Author’s response to reviews

Title: The Effect of Exercise as Adjunctive Treatment on Quality of Life for Individuals with Alcohol Use Disorders: a randomized controlled trial

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The Effect of Exercise as Adjunctive Treatment on Quality of Life for Individuals with Alcohol Use Disorders: a randomized controlled trial

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BMC Public Health

Dear reviewers,

We truly appreciate the effort you have showed by reviewing our manuscript The Effect of Exercise as Adjunctive Treatment on Quality of Life for Individuals with Alcohol Use Disorder. Beneath our response to your comments, and our action based on these comments are shown point by point. We have highlighted the changes in the manuscript with yellow color.
Reviewer comments   Authors’ comments and actions

Jonathan Ling (Reviewer 1)

However, clarification of the theory underlying the study would help with the interpretation of the results. Why is exercise felt to be a good candidate for an adjunct treatment for people with AUD? Is it distraction, an endorphin high, the potential for socialising in a different environment?

Thank you for pointing this out. In our study protocol we have described the potential benefits of exercise for patients in treatment for AUD:

“Exercise, especially moderate exercise

(Monti et al., 2000), can decrease the urge to drink. Exercise may offer positive alternatives to alcohol by triggering pleasurable states, for example through dopaminergic reinforcement (Read & Brown, 2003). Exercise also improves psychosocial outcomes in the areas of mood management (Lane & Lovejoy, 2005) and reduces depression and anxiety (Martinsen, 2008; Babyak et al., 2000; DiLorenzo et al., 1999). In addition, resilience factors such as individual and social resources (for example self-confidence) are strengthened by regular physical activity, especially as group activity (Brown et al., 2009; Read & Brown, 2003).” (Sari et al., 2013)

The following has been added to page 5, line 6:

Theoretically, exercise programs can be lifestyle interventions providing people with AUD with skills to undertake a positive health promoting behavior, simultaneously providing self-control strategies, coping strategies and an alternative to drinking (Marlatt & Gordon, 1985; Murphy et al., 1986). The concept Runner’s high, which is the feel-good effect of running due to release of endorphins that has been considered as natural painkillers (Sacks & Sachs, 1981), may also have potential to substitute alcohol with exercise (Biddle & Mutrie, 2008).

Why was the intervention chosen to run for 6 months?

This had two reasons:

1) We wanted the participants to start with short bouts of exercise to avoid injuries, and then gradually increase the duration and intensity of the exercise sessions.

2) Many former studies had intervention durations of 3 months, while we wanted to test the long-term effect of the intervention on primary and secondary outcomes. To measure changes on physical outcomes, a shorter intervention period was not found realistic.
There was no sample-size calculation presented. Were the numbers of participants recruited to each arm sufficient to detect a difference between them? This is particularly relevant given that there was a trend towards a significant difference for the pain dimension of EQ5D.

Because the nature of this manuscript which demonstrates findings on secondary outcomes, we did not describe the power calculation and other aspects, which we already have described in our published study protocol. However, we added a comment to the discussion section under limitations, that highlights this issue:

The power calculation for the present study was made on the primary outcome variable. In addition, it proved difficult to recruit the estimated number of participants. It is thus a limitation of the present sub-study that no power calculation was made to estimate the number of included patients necessary to detect differences in relation to changes in quality of life, and we cannot rule out that the present sub-study is under-powered.

The Results section is somewhat underdeveloped. Narrative giving an interpretation of the tables and figure would help the reader. Some of this, such as reference to the scores on the pain dimension is presented in the Discussion and would be better moved to the Results, with the interpretation of this kept in the Discussion.

Thank you for this very helpful comment. We have added more information to the results section.

In the Discussion, some further analysis of why participants didn't benefit from the intervention is needed. Why do the authors believe they obtained different results to those studies presented in the Introduction that found exercise to be beneficial for people with AUD?

We have added the following to the Discussion section:

Compared to other studies, our study had a longer follow-up period, and similarly to Brown et al. we found no effect of the intervention at the six months follow-up. The potential effect of adding exercise interventions to treatment as usual may therefore no longer be existing on long term. An explanation to this could be that participants’ adherence and motivation to exercise decreases in the months after initiation, e.g. due to the lack of an individually tailored exercise program or social support which we found were important reasons to drop out (Sari et al., 2016), and this may explain why no intervention effect was observed at six months follow-up. Nevertheless, the dropout rate in the present study was 37.1%, which is lower than the 40% reported by Hallgren et al. in their recent meta-analysis.

Regarding the discussion of the pain dimension - and of course we should be wary of spending much time on non-significant results - can the authors expand on why this is ‘interesting’?
The section in the Discussion on the meaning of pain (p11, l41 on) does go beyond the scope of the study and the results, so should be removed.

We have elaborated that the finding is interesting as it supports the pain reducing effect of exercise suggested in prior research.

We have removed the section.

A high drop-out rate for people undergoing treatment for AUD does not seem surprising - how does this compare to similar studies?

We have added how our study differs from dropout rates in other studies.

Nevertheless, the dropout rate in the present study was 37.1%, which is lower than the 40% reported by Hallgren et al. [12] in their recent meta-analysis.

Some qualitative work would have helped answer the question of why there was no benefit of exercise and I would suggest this as a recommendation for future research.

We have already conducted and published a qualitative article describing reasons to drop out from the study: Sari, S., Muller, A. E., & Roessler, K. K. (2017). Exercising alcohol patients don’t lack motivation but struggle with structures, emotions and social context - a qualitative dropout study. BMC Family Practice, 18(1), 45. doi:10.1186/s12875-017-0606-4

We also believe that the section added to the discussion in a way explains why the intervention had no effect.

In most of the paper AUD is used, but sometimes AUDs (and SUDs) is adopted. Suggest amending latter for consistency.

Use 'participants' throughout, rather than 'subjects'.

Thank you for your suggestions. We now use AUDs and participants throughout the paper.

John Daniel Mooney, BSc., MPH (Reviewer 2)

As it is currently presented however, the investigation seems to suffer from some key omissions which would enhance the usefulness of the paper. The most central of these in my own opinion is the lack of any information on the extent of the impact which the intervention might have had on the primary outcome of interest for this population, which is surely the impact on respective level of alcohol consumption? Since the exercise intervention is (principally) an 'an adjunctive tool' in the treatment of AUDs', this begs the immediate question of how successful the treatment was?
Thank you for this comment. We have added findings from our primary outcome paper on pages 5-6:

The intervention effect on primary outcome which was consumed amount of alcohol per week showed an OR of 0.99 [95% CI: 0.46; 2.14], p = 0.976 for excessive drinking in the group exercise condition, and 1.02 [95% CI: 0.47; 2.18], p = 0.968 in the individual exercise condition, which, when compared to the control group as reference, did not differ statistically significantly. This may indicate that the AUD treatment itself is successful regardless of the intervention. However, participants with moderate level general physical activity had lower odds for excessive drinking OR = 0.12 [0.05; 0.31], p<0.001 than participants with low level general physical activity. Furthermore, the amount of alcohol consumption in the intervention groups decreased by 4% [95% CI: 0.03; 6.8], p = 0.015 for each increased exercising day. This suggests a dose-response effect of exercise on drinking outcome and supports the need for implementing physically active lifestyles for patients in treatment for alcohol use disorder (Roessler et al., 2017).

Abstract:

Results and conclusion are very minimalist - it might be more interesting to highlight any difference (and its direction) - while of course highlighting that it was not statistically significant (e.g. the results around reported levels of pain and mobility on P11 & P12).

We have added more information to the results section of the abstract.

Methods:

Was randomization blinded for assessors?

No, and we have added this information to the design section, page 6.

P6 lines 12-17, authors say: The treatment offered consists of motivational interviewing, cognitive behavioral therapy and family therapy. Further, acute treatment for withdrawal symptoms and other kinds of pharmacological treatment may also be offered.

It would be useful to have a breakdown of how many participants (from presumably the 'usual care' arm') had each of these treatments, including any treated for withdrawal symptoms.

All participants received treatment as usual (TAU). The exercise intervention was an add-on to the TAU. We have not collected data on treatment type, however the randomization
secures us that all participants are almost equally distributed in the three arms. The most commonly offered treatment approach was cognitive behavioral therapy.

P6 Line 51 - 53: Participants - non completers / drop outs had higher addiction severity scores - not surprising - but check covered in discussion..

Thank you for pointing this out. We have now added this discussion to the limitations section.

P6-P7: 'either alone or in a training group' would be useful to have breakdown of how many were in each. This information is already given in the Participants section, but we have added N in parentheses now.

Discussion

P11: lines: Odd phrasing - not sure what is meant by 'feeling nothing' - is this the authors own interpretation / expression "Is it better to actually feel that you have used your body, even though it hurts, rather than doping your body with drugs and feel nothing?"

We have removed this section as suggested by the other reviewer.