

Is population-based screening for rheumatic heart disease precluded by the Cairo accord? Echocardiography...and beyond

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Abstract

In the 2017, "Cairo Accord on Rheumatic Heart Disease—From Molecules to The Global Community" experts from endemic areas enumerated an approach to reduce the population burden of rheumatic heart disease. The 10 key recommendations include immediate logistical objectives as well as domains for further study. Echocardiographic population screening programs were relegated to research alone. Given the large body of supporting data, relegating echo screening to an investigational modality is an opportunity lost.

KEYWORDS

children, cost-effectiveness, echocardiography, health care policy rheumatic heart disease, screening

The recently promulgated 2017 "Cairo Accord on Rheumatic Heart Disease—From Molecules to The Global Community" was a landmark in global cardiology wherein stakeholders from low and middle per capita income countries (LMIC) set international priorities for a disease largely affecting their own populations, in lieu of directives from high income country experts.¹ The Accord addresses the consequences of rheumatic fever (RF) which affects the most disadvantaged LMIC citizens who are often impoverished, living in overcrowded circumstances, with marginal health literacy and inadequate health care access.² While the Accord does not give detailed arguments for the recommendations endorsed, on balanced reading, invested stakeholders may fret over a possible opportunity lost.

RF is a systemic inflammatory disease caused by the Group A beta-hemolytic Streptococcus and occurs in conjunction with an individual's genetic susceptibility and aberrant immune response.^{2,3} A key RF consequence is rheumatic heart disease (RHD), most often characterized by valvulitis of the mitral and aortic valves. The valvular disease can continue to smolder and progress to congestive heart failure, stroke, serious arrhythmia, and/or death. RF affects 33 million people worldwide and is responsible for 275,000 deaths annually, often in the maximal earning period of the life course. Estimates on the undiscounted direct financial cost of these deaths were \$2.2 trillion in 2010.⁴ Therefore, the burden of RHD is the human tragedy

of lives debilitated but also includes the direct economic costs and ripple effects in society of lost human capital. These losses are sustained by the most vulnerable communities of LMIC countries.

The Accord endeavors to systematically set policy priorities for future RHD mitigation. The 10 key recommendations include logistical objectives such as improving case counting within rigorous databases preferably with data exchange interoperability; ensuring provision of high-quality penicillin in endemic areas; nucleating RHD centers of excellence; and percolating valve repair techniques in endemic areas. Deemed as emerging investigational recommendations are creation of tissue engineered and percutaneous valves; establishment of anti-inflammatory and anti-arrhythmic therapies; development of a group A streptococcus vaccine; discovery of RHD susceptibility genes; elucidation of diagnostic and prognostic biomarkers; and most curiously, relegation of echocardiographic screening programs to research.

Detection and treatment of RHD affected individuals at an early, modifiable stage must be at the center of RHD management. Published literature shows primary prophylaxis at the pharyngitis stage and secondary prophylaxis after the RF stage is the interventions that alleviate the burden of RHD.⁵⁻⁷ Importantly, neither surgical nor interventional catheterization on RHD-affected valves are demonstrated to mitigate the public health burden of

RHD and moreover are plagued by chronic medication use for residual congestive heart failure, arrhythmia control, and thrombosis prophylaxis. On the contrary, the effective strategies for RHD mitigation are either (a) public health infrastructure interventions like consistently delivering RHD prophylaxis or (b) raising the per capita income which appears correlated to RHD eradication. Of these two solution strategies, the former seems unpalatable in an era enchanted by turning health care into a discrete commodity which can be sold at sufficiently high prices. The latter is outside the purview of health care professionals. In this epoch of so-called disruptive innovations where societies are leapfrogging in the communication domain by bypassing fixed phone lines in favor of cellular phone technology and in the banking domain by eschewing brick-and-mortar financial institutions in favor of mobile, decentralized banking platforms, population-based echo screening appears to be a congruous, contemporary health care solution. Population-based screening would enable endemic locations to identify individual RHD cases at a modifiable point. By counting existing cases within a known population, echo screening can help establish the RHD population burden. Crucially, estimating the disease burden can establish the expected demand for high-quality penicillin and thereby facilitate the Accord's own recommendation for health policy stakeholders to negotiate better penicillin prices at scale.

Disconcertingly, the Cairo Accord consigns the most exciting and effective recent tool in RHD, namely echocardiographic population screening, to a research methodology "until further evidence regarding its impact on prognosis and cost-effectiveness is made available." As background, it is well known that atypical clinical RHD presentations occur, a substantial proportion of RHD affected individuals in the modern era present at a late stage of disease, and a substantial proportion of RHD-affected individuals do not recall a primary pharyngitis or acute RF event.^{2,4,8} These three facts cast doubt on the effectiveness of existing clinical exam-based diagnostic methods being sufficient to mitigate RHD. Numerous studies from myriad RHD endemic areas have demonstrated that echocardiographic screening detects many-fold more cases of RHD than clinical exam.^{9,10} The echo-only cases are ultrasonographically indistinguishable from clinically evident cases. Conversely, echo can detect even very mild clinical cases to which a child may have accommodated and thereby bring them to attention before the youth presents with uncompensated severe symptoms. Theoretical criticism of echocardiographic screening includes it being unrepeatably in RHD high-risk but low-income areas; being of unclear significance in borderline echo cases; and being expensive or societally cost-ineffective. But actual data show that it is repeatably deployable in LMIC settings and every analysis performed on actually existing screening programs with real world characteristics as well as modeling exercises using virtual cohorts with nearly all possible ranges of costs and disease prevalence has shown population-based screening to be cost-effective or even cost-saving.¹⁰⁻¹⁴ Therefore, the Accord's explicit request for "... further evidence regarding its ... cost-effectiveness" is most peculiar and not likely to be forthcoming.

In summary, strategies for population screening of RHD should be ideally be minimally resource-intensive with respect to equipment, time, and staff, especially through task shifting; maximally sensitive; and highly specific. Within these boundaries, echocardiographic, circulating biomarker, genetic, sociodemographic, or other strategies may be of potential screening value. Such population screening strategies could address the delay in seeking clinical attention in favor of intervening on RHD at a more modifiable stage, would leverage enthusiasm about the emerging screening strategy, and would support public health procurement of the most effective RHD-arresting treatment, penicillin. Instead of explicit endorsements of high-intensity salvage therapy or vaccines already three decades on in the making, the Cairo Accord would have been well served to endorse population-based screening as a "disruptive" strategy for improving LMIC public health. To paraphrase the old aphorism, Opportunity does not often knock twice.

CONFLICT OF INTEREST

We the authors we declare we have no financial conflicts of interest.

AUTHOR CONTRIBUTIONS

CEBB and JPZ: Conceived and drafted the manuscript.

ROS and FT: Critically revised and approved the article.

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