



Snapshot of **Strep A**, **ARF** and **RHD** Research Activities in Australia

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Approximately 10,000 people have had acute rheumatic fever (ARF) and rheumatic heart disease (RHD) in Australia. Nine out of every ten people with ARF and RHD are Aboriginal and/or Torres Strait Islander people – with profound effects on health, community and culture. This disproportionate burden of disease is a consequence of colonisation, racism and social determinants of health. RHD is preventable.

Australia has committed to ending RHD by 2031 in the Long-Term National Health Plan and the National Aboriginal and Torres Strait Islander Health Plan. Aboriginal and Torres Strait Islander people and organisations are the right leaders of this work.

Research activities are also underway to accelerate progress towards the end of RHD, including local, national and international collaborations. Some of this work will be highlighted at the World Congress of Rheumatic Heart Disease in Abu Dhabi in November 2023. The World Congress is hosted by World Heart Federation, with the support of the National Heart Foundation of Australia and other partners.

Ahead of the World Congress, an Australia Pre-World Congress is being held to connect people living with RHD, implementers, researchers, clinicians and advocates. This provides an opportunity for collaboration knowledge exchange and to prepare for international discussions.

This briefing document provides a plain language snapshot to support all participants to engage with the Pre-World Congress event. It is not exclusive or exhaustive but intended as a shared foundation for interdisciplinary discussion to progress the end of RHD in Australia.

Introduction to Strep A infections and complications

The Strep A bacteria causes a range of infections in humans. Some are very serious 'invasive' infections, including of the joints or deep skin which can lead to blood stream infection (sepsis) and death. Other infections caused by Strep A such as sore throat and skin sores are not immediately life threatening but without treatment can cause long-term effects.

One long-term effect of Strep A infection is the abnormal immune reaction acute post-streptococcal glomerulonephritis (APSGN) which can lead to chronic kidney disease and the need for dialysis.

Another long-term effect is the result of an abnormal immune reaction to Strep A skin and throat infections, leading to acute rheumatic fever (ARF). ARF begins some weeks after the Strep A infection and causes joint pain, fevers, skin rash, movement changes and inflammation of the heart. Although other symptoms resolve, the heart inflammation can cause permanent scarring to the heart valves. Damage to heart valves is generally permanent and called rheumatic heart disease (RHD). People who have had multiple Strep A infections as babies and children are more likely to develop ARF and RHD in adolescence or early adulthood.

Strep A infection burden in Australia

Strep A skin and throat infections are common childhood infections throughout Australia. Aboriginal and Torres Strait Islander young people, especially in remote communities, have a very high burden of Strep A skin infections. The risk of these skin infections is increased where people live in overcrowded houses with inadequate facilities for washing people and clothing and coinfection with other conditions such as scabies. The effects of colonisation, racism and socioeconomic marginalisation concentrate these risk factors for Aboriginal and Torres Strait Islander people in remote Northern Australia. This leads to an increased risk of ARF and RHD.

Invasive Strep A infections occur throughout Australia, but are more common for remote living Aboriginal and Torres Strait Islander people. Infections are most common in young people, older people or people with pre-existing health conditions but can also occur in people who are otherwise well and with no risk factors.

Research activities

Many of the medications and treatments for Strep A infection that were developed in the 1950s and 1960s are still effective today. It is possible to reduce the burden and impact of Strep A infections with the medications, and treatments from the 1950s and current technology. However, research could make prevention and treatment of Strep A infections even better – by making them more effective, more acceptable or disrupting the spread of Strep A. Improved understanding of Strep A, and new technologies and approaches could significantly reduce the burden of disease and current inequity. Research about lived experience, policy, implementation, epidemiology, diagnostics and prevention could all contribute to this goal. This document outlines some of the different research underway in Australia. It does not cover all the research activity or opportunities but is a snapshot of some of the larger programs of work.

Indirect contributors to Strep A infections, ARF and RHD risk and outcomes
The pervasive effects of colonisation, disempowerment and social, political and economic marginalisation need to be addressed through structural change and decolonising approaches

Direct contributors to Strep A, ARF and RHD risk
addressed through largely biomedical approaches

Exposure to Strep A
Transmission through large respiratory droplets and skin to skin contact

1. Environmental, housing and structural drivers of Strep A infections

Strep A infection
sore throats and skin sores

2. Healthy Skin

3. Strep A vaccine development

4. Point of care diagnosis of Strep A infections

Acute rheumatic fever (ARF)

5. ARF diagnostics

6. ARF therapeutics

7. More acceptable forms of prophylaxis

Rheumatic heart disease (RHD)

8. Early diagnosis of RHD

Consequences & complications of RHD

9. Improved treatment and support for people living with RHD

10. Epidemiology, burden of disease and progression

1. Environmental and social drivers of Strep A infections

Addressing environmental and social drivers is crucial in reducing the burden of Strep A infections, ARF, and RHD, particularly for Aboriginal and Torres Strait Islander people who experience the greatest burden of disease. Collaborative research projects such as the **STopping Acute Rheumatic Fever Infections to Strengthen Health (STARFISH)** and **The See, Treat and Prevent (SToP) skin sores and scabies trial**, focus on understanding transmission patterns, evaluating environmental health initiatives and improving diagnosis and treatment of Strep A related skin conditions respectively.

2. Healthy Skin

Achieving healthy skin by increasing the recognition and treatment of skin sores is a high priority. **The SToP trial** is a partnership between Telethon Kids Institute, Kimberley Aboriginal Medical Services, Nirrumbuk Environmental Health Services and WA Country Health Services-Kimberley and spans across the areas of exposure to Strep A using community driven, co-designed prevention initiatives. These include healthy skin books in local languages, through to implementing training to ensure correct diagnosis and access to better treatments for skin infections. The programmatic approach to reducing skin infections is further supported by the development of National Healthy Skin Guidelines and the recent introduction of ivermectin for treatment of scabies, which may facilitate the use of community driven scabies elimination activities.

3. Strep A Vaccine

The development of a Strep A vaccine is a promising approach to prevent Strep A infections and reduce the risk of ARF and deadly invasive diseases. Several Australian-led projects, such as the **Australian Strep A Vaccine Initiative (ASAVI)**, **Griffiths University Institute of Glycomics Strep A Vaccine program**, **University of Queensland Institute for Molecular Bioscience Strep A pathogenesis and treatment research program** are aiming to develop effective and affordable Strep A vaccines. Australian researchers also hold leadership positions on the Strep A Vaccine Global Consortium (SAVAC), advocating for the development and use of safe, effective and affordable Strep A vaccines.

4. Point of Care Diagnosis of Strep A infections

Point-of-care testing (PoCT) for Strep A sore throats can improve primary prevention of ARF by enabling timely diagnosis and appropriate use of antibiotics. **The scaling up of infectious disease PoCT in Aboriginal rural and remote communities** project supports accurate diagnosis and treatment, contributing to controlling ARF. This programme of work will scale-up infectious disease PoCT nationally in partnership with rural and remote primary care services.

5. ARF diagnostics

Improving ARF diagnostics is another area of focus. Research studies like **Searching for a technology-driven acute rheumatic fever test (START)** and the **Acute Rheumatic Fever Diagnosis Collaborative (ARC) Network** aim to develop diagnostic tests and biomarkers for accurate ARF diagnosis, enabling prompt initiation of treatment. Other studies are exploring MRI scans to measure inflammation and improve diagnosis of ARF.

6. ARF therapeutics

Exploring potential therapeutics for ARF, such as hydroxychloroquine (antirheumatic drug) and steroids for abnormal movements associated with ARF, are underway to reduce the risk of developing RHD.

7. Development of more acceptable forms of prophylaxis

Regular antibiotic use (secondary prophylaxis) can slow or prevent the development of RHD once people have had ARF. Currently, people with ARF need to have painful monthly antibiotic injections for five years or longer to prevent recurrence. Most people are not receiving the required dose to

protect them from ARF recurrences. An alternative, more acceptable method of penicillin delivery is needed to reduce pain and inconvenience to the patient and reduce burden on the health system.

Research studies are generating knowledge on dosing, delivery sites and methods and patient, family, and clinician preferences to inform development of improved forms of prophylaxis. The development of more acceptable forms of prophylaxis is crucial to reduce the burden of ARF recurrences. Currently the **Safety, tolerability and pharmacokinetics of high dose, subcutaneous infusions of benzathine penicillin G (Bicillin® L-A) (SCIP)** project is investigating the safety and tolerability of high doses of penicillin to determine if penicillin concentrations measured at 6 months were sufficient to prevent recurrent Strep A infections. The **Development of a self-administered long-acting penicillin for prevention of rheumatic heart-disease (miniSCIP)** project is exploring a weekly self-dosing schedule of a low dose of penicillin. The **Controlled human infection for penicillin against *Streptococcus pyogenes* – a double blinded randomised trial (CHIPS)** is aiming to determine the lowest penicillin concentration to prevent sore throat and rheumatic fever in individuals with Strep A and the **Good Paths for Healthy Hearts: Bringing choice and flexibility to long-acting penicillins for RHD project** will focus on the development of a suite of culturally appropriate, co-designed patient information tools and health care provider training materials for Strep A vaccine development projects in WA and NT.

8. Early diagnosis of RHD

Early diagnosis of RHD is facilitated by routinely performing an ultrasound of the heart via echocardiogram. Projects like the **Non-Expert Acquisition and Remote Expert Review of Screening echocardiography images from Child health and Ante Natal clinics (NEARER SCAN)** and **Rapid Echocardiography for Congenital and Rheumatic heart Disease – Investigating a New Approach (RECARDINA)** aim to incorporate and improve the current elements of echocardiographic screening in remote communities. By improving the current elements of echocardiographic screening, the NEARER SCAN and RECARDINA projects aim to empower and improve capacity of non-expert practitioners from remote communities to deliver echocardiography to improve early diagnosis of RHD within their respective communities.

9. Improved treatment of RHD

Early phase studies to understand damage to heart valves and explore new ways of reversing this damage are underway, alongside lived experience research to provide better support to young people living with RHD.

10. Epidemiology, burden of disease and disease progression

To inform public health strategies and vaccine development, epidemiological studies and surveillance programs, initiatives like the **End Rheumatic Heart Disease in Australia Study of Epidemiology (ERASE) Project, Sore Throat Study, The Missing Piece Study, Development of passive surveillance of Strep A in Primary Care and Laboratory Dashboards** are being conducted to understand the burden of Strep A, ARF, and RHD and guide prevention efforts. To further understand the development (pathogenesis) and transmission of Strep A, laboratory studies such as the **Laboratory studies on Strep A pathogenesis, Characterising a novel molecular pathway to reduce penicillin failure for Strep throat and Strep A modelling work** are currently underway.

Term/abbreviation	Definition	
ARF	Acute rheumatic fever	An illness caused by an autoimmune response to Strep A infection.
Echocardiography	Ultrasound of the heart used for diagnosis of ARF and RHD.	
MRI	Magnetic Resonance Imaging	Medical imaging using magnetic fields to scan the heart or other body parts.
Primary prevention	Treatment of Strep A sore throat or skin sores with antibiotics to reduce the risk of developing ARF.	
PoCT	Point of care testing	Technology to test for Strep A in primary care services with results available within an hour.
RHD	Rheumatic heart disease	Chronic damage to the valves of the heart caused by a severe episode of ARF or repeated episodes.
Secondary prophylaxis	Regular antibiotics (usually injections of benzathine benzyl penicillin) used to reduce the risk of further Strep A sore throats that lead to ARF recurrence and progression to RHD.	