Author's response to reviews

Title: Measuring adherence to antiretroviral therapy in northern Tanzania: feasibility and acceptability of the Medication Event Monitoring System

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Author's response to reviews: see over
To: Dr. Diana Boy (for Dr. Sabina Alam)
Senior Executive Editor
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From: Ramsey Lyimo
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Moshi, 24th January, 2011

Dear Dr. Diana Boy and Dr. Sabina Alam,

Again, we were very grateful to receive your positive response and valuable comments on our revised paper entitled: “Measuring adherence to antiretroviral therapy in northern Tanzania: feasibility and acceptability of the Medication Event Monitoring System” (MS: 1137749058432002). We have made changes in the text accordingly (by using the ‘track changes’ function) as explained point to point below.

We hope that we have successfully addressed your concerns.

Yours sincerely,

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Comments of reviewer 1:

Minor essential revisions:

1a. I think there is still some confusion over my previous comment 11, regarding the authors’ statement that “interviews were examined for reports of interrupted MEMS use” – now lines 175-176. The authors responded that this point is described in the Methods section, line 140. However, if I’m understanding correctly, this section of text refers to the researcher’s meeting with the patients prior to the beginning of data collection to explain the use of MEMS, rather than to the post-data collection qualitative interviews. In the first paragraph of the Data collection and analysis section (line 155+), the authors describe three topics explored in the interviews: the MEMS design, the feasibility of using MEMS, and the impact of MEMS on adherence. So I am still not sure whether the participants were directly asked during this interview about any periods of non-MEMS use that were evident from their MEMS data. The authors’ statement on lines 175-176 makes it sound like they did not directly ask this question, but examined the interviews to see if the participants spontaneously mentioned any periods of non-MEMS use on their own accord. If this is the case, I think the authors should state this more directly.

1b. Authors’ response:
We are sorry that we raised confusion with regard to the “examining of interviews for periods of interrupted MEMS use”. We did ask interviewees directly about whether they used the MEMS always and correctly, but we did not examine their MEMS-data before or during that interview. We examined MEMS-data for the reasons explained in the article, but after the interviews. During these interviews, some patients spontaneously mentioned that they had not used MEMS on travel occasions. We confirmed these statements by checking the MEMS data. While doing so, we encountered some non-monitored periods from other patients as well, but who did not report periods of inaccurate MEMS-use. That is why we decided to re-contact those few patients with unexplained non-monitored periods (periods >3 days).

To better clarify this, we have rephrased 2 sections in the text. First, in the Methods. Second, in the Results.

Methods (lines 166-179): Since self-reports on proper use of the MEMS-bottle may be biased by social desirability, misinterpretation of questions and responses, or memory retrieval problems, following the interviews we also examined the MEMS-data of all patients for: (a) patterns of overdosing (more openings on a day than prescribed) without MEMS-reports showing that patients ran out of medication before their next clinic visit (which should be the case if the overdoses are actual medication intakes and not curiosity openings); and (b) periods of >3 days during which the MEMS-cap registered no medication intake events, which could, apart from non-adherence, also indicate non-MEMS use. To distinguish between non-adherence and non-MEMS use, we first examined the interviews for patients reporting periods of non-MEMS-use. If patients had
missing data but did not report inaccurate MEMS-use, we retrieved information on whether patients had collected their medication on time. If patients collected their medication too late in that period, the MEMS-data were considered accurate and the patient as non-adherent. If patients did not report inaccurate MEMS-use in the interview and were always on time to collect their medication, they were approached again and asked what happened in that period.

Results (lines 268-280): There were six patients whose MEMS-data showed periods of more than three days of missed medication (observed range was 12 to 71 days). Two of these patients reported during the initial interviews that they had left the MEMS-bottle at home when travelling, fearing that it might be stolen. Hence, they were not considered as non-adherent, but as not using the MEMS-cap. Two of the four remaining patients, who reported in the initial interviews to have always used the MEMS-cap as prescribed, showed up too late for collecting their medication in that period. Their missing MEMS-data was therefore considered to accurately describe their medication intake (i.e., non-adherence). Of the two remaining patients, who did not self-report inaccurate MEMS-use and were on time for collecting their medication, one could be re-contacted to explain the data. This patient reported to have left the MEMS-bottle at home when travelling for a period of six weeks. The non-monitored period was indeed 6 weeks, and this was thus considered to be non-MEMS-use rather than non-adherence. Hence, the MEMS-caps seemed to have been used accurately by all patients, except by three patients who did not use it during long-distance travels.

2a. After reading the authors’ response 12b, I understand more clearly the methodology regarding the handling of missing MEMS data and how adherence was calculated in these cases. My only remaining comment is that a statement should be added to the paragraph in which study limitations are discussed. This should note something about the fact that adherence cannot be verified for the periods of missing data (non-MEMS-use), and so interpretations about adherence based on the data available should keep this in mind.

2b. Authors’ response:
Thank you very much for the observation, we have now added a statement in the paragraph that refers to this limitation (lines 363-365): “Third, the average adherence of patients with long periods of non-MEMS use should be interpreted with caution, since it cannot be verified whether medication was taken as prescribed in that period.”

3a. A few comments on grammar and spelling. In the abstract, line 40, "interviews" should be "interview" (singular). Line 44, delete the comma after "monitored". On page 14 line 322, "loosing" should be "losing". Final paragraph, line 365 - awkward wording: "recommended" should be changed to "advised".

3b. Authors’ response:
We have corrected all errors accordingly.
Comments by reviewer 2:

4a. Typos: line 322 should be 'losing' and in line 282 'patients' needs an apostrophe

4b. Authors’ response:
The corrections have been made accordingly.

5a. Line 97: I still don't understand the description of the cost of MEMS. What is the denominator for the cost you present? In other words, per 100 WHAT?

5b. Authors’ response:
Apologies, that is indeed unclear. If refers to the amount of MEMS-caps bought. As with many technologies, the more you order, the cheaper they become. The statement has been rephrased accordingly and now reads “… (30 USD per 100 MEMS-caps for one year of data, 22 USD per 5,000 MEMS-caps for one year of data) …” (lines 95-96).

6a. Since health care provider data is removed, the abstract needs to be updated accordingly.

6b. Authors’ response:
Thank you very much for the valid observation; we have now updated the abstract by removing the information about health care providers.