Author's response to reviews

Title: Cost effectiveness of a computer-delivered intervention to improve HIV medication adherence

Authors:

Raymond L Ownby (ro71@nova.edu)
Drenna Waldrop-Valverde (drenna.waldrop-valverde@emory.du)
Robin J Jacobs (riacobs@nova.edu)
Amarilis Acevedo (aa1011@nvova.edu)
Joshua Caballero (jcaballe@nova.edu)

Version: 3 Date: 24 January 2013

Author's response to reviews: see over
January 24, 2013

Adrian Aldcroft, Executive Editor
BMC Bioinformatics and Medical Decision Making

Dear Professor Aldcroft:

We thank you and the dedicated reviewers for their comments on the revised submission of our manuscript. We have responded to your and the reviewers’ comments as follows in the revision that accompanies this letter:

**Editorial concerns:**

*We would ask you to remove the figures from the text leaving only the figure legends there. The actual figures are already correctly uploaded in the Figures file.*

The figures have been removed.

*We would also request that you go through the manuscript formatting checklist one more time and ensure that your revised manuscript conforms to all of the points.*

We reviewed the checklist and have added country to each authors’ address.

**Rev 1**

*The methods and results are clearer now, and the discussion more balanced. The additional details in the tables and appendices are also helpful.*

*A couple of minor details: Table 1 has four references that need to be updated or included. Page 30, which is blank, should be removed.*

Table 1 has been edited to include the missing references, and page 30 has been removed.

**Rev 2**

The authors have addressed my concerns adequately except for one, which they admit they are unable to address given the parameters of the study. The pre-/post- adherence is only for one month and not an adequate time period for adherence analysis. This is why not all datasets can be used for all analyses. I fear a biased analysis with this short time period. I would suggest eliminating this part of the analysis. However, if the authors feel that this would completely undermine their paper, then this must be discussed in the limitations section--at
present, not done.

*It appears that we cannot address this concern as it requires data that do not exist. We added material on the persistence of the effects of other interventions, including a reference to a meta-analysis. We have added this as a limitation in the discussion section as requested.*

**Rev 3**

After reviewing the manuscript and explanation from the authors, I believe they have successfully addressed each of my comments. The paper is now suitable for publication in my opinion.

**Rev 4**

The authors have comprehensively addressed many of the concerns from the reviewers. In doing so, however, this reviewer did experience some discomfort over the amount of text devoted to discussing intervention efficacy and implications of the intervention itself rather than remaining focused on cost effectiveness of an intervention estimated to have X through Y efficacy.

*We believe that much of this material was added in response to other reviewers’ comments on the first version of the MS.*

*Specific areas where text seemed excessive in this are noted below. This is a complex manuscript and the authors have clearly taken on the herculean task of estimating costs and potential benefits through available data and pulling from published literature.*

*The addition of Table 1 is appreciated, however, perhaps the authors could consider adding in monetary value to the factors. Because many of these estimated were identified through extensive literature review on the part of the authors, the research community could greatly benefit from having an easy-to-access table of estimates that they could use in estimating cost effectiveness.*

References have been added where possible; some costs were drawn directly from the grant accounting and provided in detail in other tables (e.g., Table 3) and others are labeled as assumptions. Not all amounts can be effectively listed in the table, as they vary by level of CD4 count or adherence but average amounts have been provided. References to the figures are added to direct the reader to the actual amounts in Table 3, and additional explanation on how costs were calculated has been added to the Table 1.

*Several smaller considerations are noted below.*
Abstract:
*Typo: “…but many patients to not achieve…” should be “…but many patients do not achieve…”

This has been corrected.

*Results: Consider revising or deleting first line- ‘The intervention’s cost effectiveness…’ as this is pretty much expected. If retained, as ‘efficacy’ or ‘effectiveness’ of the intervention as well as a driver of cost effectiveness.

We believe this sentence is a concise summary of the results, which while perhaps expected is an appropriate expression of the study’s outcome (for example, it is possible that the intervention might not have been cost effective in any scenario).

Also here and throughout- it would be good to distinguish between continued increase over time (eg., intervention effects continue to amass over time) vs. durability of intervention effects (eg., intervention effects are retained post intervention).

*Duration of greater than one month are noted in abstract but results largely focus on 4 time scenarios (3, 6, 9 and 12) months- it is not clear where the one month reference to outcomes is coming from.

At the insistence of another reviewer, we evaluated outcomes at one month but for the reasons outlined in the MS have chosen not to emphasize them. The sentence has been revised.

Background:

*It would be helpful to note geography of work early on. The extent to which interventions are available and what they are depends on location or, at a very gross level, country, and feasibility of internet based scenarios will depend on use if internet in communities (also dependent on country).

It is not clear why this would be more important than any other material in the abstract which is at the editorially-prescribed word limit. We agree that this is an important issue and have noted our site in the description of costs when relevant (page 14) since office costs are likely to vary widely by geography and included this point in the discussion section (page 27).

*Typo? Page 6 ‘Few clinicians are likely to have the time to spend one hour in providing…’ Should “in” be deleted? ‘Few clinicians are likely to have the time to spend one hour providing…’

The offending “in” has been deleted.

*Consider changing ‘efficacious’ to ‘effective’ in paragraph 2 page 6.
Here we follow the common practice of distinguishing between “efficacy” in controlled research environments and “effectiveness” in actual clinical deployment. We believe that “efficacious” is the correct usage although we agree with the reviewer that the word is awkward.

*Here and other places, it seems there is text that promotes or ‘defends’ computer delivered approaches. At the end of page 6 the authors note the savings in clinician time. It does not appear that saving of clinical hours/time is in the formula for savings, which is fine as standard of care is not an hour with a clinician and cost effectiveness was in relation to currently available SOC and not to an alternative clinician-delivered intervention. However, given that it is not really a key part of methods or results, it feels odd to have this text in the introduction. It would be sufficient to say that for a variety of reasons computer delivered ART education and aspects of counseling have multiple advantages that impact evaluations of cost-effectiveness, include X, Y and Z, and leave it at that.

Much of the material here was added to the MS in response to this reviewer’s first review, and perhaps we were too diligent in making this response. This section has now been shortened by deleting portions of two sentences.

*Page 7- The authors may want to revise first sentence on page- presently it is really long (5 lines) and has two uses of ‘delivered’ in close proximity.

This sentence has been rewritten.

*Paragraph 2, page 7- As noted previously, it is not clear why the authors are going into so much detail on why computer delivered may be better that clinician delivered. This seems outside the scope of the research question presented in this manuscript.

As noted above, the material here was also added to the MS in response to this reviewer’s first review, including the addition of several references. This paragraph has also been shortened.

*Page 9 through before final sentence in Background- While the added details on the intervention itself is likely in response to reviewer requests, this reviewer strongly preferred the original introduction’s more streamlined approach. From a reader perspective, the content of cost effectiveness analyses is necessarily dense and adding in full coverage of the intervention and intervention efficacy pulls the reader in too many directions. My preference would be to refer people the manuscript describing the intervention, limit details to those that are critical to assumptions in the current manuscript’s analyses, and note range in effect size used. Obviously, publishing outcomes would resolve much of this.
The reviewer is correct that the material was added in response to another reviewer’s comments.

*Page 11, Table 2 + Figure 2. It is not entirely clear that the combination of Table 2 and Figure 2 is really accomplishing proving added clarity to readers. Having to toggle between the two and with text is concerning. Is there any way to combine the two?

We do not see any effective way to combine the two – we would combine two fairly straightforward elements into one excessively complex figure (e.g., by replacing the expression p(t) = x with a vector of probabilities). Perhaps the two elements can be placed on the same page during typesetting, reducing the burden on the reader to move back and forth between the two elements?

The meaning of the numbers in the circles on top of Figure 2 are not immediately apparent. Clearly, this is critical in the presentation of results. It may simply need to remain as is. However, if the authors can identify a way to consolidate it would be less cumbersome for the reader.

The figure labels include, in two locations, “CD4 count ranges.” We’re not sure how to make this much clearer, especially as the text clearly refers to the ranges in several places.

*Table 2- None of the effectiveness scenarios influenced movement in upper end (over 500 CD4). The reviewer did not see commentary on this- but it is curious and may be worth noting.

We assumed that persons with high CD4 counts were likely to have high levels of adherence and thus, consistent with our evaluation of baseline adherence and response to the intervention now reported as reference 44. This assumption has now been made explicit through an addition on page 17.

*Page 12- Costs of lost salary and wages to travel to and from intervention site are included as “development” cost. Should that be “implementation” cost? Alternatively, if they were included for development because development included the need for evaluation, perhaps simply note that costs associated with efficacy evaluation are included as necessarily R&D.

In response to another reviewers’ comments, we have included transportation costs as part of the development costs as well as implementation costs. The cost described on page 12 correctly refers to a development cost, and in another portion of the MS we cite implementation costs (e.g., the cost of transportation for rural users).

*Costs section- Consider adding headers to this section delineating each area in which costs were estimated or known.
Several second-level headings have been added in this section.

RESULTS
*Page 21- Is it possible to anchor the Internet scenario presented in terms of cost per 1% increase, consistent with presentation of clinician office outcomes.

These estimates have been added.

DISCUSSION
*Page 24- Typo? Should first line read “…its effects in decreasing treatment costs due to improving health status” ?

The sentence has been revised

*Page 25- consider tapering comment regarding no decrease in adherence over time from Amico et al. In that research, a number of interventions evaluated did not have a true follow-up period where the intervention was completely removed and individuals were followed over time. While no difference was found in terms of intervention effects and number of weeks post baseline for intervention, it is somewhat of an overstatement to say that adherence over time would remain unchanged in the treatment condition. Consider revising to ‘…suggested no marked deterioration in intervention effects over time.”

The sentence has been revised as suggested.

Page 28- the paragraph on uptake of computer interventions and limitations in such delivery strategies seems out of place in the current manuscript.

It appears logical to us – if computer-delivered interventions are cost effective, it seems reasonable to ask why they are not more commonly adopted. Barriers to acceptance of electronic interventions is an active area of research in informatics.

CONCLUSIONS

Page 29- noting that cost effectiveness depends on effectiveness and reach seems unnecessary.

This appears to be a reasonable summary statement, especially since the data presented show that the intervention may not be cost effective for small numbers of users.

Page 29- review of pros and cons of computer delivered intervention (Table 8) is interesting but seems beyond the stated scope of the manuscript.

This table was added at the suggestion of reviewer 3 comments on the original MS.
TABLE 1 - Is it possible to add costs to these? Also, there are a few “[ref]” in the table.

As noted above, these issues have been addressed.