Global burden of rheumatic fever and what to do about it

The Science of Rheumatic Fever Surveillance and Control Feb 4, 2013

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Acute rheumatic fever and Rheumatic heart disease





Case

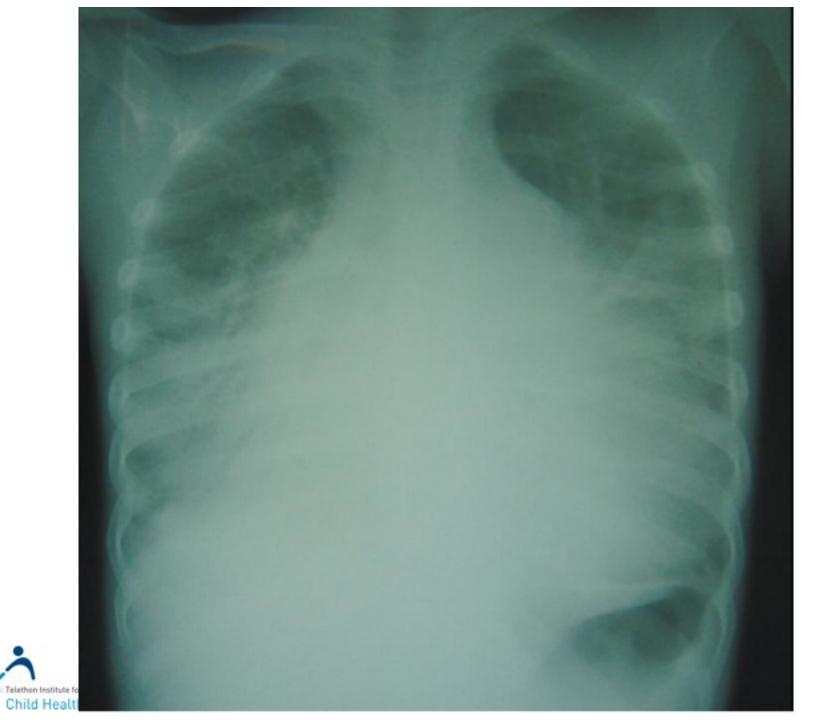
7 yo girl from rural Fijian village

Presented to a rural health centre with shortness of breath

Transferred to the main hospital in Suva







In Hospital:

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Transferred to ICU
Rapidly developed cardiogenic shock

Died within 3 hours of arrival

Post-mortem: severe RHD

The tragedy:

She had presented on multiple occasions with symptoms suggestive of rheumatic fever

At her last presentation, a nurse who had been to one of the Fiji RHD Program workshops, recognised that this could have been a case of RHD



In the 1930s and 1940s, RHD was the leading cause of death of American school-aged children. Paediatric wards were full of children with the disease and whole hospitals were devoted to its





care.

Global burden of disease

Summary report: Lancet Infect Dis 2005;5:685-94

The global burden of group A streptococcal diseases

Jonathan R Carapetis, Andrew C Steer, E Kim Mulholland, Martin Weber

The global burden of disease caused by group A streptococcus (GAS) is not known. We review recent populationLancet Infect DIs 2005; based data to estimate the burden of GAS diseases and highlight deficiencies in the available data. We estimate that

5: 685-94

Full report available on WHO website:

The current evidence for the burden of group A streptococcal diseases. WHO/FCH/CAH/05.



Global number of RHD cases 5-14 years old

Region	No. of studies (no. using echo)	RHD prevalence (per thousand)	Population 5-14 yrs (Millions)	Estimated RHD cases aged 5-14
	1.4.(1.0)		1.55	yrs
Subsaharan Africa	14 (10)	5.7	177	1008207
South-Central Asia	14 (12)	2.2	341	734786
Asia other	6 (0)	0.8	125	101822
Latin America	7 (4)	1.3	108	136971
ME and Nth Africa	7 (4)	1.8	84	153679
Eastern Europe†	1 (0)	1.0	411	40366
Pacific and indig Aust/NZ	7 (6)	3.5	22	7744
Established market economies	1 (1)	0.3	111	33330
China	1 (0)	0.8	220	176576
Total		1.3	1209	2393482



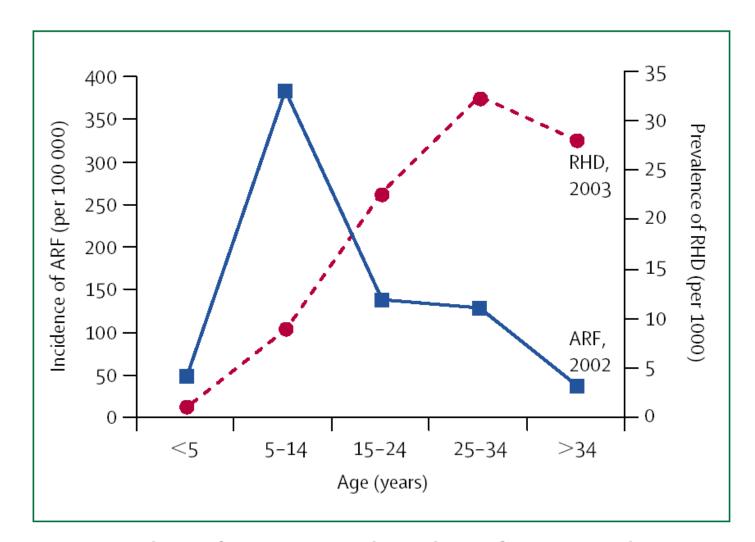


Figure 1: Incidence of ARF in 2002 and prevalence of RHD in 2003 by age in Aboriginal Australians from the top end of the Northern Territory (personal community, Top End RHD Control Program, Department of Health and Community Services, Darwin, Australia)

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Global number of RHD cases All ages

Age group and	No. of RHD cases	Prevalence in Less		
assumption		Developed countries		
5-14 years	2393482			
All ages (5.5 multiplication factor)	15.5 million	2.5		
All ages (7.2 multiplication factor)	19.6 million	3.2		



Global RHD deaths

Estimate of RHD cases	Estimated global number of RHD cases	Number of RHD deaths each year (assuming 1.5% per
Low-range estimate	15557632	233364
High-range estimate	19626551	294398

Applying cause-specific mortality rates:

- LDCs: 468,000 RHD deaths

- MDCs: 24,000 RHD deaths Total 492,000

Poor quality cause of death data from developing countries



Summary of estimated global burden of RF/RHD

Disease	Number of existing cases	Number of new cases each year	Number of deaths each year
Rheumatic heart disease	15.6 million	282,000	233,000
History of acute rheumatic fever without carditis, requiring secondary prophylaxis RHD-related infective endocarditis	1.88 million	188,000	8,000
RHD-related stroke	640,000	144,000	108,000
Total	>18 million	>640,000	~350,000

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Lancet Infect Dis 2005;5:685-94

Limitations of existing RHD disease burden estimates

- Poor quality data from most-affected regions
 - esp mortality, incidence of RHD, natural history
 - some regions with no data
- Lack of DALY data
 - Burden expressed as prevalence, number of cases, number of deaths
 - Prevalence extrapolated from 5-14yo
 - Mortality extrapolated from USA natural history studies in 1950s-60s
- Reliability of clinical vs echo-confirmed data





THE GLOBAL BURDEN OF DISEASES, INJURIES, AND RISK FACTORS STUDY

HARVARD UNIVERSITY

INSTITUTE FOR HEALTH METRICS AND EVALUATION AT THE UNIVERSITY OF WASHINGTON

JOHNS HOPKINS UNIVERSITY

University of Queensland

WORLD HEALTH ORGANIZATION



The Global Burden of Disease Study

• GBD 1990:

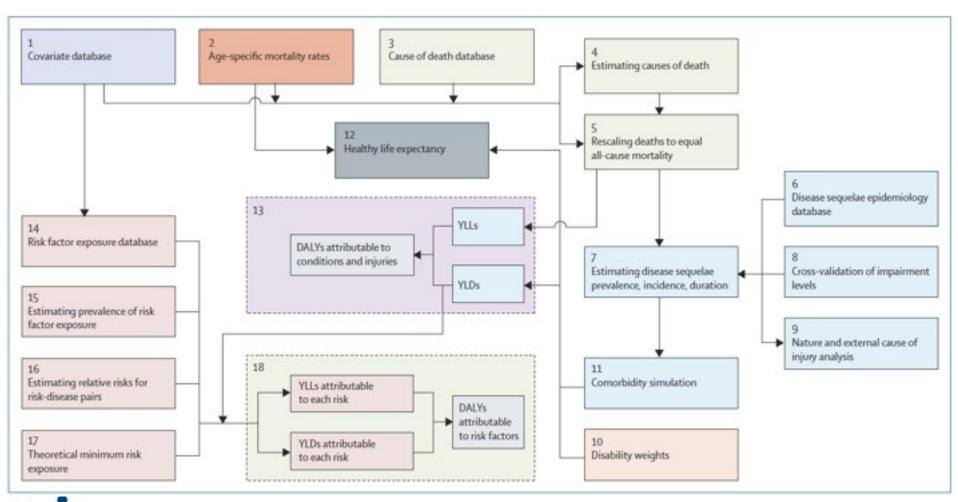
- Commissioned by World Bank 1991
- 8 regions
- 107 diseases/injuries,10 risk factors

• GBD 2010:

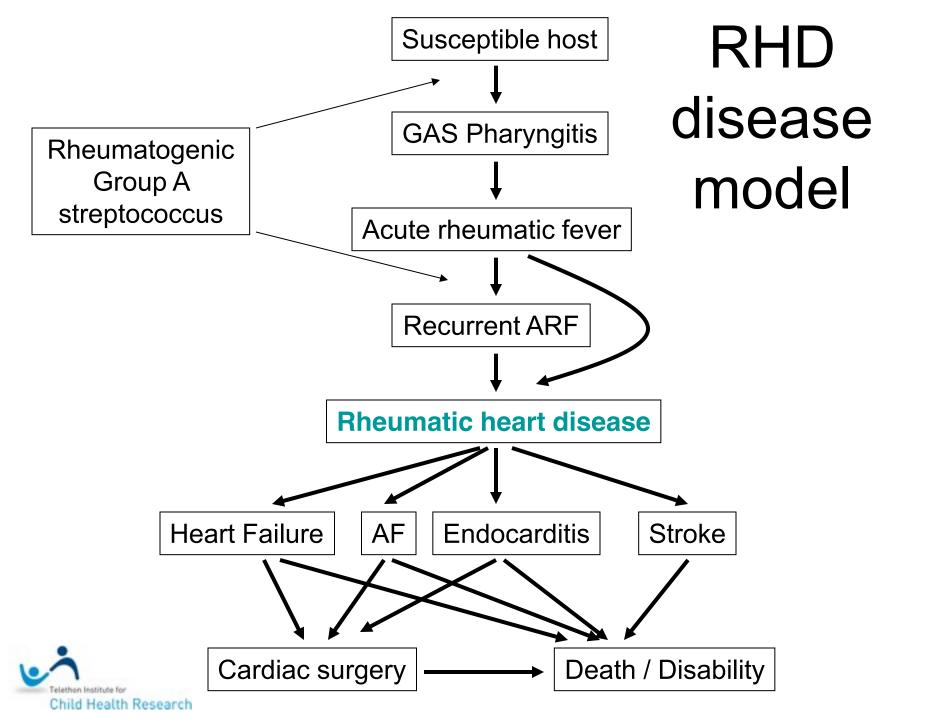
- 291 diseases and injuries
- 1160 sequelae → 220 "health states"
- 69 risk factors
- 21 regions
- DALYs

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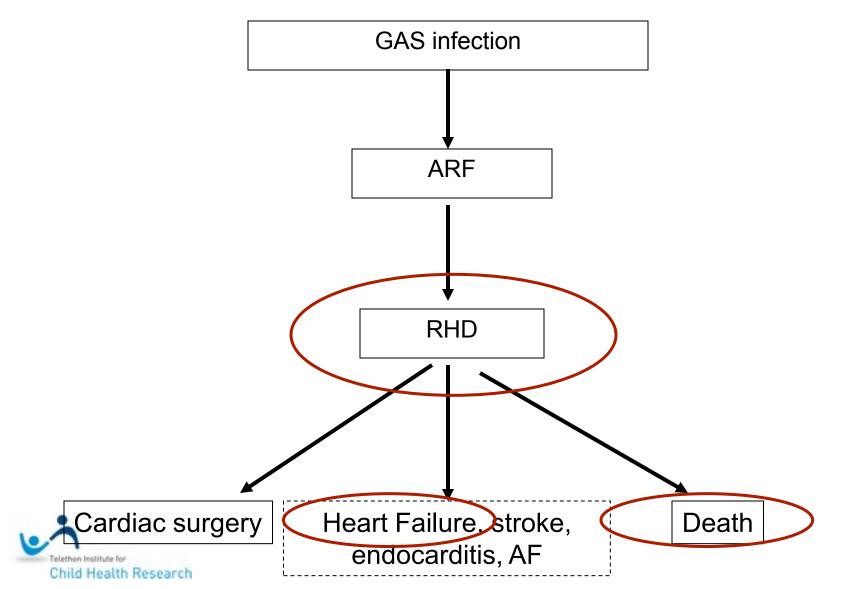
GBD 2010

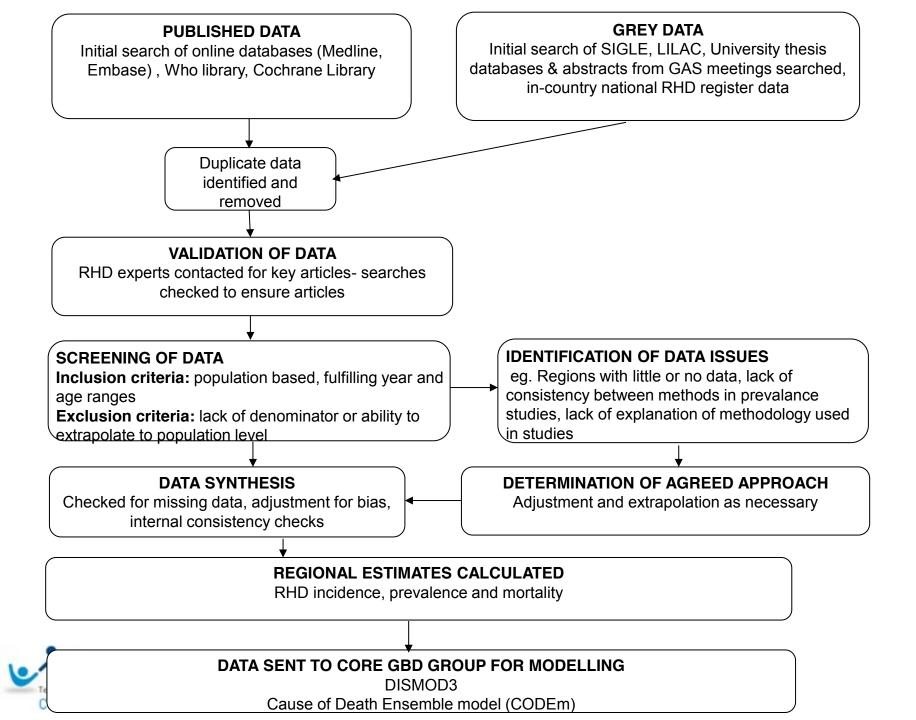






Simplified RHD disease model





Results

- 22 new studies of RHD prevalence since 2002 estimate
- 54% of published studies in school aged children- RHD prevalence only.
- Recent studies: echo confirmed diagnosis
- Earlier studies: clinical diagnosis alone.
- Only 5 studies documenting RHD incidence



GBD estimates

	1990	2005	2010
Prevalence	29,172,383	33,468,203	34,232,795
YLL	13,267,810	9,670,605	8,720,292
YLD	1,150,422	1,365,502	1,429,575
DALY	14,418,232	11,036,107	10,149,867
Deaths	462,579	363,864	345,110

Compared to previous 2005 publication: 15.6 million cases 233,000 deaths



Burden of RHD in Africa (estimated number of prevalent cases)

Region	1990	2005	2010
Sub-Saharan Africa, West	1,449,771	2,278,781	2,559,252
Sub-Saharan Africa, Southern	337,987	445,303	444,700
Sub-Saharan Africa, East	1,603,523	2,440,767	2,736,701
Sub-Saharan Africa, Central	397,010	496,000	584,780
North Africa / Middle East	767,257	993,260	1,065,011

Estimated incidence of RHD (number of cases)

Region	1990	2005	2010
Sub-Saharan Africa, West	103,051	132,118	148,031
Sub-Saharan Africa, Southern	18,184	22,899	25,558
Sub-Saharan Africa, East	100,029	132,281	145,064
Sub-Saharan Africa, Central	27,736	28,634	32,435
North Africa / Middle East	282,074	196,009	364,017



	RHD pre	evalent cas	es 1990	RHD pre	evalent cas	es 2010
GBD Region	Males	Females	Total	Males	Females	Total
North America, High Income	373,185	732,236	1,105,421	436,101	645,954	1,082,055
Latin America, Southern	71,587	113,809	185,396	73,569	115,669	189,238
Europe, Western	597,643	970,904	1,568,547	550,786	904,295	1,455,081
Australasia	10,901	17,486	28,387	10,417	17,588	28,005
Asia Pacific, High Income	220,117	353,705	573,822	184,508	299,153	483,661
Europe, Eastern	957,948	1,585,936	2,543,884	784,917	1,281,033	2,065,950
Europe, Central	278,849	422,737	701,586	242,003	305,447	547,450
Asia, Central	187,347	289,637	476,984	210,002	308,637	518,639
Sub-Saharan Africa, West	546,804	902,967	1,449,771	1,037,326	1,521,926	2,559,252
Sub-Saharan Africa, Southern	130,993	206,994	337,987	177,775	266,925	444,700
Sub-Saharan Africa, East	648,346	955,177	1,603,523	1,080,809	1,655,892	2,736,701
Sub-Saharan Africa, Central	155,691	241,319	397,010	234,722	350,058	584,780
North Africa / Middle East	307,891	459,366	767,257	441,109	623,902	1,065,011
Asia, South	1,965,424	3,057,358	5,022,782	4,220,195	5,662,012	9,882,207
Oceania	24,300	33,110	57,410	38,978	52,469	91,447
Asia, Southeast	1,236,225	1,979,432	3,215,657	1,576,475	2,343,023	3,919,498
Asia, East	3,344,926	5,093,119	8,438,045	2,326,592	3,446,920	5,773,512
Latin America, Tropical	118,837	188,038	306,875	133,412	192,513	325,925
Latin America, Central	96,849	149,009	245,858	118,068	193,062	311,130
Latin America, Andean	32,409	50,948	83,357	37,959	60,507	98,466
Caribbean	24,384	38,437	62,821	27,661	42,427	70,088
Global	11,330,658	17,841,725	29,172,383	13,943,383	20,289,412	34,232,795

Difficult issues

- Almost complete lack of data on:
 - Cause specific mortality
 - Relative risk of dying from all causes relative to those without disease
 - Average duration of disability for incident cases
 - Average duration to death
 - RHD incidence
- Attributable risk of cases/deaths due to stroke, AF, endocarditis
- Acute rheumatic fever

RHD mortality in NT, Australia

NT age-specific RHD deaths* (number and rate), 1977-2005

	/lale			Female		
	/lale			remale		
Age-group	n	rate	CI	n	rate	CI
Indigenous						
0-4	1	1.0	0.2-7.3	2	2.1	0.5-8.4
5-24	34	10.7	7.6-14.9	26	8.2	5.6-12.0
25-44	42	22.8	16.9-30.9	64	33.6	26.3-42.9
45-64	20	30.1	19.4-46.7	45	57.2	42.7-76.6
65+	5	31.4	13.1-75.4	14	67.4	39.9-113.8
non-Indigenoเ	US					
0-4	0	0.0	na	0	0.0	na
5-24	3	0.5	0.2-1.7	1	0.2	0.0-1.4
25-44	1	0.1	0.0-1.0	1	0.2	0.2-1.2
45-64	4	1.2	0.4-3.1	2	8.0	0.2-3.3
65+	6	10.5	4.7-23.1	9	19.2	10.0-36.8



Applying Australian RHD mortality rates to world population (2000 estimates)

More developed regions

	Male				Female	
Age	Popul'n	Rate	Number	Popul'n	Rate	Number
0-4	33821	0	0	32119	0	0
5 - 24	160752	0.5	804	153718	0.2	307
25-44	178781	0.1	179	175731	0.2	351
45-64	138847	1.2	1666	147330	0.8	1179
65+	67327	10.5	7069	103005	19.2	19777
All ages			9718			21614

Less developed regions

	Male				Female	
Age	Popul'n	Rate	Number	Popul'n	Rate	Number
0-4	281129	1	2811	266410	2.1	5595
5 - 24	1000221	10.7	107024	948638	8.2	77788
25-44	720252	22.8	164217	691666	33.6	232400
45-64	356366	30.1	107266	352515	57.2	201639
65+	113604	31.4	35672	134485	67.4	90643
All ages			416990			608064

Total: ~1 million RHD deaths per year

Global Burden of ARF/RHD

- GBD 2010 probably brings us closer to the truth, but still many holes in data
- Assumptions continue to underestimate the true burden
- Burden needs to be put into context:
 - Disease of the young
 - Disease of poverty and social injustice
 - Many cases and deaths eminently preventable



What to do about it?



Current status

- Disease of children and poverty
- Disease burden
- Cost effective interventions
- Enthusiastic individuals in developing countries
- New interventions on the horizon
- Interest of international community
- Interest of governments and health officials
- Interest of industry
- Interest of funding bodies
- Implementation of known strategies



4 challenges to ARF/RHD control

- Challenge 1: Translating what we know already into practical RHD control
- Challenge 2: How to identify people with RHD earlier, so that preventive measures have a higher chance of success
- Challenge 3: Better understanding of disease pathogenesis, with a view to improved diagnosis and treatment of ARF and RHD
- Challenge 4: Finding an effective approach
 to primary prevention

1. Practical RHD control

- Improving uptake of proven RHD control strategies around the world
 - Advocacy
 - Policy
 - Research
 - Implementation science



The Cerdiac Society of Australia
and New Zealand







New Zealand

Guidelines

Rheumatic Fever

1. Diagnosis, Management and Secondary Prevention

Evidence-based, best practice Guidelines on:

- 1. Diagnosis, Management and Secondary Prevention
- 2. Sore Throat Management
- 3. Proposed Pheurustic Fever Primary Prevention Programme



RHEUMATIC FEVER AND RHEUMATIC HEART DISEASE

Report of a WHO Expert Consultation Geneva, 29 October—1 November 2001



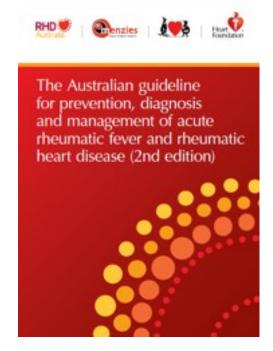
Rheumatic heart disease control programs

- Centralised register, linked to local registers
- Commitment from government to ensure long-term funding
- Activities guided by locally relevant, evidence-based guidelines
- A dedicated, centrally based coordinator for each control program
- An effective advisory committee
- Prioritisation of secondary prophylaxis
- A stable supply of benzathine penicillin
- Procedures to find new cases of ARF and RHD and to monitor burden of disease
- Education for health practitioners, the community, patients and families
- Legislation and/or regulations warranting the notification of ARF/RHD
- A priority system that ensures services are delivered to those at highest risk



Australian RHD Control

- 1997: Top End Programme (Australia's first)
- 2001: Central Australian Programme
- 2006: National Best Practice Guidelines
- 2009: National RF Strategy





Australia's National RF Strategy

- Announced 2009
- A national, coordinated approach to RHD control -RHDAustralia
- Core funding for RHD control programs across:
- Western Australia, Queensland & Northern Territory







- Menzies School of Health Research (NT)
- Baker-IDI (NT / Vic)
- James Cook University (Qld)



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PROFESSIONAL DEVELOPMENT



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WHAT IS RHEUMATIC HEART DISEASE?

Rheumatic heart disease (RHD) is chronic damage to the valves in the heart that is caused by repeated

ABOUT RHD AUSTRALIA

We work with Rheumatic Heart Disease control programs and other partners throughout Australia to



WHF Pacific RHD Control Program

Aims

 To develop a regional comprehensive model for RHD control based on secondary prevention

Methods

- Establish Demonstration sites
 - Fiji (2005)
 - Samoa (2007)
 - Tonga (2009-10)
- Share knowledge
 - RHDnet
 - Regional meetings
 - ? Regional strategy







WHF Pacific RHD Control Program

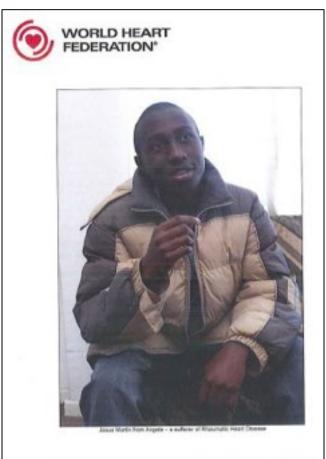
Progress

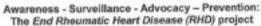
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- Fiji
 - Now national programme
 - All core costs now met by Fiji MoH
 - All training done locally
 - Minimal ongoing technical assistance
- Fiji, Tonga, Samoa
 - After initial assistance, now running essentially independently and locally funded.
- Next: AusAID funded program in 5 other
 countries

Africa

- ASAP programme
 - Awareness
 - Surveillance
 - Advocacy
 - Prevention
- World Heart Federation, PASCAR
- Funding: Else Kröner Foundation
- Multiple countries
- Leadership: Prof Bongani Mayosi





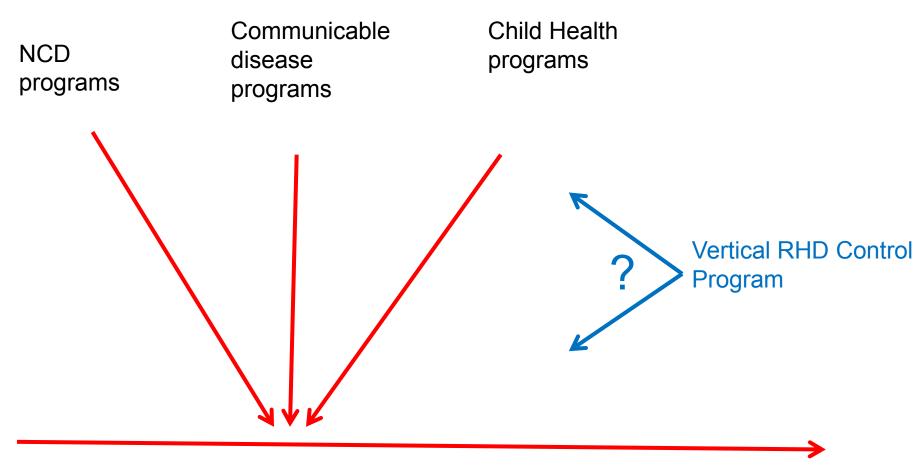


1. Practical RHD control

 New approaches to integrating centralised control programmes with primary care and with overall chronic disease care



Challenge





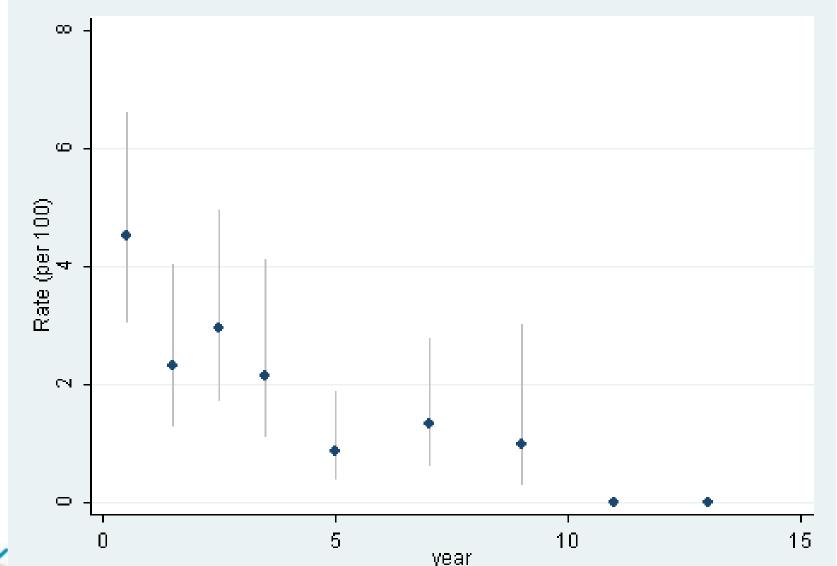
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1. Practical RHD control

- New approaches to integrating centralised control programmes with primary care and with overall chronic disease care
- Better quality and analysis of routinely collected data to study trends and outcomes



ARF recurrence rates by years since diagnosis, NT, 1997-2010





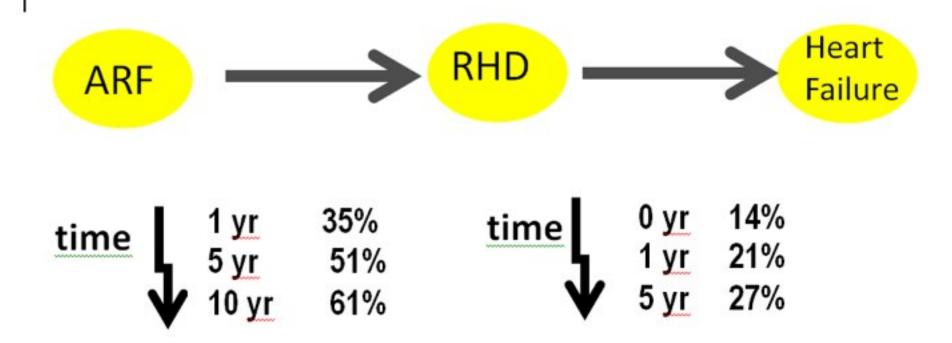
Lawrence J. et al. unpublished

Recurrences of ARF in NT, 1997-2010

	Hazards Ratio ¹	p-value	95% CI
Indigenous status	1.92	0.52	0.27-13.9
Female gender	0.79	0.30	0.50-1.23
Age at first ARF episode ²	0.93	<0.01	0.90-0.97
Year	0.91	0.01	0.84-0.97



Figure 6 Progression of ARF to RHD and cardiac failure among Indigenous subjects





Incidence and characteristics of newly diagnosed rheumatic heart disease in Urban African adults: insights from the Heart of Soweto Study

Karen Sliwa¹*, Melinda Carrington^{1,4}, Bongani M. Mayosi³, Elias Zigiriadis², Robert Mvungi¹, and Simon Stewart^{1,4}

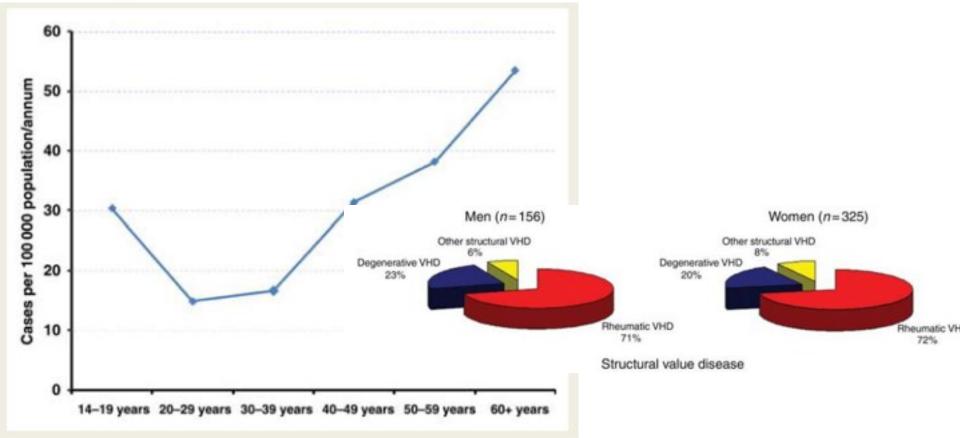


Figure 2 Estimated incidence of rheumatic heart disease (de novo hospital presentations).

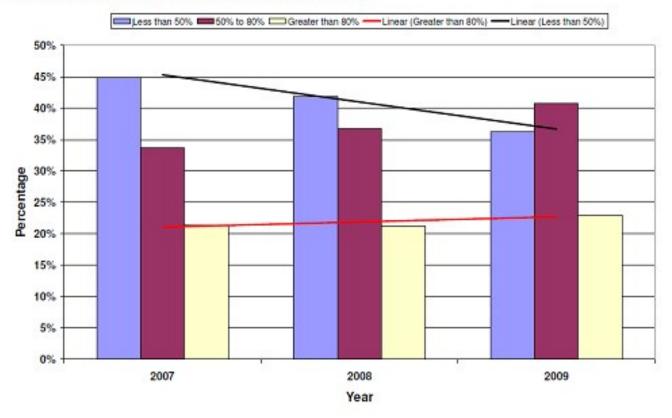
1. Practical RHD control

- New approaches to integrating centralised control programmes with primary care and with overall chronic disease care
- Better quality and analysis of routinely collected data to study trends and outcomes
- Improving uptake of secondary prophylaxis
 - Understanding determinants of adherence

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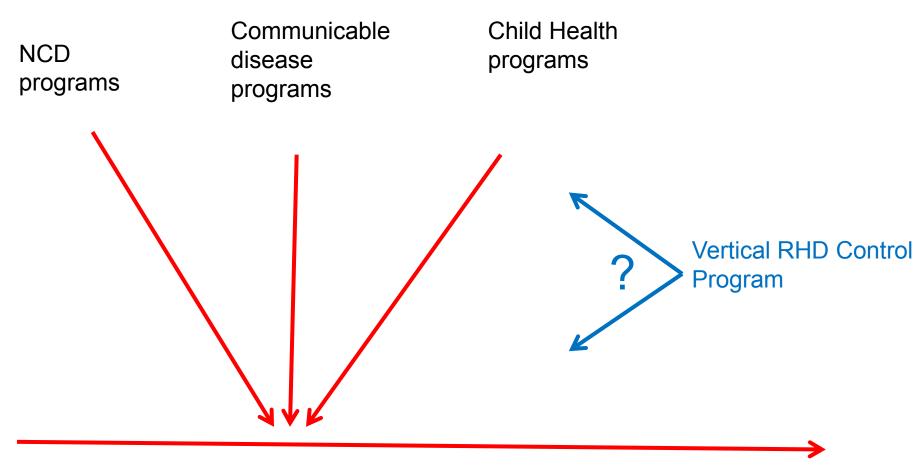
- Trials of new strategies to improve adherence
- Quality and availability of benzathine penicillin G
- Implantable penicillin or longer acting benzathine penicillin G

Fig 1. SP coverage, NT 2007-9. (NT RHD Control Programme Report 2010).



Year	<50%	50-80%	>80%	Overall Coverage
2007	44%	34%	22%	55%
2008	42%	36%	21%	56%
2009	35%	41%	24%	60%
2010	33%	42%	26%	61%
Grand Total	38%	38%	23%	58%

Challenge





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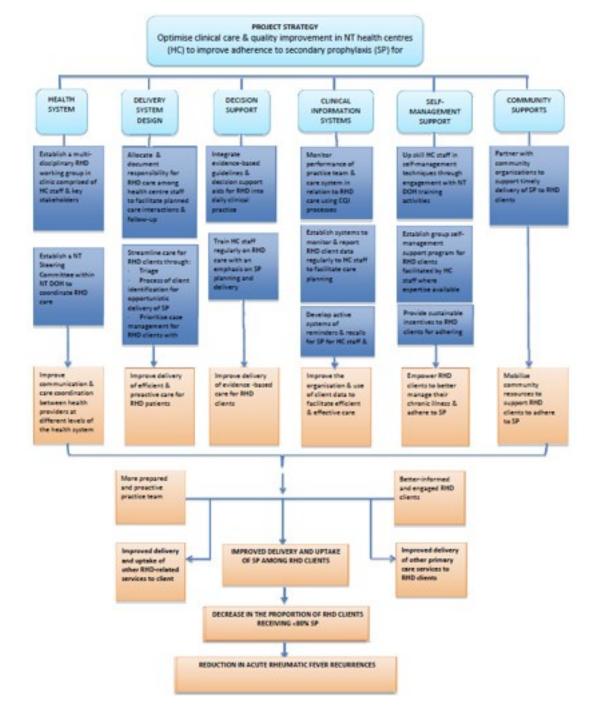
Continuous Quality Improvement in Australian health centres

	Risk classification ¹	2008	2009	2010	p- value
Received 80%+ of scheduled injections	All	25% (29/116)	26% (25/97)	23% (24/103)	0.78
	High/Med	30% (17/57)	32% (14/44)	28% (13/47)	0.83
Received 60%+ of scheduled injections	All	42% (49/116)	53% (51/97)	52% (54/103)	0.13
Received 40%+ of scheduled injections	All	70% (81/116)	76% (74/97)	82% (84/103)	0.04
Frequency of BPG injections scheduled at four weekly	All clients with documented requirement for regular BPG injections	20% (23/116)	32% (31/97)	52% (54/103)	<0.001
Actions to improve uptake for clients who received <80% of	Active recall	81% 70/86	94% 68/72	89% 70/79	0.15
injections	Arrange BPG if out of community	59% 51/86	62% 45/72	63% 50/79	0.60
	Prevention advice	64% 55/86	76% 38/72	39% 31/79	0.002
	Family meeting	31% 27/86	17% 12/72	8% 6/79	<0.001
	Action plan	28% 24/86	18% 13/72	5% 4/79	<0.001
	Other action	27% 23/86	24% 17/72	46% 36/79	0.01
* Active recall plus at least one other of the above strategies	for clients who received <80% of injections	69% 59/86	85% 61/72	72% 57/79	0.56
Echocardiogram	all within three years	55% (85/154)	60% (87/145)	62% (97/156)	0.21
	high and medium risk within 12 months ¹	39% (23/69)	42% (22/52)	44% (27/61)	0.20
Documented review by doctor	All within 2 years	73% (112/154)	83% (121/145)	86% (134/156)	0.003
within 6 months	High/medium	46%	67%	74%	0.004

Prophylaxis
project
- An RCT in the
Northern
Territory

Program and evaluation logic (courtesy V Johnston)





2. How to identify people with RHD earlier, so that preventive measures have a higher chance of success





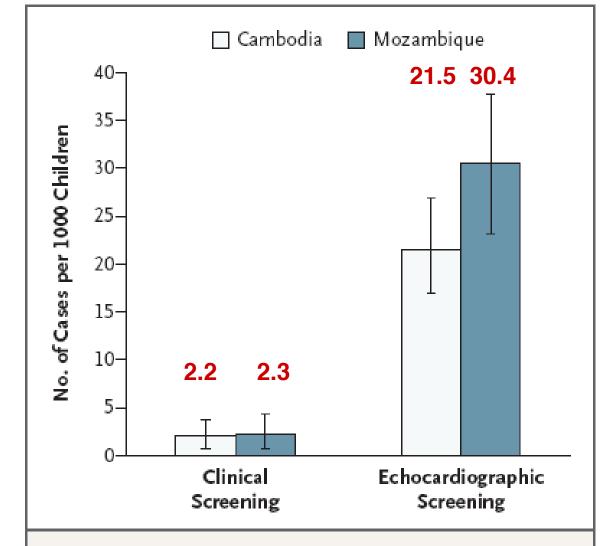


Figure 1. Prevalence of Rheumatic Valvular Abnormalities among Schoolchildren in Cambodia and Mozambique as Detected by Clinical Screening with Echocardiographic Confirmation and by Echocardiographic Screening.

The I bars indicate 95% confidence intervals.



N Engl J Med 2007;357:470-6.

RHD screening – recent studies

Place, year	Number screened	Screening method	RHD prevalence (echo confirmed)
Mozambique, 2005	2170	Clinical (sig murmur)	2.3
Cambodia, 2001-2	3677	Clinical (sig murmur)	2.2
Nicaragua	3150	Clinical (sig murmur)	5
Fiji, 2006-7	3470	Clinical (sig murmur)	8.4
Tonga, 2003-4	4794	Clinical (any murmur)	33.2
Cambodia, 2001-2	3677	Echo all	21.5
Mozambique, 2005	2170	Echo all	30.4
Nicaragua 2006-9	3150	Echo all	38

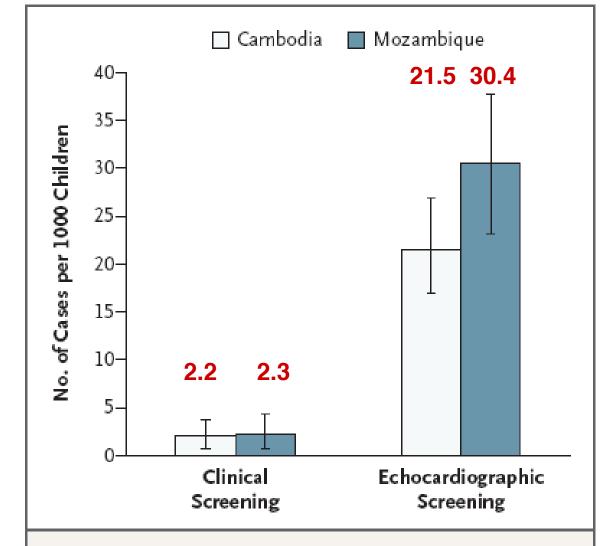


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N Engl J Med 2007;357:470-6.

- 2. How to identify people with RHD earlier, so that preventive measures have a higher chance of success
- Standardisation of echocardiographic screening for RHD
- Evidence-based diagnostic criteria for RHD
- Determining the significance of subclinical carditis
 - Follow-up studies
 - ? RCT

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Making echocardiographic screening practical
 and affordable

REVIEWS

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

Reményi, B. et al. Nat. Rev. Cardiol. advance online publication 28 February 2012; doi:10.1038/nrcardio.2012.7













The gECHO Study (Getting Every Child's Heart OK)

Between 2008 and 2010, teams from the gECHO study visited schools in the Northern Territory, Central Australia, Far North Queensland and the Kimberley region of Western Australia

What we did:

Heart checks using an ultrasound (called an 'echo') on 5000 children looking for Rheumatic heart disease (RHD).

RHD is permanent damage to the heart that can occur after Acute Rheumatic Fever (ARF).

What we found:

- Over 99% of children have healthy hearts!
- Less than 1 in 100 children have RHD.
- Children in remote communities had more RHD than children in Darwin and Cairns.

How did this study help?

- The children we found with RHD were referred to the clinic to start penicillin treatment.
- By starting treatment early, we can prevent their RHD from getting worse.
- This is the first study that shows us how many children have RHD in different communities.
- We can use this information to improve services for people with RHD in northern Australia.

Want to know more?

For more information about the gECHO study, call Dr Kathryn Roberts, Menzies School of Health Research on 08 8922 8196.

For any information about RHD or ARF, check out the RHDAustralia website: www.mdaustralia.org.au

The gECHO study would like to thank all children and their families, plus staff at the school and the clinic for participating in this important study.

We would also like to thank the Australian Government, Children's First Foundation, Cabrini Health and Kiwanis for their generous support









Overall results from the gECHO study

5245 children had heart ultrasounds

1015 children also had their heart listened to by a doctor or nurse:

(We found that this was not a good way to detect RHD)

Overall, in remote Indigenous communities we found that:

- •1 in every 140 children had Definite RHD
- •1 in every 80 children had Borderline RHD

In non-Indigenous children in Darwin and Cairns, we found that:

- No children had Definite RHD
- •1 in every 200 children had Borderline RHD

3. Better understanding of disease pathogenesis, with a view to improved diagnosis and treatment of ARF and RHD

- Immunology
- Genetics
- Prospective studies, with a view to
 - Diagnostics
 - Therapeutics



4. Finding an effective approach to primary prevention

- A vaccine for rheumatic fever
- The role of primary prophylaxis of streptococcal sore throat
 - Systematic screening based approaches vs
 strengthening primary health care treatment
- The role of controlling skin infections
 - Expanded implementation and evaluation of skin disease control programs
 - Mapping of skin disease and ARF and RHD



Also

- Surgery for RHD
 - Role, esp in developing countries



Group A streptococcal diseases

- Superficial infection
 - Pharyngitis
 - Pyoderma



- Septicaemia
- Pneumonia, osteomyelitis...
- Necrotising fasciitis



- Scarlet fever
- Streptococcal toxic shock syndrome
- Post-streptococcal autoimmune sequelae
 - Acute rheumatic fever / rheumatic heart disease









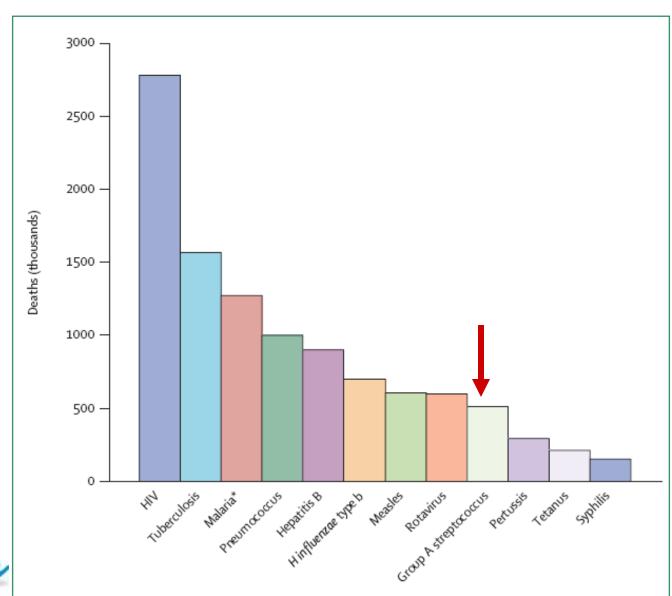








Estimated global mortality from individual pathogens, 2002

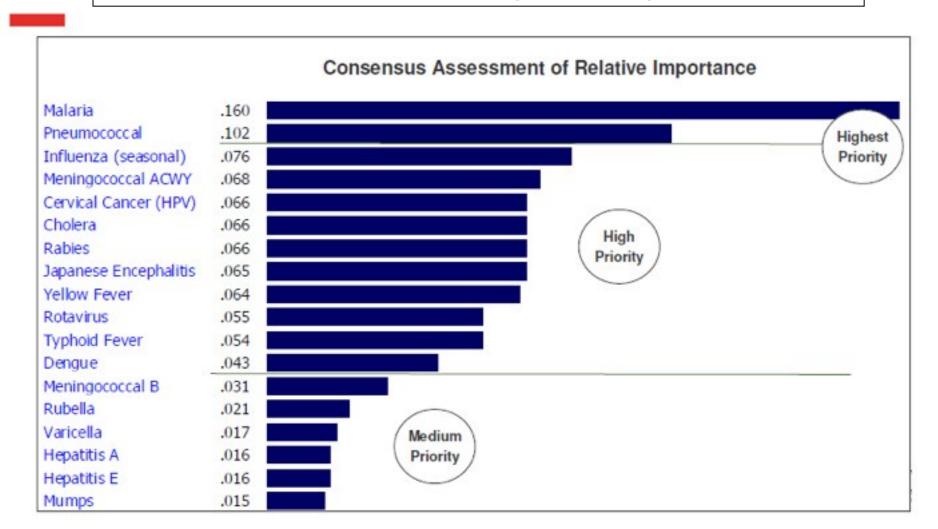




Lancet Infect Dis 2005;5:685-94

WHO disease prioritization (Nov 2007)

From GAVI Research Forum 2008, see: http://www.who.int/vaccine_research/about/gvrf/Kallenberg%20presentation.pdf



Conclusions

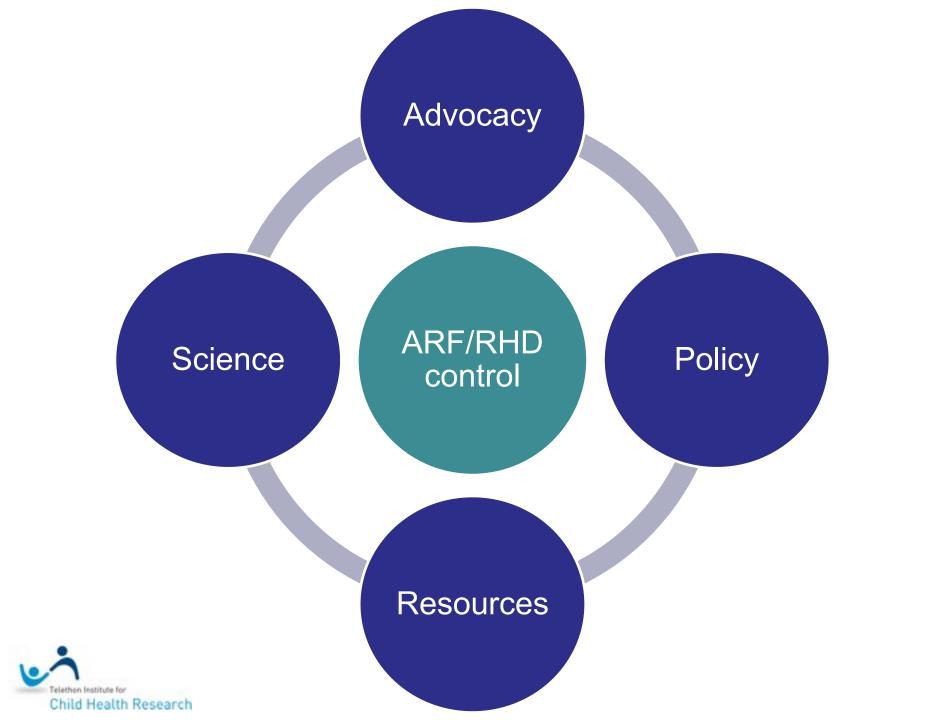
- Main obstacles:
 - Awareness
 - Advocacy
 - Political will
- Money shouldn't be an obstacle
- New developments in RHD demonstrate leadership from developing countries
 - Expansion of register-based RHD control programs
 - Screening using echocardiography in the field
 - Vaccine studies.



Conclusions

- Balance: Primary Secondary Tertiary prevention
- Diagonal integration
 - "Niche Disease"
 - Vagaries of workforce (training/transience)
 - Specific strategies, not common to other communicable or NCDs
 - Incorporation into overall NCD programmes





Social determinants and primordial prevention

- Housing
- Education
- Employment
- Communications
- Transport & access to services



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