Author's response to reviews

Title: Autonomous exercise game use improves metabolic control and quality of life in type 2 diabetes patients - a randomized controlled trial

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Version: 3 Date: 13 September 2013

Author's response to reviews: see over
Reply to referee 2

1. Cases should be missing completely at random (this needs to be demonstrated)

Reply to 1. I am sorry, but I did not understand this comment. Could you please specify your intention?

2. Last observation carried forward ignores whether the participant's condition was improving or deteriorating at the time of dropout. If there are more dropouts in the treatment group than in the control group, such an approach to analysis will bias results in favor of the intervention, since a greater proportion of patients in the treatment group will have their decline artificially stabilized at an earlier stage. (Thus - we do not know whether or not the patients were deteriorating before baseline - this can affect the follow-up).

Reply to 2. We only analyzed those participants who completed the 12-week study. These have been 93 out of 120 in the intervention group and 83 out of 100 in the control group. The percentage of dropouts did not differ significantly between the intervention and the control group. The primary and secondary outcome parameters have been measured at baseline and after 12 weeks. For analysis of the primary endpoint HbA1c there had been no missing values, i.e. we have 93 HbA1c values for the intervention group and 83 for the control group. Missing values of secondary outcomes from the completers were substituted by LOCF, i.e. the effect of intervention set to zero. Missing values which have been substituted by LOCF only occurred for total cholesterol, HDL cholesterol, LDL cholesterol and triglycerides and the numbers of missing values did not differ between both groups. For those parameters no significant difference had been observed between both groups after the study period. Therefore, a potential bias induced by LOCF should rather have led to an underestimation of effect.

3. Please state more clearly, that the waiting controls are not included in the analysis after intervention (it is stated, but I was still a bit confused until I saw the flow-chart). I think this would improve this section.

Reply to 3. We decelerated the analysis of the waiting controls now secondary analysis (please see Fig.1) and stated that they have not been included in the primary analysis on page 3, line 65, page 4, lines 85-86: “Results from the waiting controls after their 12 weeks of exercise game intervention were analyzed separately in a secondary analysis.”, and page 5, line 133.

2. Line 72-75: What was the recall period?

Reply to 4. The participants had to report their physical activity during the last 12 weeks (page 4, line 75).
3. How are the results reported? Are the () SEM's? If they are SD's, please add CI's instead where the statistics are analytic and SD's when descriptive.

Reply to 5. In the legends to figures and tables we stated if SD or SEM had been shown. Throughout the manuscript we never used (SEM) or (SD) in brackets. Do you want all tables to be presented with mean and interquartile range?

4. In Table 2: Please add effect size, confidence intervals and N, as it is important to see how the effect sizes change across models

Reply to 6. We added effect size and SEM in the table 2 and N in the table legend. Since a linear regression analysis had been performed only SEM but not confidence intervals are available.

5. Regarding the models presented in table 2 this is what I meant in the previous review (comment 13). That is analyzing the difference in change between groups. However, I wondered about the weight adjustment. One assumption in confounder control is that a confounder cannot on the causal pathway. It is possible that Wii affects weight (as a proxy for adiposity) and that would affect Hb1Ac, right? Otherwise you’re checking for effect mediation. I suggest you leave out the particular adjustment.

Reply to 7. As suggested by the associate editor we provided several models in Table 3. Only Model 3 includes adjustment to weight difference. We added the information on page 5, lines 128-129: “Even after adjustment for weight reduction, which might be considered as a mediator for HbA1c improvement, the effect remained significant.”

6. Please discuss the potential bias introduced by applying a complete case analysis and how the large drop-out (more than 20 %) affect the interpretation of your data. I think a discussion regarding the missing is handled is appropriate.

Reply to 8. We added this discussion on page 9, lines 252-259: “Our study has several limitations that need to be considered. First, a completer rate of only 67% was achieved and of those a completer analysis had been performed. The patients who managed to improve their glucometabolic control may have been more strongly motivated to stay with the program. This might have biased the results and the effects might have been weakened in the complete study population. Nevertheless, the percentage of drop out in our study are comparable to those seen in other exercise interventions for older adults [22] …”

7. The argument (l. 253-256) regarding no differences at baseline should be directed against a comparison between the included and the drop-outs/missing data subjects rather than a comparison of effect sizes between the ones who completed the intervention.
Reply to 9. We added this information on page 9, lines 256-259: “… and the fact that the baseline characteristics of completers and dropouts as well as the outcomes in both groups after exercise intervention did not differ, argues against such a responder bias.”

8. So please check differences baseline results on Hb1Ac and other key variables between completers and drop outs - stratified by allocation and report that.

Reply to 1. According to the referees’ suggestion we added a new Table 2 for comparison of the baseline characteristics of completers and dropouts and stated on page 5, lines 116-117: “The drop outs did not significantly differ from completers concerning their baseline characteristics (Table 2).”