

# End Rheumatic Heart Disease Centre of Research Excellence

**Impact Report 2014 - 2021**

*Creating the blueprint to eliminate  
rheumatic heart disease in Australia*



# Acknowledgements

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The END RHD CRE investigators would like to thank the Aboriginal and Torres Strait Islander people who have shared their stories over the life of the CRE. We acknowledge that the figures outlined in our research represent the loss of human life with profound impact and sadness for people, families, community, and culture.

We thank all those who have contributed their technical expertise, time, and advice to the research undertaken over the past six years of the CRE.

The Telethon Kids Institute acknowledges Aboriginal and Torres Strait Islander peoples as the Traditional Custodians of the land and waters of Australia, and the lands upon which this report was produced. We also acknowledge the Nyoongar Wadjuk, Yawuru, Kariyarra and Kurna Elders, their peoples and their land upon which the Institute is located, and seek their wisdom in our work to improve the health and development of all children.

This document should be read in conjunction with Wyber R, et al. *The RHD Endgame Strategy: The blueprint to eliminate rheumatic heart disease in Australia by 2031*. Perth: The END RHD Centre of Research Excellence, Telethon Kids Institute, 2020.

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## What is RHD?

**Rheumatic heart disease (RHD)** starts with a Strep A infection of the throat or skin. When left untreated, the infection can lead to acute rheumatic fever (ARF), which causes sore joints, rash, fevers, and heart inflammation. While the other symptoms of ARF go away, the heart damage remains – and this is known as rheumatic heart disease.

# A MESSAGE FROM PROFESSOR JONATHAN CARAPETIS

## END RHD CRE CHIEF INVESTIGATOR

Our goal when establishing the *End Rheumatic Heart Disease Centre of Research Excellence (END RHD CRE)* in 2014 was to create a blueprint to prevent the next generation of Aboriginal and Torres Strait Islander children from bearing the emotional and physical scars of rheumatic heart disease (RHD), and to ensure those already living with the disease were afforded the best quality of life.

With the release in September 2020 of the *RHD Endgame Strategy: The blueprint to eliminate rheumatic heart disease in Australia by 2031*, we have achieved this goal. If fully implemented, the *RHD Endgame Strategy* provides the opportunity to prevent another 8,000 Aboriginal and Torres Strait Islander people from developing rheumatic heart disease or its precursor, acute rheumatic fever (ARF), within the next decade. In doing this, we will prevent 650 deaths and another 1,370 people will avoid open heart surgery as a result of RHD.

Behind each of these statistics is a person, a family and a community – and a chance to change the course of their life immeasurably.

While I am immensely proud of the *RHD Endgame Strategy*, and the solutions it offers to end RHD in this country, I am even prouder of the way we have gone about creating this critical piece of work. Pairing the research of leading infectious diseases specialists from the END RHD CRE with the knowledge and experience of Aboriginal and Torres Strait Islander leaders across the country, the *RHD Endgame Strategy* marks a true example of collaboration across communities, sectors and backgrounds.

While on paper the END RHD CRE constitutes 20 investigators from 16 institutions across Australia, in reality the sum of the centre is far greater. At the heart of all of our work has been those living with and at risk of RHD. These voices have been integral to creating the recommendations that will translate into acceptable, culturally appropriate strategies that will be both welcomed by and successful within communities to end RHD once and for all.

The *RHD Endgame Strategy* has been endorsed by 26 leading health and research organisations, including the National Aboriginal Community Controlled Health Organisation (NACCHO). As the backbone of the organisations on the frontline working to prevent new cases and support those living with the disease, the Aboriginal and Torres Strait Islander health workforce is integral to actualising the vision of the *RHD Endgame Strategy*, and seeing this disease eliminated. I thank them enormously for their time, wisdom and passion, and stand ready to support them as they lead the next phase of implementation.

From the beginning, we have also engaged governments and other key stakeholders to ensure that the recommendations of the *RHD Endgame Strategy* are funded – and that this is not a report that sits on the shelves of powerbrokers gathering dust. As a founding member of the END RHD alliance, we have engaged politicians and policymakers from across the political spectrum. For too long, RHD has been seen as a problem too large and too multifaceted to be solved. With the *RHD Endgame Strategy*, we have proven not



END RHD CRE Chief Investigator Professor Jonathan Carapetis, examines Laqueisha, aged 5, as she recovers from open heart surgery to repair heart damage caused by rheumatic heart disease

only that it can be ended, but that in fact, it is unconscionable not to do so.

It has been my honour and privilege to lead the END RHD CRE over the past six years and I thank every single person who has contributed their wisdom, technical expertise and lived experience along the way.

After nearly 30 years working to eliminate RHD in Australia, I have never been more confident that the end is in sight. We have the Aboriginal and Torres Strait Islander leadership, community demand and, with the release of the *RHD*

*Endgame Strategy*, the evidence base to make our vision to see this disease eliminated by 2031 a reality. We simply cannot stop until this disease is ended – the next generation of Aboriginal and Torres Strait Islander children is depending on us.

**Professor Jonathan Carapetis AM**

A handwritten signature in blue ink that reads "Jonathan Carapetis".

## Vision



The END RHD Centre of Research Excellence was created with the vision of eliminating rheumatic heart disease as a public health priority in Australia

## How we worked: Science to Strategy

The END RHD Centre of Research Excellence was designed as a research-policy-service partnership to develop the first evidence-based strategy to end rheumatic heart disease in Australia, bringing the prevalence of rheumatic heart disease for Aboriginal and Torres Strait Islander peoples down to the same level as non-Indigenous people in Australians.

When the END RHD CRE was funded in 2014, RHD control was at a critical juncture in Australia. More than 20 years of research closely linked to service delivery and policymaking had placed Australia at the forefront of global ARF and RHD research, control and advocacy, however a surge of co-ordinated research and implementation strategies was needed to accelerate progress. The END RHD CRE provided an opportunity for a strategic approach targeting implementation science, encompassing all domains of disease control, consolidating existing strategies, developing new interventions with potential for rapid benefits, and modelling the effect of potential interventions.

The production of the *Endgame Strategy* involved the synthesis of information across the five-year lifespan of the END RHD CRE. Funding was allocated to priority research projects across several disciplines of research, including epidemiology, economics, biomedical sciences, clinical practice, health services research and social sciences, with a dedicated focus on engaging the RHD community and documenting the experiences of those living with the disease. Data and results from these priority projects helped inform the overall *Endgame Strategy* and were complemented by literature reviews, systematic reviews, narrative reviews and the experiences of health professionals currently working in ARF and RHD control.

The complexity of RHD means that tackling it properly requires strategies across all levels of health care. This includes different health sectors as well as sectors dealing with social determinants – requiring extensive collaboration beyond the research community. The END RHD CRE brought together Aboriginal and Torres Strait Islander community-controlled organisations, policy and practice experts from the housing, environmental health and health provider sectors, and people living with RHD to inform the development of the *Endgame Strategy*.

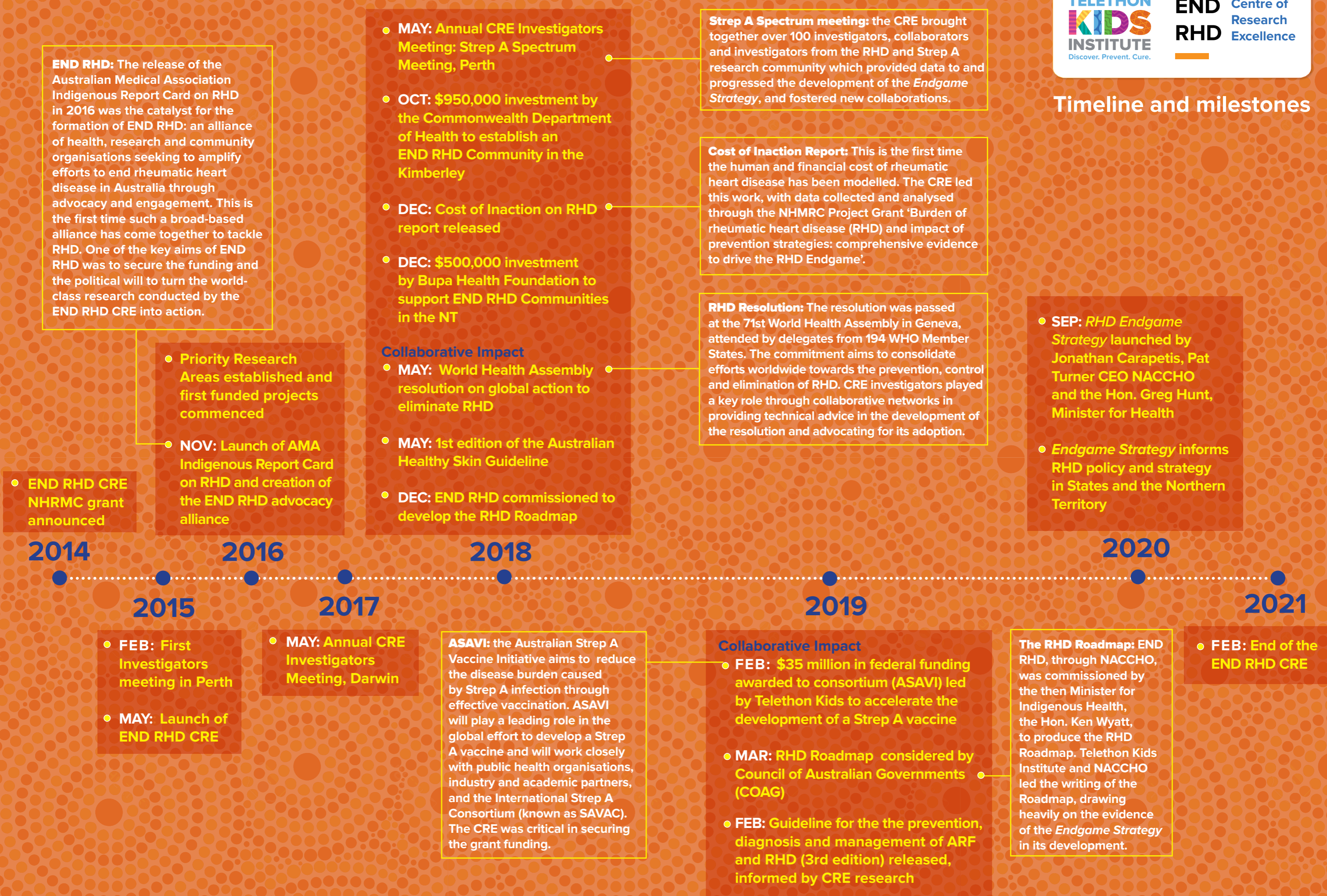
The END RHD CRE acknowledged that these stakeholders and experts – so critical in developing the *Endgame Strategy* – would also ultimately be responsible for the implementation of the recommendations of the *Endgame Strategy*. This model of stakeholder and community engagement was central to the work of the CRE and its commitment to seeing its world-class research translated into action.

## From Science to Strategy: inputs and outputs of the END RHD CRE

This diagram reflects the spectrum of work associated with the END RHD CRE. Partnerships and collaborations were strengthened across the life of the project and research findings and impact were amplified by this collaborative approach



## Timeline and milestones



# CHIEF INVESTIGATORS



**Professor Jonathan Carapetis AM**  
 Director, Telethon Kids Institute and head of the Telethon Kids Institute Strep A and Rheumatic Heart Disease Team; Consultant paediatrician, Perth Children's Hospital; Professor, The University of Western Australia; Co-director of REACH



**Professor Graeme McGuire**  
 Head of Unit, General Internal Medicine, Western Health



**Professor Bart Currie**  
 Director, Infectious Diseases, Royal Darwin Hospital; Director, HOT NORTH; lead, Tropical and Emerging Infectious Diseases team, Global and Tropical Health Division, Menzies School of Health Research



**Professor Dawn Bessarab**  
 Director, Centre for Aboriginal Medical and Dental Health, The University of Western Australia



**Assoc/Prof Dan McAullay**  
 Centre Director, ISAC, The University of Western Australia; Principal Research Consultant, Kurongkurl Katitjin, Edith Cowan University



**Heather D'Antoine**  
 Distinguished Honorary Fellow, Menzies School of Health Research



**Professor Alex Brown**  
 Theme Leader, Aboriginal Health Equity, SAHMRI; Professor of Aboriginal Health, University of Adelaide; Scientific Director, Aboriginal Grand Challenge, Telethon Kids Institute; Co-director of RHD Australia



**Professor Anna Ralph**  
 Director, Global and Tropical Health, Menzies School of Health Research; Co-director, RHD Australia; Medical specialist, General Medicine and Infectious Diseases, Royal Darwin Hospital



**Professor Andrew Steer**  
 Paediatric infectious diseases physician, Royal Children's Hospital Melbourne; Principal Research Fellow, Centre for International Child Health, Department of Paediatrics, University of Melbourne; Group Leader, Strep A Research Group at Murdoch Children's Research Institute



**Professor Nick de Klerk**  
 Honorary Emeritus Fellow, Telethon Kids Institute; Adjunct Professor, Occupational Respiratory Epidemiology, The University of Western Australia

# ASSOCIATE INVESTIGATORS



**Professor David Atkinson**  
 Professor, Rural Clinical School of Western Australia (Broome); Kimberley-based medical practitioner and researcher



**Rebecca Slade**  
 Project Manager, Papua New Guinea & Republic of Indonesia for the Micro Elimination of TB, Menzies School of Health Research; Program Manager, Rheumatic Heart Disease Australia 2018 - 2020



**Dr. Samantha Colquhoun**  
 Senior Fellow, National Centre for Epidemiology and Population Health, Australian National University



**Dr. Vicki Krause**  
 Director, Centre for Disease Control, Northern Territory



**Professor Christopher Reid**  
 Professorial Research Fellow, cardiovascular epidemiology, School of Population Health, Curtin University; Associate Director, Monash Centre for Cardiovascular Research and Education



**Professor Tom Snelling**  
 Director of Health and Clinical Analytics, School of Public Health, University of Sydney; Infectious diseases physician, Sydney Children's Hospital



**Dr. Stephanie Trust**  
 Principal Physician, Wunan Health, Kununurra



**Dr. Rosemary Wyber**  
 Head of Strategy for END RHD, Telethon Kids Institute; Senior Adjunct Research Fellow, The University of Western Australia; PhD student, Health Systems Science, The George Institute for Global Health



**Dr. Gavin Wheaton**  
 Medical Director of Paediatric Medicine, Women's and Children's Hospital, South Australia

**Previous investigators:  
 Karen Edmond (2015–17)  
 and Claire Boardman (2015–18).**

# THE RHD ENDGAME STRATEGY



Hon Greg Hunt MP, Jonathan Carapetis, END RHD Chief Investigator, and Pat Turner, NACCHO CEO

On Wednesday 23 September 2020, the *RHD Endgame Strategy: the blueprint to eliminate rheumatic heart disease in Australia by 2031* was virtually launched to more than 100 invited guests across the country by The Hon. Greg Hunt, MP, Minister for Health, alongside Professor Jonathan Carapetis AM, senior author of the Strategy, and Ms Pat Turner AM, CEO of the National Aboriginal Community Controlled Health Organisation.

The *Endgame Strategy* – the seminal output from the END RHD CRE – had been five years in the making and brought the collective experience of communities, clinicians, Aboriginal Community Controlled Health Organisations, government and non-government organisations together with more than 25 years of research to outline how to eliminate RHD in Australia.

Upon its launch, Professor Carapetis noted the Strategy’s release marked the first time a comprehensive evidence base had been developed showing how this could be done.

**“With the release of this *Endgame Strategy* we now have the blueprint outlining exactly what needs to happen to both prevent new cases and improve the quality of life for those already living with the disease,” Professor Carapetis said.**

RHD is rare among non-Indigenous people, yet Aboriginal and Torres Strait Islander people have some of the highest rates of the disease in the world. This is a disease that is usually only seen

in developing countries and its persistence in Australia is an ongoing injustice.

**“We know, without any shadow of a doubt, that by implementing the *Endgame Strategy*, we can prevent the next generation of Aboriginal and Torres Strait Islander children and their families from bearing the physical and emotional scars of rheumatic heart disease.**

“We can also have an impact on other diseases with similar risk factors, such as otitis media, trachoma and renal disease.”

Developed with the input and endorsement of the Aboriginal and Torres Strait Islander Community Controlled Health Sector via END RHD – the peak body leading work to end rheumatic heart disease in Australia – and more than 20 of Australia’s leading health and research organisations, the *Endgame Strategy* has the widespread support of both those living with the disease and those working to end it.

The *Endgame Strategy* proposes a series of initiatives which take into account the individual context and needs of remote communities and ensure Aboriginal and Torres Strait Islander leadership is guaranteed.

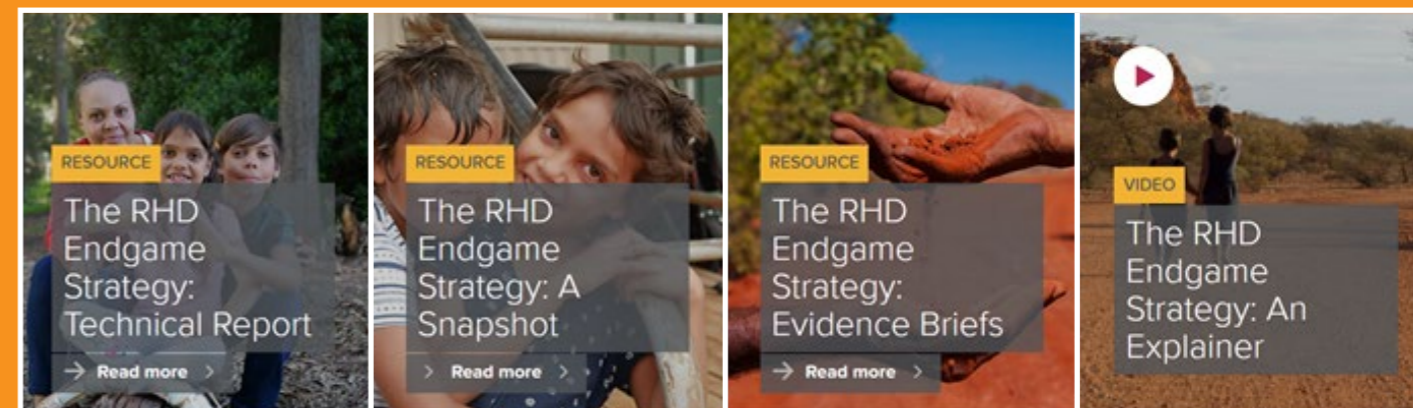
To set the foundations needed to make ending RHD achievable within the next decade, the Strategy outlines five key priorities for immediate attention which, collectively, have the greatest potential to bring about change.

## RHD Endgame Strategy inputs



From research to action: this implementation framework comprises Five Priority Action Areas designed to operationalise the *Endgame Strategy*. This framework was developed through an analysis of the range of strategies identified in the *Endgame Strategy* as being the most impactful, acceptable, practical and readily implementable with appropriate investment.

## RHD Endgame Strategy outputs



<https://endrhd.telethonkids.org.au/>

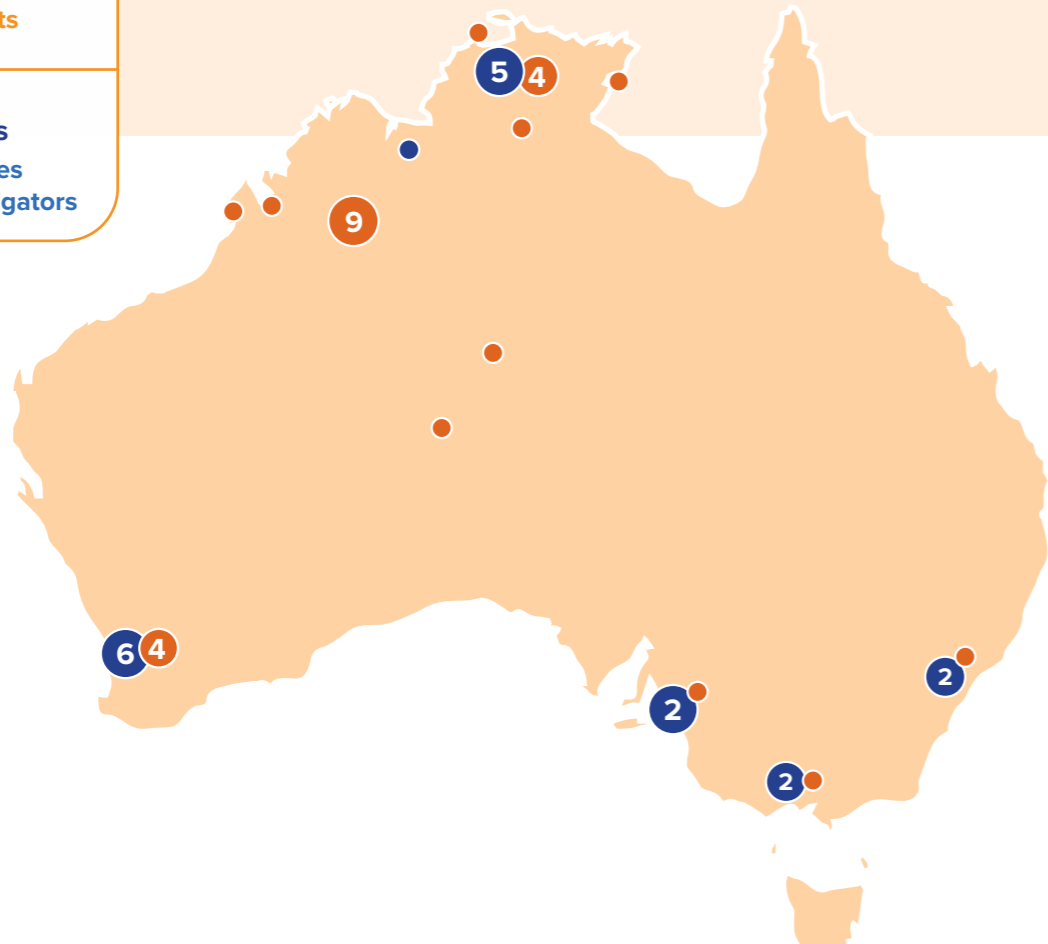
### Publications

1. R Wyber, K Noonan, C Halkon, S Enkel, J Cannon, E Haynes E, et al. *Ending rheumatic heart disease in Australia: the evidence for a new approach*. Medical Journal of Australia. 2020;213:S3-S31.
2. R Wyber, K Noonan, C Halkon, S Enkel, A Ralph, AC Bowen, et al. *The RHD Endgame Strategy: A Snapshot. The blueprint to eliminate rheumatic heart disease in Australia by 2031*. Perth: The END RHD Centre of Research Excellence, Telethon Kids Institute; 2020.
3. R Wyber, K Noonan, C Halkon, S Enkel, A Ralph, AC Bowen, et al. *The RHD Endgame Strategy: The blueprint to eliminate rheumatic heart disease in Australia by 2031*. Perth: The END RHD Centre of Research Excellence, Telethon Kids Institute; 2020.
4. R Wyber, J Cannon, JM Katzenellenbogen. *The cost of inaction on rheumatic heart disease: the predicted human and financial costs of rheumatic heart disease for Aboriginal and Torres Strait Islander people 2016-2031*. Perth: The END RHD Centre of Research Excellence, Telethon Kids Institute; 2018.
5. J Cannon, J Katzenellenbogen, R Wyber et al. *The Cost of Inaction on Rheumatic Heart Disease in Australia*. Heart, Lung and Circulation. 2019; 28(2): S50

# CRE IN NUMBERS

**Project locations**  
Number relates to # of projects

**Investigators**  
Number relates to # of investigators



**21** research projects across Australia

**22** locations in Australia

**19** investigators located across 6 cities and 1 rural town

**6** investigators in the top 30 world-rankings for RHD research

**5** investigators in the top 30 world-rankings for acute rheumatic fever research

**200+** collaborators

Scholarships and support for **6** PhD students

**5** very high impact publications

and more than

**200** networked collaborator publications

## IN FOCUS: THE MISSING PIECE STUDY



Dr Dylan Barth and the Missing Pieces team on school surveillance visits in Broome and Derby

### 'The Missing Piece': A surveillance study to understand the contribution of Strep A pharyngitis in the context of high impetigo prevalence to inform primary prevention of Acute Rheumatic Fever

Associate Professor Asha Bowen, Telethon Kids Institute

There is a well-established causal pathogenic link between infection of the throat with Strep A and subsequent development of ARF. What is less clear is whether other types of Strep A infections, such as impetigo (skin sores), may also contribute to the development of ARF.

It is reasonable to suggest that an impetigo-ARF link does exist in Australian Aboriginal populations where rates of ARF and RHD are high, but where skin sores are endemic and pharyngitis is seemingly uncommon. This hypothesis is also backed by molecular analysis of Strep A bacteria in remote Aboriginal communities.

Given that primary prevention strategies and efforts in vaccine development have long been based on the belief that ARF is caused exclusively by Strep A pharyngitis, it is vital that we better understand the concurrent burden of Strep A skin and throat infections in individuals in endemic, tropical and resource-limited settings, so as to better target primary prevention strategies.

Hence, the Missing Piece study – launched in 2019 and still ongoing – aims to comprehensively evaluate the concurrent burden (prevalence

and incidence) of Strep A impetigo and Strep A pharyngitis in Aboriginal children aged 5–15 years in the Western Australian Kimberley region. The two schools participating in this study are based in Broome and Derby, Western Australia.

To date, the Missing Piece Study has completed three screening visits, including 438 participants and collection of 405 throat and 118 skin swabs. Swabs of the classroom environment have also been undertaken to determine if Strep A persists on classroom surfaces.

In 2020 an Honours student worked on this study to analyse the baseline data for sore throats and skin sores. This was the first description of Strep A sore throats in remote-living Aboriginal children at high risk of acute rheumatic fever (ARF) in more than a decade, confirming higher than expected rates of Strep A pharyngitis.

As a result of activities having been disrupted by COVID-19 across the Kimberley, the Missing Piece study has secured a successful WA Child Health Research Fund grant to continue surveillance activities in 2021 and progress research on enhancing primary prevention strategies for ARF.

**Peer-reviewed publications**

1. S Pearce, AC Bowen, ME Engel, M de la Lande, DD Barth. *The incidence of sore throat and group A streptococcal pharyngitis in children at high risk of developing acute rheumatic fever: A systematic review and meta-analysis.* PLoS One, 2020. 15(11): e0242107.
2. J Pickering, DD Barth, AC Bowen. *Performance and practicality of a rapid molecular test for the diagnosis of Strep A pharyngitis in a remote Australian setting.* American Journal of Tropical Medicine & Hygiene, 2020. 103(6): 2530-2532.
3. DD Barth, J Daw, R Xu, S Enkel, J Pickering, T McRae, ME Engel, JR Carapetis, R Wyber and AC Bowen. *Modes of transmission and attack rates of group A Streptococcal infection: a protocol for a systematic review and meta-analysis.* BMC Systematic Reviews, 2021. 10: 90.
4. DD Barth DD, M Mullane, C Chou, JR Carapetis, AC Bowen A. *The design and rationale of the Missing Piece Surveillance Study for Strep A pharyngitis and impetigo infections in Australia.* BMJ Open. Manuscript under preparation.



# IN FOCUS: END RHD COMMUNITIES



Valerina Mungatopi, Anne-Marie Lee, Nina Black, Angela Kelly, Segora Babui at an END RHD Communities training day held in Darwin

Building on the learnings of the CRE-funded SP Plus Project, in 2018 the 'END RHD Communities' project commenced in two remote Aboriginal Communities in the Northern Territory, supported by the Bupa Health Foundation and driven by the END RHD CRE in conjunction with the Menzies School of Health Research.

The project aimed to bring together the community, service providers, local schools and researchers to develop culturally appropriate strategies to prevent RHD and ensure those already living with the disease received the support they needed.

General Practitioner and Co-Investigator, Dr Rosemary Wyber, said the project differed from other established RHD control programs, which were largely clinic-based and focused solely on treatment of the disease.

**“Central to the project is the leadership of Aboriginal Community Workers who live in communities with a high burden of RHD,” Dr Wyber said.**

“We are working with those community workers to raise awareness about how to prevent Strep A infection, as well as to help those with ARF and RHD navigate the healthcare system and other service providers.”

Associate Professor Anna Ralph, who is leading the project at the Menzies School of Health Research, said this approach was exciting because it was the kind of model Aboriginal people had been asking for.

“Our research to date shows how fundamental community engagement is for effective delivery of care, yet it’s not possible to do this effectively by reaching out from the clinic. It needs to be a grass-roots initiative starting with and driven by community members themselves,” Associate Professor Ralph said.

Project manager Angela Kelly, who is working with Associate Professor Ralph and who travels regularly to participating communities to support Aboriginal Community Workers, said creating a community-led model of care was pivotal to ending the disease.

“Take for example, complexities around local language,” Ms Kelly said. “Germ theory as causation of disease is a difficult concept to translate, so Aboriginal Community Workers play the critical role of being able to explain the best way to prevent contracting a Strep A infection in the local context.”

Given that preventing Strep A infection requires people to have access to appropriate health and hygiene infrastructure – in turn helping to close the gap – researchers hope its benefits will stretch beyond simply tackling RHD.

**“This model can address a lot more than just rheumatic heart disease. Knowledge of working health hardware and hygiene practices can help prevent other serious streptococcal infections and trachoma,” Ms Kelly said.**

The community was increasingly advocating for these basic rights, she added.

“Recently, one of the Aboriginal Community Workers was told that someone at high risk of rheumatic fever recurrence in the community had no access to hot water,” she said.

“The worker went straight to the Department of Housing representative in the community and said it needed to be fixed – and the next day, it was.”

R Wyber, A Kelly, A Lee, V Mungatopi, V Kerrigan, S Babui, N Black, V Wade, C Fitzgeragl, D Peris, A Ralph, *Formative evaluation of a community-based approach to reduce the incidence of Strep A infections and acute rheumatic fever*, (in press 2020), Australian & New Zealand Journal of Public Health.



Six activity domains of END RHD Communities

## Boom Boom: A health promotion video created for kids, by kids



The children filmed a western-themed music video titled 'Boom Boom' to teach other children how they can prevent RHD

When the END RHD Communities project was first established in Barunga, one of the most common suggestions to come out of the initial community consultation was a desire from the local school kids to create a music video to spread the RHD prevention messages they were learning as part of the project.

Their goal was to help those in other communities at risk of RHD by developing a song that was informative, culturally appropriate and would resonate. It was from here that the idea of 'Boom Boom' was born, and ABC presenter Justine Clarke and Darwin record label Skinnyfish Music were enlisted to help bring the vision to life.

The song was launched at the opening ceremony of the Barunga Festival in 2019 and then turned into a music video to be shared throughout communities at high risk of RHD.

For Anne-Marie Lee, the Aboriginal Community Worker leading the project in Barunga, the song and accompanying music video was a powerful way to engage with those in her community, and further afield, about the dangers of leaving skin sores and sore throats untreated.

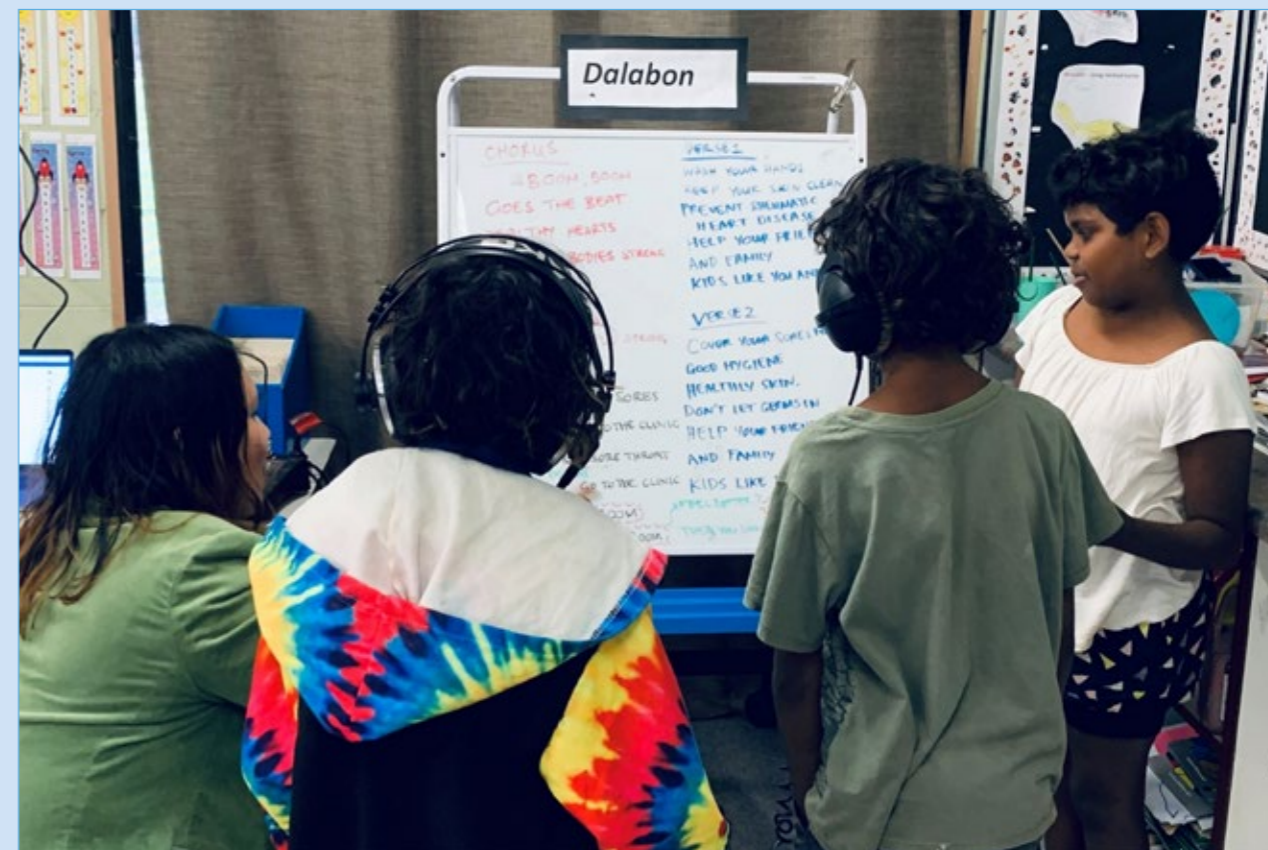
**“By doing this video in an Indigenous community it opens the eyes of a lot of families that have kids with rheumatic heart disease - and families with kids that don't - about how it's important that they get treatment for skin sores and sore throats,” Ms Lee said.**

Especially poignant was the fact that three of the children on stage had RHD, including one child who had only recently returned home from Melbourne after undergoing life-saving open heart surgery.

Since its launch, the video has been shared thousands of times across social media as well as in schools and Aboriginal and Torres Strait Islander clinics around the country, to much praise and many comments about the catchy nature of the song!



*The development of Boom Boom was made possible thanks to funding from Bupa Health Foundation*



The children in Barunga wrote the lyrics for 'Boom Boom' based on what they had learnt as part of the END RHD Communities project about how to prevent the transmission of Strep A



Boom Boom was premiered as part of the opening session of Barunga Festival, which attracts over 3,000 attendees every year. Credit: Britten Andrews

# RESEARCH SUPPORT



**Dr. Josh Osowicki**

Group A Streptococcal (Strep A) infection is a major cause of death and disability globally, with a disproportionately high burden in indigenous Australians, the Pacific region, and in settings of disadvantage worldwide. Development of a Strep A vaccine is recognised as a global priority, however progress has faltered.

Dr. Osowicki's PhD aims to establish a Strep A pharyngitis human challenge model using an observational, dose-escalation, inpatient trial. This will assist in determining the dose of Strep A administered by direct oropharyngeal inoculation required to reliably produce pharyngitis in more than 60% of healthy adult volunteers.

A successful strep A human challenge model will be a much-needed catalyst for fast-tracking Strep A vaccine development, providing proof-of-concept efficacy data for vaccine candidates to give industry and large public funders confidence to progress to larger Phase 3 vaccine trials. A challenge model could also deliver insight into identifying immune correlates of protection, and test new diagnostics (e.g. point of care Strep A pharyngitis tests) and treatments (e.g. alternatives to painful penicillin injections).

#### Peer-reviewed publications

- J Osowicki, K Azzopardi, L Fabri, HR Frost, T Rivera-Hernandez, M Neeland et al. A controlled human infection model of Streptococcus pyogenes pharyngitis (CHIVAS-M75): an observational, dose-finding study. *The Lancet*. 2021.
- J Osowicki, K Azzopardi, L McIntyre, T Rivera-Hernandez, C Ong, C Baker, et al. A Controlled Human Infection Model of Group A Streptococcus Pharyngitis: Which Strain and Why? *mSphere*. 2019;4(1):e00647-18.
- J Osowicki, K Azzopardi, C Baker, C Waddington, M Pandey, T Schuster T, et al. Controlled human infection for vaccination against Streptococcus pyogenes (CHIVAS): Establishing a group A Streptococcus pharyngitis human infection study. *Vaccine*. 2019;37(26):3485-94.



**Dr. Geri Vaughan**

The 'RHD in pregnancy: challenges of health services' doctoral study focused on the barriers and facilitators of health service provision for pregnant Australian women with RHD. It addressed important public health issues, particularly for Aboriginal and Torres Strait Islander women with complex pregnancies due to RHD, who remain at both an unequal and higher risk of this disease as well as its adverse sequelae. The study aimed to identify what works – and what doesn't – in the access of effective, timely maternity and cardiovascular care for pregnant women with RHD. It involved a systematic review of the literature on health professionals' perspectives regarding care for pregnant women with RHD; a quantitative study of surveillance and health information systems related to RHD in pregnancy; and a qualitative examination of health professionals' knowledge, experiences of and attitudes to provision of care for pregnant women with RHD.

The study found that a complex interplay of systemic and cultural factors impacts the provision of optimal care for pregnant women with RHD. Characteristics that underpin and support improved outcomes for mother and baby include early diagnosis, timely access to multidisciplinary care, effective health information systems and collaborative, respectful care. Dr. Vaughan wrote two peer-reviewed papers regarding her PhD work and contributed to the Women and RHD chapter in the 3rd Edition Australian Guidelines for Rheumatic Fever and Rheumatic Heart Disease released in 2020.

#### Peer-reviewed publications

- G Vaughan, S Belton, S La Vincente, L Bootle. Using research: educational resources for rheumatic heart disease in Women. *Heart, Lung and Circulation*. 2019;28(Suppl 2):S61.
- G Vaughan, K Tune, MJ Peek, L Jackson Pulver, B Remenyi, S Belton, EA Sullivan. Rheumatic heart disease in pregnancy: strategies and lessons learnt implementing a population-based study in Australia. *International Health*. 2018;10(6): 480–489.



**Dr. Emma Haynes**

This PhD study, titled 'Understanding the lived experience of rheumatic heart disease among Aboriginal and Torres Strait Islander people and their communities' aimed to investigate the lived experience of people living with RHD, (PLWRHD) and their communities, and those within the health system providing care for PLWRHD. An understanding of what is known and what is not known about the lived experience of RHD formed a foundation to the design of this study. The use of qualitative research methods, in particular a critical ethnographic approach based on field work over long periods of time, has allowed a deeper understanding of lived experience whilst also paying attention to factors such as systemic racism.

As part of this research, Dr. Haynes lived in a small, very remote Aboriginal community in North East Arnhem Land for 15 months, mentored by a local community researcher. An estimated 15% of the population has ARF or RHD in this community, with the study reflecting local desires to tackle this burden. As a result, 'On Track Watch' developed, reflecting community desire to keep young people on track with their monthly penicillin injections as well as watching out for, and preventing new cases of ARF. Community-based participatory action research was an integral part of this process.

#### Peer-reviewed publications

- E Haynes, A Mitchell, S Enkel, R Wyber, D Bessarab. Voices behind the statistics: a systematic literature review of the lived experience of rheumatic heart disease. *International Journal of Environmental Research and Public Health*. 2020;17(1347).



**Dr. Simone Reynolds**

Whilst being funded as an Indigenous Postdoctoral researcher, Dr Reynolds worked on a number of projects primarily focused around Group A Strep Vaccine Development. The first project's research focused on delivery of a GAS peptide vaccine through a patch containing vaccine-coated micro-projections. The micro-projections release the GAS peptide directly to immune cells immediately below the skin surface. This was a collaborative project with the proprietors of the micro-projection patch system. The vaccine peptide was tested in a Strep A skin infection mouse model with the well-studied vaccine candidate, J8-DT, developed by the Institute for Glycomics, Griffith University. Results indicated that the patch technology delivered sufficient vaccine to elicit an immune response that is comparable to traditional intramuscular-administered vaccine. Upcoming studies will examine mucosal protection.

In addition Dr Reynolds has been working on the submission process for Phase 1 clinical trials of the J8-CRM skin vaccine, to be based in Canada – the clinical trial application for the trial has recently been made. It is hoped the clinical trial will have commenced by mid-2021. Extensive pre-clinical evidence was required for the clinical trial application submission, which is the subject of two peer review papers with links below.

#### Peer-reviewed publications

- V Ozberk, S Reynolds, Y Huo, A Calcutt, S Eskandari, J Dooley, et al. Prime-Pull Immunization with a Bivalent M-Protein and Spy-CEP Peptide Vaccine Adjuvanted with CAF®01 Liposomes Induces Both Mucosal and Peripheral Protection from covR/S Mutant Streptococcus pyogenes. *mBio*. 2021;12(1):e03537-20.
- S Reynolds, M Pandey, J Dooley, A Calcutt, M Batzloff, V Ozberk, et al. Preclinical safety and immunogenicity of Streptococcus pyogenes (Strep A) peptide vaccines. *Nature Scientific Reports*. 2021;11(1):127.
- JLS Mills, CM Flores Jayashi, S Reynolds, C Wun, A Calcutt., B Baker, et al. M-Protein Based Vaccine Induces Immunogenicity and Protection from Streptococcus Pyogenes When Delivered on a High-Density Microarray Patch (HD-MAP). *NPJ Vaccines*. 2020;5(1),1-11.

# FUNDED PROJECTS

## 'SP Plus' – an expanded model of secondary prevention for individuals with rheumatic fever and their families

Professor Anna Ralph and Dr Vicki Krause, Menzies School of Health Research

SP Plus was a pilot study undertaken in select Top End NT communities, exploring the role of local Care Navigators at the community level. The project aimed to stop recurrences of ARF and develop strategies to reduce Strep A infections in households which include a person who has had rheumatic fever. This project has expanded to become the END RHD (see profile of communities project, pp 16-17).



Valerina Mungatopi undergoes training with Dr Robyn Marsh in her role as an Aboriginal Community Worker with the END RHD Communities Project (formerly 'SP Plus').

## Using the National Deaths Index to identify deaths of people on the Northern Territory RHD Register

Jessica de Dassel, Menzies School of Health Research

A retrospective cohort study which linked data from the NT RHD Register to the National Death Index (NDI), this project investigated the mortality of people with RHD in the NT, including cause of death. The project provided immediate practical benefits to the NT RHD Control Program, improving the reliability and effectiveness of the Register. Study findings were used to improve information available to patients, their families and healthcare providers when making important decisions about treatment options and personal decisions around RHD. The findings also aided resource development by RHD Australia, informing chapter revisions of the 3rd edition of the ARF/RHD Guidelines.

### Peer-reviewed publications

1. JL de Dassel, H Malik, AP Ralph, K Hardie, B Remenyi, JR Francis. *Four-Weekly Benzathine Penicillin G Provides Inadequate Protection against Acute Rheumatic Fever in Some Children*. American Journal of Tropical Medicine and Hygiene. 2019;100(5):1118-1120.
2. JV Holland, K Hardie, JL de Dassel, AP Ralph. *Rheumatic Heart Disease Prophylaxis in Older Patients: A Register-Based Audit of Adherence to Guidelines*. Open Forum Infectious Diseases. 2018;5(6):ofy125.
3. JL de Dassel, N de Klerk, JR Carapetis, AP Ralph. *How Many Doses Make a Difference? An Analysis of Secondary Prevention of Rheumatic Fever and Rheumatic Heart Disease*. Journal of the American Heart Association. 2018;7(24):e010223.
4. JL de Dassel, MT Fittock, SC Wilks, JE Poole, JR Carapetis, AP Ralph AP. *Adherence to secondary prophylaxis for rheumatic heart disease is underestimated by register data*. PLoS One. 2017;12(5):e0178264.

## Improving wellbeing for young people living with RHD – a peer support program through Danila Dilba Health Service

Dr Joe Kado, Telethon Kids Institute and Dr Rosemary Wyber, Telethon Kids Institute

This pilot program aimed to determine the suitability of an ongoing peer support program to address the needs of young people living with RHD in urban Darwin and receiving care from Danila Dilba Health Service (DDHS). Five participants took part in three sessions. Findings demonstrated participants' willingness to share their experiences and perspectives of living with RHD with facilitators and each other within a peer support setting, as well as improved knowledge about ARF and RHD. Learnings from this pilot will aid in informing elements of ongoing programs, including characteristics of facilitators and external presenters, program format, and session outlines and resourcing. An evaluation report for this project has been provided for Danila Dilba and a peer-reviewed paper submitted to share learnings more widely.

## Improving acceptability of products for secondary prophylaxis including penicillin reformulation

Dr Joe Kado, Telethon Kids Institute

This study addressed three outstanding knowledge gaps required to progress the penicillin reformulation agenda. Addressing these gaps will inform the target product profile for a long-acting penicillin formulation, identify feasible technologies, and support development of a regulatory dossier for eventual licensure.

1. Develop a protocol to use the Strep A human challenge model to investigate whether a trough level of penicillin is sufficient for secondary prophylaxis
2. Investigate the absorption and distribution of benzathine benzylpenicillin after intramuscular and subcutaneous injection in healthy adult volunteers
3. Explore globally available technologies for adaptation reformulate BPG

Success in addressing each of these three questions has facilitated the growth of further research specifically aiming to develop less painful and longer-acting penicillin treatments for those living with ARF and RHD.

### Peer-reviewed publications

1. RM Hand, S Salman, N Newall, J Vine, M Page-Sharp, AC Bowen, et al. *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. 2019;74(7):1984-1991.
2. JH Kado, S Salman, R Henderson, R Hand, R Wyber R, M Page-Sharp, et al. *Subcutaneous administration of benzathine benzylpenicillin G has favourable pharmacokinetic characteristics for the prevention of rheumatic heart disease compared with intramuscular injection: a randomized, crossover, population pharmacokinetic study in healthy adult volunteers*. Journal of Antimicrobial Chemotherapy. 2020;75(10):2951-2959.

## Understanding the burden of ARF and RHD; data linkage study

Associate Professor Judy Katzenellenbogen, The University of Western Australia

Eliminating RHD requires a robust evidence base, however the data required to support policy recommendations to achieve this is fragmented and incomplete. This study aimed to use linked data to provide a comprehensive database of ARF and RHD cases in Australia as a basis for improved monitoring and to assess prevention and treatment strategies. Additional funding has been secured for this project, making it possible to produce the most comprehensive dataset on the burden of ARF and RHD in Australia. The study concluded that previous methods of estimating cases of ARF and RHD in Australia heavily underestimated the burden, with the use of linked administrative data from five Australian jurisdictions providing a robust assessment to inform policy interventions more appropriately.

### Peer-reviewed publications

1. JM Katzenellenbogen, D Bond-Smith, RJ Seth, K Dempsey, J Cannon, I Stacey, et al. *Contemporary incidence and prevalence of rheumatic fever and rheumatic heart disease in Australia using linked data: the case for policy change*. Journal of the American Heart Association. 2020;9:e016851.
2. JM Katzenellenbogen, D Bond-Smith, RJ Seth, K Dempsey, J Cannon, L Nedkoff, et al. *The End Rheumatic Heart Disease in Australia Study of Epidemiology (ERASE) Project: data sources, case ascertainment and cohort profile*. Clinical Epidemiology. 2019;15:11:997-1010.
3. JM Katzenellenbogen, AP Ralph, R Wyber, JR Carapetis. *Rheumatic heart disease: infectious disease origin, chronic care approach*. BMC Health Services Research. 2017;17(1):793.

## MASTD-RHD: Using MRI to Aid Surgical Timing Decisions in RHD

Professor Alex Brown and Dr Ross Robert-Thompson, South Australian Health and Medical Research Institute

MASTD-RHD aimed to improve outcomes for people with established moderate-severe RHD by validating early markers of poor prognosis in mitral valve disease, the most common valvular disease in RHD. This will allow identification of people who will likely benefit from earlier surgery compared to those who can be safely monitored, helping to reduce complications such as stroke, atrial fibrillation and heart failure for patients with RHD. Specifically, the project used cardiovascular magnetic resonance (CMR) and examined whether this method can predict outcomes better than echocardiography or exercise stress testing alone.

## 'On Track Watch': a grassroots RHD initiative in the NT

Professor Anna Ralph, Menzies School of Health Research



Dr Haynes and Yolju community researchers Yunutju Gondarra and Minitja Marawili coding interview data in NVivo

On Track Watch (OTW) was a community-based participatory action research project undertaken in the East Arnhem land community of Baniyala, Northern Territory. Following on from the results from previous investigations, the community identified a need for children to be supported to stay 'on track' with their secondary prophylaxis, and for the community to be 'on watch' for the symptoms of ARF/RHD and of streptococcal infections. OTW aimed to build a local research workforce and empower local residents in community-based participatory action research methods; foster a community with health literacy relating to ARF and RHD; and improve the prevention, detection and management of ARF and antecedent streptococcal infections. As a result of this study, community members have articulated research priorities and identified holistic strategies to address the socioeconomic factors perpetuating infection transmission in remote Aboriginal communities.

### Peer-reviewed publications

1. E Haynes, M Marawili, Y Gondarra, BM Marika, AG Mitchell, J Phillips, et al. *Community-based participatory action research on rheumatic heart disease in an Australian Aboriginal homeland: evaluation of the 'On Track Watch' project*. Evaluation and Program Planning. 2019;74(1):38-53.

## Indigenous research capacity building through both-way learning

Professor Dawn Bessarab, Ms Heather D'Antoine, Professor Anna Ralph and Ms Emma Haynes, Menzies School of Health Research

This project extended 'On Track Watch' and expanded the training of two community researchers. This contributed to the original goals of OTW, strengthening the Lived Experience of RHD research, and developing CRE knowledge of Indigenous research and knowledge translation. Community researchers gained additional on-the-job training with other more experienced researchers (both Yolju and non-Aboriginal) to put new knowledge into practice, e.g. further interviews and focus groups and gained experience in validation of transcriptions, thematic analysis, and reporting. In addition, community researchers were able to gain skills in knowledge translation, including presentation of findings back to communities and at conferences.

## The South Australian Rheumatic Heart Disease (SACRHD) screening project

Professor Alex Brown and Ms Sara Noonan, South Australian Health and Medical Research Institute

The SACRHD Study aimed to determine the prevalence of RHD in Aboriginal and Torres Strait Islander children in South Australia. A component of the SACRHD screening project sought to gain a better understanding of the personal and practical impact of cardiac screening on children, and to determine the level of care provided to children following a screening diagnosis. It was determined that echocardiographic screening using portable echocardiography and performed by skilled sonographers is effective and feasible in the State. Several recommendations for future screening in South Australia were proposed based on the clinical findings and discussions with stakeholders and consideration of the accepted criteria for screening programs internationally. A peer-reviewed publication is in late-stage publication.

## Development of 3rd edition of the Australian guideline for prevention, diagnosis and management of ARF and RHD in partnership with RHD Australia and Heart Foundation

Ms Rebecca Slade, Professor Bart Currie, Professor Anna Ralph, Menzies School of Health Research

The Australian Guidelines for the prevention, diagnosis and management of ARF and RHD were updated in 2020 to reflect the translation of new research into clinical practice. The 3rd edition was also written with an aim to reflect clinically sound and culturally safe practice in Australia. Relevant additions included updated data of the burden of ARF and RHD, and a new chapter on primordial prevention and social determinants of ARF guided by the CRE.

### Peer-reviewed publications

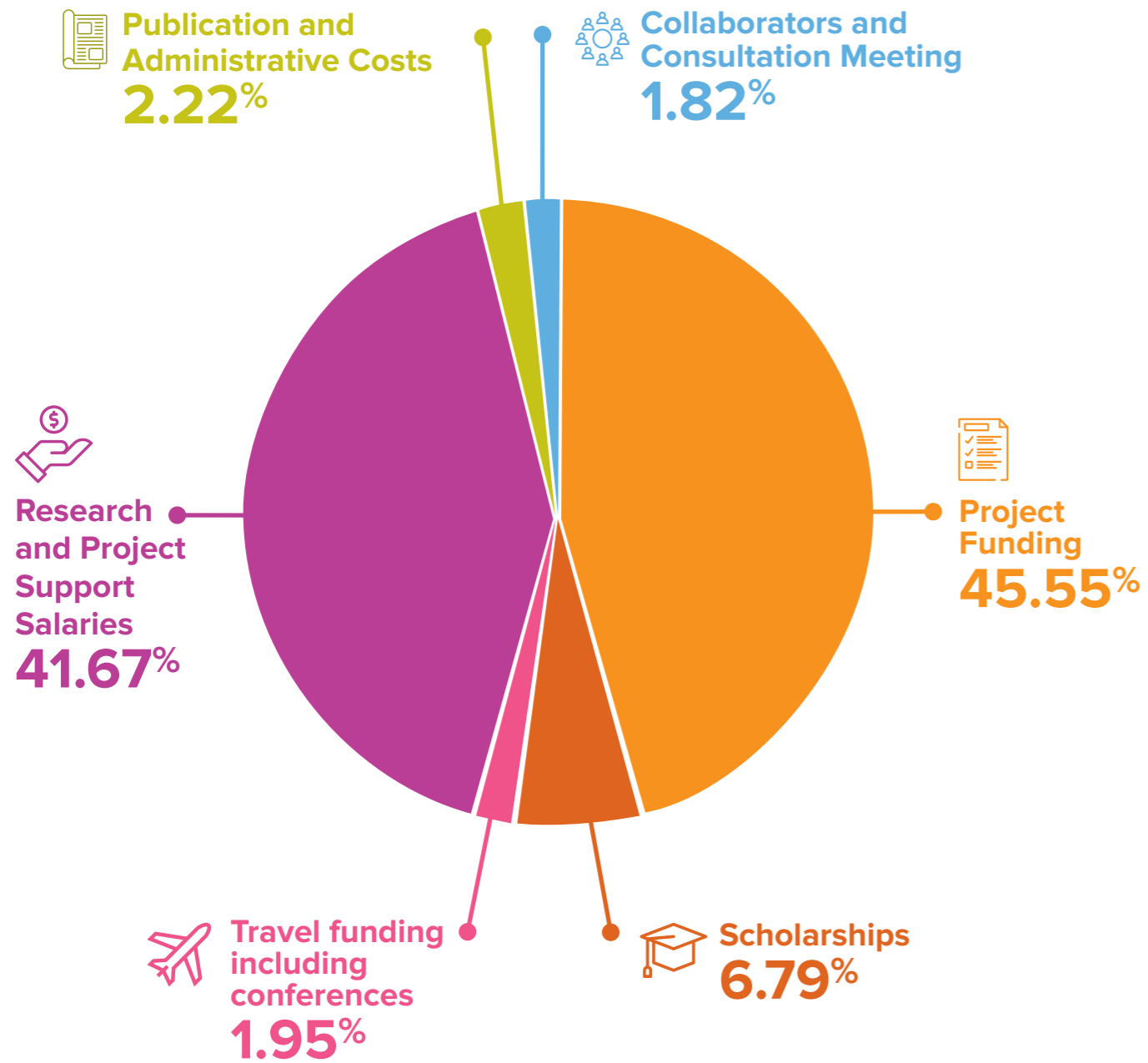
1. RHD Australia (ARF/RHD writing group). *The 2020 Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease (3rd edition)*. Darwin: Menzies School of Health Research; 2020.
2. A Ralph, S Noonan, V Wade and B Currie. The 2020 Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease. *Medical Journal of Australia*. 2021; 214 (5): 220-227

## Non-invasive identification of carditis in acute rheumatic fever

Dr. Sarah Gutman, Baker Heart and Diabetes Institute

This investigation, undertaken at The Baker Heart and Diabetes Institute, aimed to identify heart inflammation (carditis) in patients with ARF using new diagnostic methods, specifically cardiac magnetic resonance (CMR) scans. This new technology can identify subtle dysfunction of heart muscles which may be difficult to detect using conventional methods. Whilst widespread inflammation of the heart is believed to be a fundamental manifestation of acute rheumatic fever (ARF), its clinical confirmation is difficult. Patients who fulfilled the Australian-modified Jones Criteria for the diagnosis of ARF, patients with stable rheumatic heart disease (RHD) and people without underlying ARF/RHD were recruited to participate in the study and their CMR results compared. Results from a cohort of 62 participants indicated that those with ARF have a distinct picture of carditis on CMR scanning, even when usual assessment with heart ultrasound appeared relatively normal. Therefore, incorporating features of CMR scans into the diagnostic algorithm for ARF may improve diagnostic certainty and lead to more appropriate delivery of penicillin prophylaxis.

# FINANCIAL OVERVIEW



**Total Funding**

			<b>\$3,040,874.30</b>
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Tenaya Bell, diagnosed with RHD aged seven

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Discover. Prevent. Cure.

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