

# The stark reality of rheumatic heart disease

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**This editorial refers to ‘Characteristics, complications, and gaps in evidence-based interventions in rheumatic heart disease: the Global Rheumatic Heart Disease Registry (the REMEDY study)’<sup>†</sup>, by L. Zühlke et al., on page 1115.**

It is a disease that, according to the Global Burden of Disease 2010 study, affects >34 million people, causing >345 000 deaths and 10 million disability-adjusted life years (DALYs) lost per year, almost all in low and middle income countries.<sup>1,2</sup> The cause—the group A *Streptococcus* (GAS) bacterium—is one of the top-10 infectious causes of deaths in the world.<sup>3</sup> Most cases and deaths occur in children, adolescents, and young adults, depriving developing countries of many young people who would otherwise be at their most productive economically and socially. It is a disease of poverty and social injustice.<sup>4</sup> The greatest tragedy of all is that it is eminently preventable. We know the cause, and we have proven cost-effective tools to avert most new cases and avoid mortality, using one of the cheapest and oldest antibiotics known—penicillin. The disease has all the characteristics to make it a priority for international control efforts, but the urgency for disease control is yet to be recognized at a high level. For years it has not been a significant focus for the World Health Organization, it is largely ignored by other international organizations, receives only 0.1% of global research and development funding for neglected diseases, and less than a handful of affected countries has any co-ordinated strategy to implement control programmes.<sup>5</sup>

I refer, of course, to rheumatic heart disease (RHD). The mid 20th century was the heyday of RHD research, driven by high rates of the disease in the USA. Yet waning RHD rates in affluent countries saw a simultaneous decline of research interest towards the end of the century (Figure 1). Many of us have spent the last decade trying to raise awareness of RHD and its devastating impact, and searching for ways to improve the delivery of proven control strategies to affected people and communities. This has inevitably meant a move sideways for the research community into the policy, service, and advocacy arenas. Yet this pathway is difficult to navigate for a disease that has no obvious ‘home’. It is both a communicable and a non-communicable disease. It spans the child, adolescent, maternal, and adult health domains. Disciplines including cardiology,

paediatrics, infectious diseases, and public health have a stake in it. Primary, secondary, and tertiary services all have a role to play in prevention and treatment.

## A decade of progress

Almost 10 years ago, my colleagues and I published an estimate of the global burden of GAS diseases, based on a comprehensive analysis of the available data.<sup>3</sup> That 2005 publication had something of a catalysing effect. At last we had some numbers to guide our planning, and to use to influence decision-makers. And, most heartening of all, they gave a quantifiable voice to the growing cohort of individuals, primarily clinicians, working in low and middle income countries, frustrated by the constant flow of young people with end-stage cardiac failure presenting in settings with no capacity to either offer high-end tertiary care or to administer the primary and secondary preventive approaches to stem the tide of new cases.

The most confident GAS disease estimates were for RHD, but we also highlighted the paucity of high quality data on incidence, prevalence, and mortality from the countries most affected by the disease. Diseases of the poor inevitably happen in places with the least developed data collection systems. We called for more research in low and middle income countries, a call that would require leadership to emerge from those same countries.

## Leadership from rheumatic heart disease-endemic countries

The story since then has been one of such leadership indeed stepping forward. This has been evident in international cardiology meetings in recent years. The World Congress of Cardiology and the World Congress of Pediatric Cardiology and Cardiac Surgery meetings since 2012 have seen RHD become an increasingly prominent part of the programme, and satellite RHD Forums have been oversubscribed.<sup>6</sup>

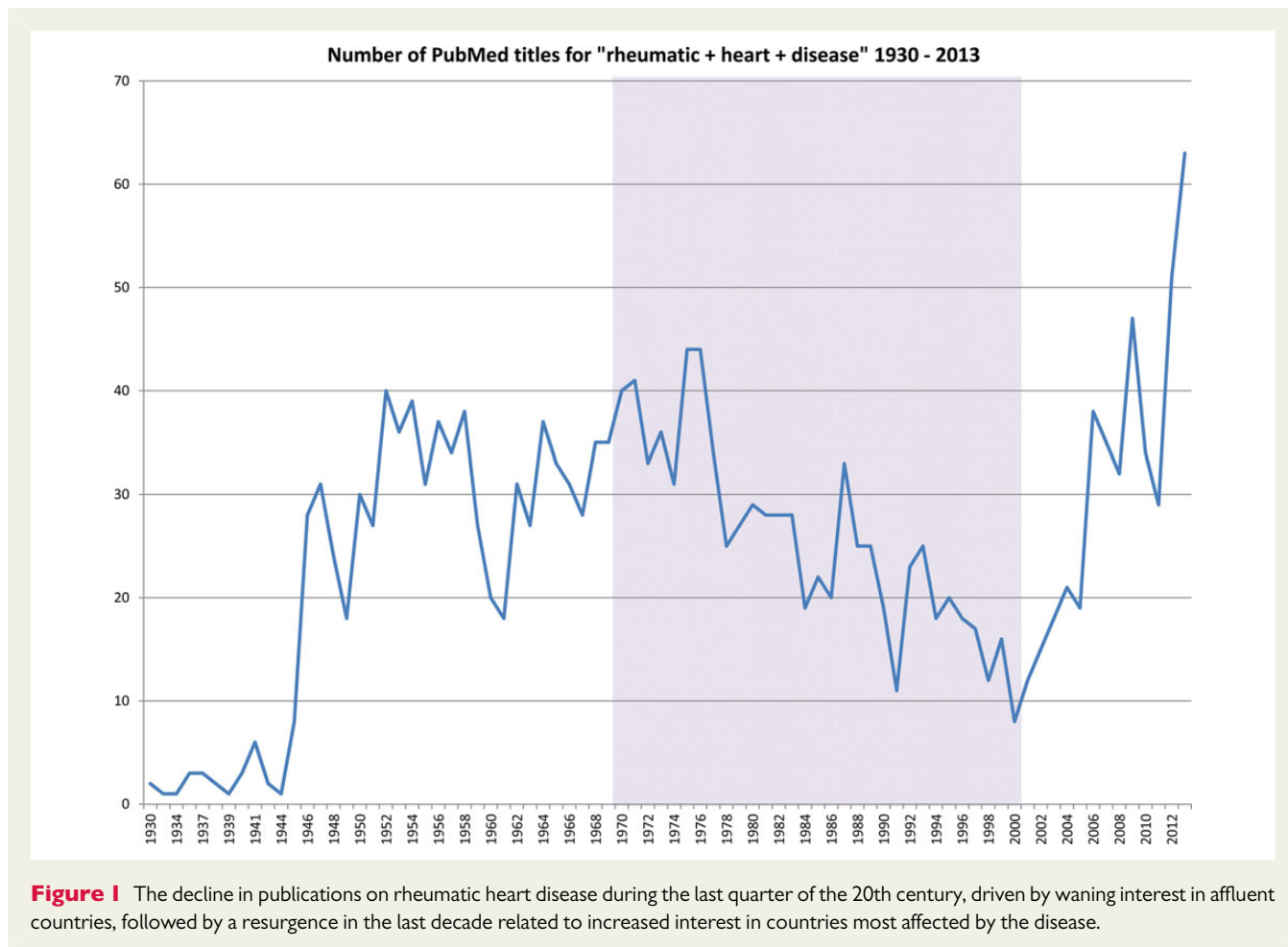
The REMEDY study is the latest example of how the tide has turned for RHD, spurred by research and advocacy emanating from the countries where the disease continues unabated. The baseline results from the pilot phase of REMEDY are reported in this

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journal, and the results are sobering.<sup>7</sup> The data are a great contribution to our understanding of the reality of RHD in developing countries, but the most illuminating aspect is the author list; 49 authors, all but one of whom is from Africa, the Middle East, or India. These are the current and future leaders of the growing RHD community, and we have a responsibility to support this powerful group in any way we can. In wealthy countries, that should include helping to find the financial resources that will allow new data and solutions to emerge from the countries that need them the most.

## The reality of rheumatic heart disease in developing countries

The REMEDY study paints a bleak picture of RHD, particularly in Africa. Remarkable features include the following (see *Box 1*).

- (i) The disease is severe. Atrial fibrillation was present in 22% of patients at enrolment, almost two-thirds had moderate to severe valvular disease, one-third had cardiac failure, and 24% had New York Heart Association (NYHA) functional class III or IV disease. This accords with Soweto data showing that 22% of new RHD patients required valve surgery within a year and even more concerning data from Ethiopia suggesting a 12.5% annual mortality rate for RHD patients.<sup>8,9</sup> Clearly, far too many

- patients in low and middle income countries are first diagnosed with advanced disease, at a stage when there is little chance of a good outcome in the absence of surgical intervention.
- (ii) Surgery is a luxury not available to the poor: despite RHD being at least as severe in low income as in low–middle or high–middle income countries, only 11% of surgical interventions occurred in low income countries compared with 61% in high income countries.
- (iii) Most RHD patients do not receive adequate secondary prophylaxis, the only proven cost-effective intervention for RHD. Only 55% were prescribed secondary prophylaxis (interestingly, only 29% in the highest income countries). It is not clear how many of those prescribed prophylaxis actually received it: the term ‘adherence’ is used, but the REMEDY manuscript does not mention if they measured the proportion of prescribed doses of secondary prophylaxis that were delivered. Delivery of secondary prophylaxis is one of the greatest challenges facing any health system dealing with RHD.<sup>10</sup>
- (iv) Delivery and monitoring of anticoagulation is inadequate. Thirty per cent of patients with indications for oral anticoagulation were not prescribed them, almost half of those on anticoagulants had inappropriate monitoring, and even then only 28% had therapeutic levels. This would help to explain the high rates of stroke (7%) and major bleeding (3%) which, along with endocarditis

### Box 1 What the REMEDY study tells us about rheumatic heart disease in low and middle income countries

- People with RHD are first diagnosed when they have advanced disease.
- Surgery is a luxury available mainly to those living in high income countries.
- Most RHD patients do not receive adequate secondary prophylaxis.
- Delivery and monitoring of anticoagulation is inadequate, leading to high rates of stroke and bleeding.
- The burden of RHD in women is underappreciated, leading to high maternal and fetal mortality.
- Leadership in RHD control is emerging from the countries that bear the greatest disease burden.

(4%), are significant causes of mortality and morbidity due to RHD that are often not considered in RHD burden estimates, including those from the Global Burden of Disease study.

- (v) The particular burden of RHD on women needs more attention. Sixty-six per cent of patients were women (RHD universally affects more women than men), most of childbearing age, and only 4% of whom were on contraceptives. Pregnancy in women with RHD is a hidden cause of maternal as well as fetal mortality. In a South African study, 41% of indirect obstetric deaths were associated with heart disease, predominantly RHD (71–84%), and in a Senegal study of 50 pregnant women with heart disease, 46 had RHD, resulting in 17 maternal deaths (34%), 6 fetal deaths, and 5 therapeutic abortions.<sup>11,12</sup> Recent data suggest that 25% of maternal deaths in developing countries are from indirect causes.<sup>13</sup> As we approach the 2015 deadline for the Millennium Development Goals (MDGs), one wonders whether a focus on RHD could have been an important contributor to averting these indirect deaths and achieving MDG5?

## Limitations

The authors acknowledge that REMEDY provides a skewed view of RHD, biased by the fact that patients are enrolled through hospitals, and that patients could be enrolled at any stage in their disease history. As it turned out, participating low income sites tended to enrol newly diagnosed RHD patients, whereas the higher income sites largely enrolled people with existing diagnoses (L. Zuhlke, personal communication). So, while REMEDY is not representative of the whole RHD problem in participating countries, it is likely to be representative of the disease facing tertiary services.

## Conclusions

It is hoped that the REMEDY study will set a precedent for further comprehensive studies of RHD in low and middle income countries. We need more observational data such as these to document the true disease burden and explore the experience of affected individuals, and the next generation of studies will hopefully be more representative by recruiting all patients from all centres (not just hospitals) with newly diagnosed RHD. We need intervention studies,

particularly those that look at better ways to provide care to reduce the extraordinary mortality and morbidity after diagnosis. We need to explore ways to diagnose cases earlier in their natural history, perhaps through echocardiographic screening, so that secondary prophylaxis can be delivered at a stage when progression to severe RHD might potentially be prevented.<sup>14</sup> We need data that are most meaningful to communities living with the disease and most likely to galvanize decision-makers, such as the contribution of RHD to maternal mortality.

This search for more and better data should not detract from the most obvious conclusion of REMEDY: RHD is a major cause of preventable death and suffering in children and young adults in low and middle income countries. The social, cultural, and economic toll of RHD warrants far greater attention and resourcing than it currently receives. The REMEDY investigator list reassures us that the future of RHD control is rightly in the hands of those who confront the stark reality of this disease daily.

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**Conflict of interest:** J.R.C. has collaborated and published previously on rheumatic heart disease with a number of the authors of the related article, and is co-Director with the first author of RHEACH, a new technical support and advocacy organization working towards global RHD control.

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