Significance of RHD detected by echocardiography

Should we screen for rheumatic heart disease in New Zealand ?

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GREEN LANE

Clinical Excellence Through Research and Education

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Outline

- History of RHD echocardiography globally & in NZ
- Questions, recent research
- Future directions, the NZ context

Rationale for screening in high-risk populations

- Benzathine penicillin secondary prophylaxis after ARF prevents rheumatic fever recurrences and improves cardiac outcomes
- There is usually a latent (preclinical) phase in RHD
- Approximately 40% adults with RHD have not had a prior episode of ARF
  - 2007 Auckland Hospital RHD admissions – only 27/80 had documented prior ARF
- **RHD screening is an opportunity for case finding, initiation of prophylaxis, improving outcomes**

Tompkins, *J Chronic Disease* 1972
Feinstein, *Annals Int Med* 1964
Carapetis, *Epidemiol Infect* 2000
Silwa et al *Eur Heart J* 2010
Pointon & Webb, unpublished data

Echocardiography to screen for RHD

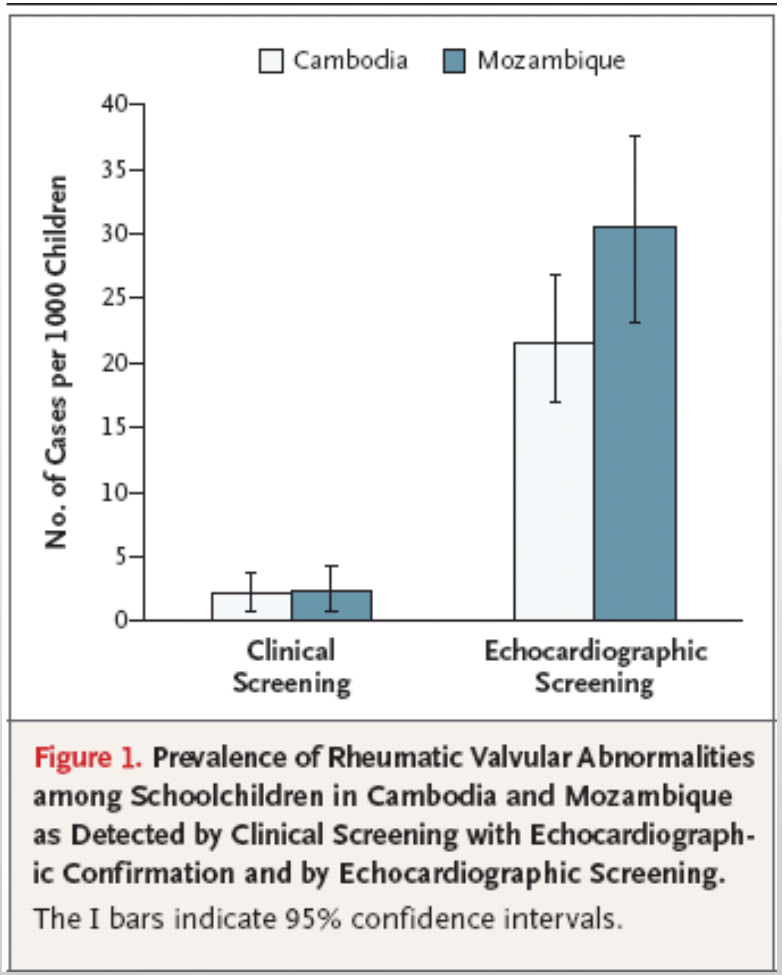
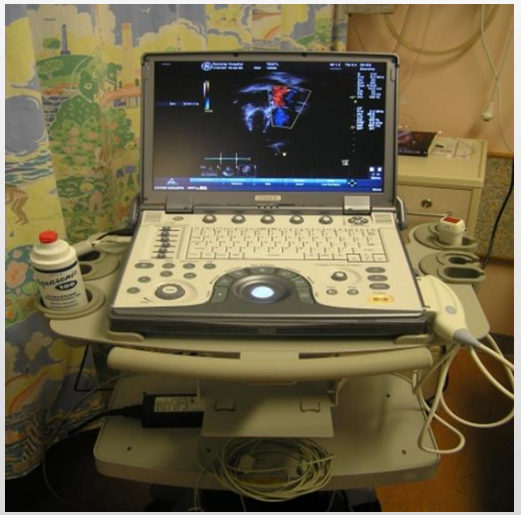


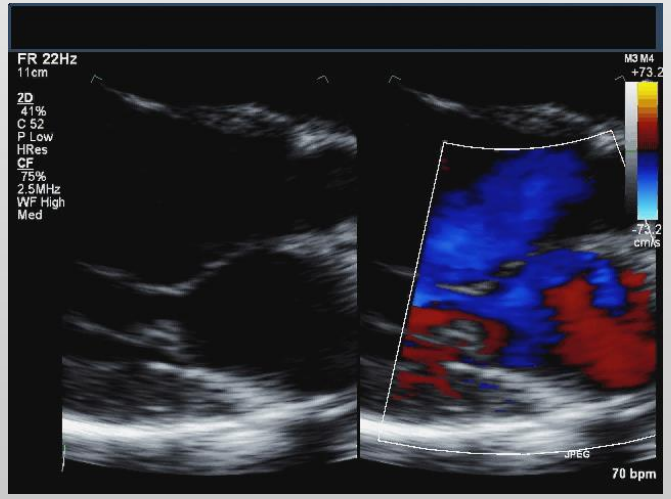
Figure 1. Prevalence of Rheumatic Valvular Abnormalities among Schoolchildren in Cambodia and Mozambique as Detected by Clinical Screening with Echocardiographic Confirmation and by Echocardiographic Screening.
The I bars indicate 95% confidence intervals.



Marijon et al, *NEJM* 2007

South Auckland 2007 – 2008 "The Healthy Hearts Study"

- Prevalence of RHD in high risk NZ children
- Sensitivity / specificity auscultation versus echo
- Feasibility of screening in NZ schools
- 1142 children 10 – 13 years
- 85% Maori/Pacific Islanders

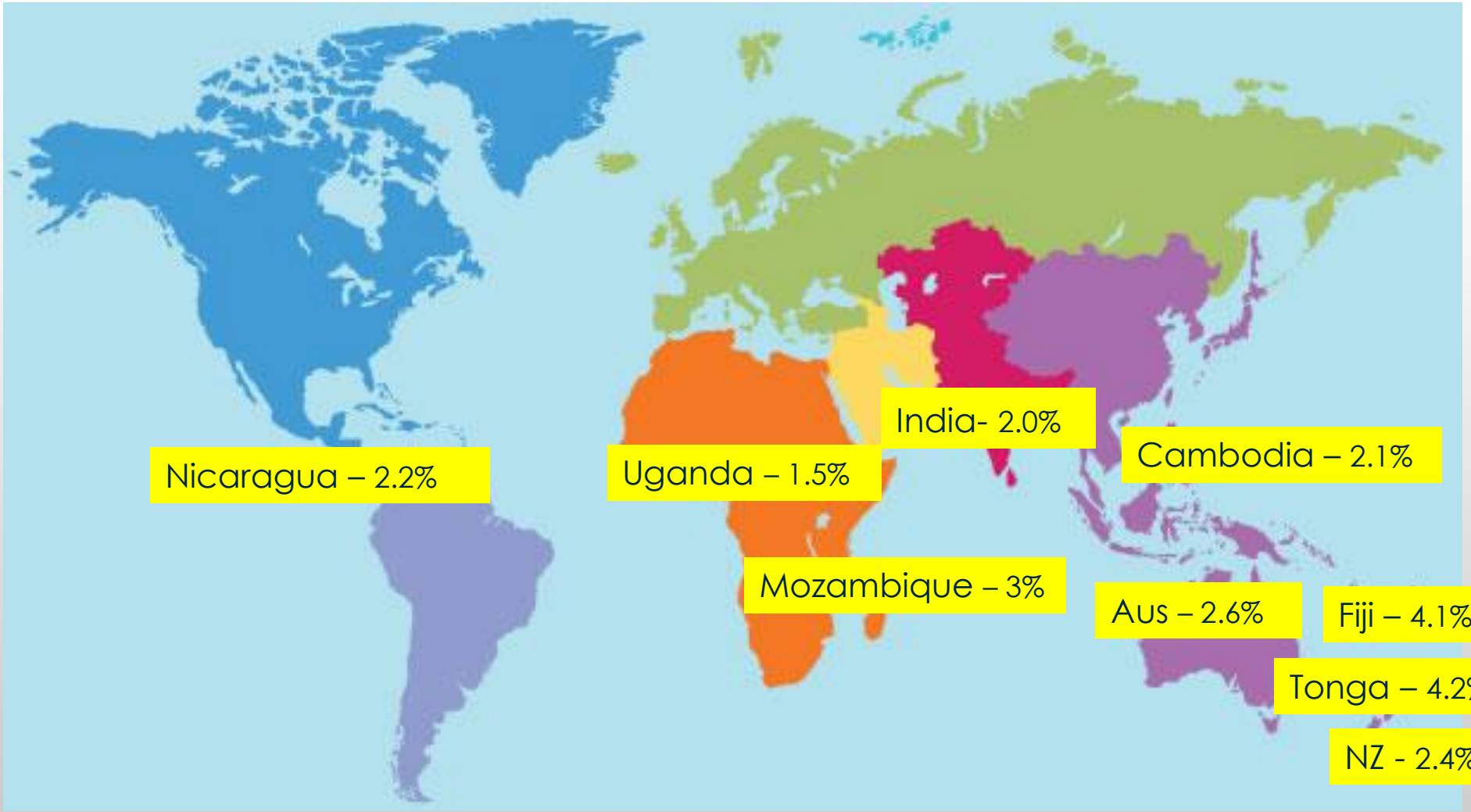


Webb, Wilson, Lennon et al. *Cardiology in the Young*, 2011

New Zealand : RHD echo findings

High prevalence regions				
	Number Surgery		**Definite RHD**	**Possible/Borderline**
South Auckland	1142	2	25 (2.4%)	30 (2.6%)
Tairawhiti	685	1	8 (1.1%)	19 (2.7%)
Bay of Plenty	553		3 (0.5%)	15 (2.7%)
Kaitaia	635	1	5 (0.8%)	16 (2.51)
Porirua (WHF)	621		8 (1.3%)	14 (2.3%)
South Auckland (adults, WHF)	425	3	7 (1.7%)	13 (3.1%)
	4090	**7**	**56** (1.4%)	**107 (2.6%)**
Low prevalence regions				
North Shore	396	0	0	2 (0.5%)

Global disease burden



Paar, *Am J Cardiol* 2010. Beaton, *Circulation* 2012. Marijon, NEJM 2007. Saxena, *Heart* 2011. Roberts, *Circulation* 2012. Steer, *J Heart Valve Dis* 2009. Carapetis, *Nat Clin Pract Cardiovasc Med* 2008. Webb, *Cardiol Young* 2011.

Questions & implications

1. Diagnostic criteria - what is abnormal and what is normal ?
2. Natural history
3. Potential harms and benefits
4. Health system capacity
5. Role of screening within ARF / RHD control programmes

World Heart Federation criteria for echocardiographic diagnosis of rheumatic heart disease—an evidence-based guideline

Bo Reményi, Nigel Wilson, Andrew Steer, Beatriz Ferreira, Joseph Kado, Krishna Kumar, John Lawrenson, Graeme Maguire, Eloi Marijon, Mariana Mirabel, Ana Olga Mocumbi, Cleonice Mota, John Paar, Anita Saxena, Janet Scheel, John Stirling, Satupaitea Viali, Vijayalakshmi I. Balekundri, Gavin Wheaton, Liesl Zühlke and Jonathan Carapetis

Nature Reviews Cardiology 2012; 9: 297 – 309

WHF criteria reduce the prevalence of RHD

	WHO-NIH	WHF
[1,2] New Zealand N =3665 2007 – 2010	2.4% Definite, Probable 2.9% Possible 5.3%	1.3% Definite 2.2% Borderline
[3] Australia N =3946 2008-2010	5.4% Definite Probable Possible	0.9% Definite 1.7% Borderline

What is normal ?

Valvular Regurgitation Using Portable Echocardiography in a Healthy Student Population: Implications for Rheumatic Heart Disease Screening

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Background: There is increasing use of portable echocardiography as a screening test for rheumatic heart disease (RHD). The prevalence of valvular regurgitation in healthy populations as determined using portable echocardiography has not been well defined. Minimal echocardiographic criteria for RHD have recently been clarified, but the overlap of normal and abnormal valvular regurgitation warrants further study. The aim of this study was to determine the spectrum of echocardiographic findings using portable echocardiography in children from a population with low prevalence of RHD.

Methods: Screening echocardiography was conducted in 396 healthy students aged 10 to 12 years using portable echocardiographic equipment. Echocardiograms were assessed according to 2012 World Heart Federation criteria for RHD. The prevalence of physiologic valvular regurgitation was compared with that found in previous studies of children using large-platform machines.

Results: Physiologic mitral regurgitation (MR) was present in 14.9% of subjects (95% CI, 11.7%–18.7%) and pathologic MR in 1.3% (95% CI, 0.6%–2.9%). Two percent (95% CI, 1.0%–3.9%) had physiologic aortic regurgitation, and none had pathologic aortic valve regurgitation. Physiologic tricuspid regurgitation was present in 72.7% of subjects (95% CI, 68.1%–76.9%) and physiologic pulmonary regurgitation in 89.6% (95% CI, 85.7%–91.8%). After cardiology review, no cases of definite RHD were found, but 0.5% of patients (95% CI, 0.1%–1.8%) had pathologic MR meeting World Heart Federation criteria for borderline RHD. Two percent (95% CI, 1.4%–4.6%) of the cohort had minor forms of congenital heart disease.

Conclusions: The spectrum of physiologic cardiac valvular regurgitation in healthy children as determined using portable echocardiography is described and is within the range of previous studies using large-platform echocardiographic equipment. The finding of two children with pathologic-grade MR, likely representing the upper limit of physiologic regurgitation, has implications for echocardiographic screening for RHD in high-prevalence regions. (J Am Soc Echocardiogr 2015;28:981-8.)

N = 396 low risk children
0.5% Borderline RHD
(all with isolated pathologic MR)

Valvular Heart Disease

Echocardiographic Screening for Rheumatic Heart Disease in High and Low Risk Australian Children

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Alex Brown, BMed, MPH, FCSANZ, FRACP (hon), PhD; David Atkinson, MBBS, MPH;
Bo Reményi, MBBS, FRACP; Gavin Wheaton, MBBS, FRACP, FCSANZ;
Andrew Kelly, MBBS, FRACP, FCSANZ; Raman K. Kumar, MD, DM;
Jiunn-Yih Su, MB, MPH; Jonathan R. Carapetis, MBBS, FRACP, FAFPHM, PhD

Background—Echocardiographic screening for rheumatic heart disease (RHD) is becoming more widespread, but screening studies to date have used different echocardiographic definitions. The World Heart Federation has recently published new criteria for the echocardiographic diagnosis of RHD. We aimed to establish the prevalence of RHD in high-risk Indigenous Australian children using these criteria and to compare the findings with a group of Australian children at low risk for RHD.

Methods and Results—Portable echocardiography was performed on high-risk Indigenous children aged 5 to15 years living in remote communities of northern Australia. A comparison group of low-risk, non-Indigenous children living in urban centers was also screened. Echocardiograms were reported in a standardized, blinded fashion. Of 3946 high-risk children, 34 met World Heart Federation criteria for definite RHD (prevalence, 8.6 per 1000 [95% confidence interval, 6.0–12.0]) and 66 for borderline RHD (prevalence, 16.7 per 1000 [95% confidence interval, 13.0–21.2]). Of 1053 low-risk children, none met the criteria for definite RHD, and 5 met the criteria for borderline RHD. High-risk children were more likely to have definite or borderline RHD than low-risk children (adjusted odds ratio, 5.7 [95% confidence interval, 2.3–14.1]; $P<0.001$).

Conclusions—The prevalence of definite RHD in high-risk Indigenous Australian children approximates what we expected in our population, and no definite RHD was identified in the low-risk group. This study suggests that definite RHD, as defined by the World Heart Federation criteria, is likely to represent true disease. Borderline RHD was identified in children at both low and high risk, highlighting the need for longitudinal studies to evaluate the clinical significance of this finding. (***Circulation*. 2014;129:1953-1961.**)

N = 1053 low risk children
0.5% Borderline RHD
(N = 5, 2 = MR, 1 = AR, 2 = MV morphology)

Imaging

Hospital

Portable

Handheld

Non-specialist sonographers, abbreviated protocols

Valvular Heart Disease

Screening for Rheumatic Heart Disease
Evaluation of a Focused Cardiac Ultrasound Approach

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Background—Rheumatic heart disease (RHD) remains a major public health problem worldwide. Although early diagnosis by echocardiography may potentially play a key role in developing active surveillance, systematic evaluation of simple approaches in resource poor settings are needed.

Methods and Results—We prospectively compared focused cardiac ultrasound (FCU) to a reference approach for RHD screening in a school children population. FCU included (1) the use of a pocket-sized echocardiography machine, (2) nonexpert staff (2 nurses with specific training), and (3) a simplified set of echocardiographic criteria. The reference approach used standardized echocardiographic examination, reviewed by an expert cardiologist, according to 2012 World Heart Federation criteria. Among the 6 different echocardiographic criteria, first tested in a preliminary phase, mitral regurgitation jet length ≥2 cm or any aortic regurgitation was considered best suited to be FCU criteria. Of the 1217 subjects enrolled (mean, 9.6±1 years; 49.6% male), 49 (4%) were diagnosed with RHD by the reference approach. The sensitivity of FCU for the detection of RHD was 83.7% (95% confidence interval, 73.3–94.0) for nurse A and 77.6% (95% confidence interval, 65.9–89.2) for nurse B. FCU yielded a specificity of 90.9% (95% confidence interval, 89.3–92.6) and 92.0% (95% confidence interval, 90.4–93.5) according to users. Percentage of agreement among nurses was 91.4%.

Conclusions—FCU by nonexperts using pocket devices seems feasible and yields acceptable sensitivity and specificity for RHD detection when compared with the state-of-the-art approach, thereby opening new perspectives for mass screening for RHD in low-resource settings. (***Circ Cardiovasc Imaging*. 2015;8:e002324. DOI: 10.1161/CIRCIMAGING.114.002324.**)

Key Words: acute rheumatic fever ■ developing countries ■ epidemiology ■ heart valve diseases ■ rheumatic heart disease ■ ultrasound

Simplified Rheumatic Heart Disease Screening Criteria for Handheld Echocardiography

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Background: Using 2012 World Heart Federation criteria, standard portable echocardiography (STAND) reveals a high burden of rheumatic heart disease (RHD) in resource-poor settings, but widespread screening is limited by cost and physician availability. Handheld echocardiography (HAND) may decrease costs, but World Heart Federation criteria are complicated for rapid field screening, particularly for nonphysician screeners. The aim of this study was to determine the best simplified screening strategy for RHD detection using HAND.

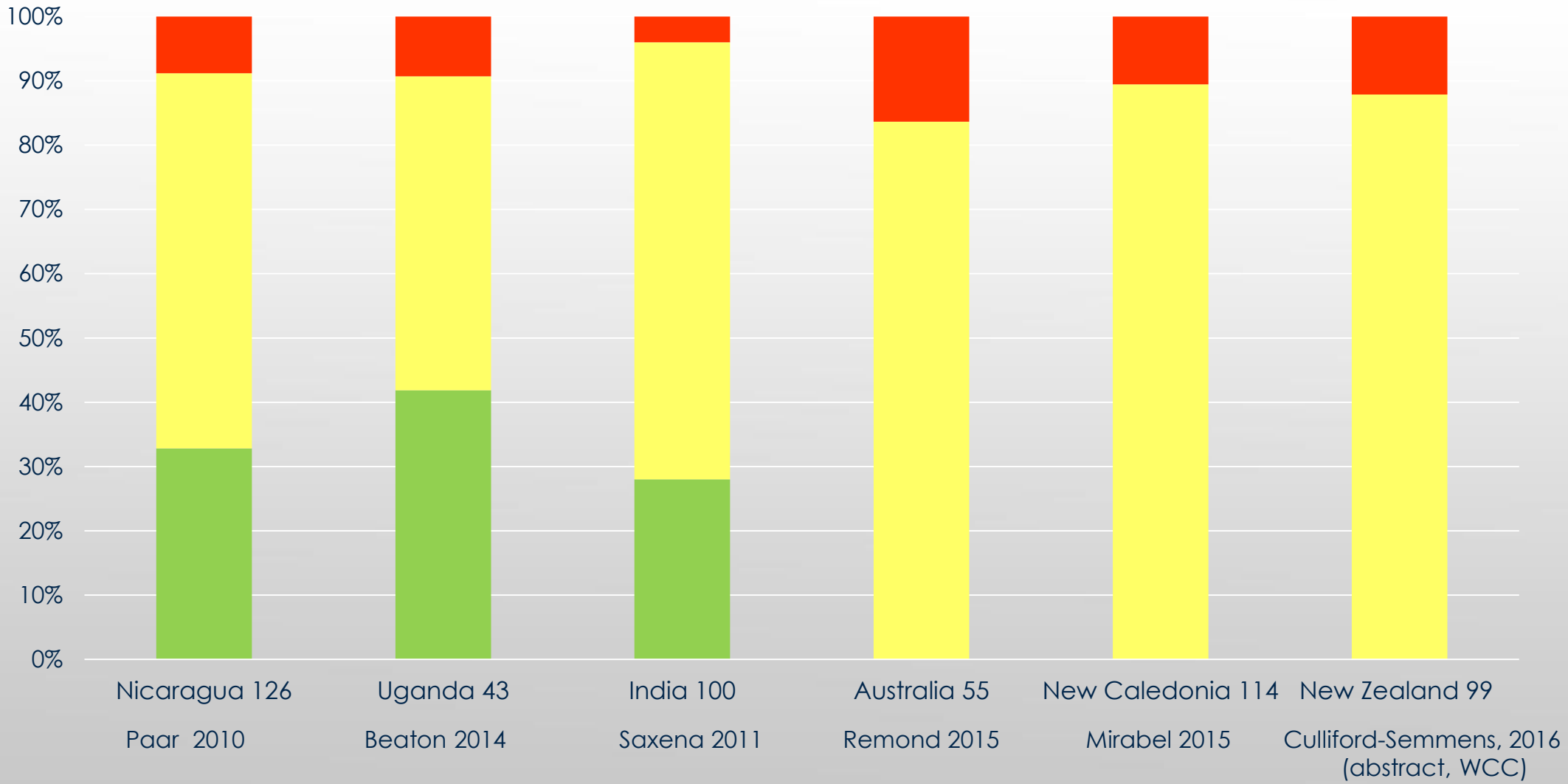
Methods: In this prospective study, STAND (GE Vivid q or i or Philips CX-50) was performed in five schools in Gulu, Uganda; a random subset plus all children with detectable mitral regurgitation or aortic insufficiency also underwent HAND (GE Vscan). Borderline or definite RHD cases were defined by 2012 World Heart Federation criteria on STAND images, by two experienced readers. HAND studies were reviewed by cardiologists blinded to STAND results. Single and combined HAND parameters were evaluated to determine the simplified screening strategy that maximized sensitivity and specificity for case detection.

Results: In 1,439 children (mean age, 10.8 ± 2.6 years; 47% male) with HAND and STAND studies, morphologic criteria and the presence of any mitral regurgitation by HAND had poor specificity. The presence of aortic insufficiency was specific but not sensitive. Combined criteria of mitral regurgitation jet length ≥ 1.5 cm or any aortic insufficiency best balanced sensitivity (73.3%) and specificity (82.4%), with excellent sensitivity for definite RHD (97.9%). With a prevalence of 4% and subsequent STAND screening of positive HAND studies, this would reduce STAND studies by 80% from a STAND-based screening strategy.

Conclusions: In resource-limited settings, HAND with simplified criteria can detect RHD with good sensitivity and specificity and decrease the need for standard echocardiography. Further study is needed to validate screening by local practitioners and long-term outcomes. (J Am Soc Echocardiogr 2015;28:463-9.)

Keywords: Rheumatic heart disease, Handheld echocardiography, Mitral regurgitation, Aortic insufficiency

Natural history



Northern Australia (RhFUSS)

Remond et al. *Int J Cardiol* 2015

	Borderline RHD Cases	Matched Controls	NSVA Cases	Matched Controls
Number	55	104	62	122
Progression to Definite RHD (n, %, 95% CI)	9 16.4% (8.9 – 28.3)	0 0%	6 9.7% (4.5 – 19.6)	2 1.6% (0.5 – 5.8)
Absolute risk difference (%, 95% CI)	16.4% (6.6 – 26.1)		8.0% (0.3 – 15.7)	
Relative risk (rr, 95% CI)	Could not be determined.		5.9 (1.2 – 28.4)	

Table 2. Progression to Definite RHD

1 in 6 Borderline -> Definite RHD

ARF Incidence RR 8.8 (1.4 – 53.8)

? An RCT

- Debated by WHF standardisation group in 2011
- Clear consensus regarding need for a multi-centre study
- Ethics of not treating Definite RHD ?
- Poor capacity for delivery of benzathine in resource-limited settings

- **Define RHD Registry**
  - **Coordinator -** Dr Amy Sims, Baylor College
  - **Collaborators** - Nigel Wilson, Liesl Zulke, Bo Remenyi, Dan Penny, Jonathan Carapetis,
  - **Goals** – Define natural history of screening-detected RHD
    - Benzathine vs no benzathine
    - RHD progression & ARF incidence / recurrence
    - To inform patient management

Potential harms & benefits

Journal of Paediatrics and Child Health

doi:10.1111/jpc.12829

ORIGINAL ARTICLE

Family acceptability of school-based echocardiographic screening for rheumatic heart disease in a high-risk population in New Zealand

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Departments of [1]Paediatrics and [3]Cardiology, Wellington Hospital, Wellington, and [2]Green Lane Pediatric and Congenital Cardiac Services, Starship Children's Hospital, Auckland, New Zealand

Aim: Echocardiographic screening for rheumatic heart disease has been piloted in high-risk areas in New Zealand and internationally, and fulfils most of the criteria for a targeted screening programme. The question of acceptability of rheumatic heart disease screening has not been assessed, and the aim of our study was to assess parental acceptability of a school-based echocardiographic screening programme in a high-risk population in New Zealand.

Methods: A post-screening questionnaire was developed to survey parents of children who underwent echocardiographic screening. The families of 34 children with abnormal scan results and a sample of 80 children with normal scan results were surveyed by phone within 4 months of screening.

Results: Positive results were seen in all survey questions in both normal and abnormal scan groups. All families were supportive of an ongoing screening programme. Of children with abnormal results, 62% of their parents reported that they would treat their child differently; however, all responses were positive health-promoting outcomes.

Conclusion: The study showed strong positive support for school-based echocardiographic screening by a community with high acute rheumatic fever incidence. The study did not detect any short-term negative effects in those with abnormal results. The survey result shows family and community support for the establishment of echocardiographic screening programmes in high acute rheumatic fever areas provided there is adequate infrastructural support.

Key words: echocardiogram screening; paediatrics; rheumatic fever; rheumatic heart disease.

Journal of Paediatrics and Child Health

doi:10.1111/jpc.12154

ORIGINAL ARTICLE

Patient and health-care impact of a pilot rheumatic heart disease screening program

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Aim: The aim of this study was to assess the impact of a pilot screening program for rheumatic heart disease (RHD) on patient quality of life (QOL) and health services.

Methods: A QOL questionnaire (CHQ-PF28) was used to assess the impact of RHD screening on children with a potentially abnormal screening echocardiogram and matched normal controls. The health service response to a potentially abnormal screening echocardiogram and the impact of the screening program on health services was evaluated using medical record review, carer interviews and surveys of health-care providers.

Results: QOL was assessed in 68 children. Potentially abnormal screening echocardiograms were associated with poorer QOL in the General Health Perception ($P < 0.05$) and Parental Impact – Emotional ($P < 0.05$) domains. Health services contacted 82% of children with potentially abnormal echocardiograms, and clinical review occurred in 56%. A potentially abnormal echocardiogram was associated with a change in management in 6% (2/34) of children. When surveyed, 49% of health providers were aware of the RHD screening program, 29% had seen children referred with screening abnormalities and 85% of these providers stated this had an impact on local health-care delivery.

Conclusions: This pilot RHD screening program was associated with poorer child and carer QOL for those with potentially abnormal results, greater health provider workload and suboptimal clinical follow-up. The adoption of screening for RHD in high-risk populations should be approached cautiously. Further research is required to facilitate and validate improved echocardiographic diagnostic criteria for RHD and the systematic assessment of the benefits and adverse effects of such screening.

Key words: cardiology; community; echocardiography; screening.

Adherence to Benzathine prophylaxis for RHD diagnosed by screening

- French Pacific[1]
  - 87% of a cohort of 114 children with RHD diagnosed by screening commenced BPG
    - 39 others lost to f/up – no data
  - 48% of 114 were receiving BPG <= 4 weekly.
- New Zealand[2]
  - 58 people started on BPG prophylaxis nation-wide 2007 – 2012
  - 45 with complete records > 2 calendar years
    - "BPG on time" defined as within 5 days of due date, 28 day cycle
    - Year 1: median 100% (range 42 – 100%)
    - Final year: median 92% (range 17 – 100%)
    - 6/45 (13%) defaulted from BPG, 3 within first 6 months

1. Mirabel et al. Int J Cardiol 2015. 2. Culliford-Semmens N, et al. Abstract accepted to WCC Mexico 2016

Cost-effectiveness

1369-6998
doi:10.3111/13696998.2015.1006366

Article 0133.R1/1006366

Original article

Echo-based screening of rheumatic heart disease in children: a cost-effectiveness Markov model

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Department of Pediatrics, Harvard Medical School, Boston, MA, USA

Abstract

Objectives:
To project the cost-effectiveness of population-based echo screening to prevent rheumatic heart disease (RHD) consequences.

Results:
The incremental costs and QALYs of the screen compared to no screen strategy were −$432 (95% CI = −$1357 to $575) and 0.007 (95% CI = −0.0101 to 0.0237), respectively. The joint probability that the screen was both less costly and more effective exceeded 80%. Sensitivity analyses suggested screen strategy dominance depends mostly on the probability of transitioning out of sub-clinical RHD.

Conclusion:
Two-stage echo RHD screening and secondary prophylaxis may achieve modestly improved outcomes at lower cost compared to clinical detection and deserves closer attention from health policy stakeholders.

EXPERT REVIEWS

Cost–effectiveness analysis of rheumatic heart disease prevention strategies

Expert Rev. Pharmacoecon. Outcomes Res. 13(6), 715–724 (2013)

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Rheumatic heart disease (RHD), secondary to group A streptococcal infection is endemic in the developing as well as parts of the developed world with significant costs to the patient, and to the healthcare system. We briefly review the prevalence and cost of RHD in developed and developing nations. We subsequently develop a Markov model to evaluate the cost-effectiveness of three strategies (vs standard no prevention) for preventing RHD in a developing world country: primary prophylaxis (throat swab to detect and subsequently treat group A streptococci as needed); primary prophylaxis (antibiotic prophylaxis for all) with benzathine penicillin G once monthly to all patients (ages 5–21 years) regardless of evidence of infection; and secondary prophylaxis with monthly only to those with echocardiographic evidence of early RHD. Our model suggests that echocardiographic screening and secondary prophylaxis is the best strategy although the strategies change depending on parameters used.

KEYWORDS: cost-effectiveness • developing and low socioeconomic status populations in developed nations • prevention strategies • primary prophylaxis • rheumatic fever • rheumatic heart disease • secondary prophylaxis

So, should we screen for RHD in NZ?

- Substantial recent progress to address many of the important questions raised in early years of RHD echo research
- Selective screening in populations where there is capacity for benzathine delivery and clinical follow-up, is logical and likely to be cost-effective
- Setting is important – NZ is in a unique position globally
- Many (including in NZ) with RHD do not have a history of ARF, and primary & secondary prevention initiatives will not benefit people with undetected RHD
- More work needed – natural history, systems & resource implications

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- Sonographers – Sandy Long, Fiona Lean, Megan Burrows, Kerry Conway, Denise Fong, Suzanne Davy-Snow, Gill Whalley, Rachel Gatland
- CMDHB - Ross Nicholson, Flo Chan Mow , Briar Peat , Adrian Trenholme
- University of Auckland – Dinny Lennon , Joanna Stewart
- Starship - Cardiology & ID teams
- SouthSeas PHO - Andrew Chan Mow & Lavinia Filiai
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- Public Health - Geoff Cramp, Jonathan Jarman, Clair Mills, Jason Gurney, Diana Sarfati

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