

CORRESPONDENCE

Global Burden of Rheumatic Heart Disease

TO THE EDITOR: Watkins et al. (Aug. 24 issue)¹ report that the health-related burden of rheumatic heart disease has declined worldwide. However, the authors emphasize mainly heart failure as the burden of rheumatic heart disease, whereas other complications were neglected. Patients with mild rheumatic heart disease that may not be clinically detectable are at increased risk for death and complications from other heart-related causes. For example, transient or sustained atrial fibrillation is sometimes observed in clinically asymptomatic patients with mild or moderate rheumatic mitral stenosis, which is often diagnosed on echocardiography after complications, such as stroke, have occurred.²⁻⁴ Stroke, peripheral-artery embolization, and ischemia in the mesenteric arteries can develop even in patients who have mild rheumatic heart disease with limited valvular involvement and who present with sinus rhythm. There is no clear relationship between the severity of rheumatic heart disease and many important complications.^{5,6} Therefore, it is misleading to exclude patients with mild rheumatic heart disease and place the emphasis on heart failure in symptomatic patients when assessing the burden of rheumatic heart disease, even in developed industrial countries.

Bahram Sohrabi, M.D.

Abdolmohammad Ranjbar, M.D.

Tabriz University of Medical Sciences
Tabriz, Iran
dr.am.ranjbar@gmail.com

No potential conflict of interest relevant to this letter was reported.

1. Watkins DA, Johnson CO, Colquhoun SM, et al. Global, regional, and national burden of rheumatic heart disease, 1990–2015. *N Engl J Med* 2017;377:713-22.
2. Zühlke LJ, Steer AC. Estimates of the global burden of rheumatic heart disease. *Glob Heart* 2013;8:189-95.
3. Singh PI, Carapetis JR, Buadromo EM, Samberkar PN, Steer AC. The high burden of rheumatic heart disease found on autopsy in Fiji. *Cardiol Young* 2008;18:62-9.
4. Marijon E, Ou P, Celermajer DS, et al. Prevalence of rheumatic heart disease detected by echocardiographic screening. *N Engl J Med* 2007;357:470-6.
5. Marijon E, Mirabel M, Celermajer DS, Jouven X. Rheumatic heart disease. *Lancet* 2012;379:953-64.

6. Wang D, Liu M, Lin S, et al. Stroke and rheumatic heart disease: a systematic review of observational studies. *Clin Neurol Neurosurg* 2013;115:1575-82.
DOI: 10.1056/NEJMc1714503

TO THE EDITOR: Watkins et al. perform a complex analysis of an impressive amount of data to estimate the global burden of rheumatic heart disease. However, we are concerned about the precision of the diagnostic criteria that were used to classify a country as having an endemic pattern of disease (i.e., an estimated rate of death from rheumatic heart disease of >0.15 deaths per 100,000 population among children 5 to 9 years of age). The typical progression from episodes of acute rheumatic fever to subclinical rheumatic heart disease to clinical rheumatic heart disease and, in some cases, heart failure and death generally occurs over a span of at least 10 years.¹ Several studies have shown that the average age at first diagnosis of acute rheumatic fever ranged from 10 to 14 years.^{2,3} Death from end-stage rheumatic heart disease usually occurs in the second or third decade of life.^{2,4} Since death from rheumatic heart disease is uncommon among children between 5 and 9 years of age, there could be a risk of serious underestimation of the endemicity of rheumatic heart disease in several countries worldwide on the basis of the criteria used in this study. In addition, the lack of a requirement for systematic confirmation of suspected rheumatic heart disease on echocardiography could compound diagnostic uncertainty in the important work of estimating the true worldwide prevalence of this disease.

Ronald A. Johannsen, M.D.

Gautam R. Shroff, M.B., B.S.

Hennepin County Medical Center
Minneapolis, MN
ronald.johannsen@hcmcd.org

No potential conflict of interest relevant to this letter was reported.

1. Lawrence JG, Carapetis JR, Griffiths K, Edwards K, Condon JR. Acute rheumatic fever and rheumatic heart disease: incidence and progression in the Northern Territory of Australia, 1997 to 2010. *Circulation* 2013;128:492-501.

2. Carapetis JR, Currie BJ. Mortality due to acute rheumatic fever and rheumatic heart disease in the Northern Territory: a preventable cause of death in Aboriginal people. *Aust N Z J Public Health* 1999;23:159-63.
3. Seckeler MD, Barton LL, Brownstein R. The persistent challenge of rheumatic fever in the Northern Mariana Islands. *Int J Infect Dis* 2010;14(3):e226-e229.
4. Günther G, Asmera J, Parry E. Death from rheumatic heart disease in rural Ethiopia. *Lancet* 2006;367:391.

DOI: 10.1056/NEJMc1714503

TO THE EDITOR: In the study by Watkins et al., more nuanced data are needed from places that continue to see the ongoing burden of rheumatic heart disease. In areas where the availability of care is poor, death rates associated with this disease can be very high. In rural central India, where we work, rheumatic heart disease contributes to 42% of all cases of heart disease that we see; approximately 18% of the cases are due to coronary heart disease, and the remaining 40% are due to other causes, predominantly cardiomyopathies.¹

Of the 48 patients with newly diagnosed rheumatic heart disease in our health program in 2015, one quarter have already died; all of these patients were under the age of 35 years. Only 2 of these patients were able to reach a hospital (in a badly decompensated state) before death. The causes of death included complications of severe pulmonary venous hypertension, stroke as a presenting manifestation, failure of anticoagulation therapy, and decompensation associated with pregnancy. Proper monitoring of anticoagulation therapy is only a dream here, since assays to calculate the international normalized ratio vary tremendously among laboratories, and such testing is not available in small towns and villages.

Yogesh Jain, M.D.

People's Health Support Group
Ganiyari, India
yogeshjain.jssbilaspur@gmail.com

Rajnish Juneja, M.D.

All India Institute of Medical Sciences
New Delhi, India

Sushil Patil, M.H.A.

People's Health Support Group
Ganiyari, India

No potential conflict of interest relevant to this letter was reported.

1. Jain Y, Kataria R, Patil S, et al. Burden & pattern of illnesses among the tribal communities in central India: a report from a community health programme. *Indian J Med Res* 2015;141:663-72.

DOI: 10.1056/NEJMc1714503

TO THE EDITOR: In the study of rheumatic heart disease from the Global Burden of Disease, the maps of whole-country prevalence of rheumatic heart disease appear to show that rheumatic fever is a disease of tropical areas, as the accompanying editorial by Marijon et al. asserts.¹ However, this perception ignores the occurrence of rheumatic fever and consequent rheumatic heart disease in socially disadvantaged areas of the highest-income countries. This phenomenon has been well described in Australia and New Zealand,² and a similar pattern occurs in Canada, where most cases of rheumatic fever occur in areas in which high concentrations of indigenous people live in impoverished circumstances.^{3,4} These cases are found largely in temperate, rather than tropical, zones. We are not familiar enough with social conditions in the United States to confidently correlate reports of rheumatic fever⁵ with social deprivation but suggest that rheumatic disease is a consequence of and marker for substandard living conditions.⁶ The so-called icebergs of this disease mark areas of social calamity, with many other medical consequences as well. The solution is not to feverishly swab the throats of children with viral pharyngitis and overdiagnose streptococcal colonization among the comfortable middle class but to focus on improving living conditions for the poorest.

James A. Dickinson, M.B., B.S., Ph.D.

Ian Johnston, M.B., Ch.B.

University of Calgary
Calgary, AB, Canada
dickinsj@ucalgary.ca

No potential conflict of interest relevant to this letter was reported.

1. Marijon E, Celermajer DS, Jouven X. Rheumatic heart disease — an iceberg in tropical waters. *N Engl J Med* 2017;377:780-1.
2. Carapetis JR, Steer AC, Mulholland EK, Weber M. The global burden of group A streptococcal diseases. *Lancet Infect Dis* 2005;5:685-94.
3. Gordon J, Kirlaw M, Schreiber Y, et al. Acute rheumatic fever in First Nations communities in northwestern Ontario: social determinants of health “bite the heart.” *Can Fam Physician* 2015;61:881-6.
4. Johnston I, Gittens C, Dickinson JA. Pharyngitis complications in North America in the 21st century. Presented at the Third Preventing Overdiagnosis Conference, Bethesda, MD, September 1–3, 2015 (http://www.preventingoverdiagnosis.net/?page_id=1054).
5. Veasy LG, Tani LY, Daly JA, et al. Temporal association of the appearance of mucoid strains of *Streptococcus pyogenes* with a continuing high incidence of rheumatic fever in Utah. *Pediatrics* 2004;113(3 Pt 1):e168-172.
6. Guilfoyle J. Out of sight, out of mind. *Can Fam Physician* 2015;61:833-4.

DOI: 10.1056/NEJMc1714503

TO THE EDITOR: In their editorial on rheumatic heart disease, Marijon and colleagues state that “the affluent world cannot afford complacency; large population movements and refugee crises can displace persons with rheumatic heart disease to developed nations.” We would like to share a provisional, retrospective analysis of ongoing operational data from screening for rheumatic heart disease that was performed in Rome from February 2016 through August 2017 by Médecins Sans Frontières in collaboration with the Cardiology Department of the Tor Vergata University Hospital and the Italian National Institute for Health, Migration, and Poverty (NIHMP). In this study, we investigated a mobile screening approach for rheumatic heart disease by providing echocardiography in centers and family houses for unaccompanied foreign minors. Persons who were identified as having definite or borderline cases according to the World Heart Federation criteria¹ were subsequently retested by cardiologists at the NIHMP outpatient clinic.²

A total of 603 persons underwent screening, with the detection of 6 definite cases of rheumatic heart disease and 263 borderline cases. Among the persons with “non-negative” results, 148 have been retested in the ongoing program; of these persons, definite disease has been diagnosed in 14 and borderline disease in 104 (provisional prevalence, 2.3% [14 of 603] for definite disease and 17.2% [104 of 603] for borderline disease). These data support the call to arms issued by Marijon et al. while promoting vigilance in rich countries.^{3,4}

Gabriele Rossi, M.D., M.P.H.

Médecins sans Frontières
Brussels, Belgium
gab.rossi@tiscali.it

No potential conflict of interest relevant to this letter was reported.

1. Reményi B, Wilson N, Steer A, et al. World Heart Federation criteria for echocardiographic diagnosis of rheumatic heart disease — an evidence-based guideline. *Nat Rev Cardiol* 2012;9:297-309.

2. De Maio G, Lupiz M, Condemi F, Pagano A, Al-Rousan A, Rossi G. Screening for rheumatic heart disease in refugee children in Europe — MSF leads, will others please follow? Presented at MSF Paediatric Days 2016, Stockholm, September 23–24, 2016. poster.

3. Rossi G, Lee VSW. Call for preventive care for rheumatic heart disease in refugee children. *BMJ* 2016;353:i2312.

4. Rossi G, Lee VSW. Assessing the burden of rheumatic heart disease among refugee children: a call to action. *J Glob Health* 2016;6:020305.

DOI: 10.1056/NEJMc1714503

THE AUTHORS REPLY: Better data are certainly needed to improve our understanding of the burden of rheumatic heart disease around the world. We agree with Sohrabi and Ranjbar that rheumatic heart disease leads to a wide range of sequelae in addition to heart failure. We note that the primary result of our analysis was the total prevalence of rheumatic heart disease, including mild, moderate, and severe cases, regardless of heart failure. Our estimates of heart failure caused by rheumatic heart disease accounted for a subgroup of the total cases and did not exclude mild cases. Unfortunately, we found no available data on subclinical or mild rheumatic heart disease in nonendemic settings, and we agree that such cases might slightly increase the small number of cases counted within administrative-health-system data in high-income countries.

We also agree with Dickinson and Johnston that subnational estimates will reveal marked variation within countries, including in nonendemic countries. Recently, we found clusters of counties in the United States that had rates of death from rheumatic heart disease that were relatively higher than the typical rates in high-income countries.¹ Dickinson and Johnston correctly emphasize that the exploration of the most proximal causes of rheumatic heart disease, including poverty and poor living conditions, is important in countries at any level of development.

Jain and colleagues note the high burden of rheumatic heart disease in rural India. Community-based studies have corroborated their observations,² and we agree that more longitudinal studies among adults in the most rural and impoverished regions are needed.

Johannsen and Shroff suggest that some countries in our analysis might have been misclassified as nonendemic according to a definition based on mortality among children between the ages of 5 and 9 years. We agree that there is a possibility of misclassifying countries on the basis of these criteria. However, after examining the rates of death from rheumatic heart disease among older persons, we do not believe that the use of different criteria would have led to substantial changes in the classification of countries. Perhaps more important to note is that, to our knowledge, no government or civil organization tracks and reports the locations in which rheumatic heart disease is endemic. We think that greater public reporting on the geographic

distribution of rheumatic heart disease is an essential step in eliminating the disease.

The Global Burden of Disease Study 2016 has recently produced subnational estimates for the prevalence of rheumatic heart disease in multiple countries, including India and China. The annual updates to the Global Burden of Disease Study continue to incorporate newer data sets and methodologic advances.

David A. Watkins, M.D., M.P.H.

Gregory A. Roth, M.D., M.P.H.

University of Washington
Seattle, WA
davidaw@uw.edu

Since publication of their article, the authors report no further potential conflict of interest.

1. Roth GA, Dwyer-Lindgren L, Bertozzi-Villa A, et al. Trends and patterns of geographic variation in cardiovascular mortality among US counties, 1980-2014. *JAMA* 2017;317:1976-92.
2. Gemechu T, Mahmoud H, Parry EH, Phillips DI, Yacoub MH. Community-based prevalence study of rheumatic heart disease in rural Ethiopia. *Eur J Prev Cardiol* 2017;24:717-23.

DOI: 10.1056/NEJMc1714503

THE EDITORIALISTS REPLY: We appreciate the important comments raised in response to our recent editorial concerning the new population data on the global burden of rheumatic heart disease. We fully agree that rheumatic heart disease is not restricted to low-income or tropical countries but is also a matter of potential concern in middle-income and even highly developed countries.^{1,2} In addition to the presentation of patients with rheumatic heart disease in almost any country owing to population flows from migration and refugee movements, local resurgences have been

observed, as we discussed in our editorial. In addition, cases have been diagnosed in Canada and western Europe, as documented by correspondents Dickinson and Johnston as well as Rossi.^{3,4} This aspect of the epidemiology of rheumatic heart disease is deserving of further emphasis. The correspondents' comments appropriately focus attention on the recent neglect of rheumatic heart disease, both in terms of research funding and medical school education. Rheumatic heart disease persists in many parts of the world and merits considerable efforts in its control and possible eventual eradication.

Eloi Marijon, M.D., Ph.D.

European Georges Pompidou Hospital
Paris, France
eloi.marijon@inserm.fr

David S. Celermajer, Ph.D., F.R.C.P.

Sydney Medical School
Sydney, NSW, Australia

Xavier Jouven, M.D., Ph.D.

European Georges Pompidou Hospital
Paris, France

Since publication of their article, the authors report no further potential conflict of interest.

1. Marijon E, Mirabel M, Celermajer DS, Jouven X. Rheumatic heart disease. *Lancet* 2012;379:953-64.
2. Marijon E, Ou P, Celermajer DS, et al. Prevalence of rheumatic heart disease detected by echocardiographic screening. *N Engl J Med* 2007;357:470-6.
3. Gordon J, Kirlew M, Schreiber Y, et al. Acute rheumatic fever in First Nations communities in northwestern Ontario: Social determinants of health "bite the heart." *Can Fam Physician* 2015; 61:881-6.
4. Rossi G, Lee VS. Assessing the burden of rheumatic heart disease among refugee children: a call to action. *J Glob Health* 2016;6(2):020305.

DOI: 10.1056/NEJMc1714503

Correspondence Copyright © 2018 Massachusetts Medical Society.