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A Proposed Methodology for Engagement, Informed Consent, and Governance for Conducting Genetic Research With Indigenous Communities: An Australian Example

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Introduction: Rheumatic heart disease (RHD) is highly prevalent in Aboriginal people in Australia. Despite decades of research, the underlying genetic mechanisms for why RHD occurs are not well understood. This genetic study was conducted to better understand why some people are susceptible to RHD and others are not. Past controversy in Indigenous genetic research has raised ethical concerns about the collection, use and storage of genetic samples. An appropriately designed methodology with a focus on cultural and ethical processes for gaining informed consent for the collection and treatment of samples was therefore vital to guide the study.
Objectives: This study; investigating the genetic association of RHD in Aboriginal communities in the Northern Territory of Australia sought to establish a range of consultative, culturally aligned and community guided mechanisms to support and ensure a robust and ethically sound approach to genetic research took place with participating Aboriginal communities.
Methods: Before individuals were approached for samples, an extensive period of Aboriginal governance, community engagement and qualitative inquiry formed stage 1 of the study. Indigenous methodology was employed to conduct five focus groups with communities, called 'yarning circles'. Genetic and health literacy material was produced, informed by communities, to ensure consent for the collection, use and storage of samples was well informed and understood. A protocol for the long-term governance of samples was established.
Results: This study demonstrates how preliminary efforts to address issues of relationship building and engagement assisted in developing community members' genetic literacy and ensured that members understood what they were consenting to when giving permission to informed consent in the context of genetic research. This was critical to clarifying researchers' responsibilities and obligations in relation to the future use of stored data and genetic samples for other research projects, and will more likely result in benefit sharing between community members and researchers.
Conclusion: This study demonstrates that such sensitive research can be ethically and successfully conducted. It can inform a pathway for ongoing research in this field and contribute to the formation of guidelines for the conduct of genetic research with Aboriginal communities.
Disclosure of Interest: None Declared

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School-Based Health Education Intervention to Increase Knowledge on Rheumatic Heart Disease: The Provar Study

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Introduction: Rheumatic Heart Disease (RHD) remains an important cause of morbidity and mortality in Brazil and other low- and middle-income countries (LMIC). Lack of public awareness of the causes and prevention of RHD limit the efficacy of primary and secondary prevention programs.
Objectives: To evaluate the efficacy of knowledge transfer that results from a structured public-school educational program on RHD.
Methods: A prospective, cohort study was conducted over 8 months (9/2014-4/2015) in 6 randomly selected low-income public schools in Belo Horizonte, Brazil. All enrolled and present students received education. A nurse and an imaging technician utilized 2 custom educational curriculums, targeting children in grades 6 - 11 (aged 11-17). Pre-tests, taken immediately prior to educational curriculum queried students' knowledge of the causes, prevention, diagnosis, and treatment of RHD. Post-tests, 1-3 weeks following education assessed the efficacy of knowledge transfer and retention.
Results: Education was delivered to 3700 students. Of these, 1176 were randomly selected to participate in pre- and post-testing including 404 (34%) in 6th/7th grades (G1), 511 (44%) in 8th/9th (G2), and 261 (22%) of in 10th/11th grades (G3). The mean interval between pre and post-tests was 10±10 days. Prior to the intervention, general knowledge regarding RHD was universally low (median score 46.7%, 40.0-60.0). Children in higher grades (G3) knew more about RHD than those in lower grades (60% vs. 43.3% G1/46.7% G2), $p<0.001$.Children showed significant gains in the post-test, raising the median score by 20% (60%, 40.0-73.3). Again, children in higher grades showed higher overall scores (73.3%, 60.0-80.0 G3; 60%, 40.0-73.3 G2; 53.3%, 33.3-66.7 G1), $p<0.001$. However, the percent increase was similar between groups (6.9% G1, 7.9% G2, 8.5% G3), $p=0.53$.
Conclusion: School-based RHD education resulted in consistent but modest gains in knowledge. Novel educational techniques and use of technology to engage young learners may lead to improved knowledge gains and retention. Further studies are needed to determine if increased knowledge leads to behavioral changes that could decrease the burden of RHD in LMIC.
Disclosure of Interest: None Declared

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Rheumatic Heart Disease Severity, Progression and Outcomes: A Multi-State Model

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Introduction: Rheumatic heart disease (RHD) remains a disease of international importance, yet little has been published about disease progression in a contemporary patient cohort. Multi-state models (MSM) provide a well-established method of estimating rates of transition between disease states, and can be used to evaluate the cost-effectiveness of potential interventions.
Objectives: We aimed to create a MSM for RHD progression using serial clinical data from a cohort of Australian patients.
Methods: The Northern Territory (NT) RHD register was used to identify all Indigenous NT residents diagnosed with RHD between the ages of 5 and 24 years in the time period 1999-2012. Disease severity over time, surgeries and deaths were evaluated for 591 patients.
Results: Ninety-six (16.2%) patients had severe RHD at diagnosis, and this proportion did not vary significantly by age. Of those diagnosed with severe disease, 42% and 60% had proceeded to surgery by 1 and 5 years respectively, and mortality 5 and 10 years after diagnosis was 14% and 22% respectively. Of those diagnosed with moderate RHD, there was a similar chance of disease regression or progression over time. The 'mild RHD' category was the most stable; after 10 years, 64% remained mild. Nonetheless 11.4% progressed to severe RHD, with half of these requiring surgery. During the study period, a total of 131 surgeries were performed in 97 patients, and there were 18 deaths.
Conclusion: The prognosis of young Indigenous Australians diagnosed with severe RHD is bleak; interventions must focus on earlier detection and treatment if the observed natural history is to be improved. This multi-state model can be used to predict the effect of different interventions on disease progression and the associated costs.
Disclosure of Interest: None Declared

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The Concept and Design of Definerhd: A Study to Evaluate the Progression of Subclinical Rheumatic Valve Lesions Diagnosed Through Echocardiographic Screening

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Introduction: Rheumatic heart disease (RHD) is the leading cause of cardiac morbidity and mortality among the world's youth. Echocardiographic (echo) screening detects subclinical RHD in asymptomatic children in endemic areas. The natural history of subclinical RHD and the impact of benzathine penicillin G (BPG) prophylaxis have not been evaluated. A randomized controlled trial comparing BPG vs. no BPG is impractical and potentially unethical given that BPG is effective at minimizing disease progression in symptomatic individuals. A registry can describe the natural history and assess the impact of secondary prophylaxis on subclinical disease.
Objectives: Delineate the natural history of subclinical RHD and the effect of BPG on subclinical lesions.
Methods: DefineRHD is a registry of echo-detected borderline and definite subclinical RHD. Enrolled sites have existing screening programs. Initial sites include Malawi, Samoa, Tonga, and Zambia. Uganda is a potential site. Cases diagnosed since 2013 will be enrolled. Yearly echos and BPG adherence data will be collected. Echos will be sent to readers for standardized diagnosis. The main outcome is the change in valve lesion grade (based on the scale below) amongst those with definite RHD at 6 years, with 2 and 4-year analyses. Rates of progression or regression of at least one grade will be compared between those with good (>80%) and poor (≤80%) BPG adherence. A secondary outcome is change in grade of lesion for the borderlines. We will also explore if there is an adherence threshold associated with disease progression. The study is powered to detect a difference in valve progression with good vs. poor adherence. Allowing 20% loss to follow-up, a total of 563 participants diagnosed with definite RHD, which equals 56,300 screened assuming a 1% definite RHD prevalence rate, are needed to power the study.

Grade	Category	WHF Nomenclature	Definition
0	No RHD	No RHD	
1	Borderline RHD	Borderline	Per WHF Criteria
2	Mild RHD	Definite	Mild MR or AR
3	Moderate RHD	Definite	Moderate MR, AR, or MS
4	Severe RHD	Definite	Severe MR, AR, or MS