Rheumatic heart disease across the Western Pacific: not just a Pacific Island problem

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ABSTRACT

Some of the highest recorded rheumatic heart disease (RHD) prevalence and mortality rates are from the World Health Organization's Western Pacific Region (WPR). RHD burden has been well documented in much of the WPR subregion of Oceania, but less is known about RHD outside the Pacific Islands and Australasia. We aimed to review RHD burden in WPR outside Oceania to identify countries with high RHD burden and those with contemporary data gaps. We searched the peer-reviewed literature for English-language primary studies published between 1980 and April 2017 that reported RHD prevalence or mortality in the 13 WPR countries/areas outside Oceania, and Taiwan. We also searched for official government reports and health indicator documents. Results were synthesised narratively and reported stratified by 2015 Human Development Index (HDI) level. 30 peer-reviewed publications fulfilling inclusion criteria were identified, representing nine countries/areas. RHD prevalence and mortality have fallen in association with economic development, particularly in very high HDI countries. In several countries that have undergone recent economic development, RHD persists particularly among older populations. In poorer WPR countries there is a persistent RHD burden, including in young populations. Some countries had no available data. Although RHD burden has declined in many high-resource settings across the WPR, in several poorer countries, the impact of RHD appears to continue. Elsewhere, insufficient contemporary data make it difficult to gauge the current status of RHD burden and control. Concerted efforts are needed to fill information gaps and implement action to address this avoidable disease.

Rheumatic heart disease (RHD), an avoidable consequence of acute rheumatic fever (ARF), disproportionately affects the world's most vulnerable people. It is estimated that there are approximately 33 million people living with RHD.[1] In high-income countries, the burden of RHD decreased markedly during the 20th century, attributable to improved living conditions associated with socioeconomic development and advances in medical management. However, RHD continues to exact a considerable toll in many low-resource settings. The epidemiology of RHD largely parallels most indicators of poverty; there are profound disparities in disease burden globally, with prevalence increasing with increasing socioeconomic inequality.[2]

Some of the highest recorded RHD prevalence and mortality rates are from countries in the Western Pacific Region (WPR) of the World Health Organization (WHO). The WPR comprises an estimated 1.8 billion people, across 37 countries and areas.[3] These culturally and developmentally diverse nations also exhibit marked variation in the size and capacity of their health systems, healthcare expenditures and health information infrastructures.[4,5]

RHD has been well documented in much of the WPR subregion of Oceania, which incorporates the 24 nations of the Pacific Islands and Australasia. Less is known about RHD in WPR nations outside Oceania. It is plausible that there are impoverished geographical areas where high RHD burden persists. Without sufficient data to inform a policy and programmatic response, RHD may be undetected, unreported and unmanaged at both the individual and population levels.

We aimed to review RHD burden in the WPR outside Oceania to identify countries with high RHD burden and those with contemporary data gaps.

METHODS

We identified publicly available official health statistics and peer-reviewed literature documenting RHD prevalence or mortality in the WHO WPR Member State countries/areas outside Oceania, as well as Taiwan (figure 1). Oceania was considered out of scope as a similar project has already been conducted for that subregion.[6]

We searched the PubMed and Global Health databases during April–June 2017 with a search strategy incorporating a combination of 'rheumatic heart' OR 'rheumatic fever' terms and individual country names. The rheumatic fever string was included to ensure all relevant papers were captured. Additionally, we searched the Institute for Health Metrics and Evaluation's Global Health Data Exchange for RHD scientific literature, and relevant studies known to the authors were reviewed for eligibility.

Studies were eligible for inclusion if they were primary studies conducted in the non-Oceania Member States and areas of the WHO's WPR or in Taiwan; reported RHD prevalence or mortality rates or proportions for the general population or in specific population or clinical subgroups (obstetric, cardiovascular/echocardiograph populations, hospital admissions); were published between 1980 and April 2017 (regardless of study period); and full texts were available in English. We included studies that ascertained disease burden using any type of data source, including auscultation-based or echocardiography-based screening, administrative data or clinical records. Studies on RHD in
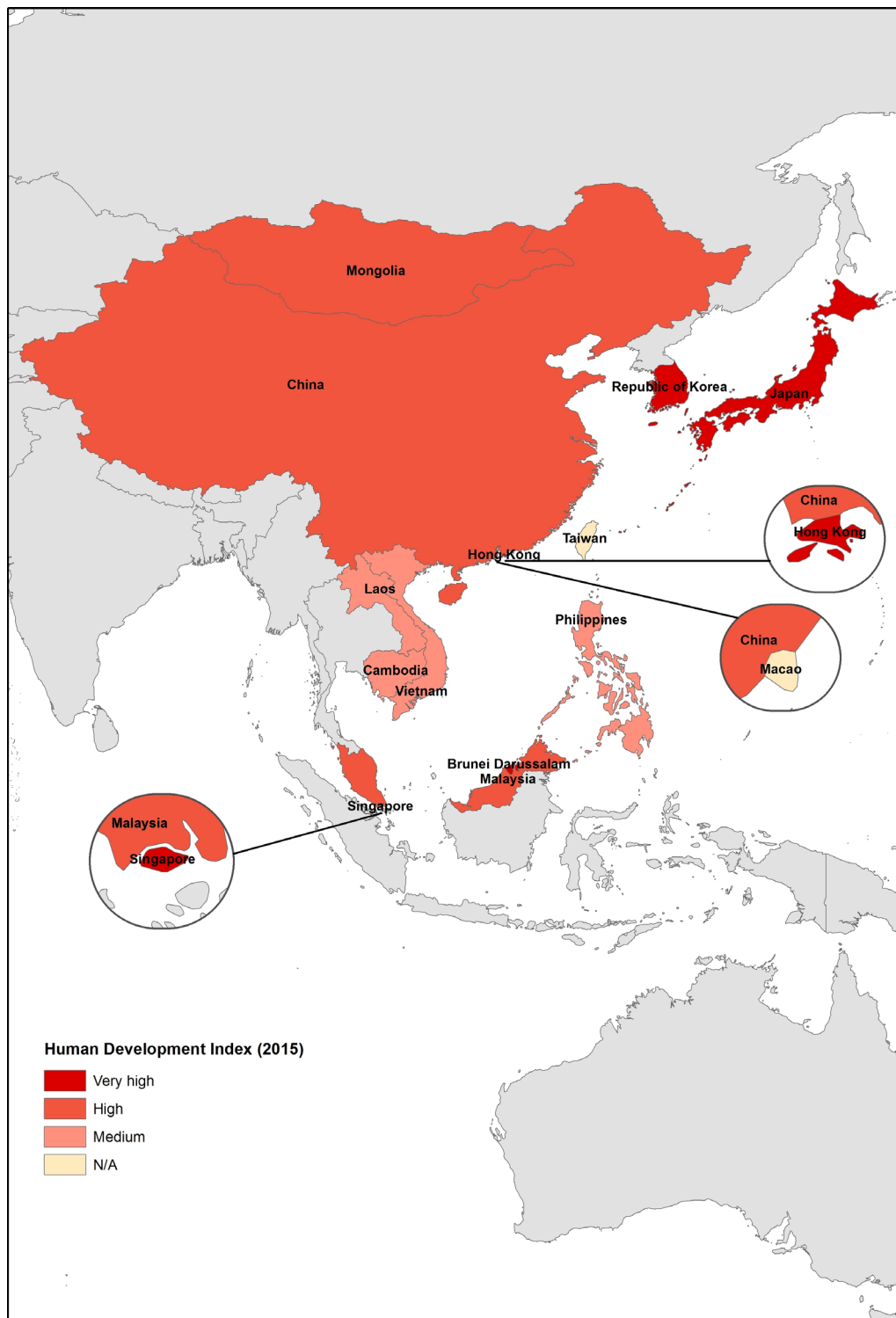
Figure 1 Countries and areas of the Western Pacific region included within the scope of this study. Taiwan does not have WHO Member State status but is within this geographical region and so was included in this study.

pregnancy were included only if the total number of pregnant women was reported, allowing calculation of the proportion with RHD. Studies focusing solely on ARF were excluded. Other specific exclusions are outlined in figure 2.

We also conducted a Google search for national statistical agency health indicator and vital statistics documents reporting RHD prevalence or mortality and published in English. Where available, summary statistics were extracted from the most recent reports.

Title and abstract screening and full text reviews were undertaken by two reviewers independently, with disagreements resolved by consensus; records retrieved via the expanded search strategy and grey literature were assessed by one reviewer. Relevant data regarding study methods and disease estimates were extracted and summarised by one reviewer, with discussion as required. In papers reporting multiple components, only those measures fulfilling inclusion criteria were included (eg, absolute numbers only with no rates were not extracted). Where multiple
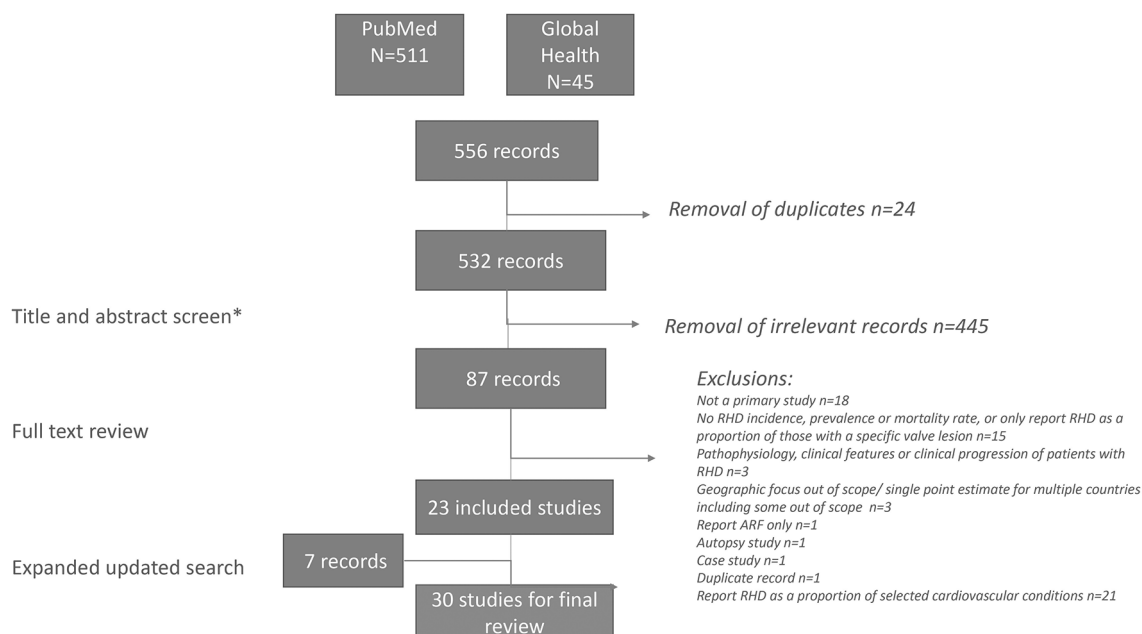
Figure 2 Summary of literature search results. *Exclusion criteria: not a primary study (including guidelines, conference proceedings, reviews); case studies; published in a language other than English; focus is pharyngitis burden/rates of group A streptococcal colonisation; focus is pathophysiology/clinical features or clinical progression of patients with ARF/RHD; focus is outcomes or treatment effectiveness in patients with ARF/RHD; report proportion of patients with a specific valve lesion due to RHD but no population denominator; does not report RHD prevalence or mortality rates (including studies that only present absolute numbers); geographical focus out of scope or report single point estimate for multiple countries, including some out of scope. ARF, acute rheumatic fever; RHD, rheumatic heart disease.

estimates over a given period were presented, the earliest and the latest estimates were extracted and temporal trends noted.

Results are presented stratified by country level of development, with classification based on the United Nations Development Programme's Human Development Index (HDI) for 2015.[5] The HDI is a composite measure that reflects life expectancy, average and expected educational attainment and gross national income per capita, with a higher score reflecting better performance on these measures. This scheme classifies countries as having very high (HDI scores ≥0.800), high (0.700–0.799), medium (0.550–0.699) and low (<0.550) human development. Studies from China were also mapped against province-level HDI.[7]

Ethics approval was not required for the conduct of this study.

RESULTS
Of 37 countries and areas in the WHO's WPR, 11 countries and two Special Administrative Regions of China lie outside Oceania, as does Taiwan.

Figure 2 outlines the search strategy and handling of records. Full text review of 87 publications was undertaken, with 23 identified as relevant and a further 7 included following an updated search and review of papers known to the authors.[8–37] Relevant RHD prevalence or mortality data were also retrieved from publicly available government documents for Brunei,[38] Hong Kong,[39 40] Japan,[41] Mongolia[42] and the Philippines[43]; no official statistics were identified for other countries/areas.

Table 1 summarises the peer-reviewed paper characteristics, representing 9 of the 14 countries/areas. Of these, 12 papers reported population-based prevalence, 13 reported RHD as a proportion of total admissions/surgeries/echos performed or proportion of deliveries, and 9 reported mortality rates. Several papers used multiple data sources and report multiple metrics.

Study periods from Hong Kong, Singapore, Malaysia, the Philippines and Taiwan were all prior to 2000.

Tables 2–5 present burden estimates from countries with very high, high, medium and unspecified 2015 HDIs, respectively, and table 6 presents official statistics.

RHD prevalence
Very high HDI: Singapore, Hong Kong, Japan, South Korea, Brunei
Two Korean papers covering 2006–2011 used administrative data to estimate prevalence, reporting high disease burden particularly among older age groups table 2.[9 10] Two other prevalence papers were early studies of younger populations that reported low RHD prevalence among university students in Hong Kong in the 1970s[12] and school children in Japan from the 1950s to 1980s.[14]

Early reports of disease burden among hospital populations in these settings also indicate a low prevalence. In South Korea in the mid-1980s, RHD comprised approximately 5% of adult cardiovascular admissions.[8] In the 1960s–1980s, RHD decreased as a proportion of cardiac admissions in Japan[14] and RHD as a proportion of hospital and cardiac admissions was also low and declining in Hong Kong among both adult and paediatric patient populations.[12 13] Recent Hong Kong government reports indicate 1736 of 79 896 heart disease inpatient discharges or deaths in hospital in 2014 were due to RHD[39] (2.2%).

Population-based or hospital-based prevalence estimates were not found for Brunei and Singapore, and the most recent data for Japan were from 1981 (prevalence in school children 0.14 per 1000).[14]

High HDI: China, Malaysia, Mongolia
Prevalence data were only available for China (table 3). Online supplementary figure S1 presents RHD data availability in China

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Table 1 Study details for peer-reviewed publications presenting estimates of RHD burden by country/area 2015 HDI status, 1980–2017

	Very high HDI countries	High HDI countries	Medium HDI countries	HDI not specified
Total number of papers	All=11 Brunei: 0 Hong Kong: 2 Japan: 3 Singapore: 2 South Korea: 4	All=12 China: 11 Malaysia: 1 Mongolia: 0	All=4 Cambodia: 2 Laos: 0 Philippines: 2 Vietnam: 0	All=3 Taiwan: 3 Macao: 0
Coverage*				
National	6	0	1	2
Subnational	3	5	2	2
Facility/facilities	5	7	1	1
Study period†				
Prior to 2000	6	3	2	3
2000 onwards	2	6	2	0
Study period spans pre-2000 and post-2000	3	2	0	0
Metric‡				
Prevalence: general population or population subgroup	4	4	2	2
RHD frequency among hospital/medical/cardiovascular/surgical/obstetric admissions	4	5	1	1
RHD as a proportion of echos performed	0	2	0	0
RHD mortality rates or proportions**	5	1	1	2
Data source				
Screening/clinical exam in other context	2	4	2	2
Hospital admissions data or surgical database	4	4	1	1
Health insurance data	2	0	0	0
Echocardiography database (including echo database for inpatients)	0	3	0	0
Mortality data	5	1	1	2

Numbers do not add to total number of papers as some reported multiple measures.

*Any study reporting on health facility populations denoted here as 'facility', regardless of whether the facility catchment area is national or subnational.

†For one paper, study period not explicitly stated.

Note several papers, particularly among those published pre-1990, have inconsistent results reported throughout the text.

‡Some studies reported ARF and RHD in the same point estimate. ** does not include absolute counts only

ARF, acute rheumatic fever; HDI, Human Development Index; RHD, rheumatic heart disease.

by province and by province HDI score. Provinces for which data were available were generally those with higher development levels; several impoverished provinces had no data. Burden estimates varied subnationally, by population subgroup, data source and over time. For example, in Dongguan City, 5 of 81 213 children aged 5–13 years screened in 2011–2012 had echo-confirmed RHD,[21] equating to 0.06 per 1000. Among adults aged 18–74 years from nine communities in urban and suburban China, prevalence of echo-detected RHD was 1.86 per 1000 in 2001–2002.[20] In a study involving 13 provinces, 91 of 29 079 subjects aged 30 and over, were reported to have RHD[29] (3.13 per 1000). Earlier clinical screening data from Panyu County, Guangdong Province, demonstrated a prevalence of 2.5% in the general population aged over 15 years.[19]

The relative contribution of RHD to cardiovascular and general medical/paediatric admissions has generally decreased over time in China but still comprises a considerable caseload. For example, in Shanghai RHD accounted for 24.23% of all medical admissions with heart disease during 1980–1989,[22] down to 2% of all cardiac admissions during 2000–2005.[23] For one facility in Zhejiang over the period 2010–2015, RHD prevalence was 1.6% in adult patients.[26] Similarly in 2008 RHD still comprised 20% of all cardiac surgery cases in Beijing.[27] At a Shanghai facility, 0.5% of 20 983 women delivering during 1993–2007 had RHD.[28] RHD also comprised 3% of all adult outpatient echocardiograms performed at a Shanghai facility in 2012[25] and 33% of all valvular disease among inpatients at a Guangdong centre in 2013.[24]

Mongolian official government documents report 24 116 new cases of ARF/RHD in 2012, and a total population of approximately 2.87 million,[42] equating to 8.4 cases per 1000. No Malaysian data were identified.

Medium HDI: Vietnam, Philippines, Laos, Cambodia

No population or hospital prevalence data were available for Vietnam or Laos (table 4).

Estimates of echocardiography-confirmed RHD prevalence among school children based on screening studies ranged from 1 per 1000 in Legazpi City, Philippines in 1998[34] (screen by auscultation) to 21.5 per 1000 among children 6–17 years old in Cambodia in 2001–2002[31] (screen by echocardiography). RHD was the indication for 43% of all Cambodian cardiac surgery procedures between 2001 and 2006 and 29% between 2007 and 2011.[32]

HDI unspecified: Taiwan, Macao

No information was available specifically for Macao. Surveys (with examination in questionnaire-positives) in Taiwan show a significant decline in RHD prevalence in 1970–1985 from 1.4 to 0.62 per 1000 (table 5).[36] ARF/RHD as a proportion of paediatric admissions fluctuated over the 1940s–1980s, to approximately 15 per 1000 admissions in 1981.[37]

RHD mortality

Mortality data in peer-reviewed literature were only available for six countries/areas.

Table 2 RHD burden estimates in countries with very high 2015 human development indices, 1980–2017

Author, publication year, title	Country (coverage)	Study period	Data source	Study population	Metric	Burden estimates*
South Korea						
Bae et al, 1987[8] *The frequency distribution of cardiovascular diseases in 13 hospital admitted patients in Korea*	South Korea (facility)	1985	Hospital discharge summary diagnosis data (WHO 1977 classification chronic RHD: ICD codes 393-398)	25 939 cardiovascular inpatients aged >15 years at 13 facilities	RHD frequency among total cardiovascular admissions	4.9% (n=1278) males 3.8% (n=528), females 6.2% (n=750)
Seo et al, 2013[9] *The economic burden of rheumatic heart disease in South Korea*	South Korea (national)	2008	Claims data from National Health Insurance Corporation of Korea (ICD-10 codes I01-I09)	General population, all ages	RHD prevalence in the general population	220.50 per 100 000 males 143.04 per 100 000 (n=34 924) females 298.67 per 100 000 (n=72 252) Age specific prevalence rates, both sexes: 0-19 years 10.27 per 100 000 20-59 years 168.78 per 100 000 60+years 791.07 per 100 000
Jang et al, 2014[10] *Changes in the etiology of valvular heart disease in the rapidly aging Korean population*	South Korea (national)	2006–2011	Korean National Health Insurance data (ICD-10 codes I05.0–2, I05.8, I05.9; I06.0–2, I06.8, I06.9)	General population	RHD prevalence in the general population	Age adjusted cumulative prevalence: 2006: 74.4 per 100 000, 95% CI 73.4–75.4 (n=22 744) 2011: 71.8 per 100 000, 95% CI 70.8–72.8 (n=21 496) Age specific prevalence rates per 100 000 (95% CI), both sexes, 2011: 20–44 years: 6.8 (6.6–7.1) 45–64 years: 31.9 (31.3–32.5) 65+ years: 33.0 (32.3–33.7)
Lee et al, 2015[11] *Thirty-year trends in mortality from cardiovascular diseases in Korea*	South Korea (national)	1983–2012	Cause of death data from Statistics Korea (ICD-10 codes ARF and chronic RHD I00-I09)	General population	Crude ARF/RHD mortality rates	1983: Males 0.3 per 100,000 Females: 0.5 per 100,000 2012: males 0.2 per 100,000 females 0.7 per 100,000
Hong Kong						
Woo et al, 1983[12] *The changing prevalence and pattern of acute rheumatic fever and rheumatic heart disease in Hong Kong – (1968–1978)*	Hong Kong (facility)	1968–1978	Admissions data from annual reports of Medical and Health Services Department of Hong Kong (ICD [1965 revision]: RHD codes 393–398)	Hospital population (*government + government assisted hospitals – 87% of all hospital beds in Hong Kong*)	RHD frequency among hospital admissions	RHD prevalence in hospital admissions 1968: 0.65% 1977: 0.51% RHD prevalence in medical admissions 1968: 2.2% 1977: 1.5%

Table 2 Continued

Author, publication year, title	Country (coverage)	Study period	Data source	Study population	Metric	Burden estimates*
		1968–1978	Registry of all cardiac patients admitted to a paediatric unit and medical unit at two hospitals	Hospital population (adult, paediatric)	RHD frequency among hospital admissions	RHD prevalence in *adult medical admissions* 1969: 6.8% 1978: 3.4% RHD prevalence in *adult cardiac admissions* 1968: 51.6% 1978: 35.9% RHD prevalence in *paediatric admissions* 1973: 0.98% (ARF+RHD:2.2%) 1977: 0.67% (ARF+RHD: 1.6%) RHD prevalence in *paediatric cardiac admissions* 1973: 34.9% 1977: 26.5%
	(national)	1972–1978	Compulsory medical examination records for all freshmen entering one university	7152 university students, ages 18-30	RHD prevalence among university students	Average annual RHD prevalence ranged from 0.13% to 0.59%, average 0.31%
Woo and Vallance-Owen, 1988[13] *Changing prevalence and pattern of cardiovascular diseases in Hong Kong. A perspective in the 1990s*	Hong Kong (facility)	1969–1985	Annual reports of medical and health services department (1969–78 used ICD 8; 1979–85 used ICD 9)	Hospital population (*government and government-assisted hospitals – 88.9% of all hospital beds in Hong Kong*)	RHD frequency among hospital admissions	RHD prevalence among *hospital population* 1969: 5.3 per 1000 1985: 3.1 per 1000 RHD prevalence among *medical admissions* 1969: 21.1 per 1000 1985: 9.1 per 1000
		1969–1987	Registry of all cardiovascular patients admitted to a medical unit and a cardiac unit at 2 hospitals	Hospital population	RHD frequency among hospital admissions	RHD prevalence among *medical admissions* 1969: 6.8% or 68 per 1000 1985: 3.4% or 34 per 1000 RHD prevalence among *cardiovascular admissions* 1969: 50.8% or 508 per 1000 1985: 8.8% or 88 per 1000
Japan						
Kawakita, 1986[14] *Rheumatic fever and rheumatic heart disease in Japan*	Japan (national)	1960–1981	Death Statistics	Total population	RHD death counts	No rates or proportions provided but dramatic decrease in absolute numbers.
	(facility)	1968–1981	Hospital admissions data	Cardiac patients	RHD frequency among cardiac admissions	Data presented graphically only: reflects decreasing contribution of RHD and increasing contribution of ischemic heart disease to total cardiac admissions

Continued

Table 2 Continued

Author, publication year, title	Country (coverage)	Study period	Data source	Study population	Metric	Burden estimates*
	(national)	1958–1981	Annual school survey (methods not stated)	School children aged 6-15 years 1958: n=26 000 1961: n=131 377 1971: n=1 135 732 1981: n=524 999	RHD prevalence in school children	1958: 4.6 per 1000 1961: 2.1 per 1000 1971: 0.27 per 1000 1981: 0.14 per 1000
	(subnational - Osaka)	1958-1981	Annual survey of heart disease	Primary and secondary school children	RHD prevalence in primary and secondary school children	1958: 4.6 per 1000 1961: 2.1 per 1000 1971: 0.2 per 1000 1981: 0.1 per 1000
Takahashi et al,2017[15] Heart disease mortality in the Life Span Study, 1950-2008	Japan (subnational)	1950–2008	Mortality data abstracted from death certificates (ICD-7 to ICD-10) and Japanese National Family Registration (koseki) system	Follow up of 86,600 Life Span Study cohort members	RHD as a percentage of total deaths	223 RHD deaths of 55 654 total deaths=0.4%
					RHD as a percentage of heart disease deaths	223 RHD deaths of 9303 cardiac deaths = 2.4%
Takamori et al, 2017[16] Mortality analysis of the Life Span Study (LSS) cohort taking into account multiple causes of death indicated in death certificates	Japan (subnational)	1950–2003	Mortality data abstracted from death certificates (ICD-7 to ICD-10) and Japanese National Family Registration (koseki) system	Follow up of 86 611 Life Span Study cohort subjects	RHD as a percentage of circulatory deaths	1950–1976: 173 of 9035 circulatory disease deaths (1.9%) 1977–2003: 84 of 10,017 circulatory disease deaths (0.84%).
Singapore						
Sheares et al, 1981[17] Surgical management of rheumatic heart disease in Singapore	Singapore (national)	1966–1977	Mortality data	General population	RHD mortality rate	1966: 3.6 per 100,000 1977: 4.4 per 100,000 1978: Ratio ischemic heart disease to RHD deaths =1749/96=18.2 Substantial increase in ratio 1962–1978 shown graphically
Loh et al, 1994[18] Maternal mortality: evolving trends	Singapore (facility)	1986-1992	Maternal death data for deaths occurring in an obstetric unit	Review of all maternal deaths among 26 173 deliveries during study period.	RHD mortality rates among obstetric population	RHD mortality rate = 1/26 173 = 3.8 per 100 000 deliveries

*Where multiple estimates were reported, for temporal trends the earliest and latest data were extracted; age-specific or sex-specific estimates are presented for the most recent year.
ARF, acute rheumatic fever; RHD, rheumatic heart disease; ICD, International Classification of Diseases

Table 3 RHD burden estimates in countries with high 2015 human development indices, 1980–2017

Study author, publication year	Country (coverage)	Study period	Data source	Study population	Metric	Burden estimates
China						
Xuan et al, 1980[19] *Epidemiology and community control of rheumatic heart disease in Panyu County*	China (subnational - Panyu County)	1972–1978	Community screening RHD: Clinical plus investigations	159 782 people aged over 15 years in a total population of 328256	RHD prevalence in general population	2.52% (male 2.0%, female 2.9%).
			Self-referral for investigation	People aged over 15 years in another population of 123 034	RHD prevalence in general population	1.7%
			Mass survey of cardiovascular diseases	11909 people of all ages including 4476 children aged 0–14 years	RHD prevalence in general population	All age groups: 0.3% 0–14 year olds: 0.6%
Zhimin et al, 2006[20] *Prevalence of chronic rheumatic heart disease in Chinese adults*	China (subnational – 9 suburban and urban communities)	Oct 2001–Feb 2002	Population-based screening (questionnaire, physical exam, echocardiography – diagnostic criteria described in paper)	General population, ages 18–74 years 9124 participants interviewed, 8652 completed questionnaires, 8080 completed echocardiographic exam	RHD prevalence in general population	186 per 100 000 (n=15) *40% (n=6) diagnosed with RHD for first time, that is, screen detected*
Kang et al, 2015[21] *Prevalence and clinical significance of cardiac murmurs in schoolchildren*	China (subnational – Dongguan City)	Nov 2011 – Nov 2012	School screening study – questionnaire plus clinical plus echocardiography in those with a murmur (echo criteria not stated)	School students attending 32 elementary schools in Dongguan (age 5–13 years); 81 213 of 81 231 school children screened (99.98%)	RHD prevalence in school children	2193 children had a murmur, underwent echocardiography – 5 had RHD. 5/81 213=6.2 per 100 000
Chen et al, 1999[22] *Changing pattern of heart disease in Shanghai from the 1950s to 1980s*	China (Two facilities, Shanghai)	1980–1989	Medical inpatient data	30 516 adult medical admissions, 7159 of which were cardiac cases	RHD as a percentage of all medical admissions with heart disease	1980–89: 24.23% (n=1743) *Reduction compared with earlier study for period 1948–1957, when RHD comprised 50.3% (n=1901)*
Cheng, 2009[23] *How much of the recent decline in rheumatic heart disease in China can be explained by changes in cardiovascular risk factors?*	China (facility, Shanghai)	1948–2005	Hospital admissions data	Total cardiac admissions	RHD frequency among total cardiac admissions	1948–57: 50% 1958–68: 44% 1969–79: 30% 1980–89: 24% 1990–99: 10% 2000–05: 2%
Liu et al, 2014[24] *Five-year epidemiological survey of valvular heart disease: changes in morbidity, etiological spectrum and management in a cardiovascular centre of Southern China*	China (facility, Guangdong)	2009–2013	Medical records / inpatient echo database	19 428 consecutive inpatients with abnormal valve structure/ function who underwent echocardiography	RHD as a percentage of total echocardiographs	RHD as a percentage of total valvular disease: 2009: 42.8% (n=1268) 2013: 32.8% (n=1680) Age-specific estimates <15 years: 7.7% 15–25 years: 28.9% 25–35 years: 60% 35–45 years: 73.6% 45–55 years: 71.8% 55–65 years: 60.2% 65–75 years: 32.0% 75–85 years: 14% 85+ years:2.9%

Table 3 Continued

Study author, publication year	Country (coverage)	Study period	Data source	Study population	Metric	Burden estimates
Lu et al. 2016[25] *Trends in the prevalence of heart diseases over a ten-year period from single-centre observations based on a large echocardiographic database*	China (facility, Shanghai)	2003–2012	Outpatient echo database (echo diagnosis based on American Society of Echocardiography recommendations)	385,682 outpatients who underwent transthoracic echocardiography, age ≥18 years	RHD as a percentage of total echocardiographs	2003: 4.04% 2012: 3.06% 2003–2007: 3.87% 2008–2012: 3.04%
Hu et al, 2017[26] *A hospital-based survey of patients with severe valvular heart disease in China*	China (facility, Zhejiang)	2010-2015	Echocardiography database (2014 AHA/ACC guidelines and EAE/ASE recommendations)	139 496 consecutive patients (inpatients and outpatients), age ≥18 years	RHD prevalence among hospital patients	1.56% (n=2179)
Wang et al, 2011[27] *Cardiopulmonary bypass techniques and clinical outcomes in Beijing Fuwai Hospital: a brief clinical review*	China (facility, Beijing)	2008	Cardiac surgery database	7606 cardiac surgery cases	RHD frequency among total cardiac surgery cases	19.45% (n=1479 cases)
Liu et al, 2010[28] *Pregnancy outcomes in women with heart disease*	China (facility, Shanghai)	1993-2007	Clinical record data	20 983 patients delivering during study period, 1142 of whom had heart disease	RHD prevalence in obstetric population	99 women with RHD among 20 983 women delivering =0.47% (RHD 8.7% of all cases with heart disease)
Zhou and Hu, 2008[29] *An epidemiological study on the prevalence of atrial fibrillation in the Chinese population of Mainland China*	China (subnational, 13 provinces)	Not stated	Population-based screening (RHD: history +/- examination and echocardiography if self-reported RHD)	29 079 subjects, age ≥30 years	RHD prevalence in general population	91 of 29 079 subjects (0.3%)
Malaysia						
Khoo et al, 1991[30] *Cardiovascular mortality in Peninsular Malaysia: 1950-1989*	Malaysia (subnational)	1950-1989	Mortality data from Registrar of Births and Deaths (1950-1960) and Department of Statistics (1965 onwards) For 1965-1989 only used data for medically certified deaths	General population	RHD as a percentage of cardiovascular deaths	1965: 4.51% 1989: 1.70% 1975–89: 2.58%
					RHD as a percentage of total deaths	1965: 0.41% 1989: 0.5% 1975–89: 0.66%

Where multiple estimates were reported, for temporal trends the earliest and latest data were extracted; age-specific and latest data were extracted; age-specific or sex-specific estimates are presented for the most recent year.
Not all published papers noted which diagnostic criteria were used. Where specified, the following abbreviations are provided in the table: AHA, American Heart Association, ACC, American College of Cardiology, ASE, American Society of Echocardiography; EAE, European Association of Echocardiography; RHD, rheumatic heart disease.

Table 4 RHD burden estimates in countries with medium 2015 human development indices, 1980–2017

Study author, publication year	Country (coverage)	Study period	Data source	Study population	Metric	Burden estimates
Cambodia						
Marijon et al, 2007[31] *Prevalence of rheumatic heart disease detected by echocardiographic screening*	Cambodia (Subnational - Phnom Penh)	2001–2002	School screening data (clinical and echocardiographic examination, echo criteria well described in paper)	3677 school children, aged 6–17 years	RHD prevalence in school children	Clinical evidence of RHD confirmed by echo: 2.2 per 1000 (95% CI 0.7-3.7). RHD prevalence on echo 21.5 per 1000 (95% CI 16.8–26.2); clinically silent RHD prevalence 19.3 per 1000
Mirabel et al, 2017[32] *Cardiac surgery in low-income settings: 10 years of experience from two countries*	Cambodia (facility)	2001–2011	Clinical data	1332 consecutive patients who underwent open heart surgery locally	RHD as a percentage of total cardiac surgery cases	Percentage of cardiac surgeries with RHD as the underlying cause: 2001–2011: 36.79% (490 surgeries) 2001–2006: 43% 2007–2011: 29%
Philippines						
Tuomihlehto et al, 1984[33] *Trends in cardiovascular diseases mortality in the Philippines*	Philippines (national)	1964–1976	Mortality data (ICD-7 A79 and A80, ICD-8 A80 and A81)	General population	ARF/RHD mortality rates	Crude annual ARF/RHD death rate per 100 000 1964: males 4.8; females 5.1 1968: males 4.8; females 5.2 1972: males 5.2; females 5.6 1976: males 5.0; females 6.0. Proportional mortality rates per 1000 (all ages): 1964: 7.2 (n=1549) 1968: 7.1 (n=1792) 1972: 7.4 (n=2116) 1976: 8.1 (n=2417) Age standardised mortality rates per 100 000 in 1976 for 40–64 year olds: males 10, females 9.
Imperial et al, 1998[34] *The Albay Province rheumatic fever/ rheumatic heart disease prevention and control program – a preliminary report*	Philippines (Subnational - Albay)	1995 to June 1998	School screening data (clinical plus echo confirmation in suspected cases)	School children, age range not stated Study was still in progress at time of publishing this preliminary report. As at June 1998, 148 592 of 238 296 school children had been screened	RHD prevalence in general population	Legazpi city - confirmed RHD 1 per 1000 (25/24 148 children screened). As of June 1998, 495 cases of confirmed ARF/RHD registered in Albay province

ICD, International Classification of Diseases; RHD, rheumatic heart disease.

The limited trend data available indicate that RHD as a proportion of total cardiovascular deaths generally decreased over time in countries across development levels, including in Malaysia[30] and Japan.[16] In Taiwan, age-adjusted RHD mortality rates decreased between the 1970s and 1980s[35], and ARF/RHD mortality rates per million population also decreased between the 1950s and 1980s[37]. In the Philippines the crude annual death rate remained relatively unchanged in 1964–1976, although the absolute number of RHD deaths increased by more than 50%[33]; in Singapore RHD mortality increased from 3.6 to 4.4 per 100 000 between 1966 and 1977.[17] RHD was the cause of an estimated 2.4% of heart disease deaths and 0.4% of total deaths in Japan during 1950–2008 collectively.[15]

Where available, contemporary RHD mortality estimates in very high development countries indicate a relatively low burden: 1.2 per 100 000 population in Hong Kong in 2014,[40] 1.8 per 100 000 population in Japan in 2014,[41] 1.4% of total cardiovascular deaths in Brunei in 2016[38] and combined ARF/RHD mortality of less than 1 per 100 000 population in Korea in 2012.[11]

Among high development settings, RHD mortality rates were not found for China. In Mongolia in 2012 there were 51 ARF/RHD deaths among 16 923 total deaths registered,[42] equating to 3.0 ARF/RHD deaths per 1000. The most recent data from Malaysia were for 1989, when RHD comprised 1.7% of cardiovascular deaths and 0.5% of total deaths.[30]

Table 5 RHD burden estimates in countries and areas with 2015 human development indices unspecified, 1980–2017

Study author, publication year	Country (coverage)	Study period	Data source	Study population	Metric	Burden estimates
Taiwan						
Tsai and Wen, 1989[35] *Mortality trends in a rapidly developing economy in Taiwan. Part 1: Comparison with the USA and Japan 1976–1983*	Taiwan (national)	1976–1983	Vital statistics data (ICD-9 codes 393–398)	General population	RHD as a proportion of total deaths	1983: Males 244 of 54 563 total deaths (0.45%) Females 258 of 35 268 total deaths (0.73%)
					RHD age-adjusted mortality rate	% change in age-adjusted mortality rate for RHD between 1976-1983: Males 28.9% decrease Females 25.2% decrease
Lue et al, 1988[36] *Establishment of a rheumatic heart disease registry in Taipei: an early appraisal*	Taiwan (subnational, Taipei)	1985	School screening study	462 373 school children aged 6–18 years administered questionnaire. 380 886 responses: 4967 suspected as having RF/RHD. 3716 examined +/- echocardiography, 121 of whom found to have RHD 371 265 with no symptoms reported on questionnaire; 4654 of whom randomly sampled for exam, 1 found with RHD	RHD prevalence among school children	Adjusted prevalence rate 0.62 per 1000 in 1985 significant decline from 1970 (1.4 per 1000 among 6–13 year-olds)
Lue et al, 1983[37] *Clinical and epidemiological features of rheumatic fever and rheumatic heart disease in Taiwan and the Far East*	Taiwan (facility)	1946–1981	Admissions data	Paediatric admissions	RF/RHD frequency among paediatric admissions	RF/RHD cases per 1000 paediatric admissions: 1946: 5 1975: 25.6 1981: ~15
	(national)	1956–1981	Mortality data	General population	RF/RHD mortality rates	1956: 175 deaths per million population 1981: 45 deaths per million population
	(subnational)	1970–71	Population survey	9425 randomised urban Taipei population, all ages	RHD prevalence in general population	2.6 per 1000 Males 2.0 per 1000 Females 2.8 per 1000

ICD International Classification of Diseases; RF, rheumatic fever; RHD, rheumatic heart disease.

From medium development settings, data were only available for the Philippines, where RHD mortality was 1.7 per 100 000 population among all ages in 2013.[43]

DISCUSSION

The WPR outside Oceania is developmentally and demographically diverse, and it follows that there is marked variation in RHD epidemiology and data availability within and between countries. Findings of this review suggest that RHD prevalence and mortality have fallen in association with economic development, particularly in very high HDI countries. In several countries that have undergone recent economic development, RHD persists particularly among older populations, a legacy of high burden in the young before socioeconomic progress. In poorer WPR countries there is a persistent RHD burden, including in young populations. This review has also highlighted considerable data gaps, particularly pronounced in less developed countries such as Laos and Vietnam. Subnational data gaps also exist in some higher HDI settings that still have substantial populations living in poverty, whose RHD burden may therefore be masked. These findings have important implications for health policy and planning nationally, regionally and globally, and reinforce that urgent and concerted efforts are required to fill the data gaps and address this avoidable disease that still exists across the region.

Consistent with known patterns of RHD distribution in different age groups by levels of economic development, in some countries with very high current HDI, RHD burden is high among older populations. For example, in South Korea crude RHD prevalence for 2008 was estimated at 220 per 100 000, with highest prevalence rates being among people aged over 60 years (791 per 100 000), and total costs being US$67.25 million[9]. Besides economic repercussions, high disease burden in older populations also has marked implications for health service planning and delivery, particularly in the context of ageing populations. A high RHD burden may generate demand on health

Table 6 National health agency RHD burden estimates, by country and year

Country	Metric	Burden estimates	Year*
Very high HDI countries			
Brunei	ARF/RHD as a percentage of total cardiovascular deaths	6 ARF/RHD deaths of 421 total cardiovascular deaths = 1.4%	2016[38]
Hong Kong	RHD mortality rate per 100,000 population (number of RHD deaths)	Male: 0.9 per 100,000 (29 deaths) Female: 1.5 per 100,000 (59 deaths) Total: 1.2 per 100,000 (88 deaths)	2014[39 40]
	RHD as a percentage of total heart disease In-patient Discharges and Deaths in Hospital	1736 of 79 896 total heart disease inpatient discharges and deaths in hospital = 2.2%	
Japan	RHD mortality rate per 100 000 population (number of RHD deaths)	Male: 1.2 per 100 000 (720 deaths) Female: 2.5 per 100 000 (1588 deaths) Total: 1.8 per 100 000 (2308 deaths)	2014[41]
Singapore			
South Korea			
High HDI countries			
China			
Malaysia			
Mongolia	ARF/RHD number of new cases Total population	Total number of new cases: 24,116 2 867 744 people 24 116/2 867 744=8.4 per 1000	2012[42]
	ARF/RHD as a proportion of total deaths	51 ARF/RHD deaths among 16 923 total deaths registered = 3.0 per 1000 deaths	
Medium HDI countries			
Cambodia			
Laos			
Philippines	RHD mortality rate per 100 000 population (number of deaths)	1.7 per 100 000 population (1705 deaths – 672 male, 1033 female)	2013[43]
Vietnam			
HDI not specified			
Taiwan			
Macao			

*Most recently available year.
ARF, acute rheumatic fever; HDI, Human Development Index; RHD, rheumatic heart disease.

services, both for treatment of the valvular disease itself and for RHD sequelae (including endocarditis, ischaemic stroke and heart failure) and comorbidities.

The high disease burden in the young in low-resource settings is also cause for concern. Peak incidence of ARF occurs at ages 5–14 years and RHD prevalence increases with age, peaking at 25–34 years.[44] The only relatively recent data from the four medium HDI countries was from Cambodia—prevalence among school children aged 6–17 years in 2001–2002 was 21.5 per 1000, with 90% being detected only on echocardiographic screen.[31] Cambodia has a young population age structure, with approximately one-third of the total population aged 0–14 years.[4] It is plausible that a similarly high burden of undetected disease exists in the other countries with similar levels of development and age structure.

In China, studies since 2000 indicate persistent burden among school children aged 5–13 years[21] and the general population aged 30 and over[29] and 18–74 years.[20] Available Chinese data were predominantly from large cities; many less developed provinces had data gaps. Despite China's considerable socioeconomic progress, pronounced socioeconomic inequality exists[7] and RHD burden may well be higher in less developed, data-poor regions. Additionally, China's large population size means that high rates translate into considerable absolute numbers of people living with RHD—prevalence of 2 per 1000 equates to an estimated 2 million middle-aged and elderly adults.[20] RHD has generally decreased as a proportion of total medical and cardiac admissions over recent decades, likely reflecting China's epidemiological transition with an associated increase in the burden of lifestyle-related conditions such as type 2 diabetes and ischaemic heart disease.

For several WPR countries, contemporary estimates of disease burden were not available in the peer-reviewed literature. In settings that now have very high HDI, this probably indicates RHD is no longer a public health priority. The prevalence study from Japan reported a progressively declining burden among school children over time, to 0.14 cases per 1000 in 1981.[14] Similarly for Hong Kong, population prevalence among university students was low and the proportion of RHD hospital admissions progressively declined over the 1960s to 1980s.[12 13] Although it is appropriate that resources are directed to areas of contemporary priority, there is no room for complacency, as highlighted by recent Japanese reports that between 2010 and 2015 there were 44 new cases of ARF occurring predominantly in large Japanese cities.[45] In WPR and beyond, it is important that even highly developed nations remain vigilant to ARF and RHD.[46]

Data gaps elsewhere warrant attention because they occur particularly in settings where socioeconomic conditions would suggest that RHD burden is likely to be high. Several countries had high burden documented but no recent follow-up studies to gauge progress. In the Philippines, an early study documented a 13% increase in the ARF/RHD proportional mortality rate between 1964 and 1976,[33] and a preliminary report on Filipino school screening (data to June 1998) indicated an RHD prevalence of 1 per 1000.[34] More contemporary estimates were not found in the published literature. However, health department reports of mortality rates of 1.7 per 100 000 in 2013[43] indicate

that RHD persists. A single Malaysian study reported cardiovascular mortality between 1950 and 1989,[30] but no contemporary mortality statistics and no population-based estimates of RHD prevalence were located, as noted by others.[47] Some developing countries had no data whatsoever. Globally, the volume of ARF/RHD research in the published literature has declined markedly over time, in parallel with and reflecting the decreased disease burden in developed nations, but this waning interest comes at the expense of information deficits in developing settings where disease burden is likely greatest.[48]

In some low-resource settings poorly developed health information infrastructure means that there are little real data about the health status of populations, including RHD burden. For example, mortality data are often unavailable because of inadequately functioning civil registration and vital statistics systems and poor rates of medical certification of cause of death.[49] Data gaps mean that there is a reliance on statistically modelled estimates such as the Global Burden of Disease study[50] to gauge disease burden.

Modelling studies help bridge information gaps. However, there are limitations, assumptions and uncertainties inherent in any model, and a model is only as good as its data inputs. For some WPR countries, modelled estimates differ considerably from other data sources. These estimates may not be directly comparable if the primary data signals are of poor quality or insufficiently described—paucity of information about diagnostic methods, case definitions, reporting requirements and other metadata may mean that modelled metrics and indicators derived from other data are not measuring the same thing, precluding direct comparison. For mortality estimates, differences may arise due to incomplete or poor quality death data requiring statistical correction for completion. In other cases, where local data are unavailable, modelled estimates are derived using data from other settings. Models are best enhanced by improving the primary data inputs. It is imperative that there is improved collection of real world data to more accurately understand the true situation on the ground.

There are several potential limitations to this work. Relevant papers may have been excluded or missed. Additionally, as this review only captured English-language peer-reviewed publications and government reports, burden estimates reported in other languages or sources were not considered. There are inherent difficulties in measuring RHD burden, including screening methodology and variation in the quality and completeness of civil registration systems and cause of death statistics across the region. Differences in study methodology, data sources, study periods, geographical coverage and study populations preclude direct comparison. In particular, the change from auscultation to echocardiographic screening (including World Heart Federation criteria for echo screening) is associated with significant changes in sensitivity.[31 51] The metrics complied in this review encompass a range of indicators, methodologies and study population groups, and the measures reported differ both within some countries and between countries. This makes it difficult to accurately gauge progress over time, but this issue reflects the difficulties arising from not having standardised, consistent and serial measurement. Finally, settings with poor information infrastructure are also the ones most likely to have a considerable disease burden; hence, official statistics may not completely capture all cases/deaths.

Nonetheless, this paper tells the story of successes achieved in controlling RHD in some parts, where falling prevalence is followed by declining representation in biomedical literature. It also highlights information gaps and evidence of disease hot spots throughout the WPR beyond Oceania, indicating a need for active and ongoing disease control initiatives, and a focused regional effort to address this issue.

Elsewhere, high disease burden has precipitated strong calls to address this avoidable disease of disadvantage, including from across Africa[52] and from the World Heart Federation, who have called for a 25% reduction in RHD mortality in those aged under 25 years by 2025.[53] In the sustainable development goals era, the impetus to address poverty and the underlying social and systemic determinants of disease has never been greater. Achieving RHD control is now on the agenda at the highest levels of global health diplomacy.[54] Concerted efforts across WPR are required to fill information gaps and ensure that targeted, contextually relevant actions are adopted where needed. Serial monitoring of disease burden is crucial to gauge progress and ensure that the whole region is on track to banishing RHD to the history books.

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