirs by the nurse on weekdays (with self-administration on the weekend). There was very positive feedback from parents/caregivers about this approach. The cost may be a limiting factor, but it could be reduced through improved processes.
- **Using blister packs for the antibiotics** (a recognised adherence aid) was not found to improve adherence to the course of antibiotics compared to those who used the standard product. Though fewer people who used the blister pack reported poor adherence at day 10, there were similar rates of positive throat swabs after their antibiotic course was finished (~21%).²⁴⁷ Thus blister packs were not implemented, although some argue that better communication of the ‘why’ alongside the ‘what’ for this intervention could improve success.
- **Daily text reminders** for medication adherence were found to be ineffective at improving adherence to antibiotics for GAS throat infections. Ninety percent of text messages sent by the system were received and only 21% of parents/caregivers responded to a final text asking if their child had completed their course of antibiotics. There was no significant difference between the proportion of children with a positive throat swab following their course of antibiotics who had the texts (18.1%) or didn’t (21.4%).

²⁴⁴ Heart Foundation. (n.d.). Guidelines on rheumatic fever, rheumatic heart disease & GAS sore throat. Retrieved 29 September, 2021, from <https://www.heartfoundation.org.nz/professionals/health-professionals/guidelines-on-rheumatic-fever-rheumatic-heart-disease-gas-sore-throat>

²⁴⁵ Mathan, J.J., Erkart, J. and Houlding, A. (2017). Clinical management and patient persistence with antibiotic course in suspected group A streptococcal pharyngitis for primary prevention of rheumatic fever: The perspective from a New Zealand emergency department. *The New Zealand Medical Journal*, 130(1457), 58-68.

²⁴⁶ National Hauora Coalition. (2019). *Rheumatic fever prevention programme: Antibiotic adherence trial*. Auckland, New Zealand: National Hauora Coalition. Retrieved from <https://www.nhc.maori.nz/wp-content/uploads/2019/12/AATreportfinal.pdf>

²⁴⁷ Ibid.

- **Using a one-off injection** of the BPG, rather than a 10-day course of amoxicillin did not significantly reduce the number of children with a GAS-positive swab (thought to be due to carriers presenting with a viral sore throat, but requiring further investigation). Over 80% of parents/caregivers were happy for their child to receive the injection and would choose that option again, a small proportion of parents/caregivers would only want to choose the injections if their child had multiple positive sore throat swabs, and some said needing to go to a clinic for the injection would be a barrier. However, injections may also remove access barriers to care by only needing one appointment and not needing to pick up a prescription. The majority (85%) of health professionals in a small focus group were happy to use it as a treatment option. The Ministry of Health has produced resources including a video of how to reduce injection pain.

Further research around medicines adherence and interventions to improve adherence is needed.

9.6 Public health communications

Stage of intervention: Preventing RF

Awareness of the risk of developing RF following GAS infection is important so people at high risk of developing RF seek antibiotic treatment when needed. Comprehensive awareness raising campaigns have been part of the multipronged approaches that led to dramatic reductions in RF rates in some settings (see section 2.1).²⁴⁸

Communications interventions to reduce the rates of RF have been delivered in Aotearoa New Zealand, at a both a national and local level. The Ministry of Health ran the Rheumatic Fever Awareness Campaign as part of the RFPP. These have thus far been targeted at sore throats and ran in 2014, 2015 and 2016.

- An evaluation of the 2014 winter campaign found that the target audience had high recollection of it and that they remembered the key messages including a call to take children with sore throats to their doctor or nurse.²⁴⁹
- An evaluation of the 2015 campaign was undertaken by a consultancy firm, informed by reviews, stakeholder interviews and call statistics to Healthline. The evaluation focused on efficacy, relevance, and effectiveness of the campaign. Aspects that were rated as ‘excellent’ included value for investment, relevance for the target audience, and reaching the target audience. Aspects rated as ‘good’ included alignment with other activities and the audience’s understanding of the campaign²⁵⁰ and were used to inform the design of the 2016 campaign. Limitations in the focus of this evaluation have been raised. There was little critical consideration of the social consequences of the messages and their presentation for Māori and Pacific families.²⁵¹

Some regions ran specific campaigns prior to and alongside the national campaign. The Toi Te Ora RF campaign run in the Bay of Plenty since 2009 led to marked increases in community awareness, from 22% prior to the campaigns up to 58% after it.²⁵² National television ads were found to be particularly effective and were the most commonly recalled.

²⁴⁸ Nordet, P., Lopez, R., Duenas, A., *et al.* (2008). Prevention and control of rheumatic fever and rheumatic heart disease: The Cuban experience (1986–1996–2002). *Cardiovascular Journal of Africa*, 19(3), 135–140. <https://doi.org/10.10520/EJC23128>; Bach, J., Chalons, S., Forier, E., *et al.* (1996). 10-year educational programme aimed at rheumatic fever in two French Caribbean islands. *The Lancet*, 347. [https://doi.org/10.1016/s0140-6736\(96\)91202-7](https://doi.org/10.1016/s0140-6736(96)91202-7)

²⁴⁹ TNS New Zealand Limited. (2015). *Rheumatic fever campaign evaluation*. Wellington, New Zealand: Health Promotion Agency. Retrieved from <https://www.health.govt.nz/publication/evaluation-2015-rheumatic-fever-awareness-campaign>

²⁵⁰ Vermillion Peirce, P., Akroyd, S. and Tafuna, P. (2015). *Evaluation of the 2015 Rheumatic Fever Awareness Campaign*. Wellington, New Zealand: Ministry of Health. Retrieved from <http://www.health.govt.nz/publication/evaluation-2015-rheumatic-fever-awareness-campaign>

²⁵¹ Anderson, A. and Spray, J. (2020). Beyond awareness: Towards a critically conscious health promotion for rheumatic fever in Aotearoa, New Zealand. *Social Science & Medicine*, 247, 112798. <https://doi.org/10.1016/j.socscimed.2020.112798>

²⁵² Lindsay Lowe, R.V., Debbie Phillips & Sarah Bunker. (2015). *Evaluation of the 2014 Bay of Plenty rheumatic fever awareness campaign*. Bay of Plenty, New Zealand: Toi Te Ora Public Health Service, Bay of Plenty District Health Board. Retrieved from <https://www.health.govt.nz/system/files/documents/publications/evaluation-2015-rheumatic-fever-awareness-campaign-december15.pdf>

Another study assessed the effectiveness of three communications strategies aimed at high school students at four different schools – public health nurses taking a school assembly, written information sheets, and classroom lessons – comparing knowledge before and after the intervention between these schools and a control school. Each of the three interventions showed a significant improvement, with the assembly presentations being the most effective and the information sheet the least.²⁵³

Despite the effectiveness of public health communication interventions at increasing awareness to date, evidence suggests that communication and education strategies could be improved by ensuring messaging does not shift blame to parents/caregivers and rather recognises the inequitable conditions that lead to disease.²⁵⁴ Messaging could also be more culturally safe, for example by focusing on healthy living arrangements with messaging of how to live healthily in multigenerational homes, rather than through a Western lens of household crowding.²⁵⁵

These assessments have focused on whether the campaigns led to increased awareness, but not whether that translated to changes in behaviour leading to a reduction in RF. Such an assumption is called into question by a study that found similarly high levels of RF awareness (92% and 95%) among people who did and did not develop RF, though more people with RF knew sore throats were the cause.²⁵⁶ This suggests that interventions aimed at raising awareness may not have significant impacts on disease rates, especially when the change needed is outside an individual's control.

These assessments have focused on whether the campaigns led to increased awareness, but not whether that translated to changes in behaviour leading to a reduction in RF.

9.7 Decision guidance and support for healthcare professionals

Stage of intervention: Preventing RF

There are guidelines for treating and preventing RF, published by the Heart Foundation in 2014 and most recently updated in 2019.²⁵⁷ Updating the RF guidelines is a priority task of Pū Manawa. Beyond this, implementation of the guidelines within the context of the workflow in primary care is critical for success.

There have been few studies that have measured whether prescribers adhere to the national RF guidelines and their regional interpretation.

- A study in Northland GP clinics found different rates of GPs adhering to national guidelines for managing GAS throat infections for Māori and non-Māori patients – 85.8% of Māori patients were given the guideline-recommended antibiotic, 10-day course and within nine days of the swab result, compared to 92.5% of non-Māori patients, despite the significantly higher risk of RF for Māori patients.²⁵⁸
- The He Ako Hiringa Epic Dashboard provides a means for GPs and other prescribers to audit their own prescribing and might provide a useful source for investigation.

²⁵³ Harré, N., Thomas, D., Brown, K., *et al.* (2000). Communicating information about sore throats and rheumatic fever to South Auckland high-school students. *The New Zealand Medical Journal*, 113(1111), 215.

²⁵⁴ Anderson, A. and Spray, J. (2020). Beyond awareness: Towards a critically conscious health promotion for rheumatic fever in Aotearoa, New Zealand. *Social Science & Medicine*, 247, 112798. <https://doi.org/10.1016/j.socscimed.2020.112798>

²⁵⁵ Bryers, C. (2021). *Rheumatic fever review: An examination and recommendations for designing a rheumatic fever awareness campaign*. Auckland, New Zealand: Auckland and Waitemātā District Health Boards.

²⁵⁶ Gurney, J.K., Chong, A., Culliford-Semmens, N., *et al.* (2017). High levels of rheumatic fever and sore throat awareness among a high-risk population screened for rheumatic heart disease. *The New Zealand Medical Journal*, 130(1450), 107-110.

²⁵⁷ National Heart Foundation of New Zealand. (2019). *Group A streptococcal sore throat management guideline. 2019 update*. Auckland, New Zealand: National Heart Foundation of New Zealand. Retrieved from <https://www.heartfoundation.org.nz/resources/group-a-streptococcal-sore-throat-management>

²⁵⁸ Shetty, A., Mills, C. and Eggleton, K. (2018). A repeat audit of primary care management of group A streptococcal pharyngitis in Northland, New Zealand 2016. *Journal of Primary Health Care*, 10(1), 18. <https://doi.org/10.1071/hc17056>

A study in Northland GP clinics found different rates of GPs adhering to national guidelines for managing GAS throat infection for Māori and non-Māori patients.

Whether or not the guidelines actually improve outcomes for patients is not well studied.

- A local study that used four GAS throat infection prediction rules found that none were reliable predictors in the high-risk population in Aotearoa New Zealand. The New Zealand Heart Foundation's prediction rule was the best at picking up positive tests but still only correctly found just over half (54%).²⁵⁹
- For prediction rules to be useful they need to be translated into accessible guidelines for healthcare professionals, which are likely key to their implementation. The extent to which healthcare professionals know they exist has not been studied.
- Further study is needed to understand how RF guidelines and prediction rules impact outcomes for patients.

Doctors new to practising in Aotearoa New Zealand may need targeted awareness raising.

- Anecdotal evidence suggests that doctors who have been trained in developed countries where RF is no longer commonly found may overlook GAS in high-risk populations.
- Raising awareness about the risk of RF in certain high-risk populations in Aotearoa New Zealand is therefore crucial for healthcare professionals new to practising in this country, e.g. locums.

9.8 Rapid diagnostics for GAS infection

Stage of intervention: Preventing RF

Attempts have been made to develop and implement rapid diagnostics for GAS throat infections so that those with the infection can have treatment started immediately, and those who have a viral infection don't need 'just-in-case' treatment while awaiting results from a throat swab culture, which can take up to 72 hours. There are different types of rapid diagnostic tests for GAS, but to our knowledge few have been evaluated in Aotearoa New Zealand.

- A recent prospective study investigated the utility of Xpert® Xpress Strep A molecular tests at Middlemore Hospital in Auckland, comparing them to culture and another molecular method (BioGX Group A Streptococcus- OSR for BD MAX™).²⁶⁰ Out of 205 swabs, 28 were GAS culture positive, 45 were positive according to the Xpert® test, and 38 were positive according to the BioGX test. The authors concluded that Xpert® test, which uses qualitative real-time PCR, was highly sensitive with a strong negative predictive value and rapid turnaround time, making it safe to introduce to front-line testing in a high-incidence RF population. The Xpert® test has also been evaluated overseas with comparable results.²⁶¹
- New Zealand researchers compared **four rapid antigen tests** for GAS to see if they were sensitive enough to be used in practice. These were tests that were commercially available in Aotearoa New Zealand in mid-2011. The study highlighted an issue with rapid antigen tests – the tests were fine at picking up samples that had high loads of GAS but were less consistent with low bacterial loads and

²⁵⁹ Kerdelmelidis, M., Lennon, D.R. and Stewart, J. (2015). How should sore throats be managed? Performance of four group A streptococcal sore throat prediction rules in New Zealand children. *Open Forum Infectious Diseases*, 2(suppl_1). <https://doi.org/10.1093/ofid/ofv133.720>

²⁶⁰ Taylor, A., Morpeth, S., Webb, R., et al. The utility of rapid Group A streptococcus molecular testing compared with throat culture for the diagnosis of Group A streptococcal pharyngitis in a high-incidence rheumatic fever population. *Journal of Clinical Microbiology*, 0(ja), JCM.00978-00921. <https://doi.org/10.1128/JCM.00978-21>

²⁶¹ Eldirdiri, S., Omojola, J., MacDonald, S., et al. (2020). Evaluation of Xpert® Xpress Strep A Test for detection of group A *Streptococcus* in throat swabs. *Access Microbiology*, 2(2). <https://doi.org/10.1099/acmi.fis2019.po0082>

the result was hard to determine, which would be an issue as sore throats with low bacterial loads can still be clinically relevant.²⁶²

- To address the low bacterial loads, another trial used different swabs (flocked vs conventional rayon) to release more bacteria into the test. However, the rapid antigen tests performed so poorly for both swabs that the study was terminated.²⁶³
- **Loop-mediated isothermal amplification (LAMP) technology.** A local study compared the *illumigene* GAS LAMP test with the traditional culture technique used on samples from a school-based sore throat clinic. The LAMP assay picked up more true positives than the culture technique (86.5% vs 73.2%) but fewer true negatives (97.6% vs 100%). A key strength was the much faster turnaround time of less than one hour compared with up to 72 hours for culture-based techniques.²⁶⁴
- An alternative type of rapid diagnostic test relying on **cameras and image processing technology** is in development. Light AI aims to distinguish between viral and bacterial throat infections, though it won't be able to distinguish between strep groups A, C or G. The technology will be applied via a handheld, point-of-care test or a smartphone and is still in the trial stage.²⁶⁵ Mana Kidz was part of an international trial but this was stopped after one term due to low GAS positives (likely associated with COVID-19 lockdowns).
- Other rapid diagnostics, such as the QuikRead go[®] Strep A test, the BD Veritor[™] system, Revogene Strep A molecular assay, and the Xpert[®] Xpress Strep A Assay, have been trialled more recently in overseas settings, and some have reported promising results (e.g. around 95% true positives and true negatives captured).²⁶⁶ **Each test would need to be replicated in the local setting before being implemented.**
- A 2020 health technology assessment for the US National Institute for Health Research systematically reviewed the evidence for 21 point-of-care tests for GAS and compared their cost effectiveness.²⁶⁷ The review highlighted promising sensitivity and specificity of rapid diagnostic tests but found there was **insufficient evidence to meaningfully compare or rank the tests against each other.** They found considerable variability of the success of tests in different settings, illustrating the importance of checking each test in the local setting it will be deployed in. The review also highlighted uncertainty about how costs and benefits would change if these tests were used instead of standard culture techniques and concluded that further research was needed to determine if the testing provides value for money.

If a rapid diagnostic test is proven to be effective in a specific setting, it would be important for the test to be widely available and accessible so that people who would otherwise not seek medical attention for a sore throat could be tested. They are currently not considered accurate enough to be recommended in Aotearoa New Zealand.

²⁶² Upton, A., Lowe, C., Stewart, J., *et al.* (2014). *In vitro* comparison of four rapid antigen tests for group A *Streptococcus* detection. *The New Zealand Medical Journal*, 127(1398).

²⁶³ Upton, A., Farrell, E., Stewart, J., *et al.* (2014). Disappointing performance of rapid antigen detection tests for group A *Streptococcus* in the Auckland school-based sore throat programme. *The New Zealand Medical Journal*, 127(1389), 103-105.

²⁶⁴ Upton, A., Bissessor, L., Farrell, E., *et al.* (2016). Comparison of *illumigene* group A *Streptococcus* assay with culture of throat swabs from children with sore throats in the New Zealand school-based rheumatic fever prevention program. *Journal of Clinical Microbiology*, 54(1), 153-156. <https://doi.org/10.1128/JCM.02440-15>

²⁶⁵ Light AI. (2021). Computer vision for medical diagnosis. Retrieved 10 August 2021, from <https://light.ai/>

²⁶⁶ Bulut, M.E., Kina, N., Büyükyanbolu, E., *et al.* (2020). A highly-sensitive rapid test for the diagnosis of streptococcal pharyngitis: BD veritor[™] system. *International Journal of Pediatric Otorhinolaryngology*, 133, 109980. <https://doi.org/10.1016/j.ijporl.2020.109980>; Azrad, M., Danilov, E., Goshen, S., *et al.* (2019). Detection of group A *Streptococcus* in pharyngitis by two rapid tests: Comparison of the BD Veritor[™] and the QuikRead go[®] Strep A. *European Journal of Clinical Microbiology & Infectious Diseases*, 38(6), 1179-1185. <https://doi.org/10.1007/s10096-019-03527-w>; Eldirdiri, S., Omojola, J., MacDonald, S., *et al.* (2020). Evaluation of Xpert[®] Xpress Strep A Test for detection of group A *Streptococcus* in throat swabs. *Access Microbiology*, 2(2). <https://doi.org/10.1099/acmi.fis2019.po0082>;

Banerjee, D., Michael, J., Schmitt, B., *et al.* (2020). Multicenter clinical evaluation of the revogene strep A molecular assay for detection of *Streptococcus pyogenes* from throat swab specimens. *Journal of Clinical Microbiology*, 58(7), e01775-01719. <https://doi.org/10.1128/JCM.01775-19>

²⁶⁷ Fraser, H., Gallacher, D., Achana, F., *et al.* (2020). Rapid antigen detection and molecular tests for group A streptococcal infections for acute sore throat: Systematic reviews and economic evaluation. *Health Technology Assessment*, 24(31), 1-232. <https://doi.org/10.3310/hta24310>

A limitation of using non-culture-based techniques is that there will not be clinical isolates available for further study either for immediate susceptibility testing or potential research at a later date.

9.9 Identifying at-risk children through hospital admissions

Stage of intervention: Preventing RF

An approach to target interventions to prevent RF for at-risk people, based on hospital admissions, was tried but was found to be ineffective. The idea was that a child who had certain health conditions may be more at risk of also developing RF and their presentation for the initial illness may provide a point to intervene to reduce their risk of later developing RF. In this study, it was hoped that three previously developed screening groups would capture people who later developed RF and could therefore be used as tool to guide interventions. The groups were based on other conditions associated with poor housing (e.g. acute bronchiolitis, asthma, non-viral pneumonia) that children might be hospitalised for were identified. The sensitivity of using these three conditions to identify children and young people who developed RF was low (ranging from 4.7% to 27%) suggesting these screening groups would not be effective at developing a predictive risk tool for RF.²⁶⁸

Despite limited efficiency for RF prevention, a significant burden of child death and repeat hospitalisation might still be avoided through housing intervention targeted to this group.

9.10 RF patient register

Stage of intervention: Preventing further episodes and development of RHD

In Aotearoa New Zealand, there are some regional registers for RF but not a national register (see section 3). Regional registers are held on different patient management systems which vary between DHBs and limit information sharing across regions. Regional registers do not address the issue of losing patients to follow up with one local study reporting that 30% of the cohort were moving between regions or overseas.²⁶⁹ A RF surveillance sector review by local experts concluded there should be an online national RF register.²⁷⁰ A register and patient management system that collects comprehensive information could support patient check-ins and targeted information sharing, and the surveillance data could be linked with relevant epidemiological information about disease determinants.

- Evidence shows that registers help to improve adherence to secondary antibiotic prophylaxis.
 - In a local study, people on a register were more compliant than those just in the usual healthcare system (94% vs 37%).²⁷¹
 - Health systems with a register and follow-up (e.g. reminder system) have higher levels of adherences than those without a register.²⁷²
 - The ability to improve outcomes depends on the quality of the register, as demonstrated by Waikato DHB assessing their regional register and finding it did not provide an accurate record of patients currently in the region and/or on BPG injections.²⁷³
- Evidence shows that data on the number of RF cases may be more accurate from registers.

²⁶⁸ Oliver, J., Foster, T., Williamson, D.A., *et al.* (2018). Using preceding hospital admissions to identify children at risk of developing acute rheumatic fever. *Journal of Paediatrics and Child Health*, 54(5), 499-505. <https://doi.org/10.1111/jpc.13786>

²⁶⁹ Culliford-Semmens, N., Tilton, E., Webb, R., *et al.* (2017). Adequate adherence to benzathine penicillin secondary prophylaxis following the diagnosis of rheumatic heart disease by echocardiographic screening. *The New Zealand Medical Journal*, 130(1457), 50.

²⁷⁰ Oliver, J., Pierse, N. and Baker, M.G. (2014). Improving rheumatic fever surveillance in New Zealand: Results of a surveillance sector review. *BMC Public Health*, 14(1), 528. <https://doi.org/10.1186/1471-2458-14-528>

²⁷¹ Culliford-Semmens, N., Tilton, E., Webb, R., *et al.* (2017). Adequate adherence to benzathine penicillin secondary prophylaxis following the diagnosis of rheumatic heart disease by echocardiographic screening. *The New Zealand Medical Journal*, 130(1457), 50.

²⁷² Barker, H., Oetzel, J.G., Scott, N., *et al.* (2017). Enablers and barriers to secondary prophylaxis for rheumatic fever among Māori aged 14–21 in New Zealand: A framework method study. *International Journal for Equity in Health*, 16(1), 201. <https://doi.org/10.1186/s12939-017-0700-1>

²⁷³ McIlhone, K. (2019). *Evaluation of Waikato District Health Board rheumatic fever secondary prevention programme*. Waikato, New Zealand: Waikato District Health Board.

- The register for Auckland was found to be more accurate than notification and hospitalisation data. Hospitalisation data overcounted patients by including those that did not meet the case definition or who had a previous diagnosis of RF. The notification data undercounted patients due to notification information not being submitted or completed, though there were also notifications for some patients who do not meet the case definition. This has now been improved in Auckland. In contrast, the registry data was more accurate as clinicians were motivated to report RF cases to ensure they get the free prophylactic injections.²⁷⁴
- Overseas evidence indicates that registers have helped to improve outcomes for patients.
 - There is international evidence of their effectiveness in improving health outcomes.²⁷⁵
- Registers still have some limitations as a source of data.
 - Depending on how they are set up, registers may grossly underestimate those with RHD as it only covers those who are on prophylactic antibiotic injections every 28 days, and this is normally only given for around 10 years after diagnosis.

Table 10: Rheumatic fever registers across DHBs in Aotearoa New Zealand.

DHB	Has register?	Area covered	Approximate number of people on register	Comments
Northland				
Auckland	Yes	Joint register for ADHB and WDHB210	220	
Waitemata	Yes	Joint register for ADHB and WDHB210	210	Includes people who have completed treatment or have been lost to follow up, or moved out of the area
Counties Manukau DHB	Yes	CMDHB only	750	~2/3 are adolescents/adults
Waikato	Yes	Waikato only	340	Includes people who have completed treatment or have been lost to follow up
Bay of Plenty	Yes	BOP only	60	Register used for some studies, e.g. checking dental care access
Lakes				
Tairāwhiti				
Hawke's Bay	Yes	Hawke's Bay only	58	All are active cases
Capital & Coast				
Hutt Valley				

9.11 Improving adherence to prophylactic antibiotics

Stage of intervention: Preventing further RF episodes and development of RHD

As discussed in section 1, high adherence to this treatment is associated with reduced recurrence of RF.²⁷⁶ There is guidance on the administration of the BPG injection on the Ministry of Health website. A few studies have estimated the levels of adherence to monthly prophylactic BPG injections:

²⁷⁴ Lennon, D., Te Aro Moxon, P.A., Leversha, A., *et al.* (2017). Is a rheumatic fever register the best surveillance tool to evaluate rheumatic fever control in the Auckland region? *The New Zealand Medical Journal*, 130(1460), 48.

²⁷⁵ Hoque, D.M.E., Kumari, V., Hoque, M., *et al.* (2017). Impact of clinical registries on quality of patient care and clinical outcomes: A systematic review. *PLOS One*, 12(9), e0183667-e0183667. <https://doi.org/10.1371/journal.pone.0183667>

²⁷⁶ de Dassel, J.L., de Klerk, N., Carapetis, J.R., *et al.* (2018). How many doses make a difference? An analysis of secondary prevention of rheumatic fever and rheumatic heart disease. *Journal of the American Heart Association*, 7(24), e010223. <https://doi.org/10.1161/JAHA.118.010223>

- In Waikato, around half of patients were fully adherent over three months and the other half were partially adherent, missing one or more injections or being late on two or three.²⁷⁷ Outpatient clinic attendance rates for secondary prophylaxis were 55% for paediatric and 64% for adult patients in this region.²⁷⁸
- An audit of the 1998 and 2000 Auckland Rheumatic Fever Register data found compliance rates across the three Auckland DHBs ranging from 80% to 100% for individual community nursing offices.²⁷⁹
- Patients diagnosed after echocardiographic screening, rather than following a symptomatic episode of RF, had good adherence. The percentage of ‘days at risk’ (when a patient needed to have an injection) went from 0% in year one to 2.7% at year five. The median adherence for the total cohort over the entire follow-up period was 92%, ranging from 0% (non-compliant) to 100% (fully compliant).²⁸⁰
- A study found 14% of their RF cohort experienced progression, suggesting patients were not able to adhere fully to secondary prophylaxis.²⁸¹

Studies of lived experience (see section 7) highlighted some of the facilitators and barriers to adhering to monthly prophylaxis. Some interventions to address these issues and raise adherence have been tried:

- **Booking and attending appointments.** An incentive was tried where individuals aged 14–21 who had a prior history of RF were given a mobile phone and monthly “top-up” (for data/calls). This was to ensure nurses could reach patients to arrange their appointments. The intervention had a strong impact for partially adherent patients, particularly during the early periods following initiation of the intervention. However, the study had a high attrition rate which may limit long-term effectiveness of such an approach. The overall incremental cost-effectiveness was \$989 per extra successful injection although costs increased sharply toward the end of the intervention.²⁸²
- **Pain reduction.** Trials of using different techniques when giving injections have found evidence of ways to reduce pain, which can address that barrier to people receiving injections. A study in Turkey found that patients reported a significant reduction in pain when manual pressure was applied to the injection site before the injection was given.²⁸³ A local study in Counties Manukau found using a ‘Buzzy’ vibrating cold pack and adding the local anaesthetic lidocaine to the injected benzathine benzylpenicillin led to a significant reduction in pain scores and fear of the injections.²⁸⁴

Home visits by nurses to deliver prophylaxis have been highlighted as a way to support adherence for some patients, but some regions trying to implement nurse home visits to administer the injections have faced barriers in the number of doses funded via practitioner supply order. This could be simply remedied.

There is also a local trial of a longer acting, slow-release prophylaxis underway, which involves a local multi-stage clinical trial of subcutaneous infusion of BPG.²⁸⁵ Phase 1 has just been completed in Perth using healthy volunteers. If successful, this may offer a less painful treatment option.

²⁷⁷ Oetzel, J.G., Lao, C., Morley, M., et al. (2019). Efficacy of an incentive intervention on secondary prophylaxis for young people with rheumatic fever: A multiple baseline study. *BMC Public Health*, 19(1), 385. <https://doi.org/10.1186/s12889-019-6695-3>

²⁷⁸ McIlhone, K. (2019). *Evaluation of Waikato District Health Board rheumatic fever secondary prevention programme*. Waikato, New Zealand: Waikato District Health Board.

²⁷⁹ Grayson, S., Horsburgh, M. and Lennon, D. (2006). An Auckland regional audit of the nurse-led rheumatic fever secondary prophylaxis programme. *The New Zealand Medical Journal*, 119(1243), U2255.

²⁸⁰ Culliford-Semmens, N., Tilton, E., Webb, R., et al. (2017). Adequate adherence to benzathine penicillin secondary prophylaxis following the diagnosis of rheumatic heart disease by echocardiographic screening. *The New Zealand Medical Journal*, 130(1457), 50.

²⁸¹ Oliver, J., Robertson, O., Zhang, J., et al. (2021). Ethnically disparate disease progression and outcomes among acute rheumatic fever patients in New Zealand, 1989–2015. *Emerging Infectious Diseases*, 27(7), 1893-1902. <https://doi.org/10.3201/eid2707.203045>

²⁸² Oetzel, J.G., Lao, C., Morley, M., et al. (2019). Efficacy of an incentive intervention on secondary prophylaxis for young people with rheumatic fever: A multiple baseline study. *BMC Public Health*, 19(1), 385. <https://doi.org/10.1186/s12889-019-6695-3>

²⁸³ Derya, E.Y., Ukke, K., Taner, Y., et al. (2015). Applying manual pressure before benzathine penicillin injection for rheumatic fever prophylaxis reduces pain in children. *Pain Management Nursing*, 16(3), 328-335. <https://doi.org/10.1016/j.pmn.2014.08.013>

²⁸⁴ Russell, K., Nicholson, R. and Naidu, R. (2014). Reducing the pain of intramuscular benzathine penicillin injections in the rheumatic fever population of Counties Manukau District Health Board. *Journal of Paediatrics and Child Health*, 50(2), 112-117. <https://doi.org/10.1111/jpc.12400>

²⁸⁵ Bennett, J. (2021). Personal communication.

The effectiveness of secondary prophylaxis programmes is not monitored. The information collected about secondary prophylaxis and its delivery should be standardised.²⁸⁶

9.12 Less stringent diagnostic criteria

Stage of intervention: Preventing further RF episodes and development of RHD

To avoid underdiagnosis of RF, the Jones criteria for diagnosing RF were revised to allow for less stringent findings in high-risk groups while maintaining stringency in low-risk groups.²⁸⁷ Overseas studies found that this improves diagnosis, with one study finding that it prevented underdiagnosis in 18% of children.²⁸⁸

An assessment of how the revised criteria has prevented underdiagnosis of RF in Aotearoa New Zealand has not been undertaken and is a complex issue – there is no gold standard diagnostic test.

A particular issue is that the cut off levels required to diagnose a recent GAS infection through serology are high in Aotearoa New Zealand which may result in cases of RF being missed – as shown by 18% more cases being defined as definite RF cases in a study that used Australian serology criteria instead of Aotearoa New Zealand's.²⁸⁹ These studies require nuanced interpretation including review of how the patients were classified and managed by clinicians.

9.13 Treatments to reduce severity of heart damage

Stage of intervention: Minimising complications of RHD

A study of two patients suggested that hydroxychloroquine suppresses some of the immune dysregulation that occurs during an episode of RF.²⁹⁰ Further studies are underway to determine whether this treatment can prevent development of RHD.

9.14 Active case finding

Stage of intervention: Minimising complications of RHD

The high proportion of patients admitted to hospital with RHD without prior RF hospitalisation in Aotearoa New Zealand (see section 4) has led to a proposal to use medical imaging of the heart (echocardiography) as a screening process to actively find cases. This has potential to locate people with unrecognised RHD who may benefit from antibiotic prophylaxis.²⁹¹ There are portable echocardiographic systems that enable a screening approach outside the hospital.

However, such an approach is not a silver bullet and a broad approach to active case finding in Aotearoa New Zealand would require infrastructure, resourcing and capacity beyond what is currently available. Some hesitate to support this approach as a study has found that it can lead to anxiety and reduction in physical

²⁸⁶ Oliver, J., Pierse, N. and Baker, M.G. (2014). Improving rheumatic fever surveillance in New Zealand: Results of a surveillance sector review. *BMC Public Health*, 14(1), 528. <https://doi.org/10.1186/1471-2458-14-528>

²⁸⁷ Bennett, J., Rentta, N.N., Leung, W., et al. (2021). Early diagnosis of acute rheumatic fever and rheumatic heart disease as part of a secondary prevention strategy: Narrative review. *Journal of Paediatrics and Child Health*. <https://doi.org/10.1111/jpc.15664>

²⁸⁸ Beaton, A. and Carapetis, J. (2015). The 2015 revision of the Jones criteria for the diagnosis of acute rheumatic fever: Implications for practice in low-income and middle-income countries. *Heart Asia*, 7(2), 7-11. <https://doi.org/10.1161/CIR.0000000000000205> Güler, M., Laloğlu, F., Olgun, H., et al. (2019). Clinical characteristics of pediatric patients with first-attack acute rheumatic fever following the updated guideline. *Turkish Archives of Pediatrics*, 54(4), 220. <https://doi.org/10.14744/TurkPediatriArs.2019.69376>

²⁸⁹ Jack, S., Moreland, N.J., Meagher, J., et al. (2019). Streptococcal serology in acute rheumatic fever patients: Findings from 2 high-income, high-burden settings. *The Pediatric Infectious Disease Journal*, 38(1), e1-e6. <https://doi.org/10.1097/INF.0000000000002190>

²⁹⁰ Wilson, N.J., Concannon, A., Malcolm, J., et al. (2020). The treatment of acute rheumatic fever: Novel use of hydroxychloroquine. *The Pediatric Infectious Disease Journal*, 39(7). <https://doi.org/10.1097/INF.0000000000002647>; Kim, M.L., Martin, W.J., Minigo, G., et al. (2018). Dysregulated IL-1 β -GM-CSF axis in acute rheumatic fever that is limited by hydroxychloroquine. *Circulation*, 138(23), 2648-2661. <https://doi.org/10.1161/CIRCULATIONAHA.118.033891>

²⁹¹ Webb, R. (2020). *Rheumatic heart disease in New Zealand children: Echocardiographic disease burden and clinical outcomes*. ResearchSpace@Auckland, Auckland, New Zealand. Retrieved from <https://onlinelibrary.wiley.com/doi/10.1111/j.1440-1754.2011.02218.x>

activity among those who received an ‘abnormal’ screening result.²⁹² The Ministry of Health have told us that they considered a pilot for antenatal RHD screening but for women with no history of RHD and no symptoms, it did not meet their criteria.

Further research is needed to determine how active case finding and initiation of antibiotic prophylaxis for people detected through screening impacts RHD outcomes.²⁹³ A randomised controlled trial in Northern Uganda aims to determine whether secondary prophylaxis improves outcomes for people with latent RHD, and therefore whether screening for RHD could improve outcomes for those who have RHD detected.²⁹⁴ The final results are not yet published, but early evidence shared through personal communications with New Zealand researchers suggests that the preventative treatment does slow disease progression for people with mild or latent RHD.²⁹⁵ If confirmed, this finding will provide motivation to take this approach, and prior research would indicate efforts to improve health literacy and provide holistic support to those who have an abnormal result would be needed as part of such a service.

An alternative strategy would be to target high-risk populations such as co-habiting whānau of those with RF or children who are hospitalised frequently. Research suggests there is positive support for such active case finding in high-risk populations.²⁹⁶ A local study found that RHD prevalence was significantly greater in siblings and parents/caregivers of cases with RF than in comparable background populations. This suggests that targeted echocardiographic case-finding among immediate family may be a good way to find unrecognised latent RHD²⁹⁷ if the system were resourced sufficiently to deal with an influx of asymptomatic cases.

This suggests that targeted echocardiographic case-finding among immediate family may be a good way to find unrecognised latent RHD.

A study in Brazil compared different strategies for screening for RHD. The researchers found that in the Brazilian setting, the highest coverage rates were achieved in primary care centres rather than schools.²⁹⁸ A similar study may be worthwhile to inform approaches in Aotearoa New Zealand.

Any consideration of screening / case finding needs to include a careful consideration on whether it meets the screening criteria as set out by the National Screening Advisory Committee.

²⁹² Gurney, J., Chong, A., Culliford-Semmens, N., *et al.* (2016). The benefits and harms of rheumatic heart disease screening from the perspective of the screened population. *International Journal of Cardiology*, 221, 734-740. <https://doi.org/https://doi.org/10.1016/j.ijcard.2016.07.025>

²⁹³ Bennett, J., Rentta, N.N., Leung, W., *et al.* (2021). Early diagnosis of acute rheumatic fever and rheumatic heart disease as part of a secondary prevention strategy: Narrative review. *Journal of Paediatrics and Child Health*. <https://doi.org/10.1111/jpc.15664>

²⁹⁴ Beaton, A., Okello, E., Engelman, D., *et al.* (2019). Determining the impact of benzathine penicillin G prophylaxis in children with latent rheumatic heart disease (GOAL trial): Study protocol for a randomized controlled trial. *American Heart Journal*, 215, 95-105. <https://doi.org/10.1016/j.ahj.2019.06.001>

²⁹⁵ Bennett, J., Rentta, N.N., Leung, W., *et al.* (2021). Early diagnosis of acute rheumatic fever and rheumatic heart disease as part of a secondary prevention strategy: Narrative review. *Journal of Paediatrics and Child Health*. <https://doi.org/10.1111/jpc.15664>

²⁹⁶ Perelini, F., Blair, N., Wilson, N., *et al.* (2015). Family acceptability of school-based echocardiographic screening for rheumatic heart disease in a high-risk population in New Zealand. *Journal of Paediatrics and Child Health*, 51(7), 682-688. <https://doi.org/10.1111/jpc.12829>

²⁹⁷ Culliford-Semmens, N., Tilton, E., Wilson, N., *et al.* (2021). Echocardiography for latent rheumatic heart disease in first degree relatives of children with acute rheumatic fever: Implications for active case finding in family members. *EClinicalMedicine*, 100935. <https://doi.org/10.1016/j.eclinm.2021.100935>; we were also provided with a copy of P Murray’s dissertation on this topic.

²⁹⁸ Nascimento, B.R., Sable, C., Nunes, M.C.P., *et al.* (2018). Comparison between different strategies of rheumatic heart disease echocardiographic screening in Brazil: Data from the PROVAR (rheumatic valve disease screening program) study. *Journal of the American Heart Association*, 7(4). <https://doi.org/10.1161/JAHA.117.008039>

10 Future developments that could significantly reduce the rates of rheumatic fever

10.1 A GAS vaccine is a top priority to prevent high rates of rheumatic fever

Preventing infection with GAS through vaccination could make a significant difference to the rates of infection and subsequent complications of RF and RHD. A vaccine that prevents 80% of GAS disease for a duration of ten years would reduce the number of healthcare episodes in the infant and child cohorts by between 16% and 29%, and the cost and health burden by between 30% and 42%.²⁹⁹ It could also contribute to a significant reduction in antibiotic use, by reducing antibiotics used to treat GAS and prevent recurrent RF, which would have positive implications for AMR. Modelling in Australia has shown that vaccine that prevents GAS skin and throat infections would be commercially viable and have cost-effectiveness in line with other recently licensed and funded vaccines in Australia.³⁰⁰

There is currently not an approved vaccine for GAS but there is a focus on it, with dedicated funding and various workstreams previously and/or currently underway in Aotearoa New Zealand and internationally.

- Researchers from Aotearoa New Zealand and Australia formed the ‘Coalition to Advance New Vaccines for Group A *Streptococcus* (CANVAS)’ that was jointly funded by HRC/NHMRC (\$1.6 million each) from 2014–2017 with the goal of developing tools to accelerate GAS vaccine development.³⁰¹
 - A repository of GAS strains that represents global disease including strains from Aotearoa New Zealand.³⁰²
 - Qualified assays to test the efficacy of GAS vaccines in the laboratory.³⁰³
 - Cost of illness and economic models of GAS disease and vaccine value³⁰⁴ as well as a clinical development plan for GAS vaccines.³⁰⁵
- Significant funding has recently been dedicated to the efforts of developing a GAS vaccine internationally.
 - In 2021 it was announced that GSK, based in Siena, Italy, will receive up to \$8.2 million from CARB-X (a non-profit partnership focused on supporting antibacterial research) to develop a GAS vaccine, with an additional \$4.2 million if the project meets certain milestones.³⁰⁶
 - Following CANVAS, there has been significant investment in Australia to accelerate the development of a GAS vaccine, with \$35 million of funding from the Australian Government

²⁹⁹ Bennett, J. (2021). Personal communication.

³⁰⁰ Cannon, J.W., Jack, S., Wu, Y., *et al.* (2018). An economic case for a vaccine to prevent group A *Streptococcus* skin infections. *Vaccine*, 36(46), 6968–6978. <https://doi.org/10.1016/j.vaccine.2018.10.001>

³⁰¹ Moreland, N.J., Waddington, C.S., Williamson, D.A., *et al.* (2014). Working towards a group A streptococcal vaccine: Report of a collaborative Trans-Tasman workshop. *Vaccine*, 32(30), 3713–3720. <https://doi.org/10.1016/j.vaccine.2014.05.017>

³⁰² Williamson, D.A., Smeesters, P.R., Steer, A.C., *et al.* (2016). Comparative M-protein analysis of *Streptococcus pyogenes* from pharyngitis and skin infections in New Zealand: Implications for vaccine development. *BMC Infectious Diseases*, 16(1), 561.

³⁰³ Davies, M.R., McIntyre, L., Mutreja, A., *et al.* (2019). Atlas of group A streptococcal vaccine candidates compiled using large-scale comparative genomics. *Nature Genetics*, 51(6), 1035–1043. <https://doi.org/10.1038/s41588-019-0417-8>

³⁰⁴ Jones, S., Moreland, N.J., Zancolli, M., *et al.* (2018). Development of an opsonophagocytic killing assay for group A *Streptococcus*.

Vaccine, 36(26), 3756–3763. <https://doi.org/10.1016/j.vaccine.2018.05.056> McGregor, R., Jones, S., Jeremy, R.M., *et al.* (2020). An opsonophagocytic killing assay for the evaluation of group A *Streptococcus* vaccine antisera. In Proft and Loh (Eds.), *Group A Streptococcus: Methods and Protocols* (pp. 323–335). New York, NY: Springer US.

³⁰⁵ Cannon, J.W., Jack, S., Wu, Y., *et al.* (2018). An economic case for a vaccine to prevent group A *Streptococcus* skin infections. *Vaccine*, 36(46), 6968–6978. <https://doi.org/10.1016/j.vaccine.2018.10.001>; Cannon, J.W., Zhung, J., Bennett, J., *et al.* (2021). The economic and health burdens of diseases caused by group A *Streptococcus* in New Zealand. *International Journal of Infectious Diseases*, 103, 176–181. <https://doi.org/10.1016/j.ijid.2020.11.193>

³⁰⁶ Schödel, F., Moreland, N.J., Wittes, J.T., *et al.* (2017). Clinical development strategy for a candidate group A streptococcal vaccine. *Vaccine*, 35(16), 2007–2014. <https://doi.org/10.1016/j.vaccine.2017.02.060>

³⁰⁷ CARB-X. (2021). CARB-X is funding GSK to support the development of two unique vaccine projects that aim to prevent serious bacterial infections killing thousands worldwide each year. Retrieved 28 July 2021, from <https://carb-x.org/carb-x-news/carb-x-is-funding-gsk-to-support-the-development-of-two-unique-vaccine-projects-that-aim-to-prevent-serious-bacterial-infections-killing-thousands-worldwide-each-year/>

and other grants, such as \$5.3 million from global philanthropic Open Philanthropy.³⁰⁷ The development is being led by the Australian Strep A Vaccine Initiative.³⁰⁸

- Methods for trialling vaccines and development of specific vaccines are underway.
 - Researchers in Australia have developed a way to test GAS vaccines in a controlled human model because animal models and other methods have limitations for studying GAS.³⁰⁹
 - Several vaccines are under development globally including those based in the GAS M protein, or combinations of conserved GAS antigens.³¹⁰ Researchers from Aotearoa New Zealand have generated a multivalent vaccine called TeeVax1, a recombinant protein that consists of a fusion of six T-antigen domains, which produces antibodies in an animal model.³¹¹

While a vaccine is highly necessary, addressing the risk factors within the wider complex determinants of health is still important for other health outcomes.

10.2 Diagnostic tool for rheumatic fever

A challenge with RF is that there is no specific diagnostic tool or accurate lab test. Instead, it relies on clinical judgement and prior evidence of GAS infection, which can lead to misdiagnoses and missed diagnoses.³¹² The dramatic fall in RF in non-Māori/non-Pacific populations in Aotearoa New Zealand (and other non-Indigenous populations overseas) has meant few physicians have seen a case of RF, making successful diagnosis even more difficult.³¹³

Improving diagnostics for RF has been the focus of recent research by Aotearoa New Zealand and Australian researchers (the START study) and promising work is in development.³¹⁴ The main areas of focus are:

- **Improving serology.** Researchers in Aotearoa New Zealand are developing immunoassays that detect GAS antibodies and improve upon the currently available tests.³¹⁵ They developed a bead-based assay that quantified the same two antibodies that the existing test does, along with a new third antibody. Validation tests found that it was accurate and reproducible and correlated well with existing technology but had the benefit of being more efficient and able to be performed high-throughput.
- **Identifying a unique biomarker.** There have been a number of studies attempting to identify biomarkers that could be utilised as a clinical biomarker for RF, with candidates including periostin, Tenascin-C, Interferon γ -induced protein 10, and IgG3 and C4 immunoglobulin and complement factors.³¹⁶ These studies have demonstrated promising sensitivity and specificity, and well as

³⁰⁷ Telethon Kids Institute. (2021, 10 March 2021). Global organisation backs Strep A vaccine. Retrieved 28 July 2021, from <https://www.telethonkids.org.au/news--events/news-and-events-nav/2021/march/global-organisation-backs-strep-a-vaccine/>

³⁰⁸ ASAVI. (2021). The Australian Strep A Vaccine Initiative. Retrieved 28 July 2021, from <https://asavi.telethonkids.org.au/>

³⁰⁹ Osowicki, J., Azzopardi, K.L., Fabri, L., et al. (2021). A controlled human infection model of *Streptococcus pyogenes* pharyngitis (CHIVAS-M75): An observational, dose-finding study. *The Lancet Microbe*, 2(7), e291-e299. [https://doi.org/10.1016/S2666-5247\(20\)30240-8](https://doi.org/10.1016/S2666-5247(20)30240-8)

³¹⁰ Moreland, N.J., Waddington, C.S., Williamson, D.A., et al. (2014). Working towards a group A streptococcal vaccine: Report of a collaborative Trans-Tasman workshop. *Vaccine*, 32(30), 3713-3720. <https://doi.org/10.1016/j.vaccine.2014.05.017>

³¹¹ Loh, J.M.S., Rivera-Hernandez, T., McGregor, R., et al. (2021). A multivalent T-antigen-based vaccine for group A *Streptococcus*. *Scientific Reports*, 11(1), 4353. <https://doi.org/10.1038/s41598-021-83673-4>

³¹² Bennett, J., Rentta, N.N., Leung, W., et al. (2021). Early diagnosis of acute rheumatic fever and rheumatic heart disease as part of a secondary prevention strategy: Narrative review. *Journal of Paediatrics and Child Health*. <https://doi.org/10.1111/jpc.15664>

³¹³ Steer, A.C. (2015). Historical aspects of rheumatic fever. *Journal of Paediatrics and Child Health*, 51(1), 21-27.

<https://doi.org/10.1111/jpc.12808> Vekemans, J., Gouvea-Reis, F., Kim, J.H., et al. (2019). The Path to Group A Streptococcus Vaccines: World Health Organization Research and Development Technology Roadmap and Preferred Product Characteristics. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*, 69(5), 877-883. <https://doi.org/10.1093/cid/ciy1143>

³¹⁴ Ralph, A.P., Webb, R., Moreland, N.J., et al. (2021). Searching for a technology-driven acute rheumatic fever test: The START study protocol. *BMJ Open*, 11(9), e053720. <https://doi.org/10.1136/bmjopen-2021-053720>

³¹⁵ Whitcombe, A.L., Hanson-Manful, P., Jack, S., et al. (2020). Development and evaluation of a new triplex immunoassay that detects group A *Streptococcus* antibodies for the diagnosis of rheumatic fever. *Journal of Clinical Microbiology*, 58(9). <https://doi.org/10.1128/JCM.00300-20>

³¹⁶ Epeçcan, S. and Yücel, E. (2020). Serum periostin levels in acute rheumatic fever: Is it useful as a new biomarker? *Paediatrics and International Child Health*, 40(2), 111-116. <https://doi.org/10.1080/20469047.2019.1682330>; Karatas, Z., Baysal, T., Alp, H., et al. (2013). Serum tenascin-C: A novel biomarker for diagnosis and predicting prognosis of rheumatic carditis? *Journal of Tropical Pediatrics*, 59(6), 476-482. <https://doi.org/10.1093/tropej/fmt058>; Kim, M.L., Martin, W.J., Minigo, G., et al. (2018). Dysregulated IL-1 β -GM-CSF axis in acute rheumatic fever that is limited by hydroxychloroquine. *Circulation*, 138(23), 2648-2661. <https://doi.org/10.1161/CIRCULATIONAHA.118.033891>; Chung, A.W., Ho, T.K., Hanson-Manful, P., et al. (2020). Systems immunology

demonstrating that using a combination of two markers, as shown for IgG3 and C4, may be beneficial. Further work is needed to determine whether effectiveness in a clinical setting.

10.3 Drug development and BPG reformulation for RF/RHD prevention

Pacific-led research work is currently underway in Aotearoa New Zealand contributing to global efforts to develop new formulations that are less painful and longer lasting for effective RF/RHD prevention. Initial work sought to identify the BPG reformulation preferences of children and youth currently receiving BPG injections, and also of their family members and health professionals who deliver the BPG injections.³¹⁷ This was to ensure acceptability for those who will use a new formulation and develop a new penicillin that encourages strong adherence by understanding the experiences and exploring the reformulation preferences of those currently receiving BPG injections.

In addition, research work was initiated in Aotearoa New Zealand to explore the pharmacokinetics of BPG in mainly Pacific and Māori children and young people with previous RF who are receiving BPG injections. This local pharmacokinetics study is in progress and is the first study of its kind in Aotearoa New Zealand.³¹⁸ Similar work in Australia explored the pharmacokinetics of BPG within an Indigenous Aboriginal population cohort and found that BMI characteristics were an important consideration for BPG injections for RF/RHD prevention.³¹⁹ This was needed as limited literature was available on the pharmacokinetic characteristics of BPG when utilised for RF/RHD prevention. Early studies exploring the pharmacokinetics of intramuscular BPG administration had been conducted in healthy, young, fit, white male military recruits, none of whom had RF or RHD.³²⁰

Research work in Aotearoa New Zealand has also been initiated to begin exploring the generation of different antibiotics better suited for RF/RHD prevention and to identify and generate the most appropriate penicillin G containing candidates for further drug development. This is the first study in Aotearoa New Zealand seeking to develop drug candidates for secondary prophylaxis for RF/RHD. It has important relevance to the evaluation of drug delivery and exploration of novel formulations of BPG with drug release periods beyond those currently available.

Efforts to support appropriate and respectful community engagement, inclusivity, involvement and communication as part of the BPG drug development research efforts in Aotearoa New Zealand and the Pacific region, have included Talanoa (discussions) and Fono (gatherings) with Pacific and Māori communities in Aotearoa New Zealand education efforts involving students in addition to consultation with health leaders and researchers in the Pacific region over the past years.³²¹

reveals a linked IgG3–C4 response in patients with acute rheumatic fever. *Immunology and Cell Biology*, 98(1), 12-21. <https://doi.org/10.1111/imcb.12298>

³¹⁷ Sika-Paotonu, D., Tiatia, R., Sung, Y.K., et al. (2017). The Benzathine Penicillin G (BPG) reformulation preferences study - towards a new Penicillin for Rheumatic Fever and Rheumatic Heart Disease. *The Journal of Immunology*, 198(1 Supplement), 213.212. ; Sika-Paotonu, D., Tiatia, R., Sung, Y.K., et al. (2018). The Benzathine Penicillin G (BPG) reformulation preferences study – the importance of cultural awareness and appropriate governance concerning Rheumatic Fever related research in New Zealand. *The Journal of Immunology*, 200(1 Supplement), 120.139. ; Sika-Paotonu, D., Tiatia, R., Sung, Y.K., et al. (2018). The Benzathine Penicillin G (BPG) reformulation preferences study-edging closer towards a new Penicillin for Rheumatic Fever and Rheumatic Heart Disease. *The Journal of Immunology*, 200(1 Supplement), 120.135.

³¹⁸ Sika-Paotonu, D., Tiatia, R., Thornley, C., et al. (2018). Understanding protective plasma levels of penicillin and monitoring antibody responses for the prevention of GAS infection in a paediatric population in New Zealand. *The Journal of Immunology*, 200(1 Supplement), 45.46.

³¹⁹ Hand, R.M., Salman, S., Newall, N., et al. (2019). A population pharmacokinetic study of benzathine benzylpenicillin G administration in children and adolescents with rheumatic heart disease: new insights for improved secondary prophylaxis strategies. *Journal of Antimicrobial Chemotherapy*, 74(7), 1984-1991. <https://doi.org/10.1093/jac/dkz076>; Sika-Paotonu, D., Marsh, J., Gray, K., et al. (2016). Understanding protective plasma levels of penicillin and monitoring antibody responses for the prevention of GAS infection in a paediatric population Paper presented at the International Congress of Immunology, Melbourne, Australia.

³²⁰ Broderick, M.P., Hansen, C.J., Russell, K.L., et al. (2011). Serum penicillin G levels are lower than expected in adults within two weeks of administration of 1.2 million units. *PLOS ONE*, 6(10), e25308. <https://doi.org/10.1371/journal.pone.0025308>; Davis, J. and Schmidt, W.C. (1957). Benzathine Penicillin G: Its effectiveness in the prevention of streptococcal infections in a heavily exposed population. *New England Journal of Medicine*, 256(8), 339-342. <https://doi.org/10.1056/NEJM195702212560803>

³²¹ Sika-Paotonu, D. (2019). STEM knowledge translational outreach efforts – connecting with Immunology in the classroom for Pacific Intermediate students. *The Journal of Immunology*, 202(1 Supplement), 61.18. ; Sika-Paotonu, D. (2021). A novel approach towards drug

11 Further research to fill knowledge gaps and develop new tools is crucial

Despite the significant amount of research that has been undertaken relating to RF over the past century, there is still further research required to better understand the emerging evidence about disease risk and transmission.

- The possible association of GAS skin infections in development of RF needs further study, with a view to establishing whether antibiotic treatment of skin infections in high-risk groups can prevent subsequent RF.
- Association of RF with eczema and whether eczema bleach baths may play a preventative role.
- There is limited understanding around the specific role of within household transmission of GAS, and whether interventions targeted at this (such as swabbing household members, administering of antibiotics (as is done for meningitis) and use of contact tracing) may be effective. The role of genomics in tracing transmission pathways should also be explored further.
- Carriage rates for GAS are not well understood and we need better diagnostics to improve this.
- Further study to understand the true prevalence of RHD is important for interventions, particularly for some high-risk populations such as pregnant women.
- A greater body of research about lived experiences with a strong social science lens may result in more strengths-based findings to inform new approaches.
- Indigenous-led research is needed to critique current Western approaches and provide more culturally responsive and safe interventions.
- Research is needed to understand how to intervene to reduce the risk associated with family history of RF without stigmatising whānau.
- A better understanding of the outcomes from different heart repair methods, including how surgeons choose their approach and what's happening on a national level in Aotearoa New Zealand, are needed.

Research into RF and RHD waned following reduced incidence of the disease in high-income countries after the 1960s but there has been a resurgence in interest more recently with increased recognition and understanding of the true burden of disease.³²² Locally, new funding for research has been announced by the HRC and Cure Kids.³²³

design. *The Journal of Immunology*, 206(1 Supplement), 95.16. ; Sika-Paotonu, D., Anderson, J., Cashin, P., et al. (2019). An immunological basis for improving interest and participation of underrepresented student groups in high school science classes. *The Journal of Immunology*, 202(1 Supplement), 61.16. ; Sika-Paotonu, D., Anitelea, T., Uiese, T., et al. (2019). Engaging with Pacific Communities to support effective dialogue, appropriate outreach and scientific knowledge translation activity. *The Journal of Immunology*, 202(1 Supplement), 61.14. ; Sika-Paotonu, D., Chandra, P., De Silva, H., et al. (2020). Appropriate contextualisation of immunology based STEM and health teaching for undergraduate medical sciences education. *The Journal of Immunology*, 204(1 Supplement), 222.232. ; Sika-Paotonu, D. and Laban, L.W. (2018). Knowledge translation for cancer immunotherapy and immunology that is culturally appropriate and relevant within a Pacific context. *The Journal of Immunology*, 200(1 Supplement), 113.119. ; Sika-Paotonu, D., Laing, B., Anitelea, T., et al. (2019). Supporting scientific knowledge communication and translation efforts by engaging appropriately with the Pacific audience. *The Journal of Immunology*, 202(1 Supplement), 61.11. ; Sika-Paotonu, D., Tiatia, R., Sung, Y.K., et al. (2017). The Benzathine Penicillin G (BPG) reformulation preferences study - towards a new Penicillin for Rheumatic Fever and Rheumatic Heart Disease. *The Journal of Immunology*, 198(1 Supplement), 213.212. ; Sika-Paotonu, D., Aho, G., 'Ulufonua, L.K., et al. (2018). The Benzathine Penicillin G (BPG) Reformulation Preferences Study - Tonga. *The Journal of Immunology*, 200(1 Supplement), 45.43. ; Sika-Paotonu, D., Tiatia, R., Sung, Y.K., et al. (2018). The Benzathine Penicillin G (BPG) reformulation preferences study-edging closer towards a new Penicillin for Rheumatic Fever and Rheumatic Heart Disease. *The Journal of Immunology*, 200(1 Supplement), 120.135. ; Sika-Paotonu, D., Viali, S.i., Naseri, L.T.T.K., et al. (2018). The Benzathine Penicillin G (BPG) Reformulation Preferences Study - Samoa. *The Journal of Immunology*, 200(1 Supplement), 45.45.

³²² Karthikeyan, G. and Guilherme, L. (2018). Acute rheumatic fever. *The Lancet*, 392(10142), 161-174. [https://doi.org/10.1016/S0140-6736\(18\)30999-1](https://doi.org/10.1016/S0140-6736(18)30999-1)

³²³ <https://www.scoop.co.nz/stories/GE2012/S00031/rheumatic-heart-disease-patients-among-those-to-benefit-from-new-research-funding-for-dhbs.htm>; <https://curekids.org.nz/news/spike-in-rheumatic-fever/>

12 Considerations relating to AMR

Antibiotic use to treat GAS throat infections and to prevent RF is likely to be a significant driver of AMR. While this use is crucial in high-risk populations, it is also contributing to the overall use of antibiotics and any use of antibiotics contributes to the development of AMR. AMR will also be driven by use of antibiotics to treat non-GAS throat infections (e.g. viral infections) and for GAS sore throat infections in individuals at low risk of RF. A balance needs to be struck to ensure appropriate use and discourage inappropriate use. An additional motivation to prevent GAS throat infections is to equitably reduce overall use of antibiotics.

A study that looked at antibiotic dispensing in Aotearoa New Zealand found higher rates of penicillins dispensed for Māori and Pacific peoples aged 5–20, likely reflecting prescriptions for GAS throat infections to prevent RF. However, the same study found higher rates of penicillin dispensing for people aged 5–20 of other ethnicities than would be expected given this group is essentially at no risk of RF, suggesting a proportion of prescribing to prevent RF is inappropriate.³²⁴ This raises questions as to who bears the AMR burden of overuse – unnecessary broad spectrum antibiotic use runs the risk of further widening the equity gap.

The threat of AMR will be discussed more broadly in the full report from our office due later this year. However, it is important to highlight how the context of a high burden of RF in Aotearoa New Zealand may be contributing to this slow-burning pandemic.

The bacteria that cause GAS infections, *S. pyogenes*, is not a top priority in terms of microbes that are developing drug resistance. So far there is limited evidence of resistant GAS strains emerging. Despite nearly 80 years of penicillin use to treat GAS, penicillin resistance for GAS is rare. Specific studies have found:

- Aotearoa New Zealand data shows:³²⁵
 - 300/7893 (3.8%) erythromycin resistant and zero resistant to penicillin (2015)
 - 316/8109 (3.9%) erythromycin resistant and zero resistant to penicillin (2014)
 - 211/8127 (2.6%) erythromycin resistant and zero resistant to penicillin (2013)
 - The absence of data beyond 2015 is a concern.
- Evidence overseas
 - In an Egyptian study, penicillin-macrolide-resistant *S. pyogenes* was detected among household pets (dogs and cats).³²⁶ (Macrolides include erythromycin and clarithromycin.)
 - Emergence of macrolide-resistant *S. pyogenes* in a range of places, such as Taiwan³²⁷ and Iceland.³²⁸
 - Emergence of *S. pyogenes* isolates with resistance to β -lactam antibiotics or reduced susceptibility to penicillin in China.³²⁹
 - Strains with erythromycin, clarithromycin and ciprofloxacin resistance in Germany.³³⁰
 - Erythromycin resistance in Tunisia.³³¹

³²⁴ Whyler, N., Tomlin, A., Tilyard, M., *et al.* (2018). Ethnic disparities in community antibacterial dispensing in New Zealand, 2015. *The New Zealand Medical Journal*, 131(1480), 50-60.

³²⁵ Institute of Environmental Science and Research Limited (ESR). (2015). *Antimicrobial resistance data from hospital and community laboratories, 2015*. Porirua, New Zealand: Institute of Environmental Science and Research Limited (ESR). Retrieved from https://surv.esr.cri.nz/PDF_surveillance/Antimicrobial/AR/National_AR_2015.pdf

³²⁶ Samir, A., Abdel-Moein, K.A. and Zaher, H.M. (2020). Emergence of penicillin-macrolide-resistant *Streptococcus pyogenes* among pet animals: An ongoing public health threat. *Comparative Immunology, Microbiology and Infectious Diseases*, 68, 101390. <https://doi.org/10.1016/j.cimid.2019.101390>

³²⁷ Tsai, W.-C., Shen, C.-F., Lin, Y.-L., *et al.* (2020). Emergence of macrolide-resistant *Streptococcus pyogenes* emm12 in southern Taiwan from 2000 to 2019. *Journal of Microbiology, Immunology and Infection*. <https://doi.org/10.1016/j.jmii.2020.08.019>

³²⁸ Southon, S.B., Beres, S.B., Kachroo, P., *et al.* (2020). Population genomic molecular epidemiological study of macrolide-resistant *Streptococcus pyogenes* in Iceland, 1995 to 2016: Identification of a large clonal population with a pbp2x mutation conferring reduced in vitro β -lactam susceptibility. *Journal of Clinical Microbiology*, 58(9), e00638-00620. <https://doi.org/10.1128/JCM.00638-20>

³²⁹ Yu, D., Zheng, Y. and Yang, Y. (2020). Is there emergence of β -lactam antibiotic-resistant *Streptococcus pyogenes* in China? *Infection and Drug Resistance*, 13, 2323-2327. <https://doi.org/10.2147/IDR.S261975>

³³⁰ Arvand, M., Hoeck, M., Hahn, H., *et al.* (2000). Antimicrobial resistance in *Streptococcus pyogenes* isolates in Berlin. *Journal of Antimicrobial Chemotherapy*, 46(4), 621-624. <https://doi.org/10.1093/jac/46.4.621>

³³¹ Ksia, S., Smaoui, H., Hraoui, M., *et al.* (2017). Molecular characteristics of erythromycin-resistant *Streptococcus pyogenes* strains isolated from children patients in Tunis, Tunisia. *Microbial Drug Resistance*, 23(5), 633-639. <https://doi.org/10.1089/mdr.2016.0129>

However, it is not only resistance in GAS bacteria that we need to be concerned about. The widespread use of antibiotics to treat and prevent GAS throat infections may contribute to resistance in other microbes. There is some emerging evidence that resistance in other microbes may contribute to cases where penicillin fails to treat a GAS pharyngeal infection.³³² This mechanism is called co-pathogenicity: other microbes in the throat produce β -lactamase enzymes, which then inactivate the penicillin before it is able to kill the GAS bacteria.

Penicillin, which was traditionally used as the treatment for GAS throat infections, is fairly narrow spectrum. Alternatives that are used to improve antibiotic adherence (e.g. once daily amoxicillin) or for patients with penicillin intolerance (e.g. cephalexin or macrolides) are broader spectrum and/or used for other significant infections. The use of these broader spectrum antibiotics may contribute to AMR by exposing other bugs to these drugs, but this is not currently monitored. BPG is considered a lower risk for developing AMR.

In order to understand the contribution of antibiotic use related to RF to the issue of AMR we need a better understanding of the rates of penicillin versus amoxicillin as first-line treatment, the former being narrower spectrum and less likely to drive resistance. Addition of indication on all antibiotic prescriptions would make this easier. We also need to understand what proportion of patients end up on a second-line agent due to penicillin intolerance as there are concerns around mislabelling for penicillin allergy which may drive greater use of broad-spectrum antibiotics.³³³ There is local/regional work being done in various DHBs to actively manage the 'allergy' alerts, e.g. in CCDHB they are reviewing and downgrading unnecessary penicillin allergy alerts for everyone who is admitted to hospital.

³³² Pichichero, M.E. and Casey, J.R. (2007). Systematic review of factors contributing to penicillin treatment failure in *Streptococcus pyogenes* pharyngitis. *Otolaryngology - Head and Neck Surgery*, 137(6), 851-857.e853. <https://doi.org/10.1016/j.otohns.2007.07.033>

³³³ Lteif, L. and Eiland, L.S. (2019). The basics of penicillin allergy: What a clinician should know. *Pharmacy*, 7(3). <https://doi.org/10.3390/pharmacy7030094>

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