Comparing the incomparable: studies of echocardiographic rheumatic heart disease prevalence

Authors' reply

We acknowledge the large heterogeneity in reported prevalence of rheumatic heart disease documented in our systematic review,[1] and concur with Peter Murray and Caroline Shaw that the statistical combination of heterogeneous studies might have drawbacks. The exploration of potential sources of heterogeneity is therefore important and could provide more insight than the mechanistic calculation of the overall measure of effect.[2]

As former US Secretary of State for Defence Donald Rumsfeld said, "There are known knowns. These are the things we know that we know. There are known unknowns. That is to say, there are things that we know we don't know. But there are also unknown unknowns. There are things we don't know we don't know."[3] The potential sources of heterogeneity addressed by Murray and Shaw fall under the category of known unknowns, for which we tried to account by taking several measures. We assessed the methodological characteristics and summarised the clinical and echocardiographic criteria for case detection of all included studies in the online appendix, did sensitivity analyses, and transparently discussed the limitations of our findings. Additionally, we presented prediction intervals. These intervals represent the true uncertainty of a pooled estimate in the presence of unexplained or only partly explained heterogeneity, as is the case here. Beyond the known unknowns that we tried to address, we are confronted with residual confounders, unknown unknowns that might be uncovered only in subsequent studies.

Nevertheless, we believe that the main findings of our study are robust. We noted a progressive increase in the prevalence of rheumatic heart disease with advancing age of children, modelling different prevalence patterns across age groups separately for each study, and pooling estimates within each age group only in a second step, while taking into account the uncertainty of our estimates. Our findings suggest the potential importance of cumulative exposure to streptococcal infections. We noted a prevalence of silent rheumatic heart disease that was several times higher than clinically manifest disease, as previously shown by Marijon and colleagues,[4] among others. Finally, we noted a statistically significant association of prevalence and social inequality. The eradication of rheumatic heart disease in high-income countries was mediated by socioeconomic change. It is a known known that the answer to rheumatic heart disease resides in a reduction of poverty and facilitated access to health care.

We declare no competing interests.

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2 Egger M, Schneider M, Davey Smith G. Spurious precision? Meta-analysis of observational studies. *BMJ* 1998; **316:** 140–44.
3 DoD News Briefing – Secretary Rumsfeld and Gen. Myers, February 12, 2002 Defense.gov News Transcript, United States Department of Defense http://www.defense.gov/transcripts/transcript.aspx?transcriptid=2636 (accessed Jan 9, 2015)
4 Marijon E, Ou P, Celermajer DS, et al. Prevalence of rheumatic heart disease detected by echocardiographic screening. *N Engl J Med* 2007; **357:** 470–76.