Reviewer’s report

Title: A systematic review of economic evaluations of interventions to tackle cardiovascular disease in low- and middle-income countries

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Reviewer: Rachel Nugent

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Nugent review for BioMed Central

Article title: A systematic review of economic evaluations of interventions to tackle cardiovascular disease in low- and middle-income countries
Authors: Suhrcke, Boluarte, Niessen

Review summary: The article is interesting and on a timely and important topic. There have been no other systematic reviews of cost-effectiveness or economic evaluation of CVD in LMICs, and the body of work covered in this review is worthy of summary and evaluation. The authors are well-respected experts in this field and the article will be heavily cited. While the article is valuable as written, there is a structural issue that should be addressed. The primary purpose of the article is to provide a systematic review of CVD economic evaluations. The article ably accomplishes this goal; however, the discussion focuses on methodological weaknesses and challenges rather than the results of the systematic review. While the discussion of methodological weaknesses of the studies reviewed is important and raises interesting questions, it seems to pertain more broadly to economic evaluation of interventions in LMICs rather than specifically to CVD intervention studies. The article would be more cohesive if it better connected the systematic review results in part 1 with the discussion in part 2. One way to connect the two parts of the article is to more specifically address particularities of CVD in the methodological section and conclusions; for instance, what are the specific transferability issues related to CVD? Other issues in the article are specified below.

Major compulsory revisions:

1. Better connect results of systematic review with discussion. See above.
2. Clarify when discussing efficacy versus effectiveness. Most studies reviewed are assessing efficacy, rather than effectiveness. In several places the article raises issues about effectiveness and real world conditions. It would be very interesting to see a discussion of how efficacy and effectiveness vary for CVD. There is literature from HIV specifically addressing adherence, access, and some of the other issues raised here. This literature might inform a discussion.
3. Provide a summary of systematic review results. Although a ranking cannot be provided because of differences across studies, the article loses power by not summarizing what is learned about the cost-effectiveness of various
interventions. More explanation of differences across studies would be useful to explain why interventions can’t be ranked.

Discretionary revisions:

1. Issues of “mass medicalization.” It’s not clear what is meant here. Is it a real issue, and if so, how would it be assessed by an economic evaluation? (3rd para in discussion section, and later)

2. Blood pressure thresholds. Most recent proposals suggest lowering thresholds such that a large number of people would be at-risk. The discussion section of the paper suggests the opposite. The point is made that extensive pharmacological treatment is expensive, which is appropriate but then the suggestion is made that population-based approaches may be more cost-effective. However, the article does not provide evidence for this supposition. In fact, in several places in the article the authors suggest a bias for prevention (also conclusion) that does not appear to be supported by the results. In fact, the article points out that such interventions (population-based, non-clinical) have not been adequately studied.

3. Transferring results from developed to developing countries. This is a major topic in the discussion, but is not well fleshed-out. Would be useful to describe what it means, how authors deal with this in different ways, and what the particular aspects are that pertain to CVDs. Discussion of ISPOR recommendation and RWD belongs earlier in the article.

4. Modeling approaches. Also an important topic in the discussion which would benefit from more fleshing out to indicate what different approaches to modeling are relevant to CVD and how much they can be relied upon.

5. Ambiguity between primary and secondary prevention. I was surprised that the review produced more studies about primary than secondary prevention as that is not what the literature normally suggests. I looked carefully at the list of studies reviewed and would re-categorize some of the studies listed as secondary rather than primary prevention (Ker, Robberstad, Araujo…) Suggest that there be a more complete definition of primary and secondary. One reason for the ambiguity is that different medical fields use these terms differently.

6. Writing is not clear and succinct. Repetitions appear throughout the article; for instance, the issue of societal perspective appears more than once, lack of data in developing countries is mentioned several times, a few words are missing (the beginning of the conclusion should mention economic evaluation rather than just burden of cardiovascular disease as a neglected topic.)