Author’s response to reviews

Title: Screening and brief interventions for hazardous and harmful alcohol use among hospital outpatients in South Africa: results from a randomized controlled trial

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Author’s response to reviews:

Reviewer’s report
Title: Screening and brief interventions for hazardous and harmful alcohol use among hospital outpatients in South Africa: results from a randomized controlled trial
Version: 3 Date: 21 January 2013
Reviewer: Simon Coulton
Reviewer’s report:

Many thanks for the opportunity to review this manuscript. The manuscript reports the results of a randomized controlled trial of screening and brief intervention for hospital outpatients in South Africa.

Some aspects of the study reporting are rather challenging and I have identified some areas where clarification is required, some of these are relatively minor and some quite major. I have addressed any issues in the order they arise in the manuscript.

Abstract

Some consistency in the use of terms to describe the nature of the population is required in the manuscript and throughout the paper generally. In the abstract the population of interest is described as hazardous and harmful alcohol users in the background, problem drinkers and medium risk drinkers in the methods.

Response (R): Corrected

The time period recruitment occurred should also be reported as should the outcomes used.
It is worth noting that the study reported is a RCT of alternative interventions, differences between groups are the primary statistic of interest rather than changes within groups and these should be reported with confidence intervals. (Minor changes).

R: Changed to differences between groups as the primary statistic

Methods
In the design section the study is described as an efficacy study, previous, in the last sentence of the background, it is described as an effectiveness study. It needs to be clarified whether efficacy or effectiveness is being addressed in this study (minor).
R: Corrected to “efficacy”

It would be useful to have the hypotheses clearly stated as null hypotheses (minor).
R: Added

The last sentence under design is not necessary (minor).
R: Removed

In study population and participants it would be useful to know over what period outpatients were screened and whether all outpatients over this period were screened.
R: Below is added

Systematic sampling of all presenting outpatients was used whereby all consecutive clients were recruited from five different out-patient departments, i.e., family practice (10.4%), general out-patient department (48.0%), cardiology (10.5%), diabetes (19.4%) and ear nose and throat department (7.1%) and from a dispensary (4.7%). All out-patients were interviewed using an interviewer-administered questionnaire by four trained research assistants (qualified nursing assistants) in private rooms as they waited for their medical visit or at the dispensary throughout all hours of clinic operation for a period of three months in one tertiary hospital.

Some of the text becomes quite repetitive and this would benefit for being more explicit in what happened and how it was conducted (minor).
R: Corrected

Under exclusion criteria a score of 20 or more on AUDIT indicates possible alcohol dependence rather than probable, it is a screening not a diagnostic tool (minor).
R: Corrected accordingly
Under randomization more detail on the randomization procedures would be useful, were they stratified? Were blocks used? You have exactly the same numbers in either group and as a reader I would want to know that the allocation was conducted appropriately. (minor)

R: as below
After baseline assessment, each patient was randomized to either a control or a brief intervention group. Patients were randomized using sequentially numbered opaque sealed envelopes prepared according to a computer-generated randomization allocation sequence. Block randomization using randomly varying block sizes (prepared using Stata version 10) ensured equal numbers of patients are recruited into each group.

Under measures indication of primary and secondary measures are required,
R: Added, as below
The total AUDIT score was used as the primary outcome measure. In addition, the third AUDIT question, for measuring the frequency of heavy episodic drinking was used as secondary outcome measure.

The Cronbach’s alpha of AUDIT is not necessary in this section (minor).
R: Removed
In the data analysis section it is not clear whether any data transformations were undertaken in testing the baseline descriptives, it is clear from the table that some of these outcomes were not normally distributed. I am not convinced that testing for differences between the groups at baseline is necessary, it only tests for those outcomes measured and if these differences are potentially influencing the observed outcome they need to be incorporated into the analysis of the primary outcome (minor). I would expect a sample size calculation presented in this section with an indication of clinically meaningful differences (major). GLM repeated measures were employed to assess the primary outcome at 12 months, AUDIT score, is this appropriate? I would have thought that considering the loss to follow-up at month 6 this would make any such analysis under-powered (major).

R: Below is added, and also sample size calculations
Data analysis
Means, standard deviations, and percentages were used for descriptive statistics. Mann-Whitney U Test for continuous data and chi-square for categorical data were used to examine differences between groups. We first
inspected all outcome variables for distribution properties. Variables that were significantly skewed, the total AUDIT score was transformed using the formula log10 (#+1) with non-transformed observed values presented in the table. To test the main study hypotheses, we conducted an analysis of covariance (ANCOVAs) for all continuous outcome variables. Differences between conditions were examined at the 6- and 12-month follow-ups using 6-month recall for alcohol use. Analyses tested for differences between conditions at the follow-ups after controlling for baseline values and potential confounds. Comparisons on categorical outcomes were tested using multilevel logistic regression for binominal variables (harmful drinking) adjusting for potential confounds and baseline differences between the two groups. IBM SPSS for Windows version 20.0 (SPSS, Inc., Chicago, IL) was used for the calculations.

When looking at the results reported I had a number of major concerns. You assessed 1500 for eligibility, 1106 were excluded, leaving 394 for randomization into two groups. Each group had 192 so 10 patients are missing from the CONSORT statement. I also note that in the baseline demographic table few of the variables add up to 192 and some, for example education and AUDIT categories add up to 196. In the text under results we are informed that 194 were allocated to each group. There is a major discrepancy in how the results have been reported and this needs to be addressed (major).

R: Thank you, this has been corrected, to 196 in each arm

Your primary outcome is AUDIT score and the primary analysis is the mean difference in AUDIT score between the control and intervention group at 12 months post-randomisation. This should be analysed using analysis of covariance adjusting for baseline values of AUDIT, as they will have greatest influence on 12 months AUDIT score. It is also likely that the AUDIT score would need to be transformed in order to conduct the analysis, it is rarely normally distributed in populations such as this. This statistic presented with estimates of the precision, such as 95% confidence intervals, is the most important finding. What we have is a cursory sentence that the intervention effect on the AUDIT score was -1.5. This is not acceptable for a study reporting a RCT and needs to be addressed (major).

R: Thank you. Corrected, as below, AUDIT total score is also transformed

Data analysis

Means, standard deviations, and percentages were used for descriptive statistics. Mann-Whitney U Test for continuous data and chi-square for categorical data were used to examine differences between groups. We first
inspected all outcome variables for distribution properties. Variables that were significantly skewed, the total AUDIT score was transformed using the formula \( \log_{10}(x+1) \) with non-transformed observed values presented in the table. To test the main study hypotheses, we conducted an analysis of covariance (ANCOVAs) for all continuous outcome variables. Differences between conditions were examined at the 6- and 12-month follow-ups using 6-month recall for alcohol use. Analyses tested for differences between conditions at the follow-ups after controlling for baseline values and potential confounds. Comparisons on categorical outcomes were tested using multilevel logistic regression for binominal variables (harmful drinking) adjusting for potential confounds and baseline differences between the two groups. IBM SPSS for Windows version 20.0 (SPSS, Inc., Chicago, IL) was used for the calculations.

Table 2 Alcohol-related outcome measures at baseline, 6-month and 12-month follow-up

<table>
<thead>
<tr>
<th>Variables</th>
<th>Time</th>
<th>Control</th>
<th>Intervention Fa</th>
<th>Fb</th>
<th>Fc</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUDIT total score (M,SD)</td>
<td>Baseline</td>
<td>11.3 (3.4)</td>
<td>6.3 (4.6)</td>
<td>7.3 (6.8)</td>
<td>12.7 (3.4)</td>
</tr>
<tr>
<td>6 months</td>
<td>12 months</td>
<td>11.3 (3.4)</td>
<td>6.3 (4.6)</td>
<td>7.3 (6.8)</td>
<td>12.7 (3.4)</td>
</tr>
<tr>
<td>6 months</td>
<td>7.0 (4.5)</td>
<td>7.2 (5.8)</td>
<td>(1,195)= 7.72**</td>
<td>(1,198)= 2.35</td>
<td>(1,194)= .06</td>
</tr>
<tr>
<td>Heavy episodic drinking score (M, SD) Baseline</td>
<td>6 months</td>
<td>1.9 (0.8)</td>
<td>0.9 (1.1)</td>
<td>1.1 (1.3)</td>
<td>1.9 (0.8)</td>
</tr>
<tr>
<td>6 months</td>
<td>1.1 (1.0)</td>
<td>1.1 (1.4)</td>
<td>(1,195)= 3.97*</td>
<td>(1,198)= .34</td>
<td>(1,194)= 1.17</td>
</tr>
<tr>
<td>Harmful alcohol use (AUDIT score=16-19 or more) Baseline</td>
<td>6 months</td>
<td>29 (14.8)</td>
<td>5 (4.6)</td>
<td>24 (17.3)</td>
<td>43 (21.9)</td>
</tr>
<tr>
<td>6 months</td>
<td>5 (3.9)</td>
<td>12 (8.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Analyses controlling for baseline scores, participant gender, age, education, and marital status
**P<0.01
aTime effects; bGroup effects; cTime x Group effects

As reported it is quite difficult to consider the conclusions as valid. The authors really need to consider what and how they are reporting the outcomes of this trial. Of particular concern is the lack of integrity in the numbers reported, the lack of a sample size calculation and significant issues in how the analysis has been undertaken and reported.

R: Adjusted

Reviewer's report
Title: Screening and brief interventions for hazardous and harmful alcohol use among hospital outpatients in South Africa: results from a randomized controlled trial
Version: 3 Date: 22 February 2013
Reviewer: Natalie Johnson

Reviewer's report:

Major Compulsory Revisions
The results of the study should be analysed and/or reported in greater detail. For example, I would like to see the subheadings “Between group differences” and “Within group differences” followed by appropriate descriptions. Similarly, I would like to see results of analyses that conform to intention-to-treat principles and then results of analyses that refer to completers-only and any subgroups of interest (eg., harmful drinkers as suggested below).

Minor essential revisions
1. There are a wide variety of terms used to describe drinkers in this manuscript (eg., hazardous, high hazardous, harmful, problem, risky, level 2 and level 3). In the introduction, the terms ‘hazardous drinking’ and ‘harmful drinking’ are described and used appropriately. In the methods section, however, the term ‘medium risk drinker’ is introduced which is atypical of the literature (an advanced google scholar search identified that exact phrase in only four articles, one of which was the trial protocol for this study). Given the use of the AUDIT to screen and classify outpatients, use of the widely used terms ‘hazardous’ and ‘harmful’
is preferable (eg., "Outpatients who screened positive for hazardous or harmful drinking (scored 8-19 for men and 7-19 for women on the AUDIT) were included in this study").
R: Changed accordingly
2. The primary outcome should be clearly described.
R: Added, as below
The total AUDIT score was used as the primary outcome measure. In addition, the third AUDIT question, for measuring the frequency of heavy episodic drinking, and harmful alcohol use (AUDIT score 16-19) were used as secondary outcome measures.

3. The phrases “universal screening” and “sampling occurred throughout all hours of clinic operation over a 4-month period” seem contradictory.
R: Corrected

4. The reference for the AUDIT should be presented when it is first mentioned in the methods section (page 5).
R: Corrected

5. Information on how the AUDIT was administered should be provided (eg., was it a self-administered paper version or an interview?).
R: Added below
using an interviewer-administered questionnaire

6. Details on the “theory-based intervention” should be provided in this manuscript so readers do not have to track down the protocol (at a minimum, the name of the theory used should be provided).
R: Below is added
The Information-Motivation-Behavioural Skills (IMB) Model was used to guide the alcohol reduction intervention.

7. Clarification as to the scope of the questionnaire should be provided earlier than is currently the case (ie., because the phrase “alcohol test section of the questionnaire” made me wonder what other sections there were).
R: The name AUDIT, as below includes the term “test”; in other places test has been removed
Alcohol Disorder Identification Test (AUDIT)

8. I am unclear what a “chronic” hospital outpatient is. I assume it refers to a person with a chronic medical condition?
R: Corrected
9. Clarification on the nature and extent of the “feedback (given to participants in the control group) on the initial alcohol screening” is required as it sounds like more than the simple provision of “a health education leaflet on responsible drinking.”

R: Thank you, corrected as below:

Participants randomized to this group were provided with a health education leaflet on responsible drinking.

10. According to the CONSORT group, “Tests of baseline differences are not necessarily wrong, just illogical.(211) Such hypothesis testing is superfluous and can mislead investigators and their readers. Rather, comparisons at baseline should be based on consideration of the prognostic strength of the variables measured and the size of any chance imbalances that have occurred.(211)” - http://www.consort-statement.org/consort-statement/13-19---results/item15_baseline-data/

R: Changed to below

We first inspected all outcome variables for distribution properties. Variables that were significantly skewed, the total AUDIT score was transformed using the formula \( \log_{10} (\#+1) \) with non-transformed observed values presented in the table. To test the main study hypotheses, we conducted analysis of covariance (ANCOVAs) for all continuous outcome variables. Differences between conditions were examined at the 6- and 12-month follow-ups using 6-month recall for alcohol use. Analyses tested for differences between conditions at the follow-ups after controlling for baseline values and potential confounds. Comparisons on categorical outcomes were tested using logistic regression adjusting for potential confounds and baseline rates, reporting odds ratios and 95% confidence intervals.

11. The information on drinking patterns is not quite clear. For example, does “976 screened negative for alcohol” mean they were non-drinkers or does it mean they screened negative for hazardous or harmful alcohol use? There is also some repetition here (eg., the fact that 51 had a score of 20+ is mentioned twice.

R: Changed accordingly

12. Tobacco and subjective health status outcomes should not be included under the heading “Alcohol Use Outcomes”. Further, as these were not included as secondary outcomes, they probably ought to be omitted entirely.

R: Removed accordingly

Discretionary revisions
13. I am uncertain about the need for Cronbach alpha results for the AUDIT. R: removed
14. Post hoc analyses to determine if there were any between group differences among harmful drinkers (AUDIT score 16-19), who may require a more intensive intervention than hazardous drinkers (AUDIT 7 or 8 to 15), might be worth investigating? R: Included

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Needs some language corrections before being published
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests: