Author's response to reviews

Title: Hypertension education and adherence in South Africa: a cost-effectiveness analysis of community health workers

Authors:

Thomas A Gaziano (tgaziano@partners.org)
Melanie Bertram (melanie.bertram@gmail.com)
Stephen M Tollman (Stephen.Tollman@wits.ac.za)
Karen J Hofman (Karen.Hofman@wits.ac.za)

Version: 2 Date: 22 February 2014

Author's response to reviews: see over
Dear Editors:

We are grateful for the opportunity to revise the manuscript and respond to the helpful reviewer comments that we received. In particular we conducted the sensitivity analyses that were suggested and feel that they have strengthened the paper. We also have responded to the other queries and suggestions and have altered the manuscript when suggested. Below you will find our responses to the reviewers’ comments in italics. Attached is a revised manuscript.

Reviewer: Jeremy Sussman

More sensitivity analyses are needed. While I hate to criticize a very good model that has already been used in publication multiple times, my biggest problems were with the two major assumptions that relied on US-based data. The CVD prediction tool was based on old Framingham scores. While this is likely the best available, multiple studies have shown that Framingham is consistently mis-calibrated outside of the US, in part due to Framingham's slightly unusual dependent variable. (See D'agostino Jama 2001, where they recalibrate the score every time and Brindle BMJ 2003.) Similarly, the rate of survival is from ISIS-2, a study that bears mixed resemblance to MI in South Africa. These limitations are not acknowledged or analyzed in sensitivity analyses.

Because of data limitations like this, I think the paper focuses too much on the mean estimated cost-effectiveness, a number that is rarely meaningful and certainly not here, and not enough on understanding the reliability of those numbers. I think a tornado diagram would be in order, or perhaps a probabilistic sensitivity analysis, so would using more meaningful values for the ranges chosen for these analyses. The estimates of the cost of an MI vary 15%, for example, which seems very optimistic. My point in saying this is not that I don't believe the results, but I think when data is as uncertain as much of this is, it is more important to see where the CEA could be wrong than to look at the take-home value. Especially considering this is in preparation for a project, not evaluation of one that's been done; it is good to see where it may go wrong.

We appreciate the concern regarding the model being based on the Framingham Risk Function. We had the same concern when the model was first developed. In 2006 when we first used the model for analyses in South Africa we had the same concern. Unfortunately to this date there are no adult cohorts to test the over or underestimation of the risk function. However, we did a simple validation at that time where we assessed the predicted ischemic heart disease (IHD) and stroke deaths using the demographic health study data for the South African population and the published national death data which was limited in precision but the best available in that setting. See table below from (Gaziano Circulation 2005). We have developed our own cohort through NHLBI funding to follow and calibrate the risk score as well as our own non-lab score but that will not be completed for another 5 years.
However, to address the appropriate concern, we ran the model in a sensitivity analysis where we varied the Framingham risk by as much as 50% of an overestimated (consistent with Brindle BMJ 2003) and as an underestimate of the risk by 50%. The results reported in the revised manuscript show that if the risk of IHD is half of what the Framingham predicted the ICER for our the CHW intervention would be $2991/DALY averted still well below the WTP of $10000/DALY (1X’s GDP/capita) or $30,000 (3X’s GDP/capita). If the IHD risk is 50% more than the Framingham predicted risk the intervention becomes cost-saving. In fact if the risk is even 20% more than what Framingham predicts the CHW intervention becomes cost-saving. We also conducted a sensitivity analysis on the MI survival rate.

We assessed the mortality assumption ranging again from half as fatal as we predicted to 50% more fatal and found the model was not sensitive to this assumption with a change from $305 to $335 per DALY across this range. Likewise, we conducted a sensitivity analysis on the cost of MI ranging it from 50% below and above our estimated costs and found the results insensitive to this range ($316-326 per DALY)

We also agree that a level of certainty would add robustness to our results. We therefore conducted a probabilistic sensitivity analysis on the key variables listed in the tables of the paper. Here we found that the mean ICER was $223/DALY with 95% interval ranging from $0.40-$402 and a maximum ICER of $441/DALY and a minimum that showed the CHW intervention was cost-saving.

Minor essential revisions:
1. The background section does not flow well. The last sentence of the first paragraph doesn't really make sense to me - I'm not sure what awareness and adherence mean together. The long second and third paragraphs shift between the rise of NCD's to the use to primary care to CHW's to infectious disease that I found confusing. Maybe it would help to separate this into a paragraph about NCDs (both WHO and then S.A.), then a paragraph specifically about CHWs. ("One proposed way to address the problems caused by NCDs is CHWs... There is experience with CHWs in infectious disease", etc.)

We appreciate the suggestions and have made the revisions to the background for both clarity and flow. The first paragraph is about the NCD burden and in particular hypertension.

2. Improve the labeling of the figures, which are not fully-understandable without the text and are missing things like dollar signs.

We made edits which we hope improve understanding.

3. Is the turn at the 0-point in both figures really correct? Isn't the point that at <$4/PY the CHW is cost-saving, so the area below 0 on the y-axis should be blue, not red?
The blue line above the red indicates that it is preferred strategy. The point at which the red line turns negative is the point at which the CHW intervention becomes cost-saving. We have added a notation for explanation in the figure.

Discretionary revisions:
3. It's unclear to me why the paper and project focus on blood pressure instead of cardiovascular risk, which these authors have convincingly shown would be a more effective way of modeling this work. It's particularly relevant because the predictive capacity of blood pressure (and hence the value of treatment) is likely to be far worse in real-world practice with CHW's than in the Framingham model, where the blood pressures were measured multiple times in a much more controlled setting.

We would agree that the focus should certainly focus on CVD risk rather than on blood pressure alone and was the focus of the (2005 Circulation paper). Nonetheless, South African authorities are still focused on blood pressure control (as is the US for that matter) and it may be sometime before they change. Furthermore, a program similar to what we evaluated is being proposed by the South African Dept of Health and we therefore sought out to evaluate the proposed plan. We have added a line in the discussion to suggest our interest in moving towards CVD risk assessment.

Reviewer: Adolfo AR Rubinstein

Reviewer's report:
Minor Discretionary Revision:
The authors rightly highlighted as one of the major limitations of this manuscript, the dearth of data on the effectiveness of task-shifting to CHW to improve care management of chronic conditions in primary care. In this regard, any intervention should demonstrate first and foremost clinical effectiveness before cost-effectiveness is calculated (not including here interventions that could be cost-effective just because they are much less costly although less effective than the alternative). In fact, they could just retrieved 2 papers to include effectiveness data into the model: a clinical trial of CHW in an inner-city population in the US and a before-after study to assess an intervention program to lower BP in Taiwan. Neither of these 2 countries probably resemble the health care system in South Africa or other developing countries, for which these results should be taken with caution. Moreover, the results of the quasi-experimental study in Taiwan could be flawed just by design.

As the reviewer suggested, we acknowledged the lack of data on task-shifting to CHWs. However, we disagree that modeling CEA in this scenario should not precede the effectiveness data in that country. First of all, if a trial as such is never done then this is when modeling is most beneficial because it can guide whether the proposal is potentially prohibitively expensive regardless or very beneficial assuming one accepts the results of the limited effectiveness studies. Second, as the previous reviewer suggested, the results of our study may serve to encourage the South African government and others to fund such CHW effectiveness studies given the potential gains if the same effectiveness data is confirmed locally. Furthermore, we were very conservative in our use of the effectiveness data from the US study given the very same concerns raised by the reviewer.

The authors may consider including another important paper of task shifting to CHW for hypertension control in underserved communities in Karachi, Pakistan (Jafar TH, Hatcher J, Poulter N, Islam M, et al. Community-based interventions to promote blood pressure control in a developing country: A cluster randomized trial. Ann Intern Med.2009; 151: 593-601). Interestingly, this 2X2 factorial RCT did not showed a larger improvement of
the CHW educational intervention alone as compared to no intervention or GP training alone (all reduced SBP by 4-8 mmHg of SBP). The only effective intervention was the combination of both GP and CHW training which reduced SBP by 10.8 (8.9–12.8).

We agree with the reviewer of including the Jafar paper in the discussion. Although the intervention in that study in Pakistan was slightly different than what we propose, ie there was training of the GPs as well. In the US and South Africa, training of GPs with regards to hypertension is substantial although there may be benefits we are not prepared to assess accept to say if one assumes the GP training is sufficient then a 10 mmHg increase with additional lay education would make our intervention cost-saving but we are unsure if this would be too much to assume. We address this study in the discussion section.

Nevertheless, this intervention because of its low cost is, according to the authors, still cost-effective at very low reductions of BP (in the range of 2mmHg). In this regard, the health benefits accrued by CHW at the community setting, for the management of chronic conditions that usually cluster in the same individuals, largely exceed the health benefits for the management of just one condition. This fact could also underestimate the cost-effectiveness of this intervention.

We agree that this is true and as the first reviewer also stated we make a statement in support of overall risk assessment and management in the discussion.

Please feel to communicate with me if there is anything else we can do to strengthen the manuscript.

Sincerely,

[Signature]