EDITORIAL COMMENT gOPINION

## Can We Eliminate Rheumatic Fever and Premature Deaths From RHD?



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It is estimated that 32.9 million individuals experience rheumatic heart disease (RHD) globally, with about 275,000 deaths occurring each year. The majority of cases occur in South Asia and sub-Saharan Africa. The disability adjusted life years (DALYs) lost from RHD is estimated to be about 9.5 million, with the majority being in low- and middle-income countries (this burden is similar to that of acute leukemia). Between 2000 and 2012, the number of deaths from RHD declined by 9% (from 372,000 to 337,000) and DALYs declined 6% (from 14.3 million to 11.9 million) globally [1]. Both of these declined the most in high income countries (-21% and -28%, respectively), where the number of deaths and DALYs were already the lowest. By contrast, Africa and the Eastern Mediterranean region showed little change. Yet both deaths and DALYs declined in many other economically less-advanced regions of the world (e.g., South America, Southeast Asia, and the Western Pacific) (Table 1). Hidden in these statistics is the remarkable progress made in several middle-income countries such as Cuba, Costa Rica, or Tunisia, and some regions within countries with high disease burdens. For example, in India, there have been marked declines in acute rheumatic fever (ARF) and RHD deaths in the southwestern states (Kerala, Tamil Nadu, Andhra Pradesh, Karnataka, Maharashtra, and Gujarat), some northern states (Punjab and Haryana), and the eastern state of Bengal. By contrast, there has been little improvement in central India (Rajasthan, Madhya Pradesh, Uttar Pradesh, Bihar, Chhattisgarh, and Odisha) and the northeast.

What accounts for the marked declines in ARF and RHD in the countries or regions of the world with success

stories? In all these locations, some or all 4 of the following social and economic changes or targeted health systems strategies were implemented.

- Economic development with greater governmental investment in health.
- Decrease in poverty.
- Improved penicillin prophylaxis for both primary and secondary prevention, and prompt treatment of sore throats
- Appropriate medical (e.g., for heart failure or atrial fibrillation) or interventional therapies (mitral valve balloon angioplasty or surgery).

Tunisia is a country that is a success story which exemplifies the impact of all 4 approaches (Habib Gamra, personal communication, 2016) (Table 2). Despite a doubling in the population from around 1980 to 2015, gross domestic product per capita increased 9-fold (from U.S. \$1,368 to U.S. \$9,900), and new cases of ARF in the country declined from about 900 cases per year to 9 per year. Key health systems changes included the following:

- 1. Making ARF a notifiable disease.
- Standardized treatment of sore throats with benzylpenicillin—G (BPG).
- 3. Screening for RHD and referral for specialized care.
- 4. Secondary prophylaxis and optional medical and surgical care with education of patients, and involvement of nurses along with physicians.

The impact of improved medical and surgical care is reflected in the results of the REMEDY (Global Rheumatic

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TABLE 1. World Health Organization estimates for trends in RHD: 2000 to 2012

	Deaths			DALYS		
	2000	2012	% change	2000	2012	% change
Global	371,937	337,335	-9%	14,312,769	11,953,850	-16%
HIC	37,740	29,690	-21%	1,191,486	858,392	-28%
AFR*	32,438	32,968	2%	1,662,132	1,643,539	-1%
AMR	11,627	11,087	-5%	425,373	357,439	-16%
SEAR	147,746	131,220	-11%	5,863,333	4,869,508	-17%
EUR	25,989	21,824	-16%	945,094	691,360	-27%
EMR*	34,523	35,305	2%	1,263,994	1,238,496	-2%
WPR	80,760	74,230	-8%	2,924,041	2,265,636	-23%

AFR, African region; AMR, American region; EMR, Eastern Mediterranean region; EUR, European region; DALYs, disability adjusted life years; HIC, high-income countries; RHD, rheumatic heart disease; SEAR, Southeastern Asia region; WPR Western Pacific region.

\*Note that in AFR and EMR there has been little change.

**TABLE 2.** Tunisia: changes in demographics, socioeconomic changes and acute rheumatic fever over 35 years

	1978/1980	2014/2015				
Population	6.3 million	11.0 million				
Life expectancy	62 yrs	76 yrs				
GDP/capita	U.S. \$1,368	U.S. \$9,900				
ARF incidence (per 100,000)	8.7	0.08				
No. of cases of ARF	~900	9				
ARF, acute rheumatic fever; GDP, gross domestic product.						

**TABLE 3.** Definitions of eradication, elimination, or control of ARF and RHD

**Eradication**: Complete, permanent, and **worldwide**reduction to zero new cases through deliberate
attempts; **no further control measures required**. This
would require all current approaches plus a vaccine.

Elimination: Reduction to zero (or a very low target rate) of new cases in a *geographical area* through deliberate efforts; *continued efforts required*. This can be achieved by current strategies, as has been done in Tunisia, Cuba, and Costa Rica.

Control: Reduction of disease incidence, prevalence, morbidity, or mortality to *locally acceptable levels* through deliberate efforts; continued interventions required. This may be a first step toward elimination and lead to rapid declines in ARF.

Abbreviations as in Tables 1 and 2.

Heart Disease Registry), conducted in 12 countries in sub-Saharan Africa, Yemen, and India [2]. The 2-year mortality rates were highest in low-income countries (20.8%), intermediate in low- to middle-income countries (16.8%), and lowest in upper middle-income countries (12.5%). This was associated with better medical therapy and more frequent surgery in the centers in the richer countries.

Although an effective vaccine against group A streptococci is highly desirable, it is not essential to eliminating ARF or mortality from RHD. Table 3 provides the definitions of the terms eradication, elimination, and control. While vaccines have been critical to the eradication of small pox globally, or the eradication of poliomyelitis in most regions of the world (except for pockets in a few African and South Asian countries), even without an effective vaccine for group A streptococci, a 99% reduction in ARF (as was achieved in Tunisia) and a substantial reduction in RHD deaths and morbidity is possible. Transferring lessons learned from the regions with success stories to the regions where ARF and RHD still pose a substantial burden can virtually eliminate premature deaths and disabilities from this condition, which predominantly affects children and young adults. Given that ARF is declining by 5% per year globally, it could be eliminated within the next 20 to 25 years (i.e., 2040 or 2045) if strategies currently known to be effective were to be implemented in sub-Saharan Africa, South Asia, and other regions of the world where ARF remains a significant burden. If this is achieved, complications and deaths from RHD will rapidly decline in the following 2 or 3 decades, representing a major public health triumph.

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## **REFERENCES**

- Karthikeyan G. Global burden of rheumatic heart disease. Presentation at: World Congress of Cardiology and Cardiovascular Health; June 4-7, 2016; Mexico City.
- Zühlke L, Karthikeyan G, Engel ME, et al. Clinical outcomes in 3343 children and adults with rheumatic heart disease from 14 low- and middle-income countries: two-year follow-up of the Global Rheumatic Heart Disease Registry (the REMEDY Study). Circulation 2016;134: 1456–66.