Title: The Efficacy of Motivational Counseling and SMS-reminders on Daily Sitting Time in Patients with Rheumatoid Arthritis: Study Protocol for a Randomized Controlled Trial

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Author's response to reviews: see over
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<th>Comments from reviewer #1</th>
<th>Comments from authors</th>
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<td><strong>1. Will the study design adequately test the hypothesis?</strong></td>
<td>Thank you very much for this important comment. We have added following sentences in the discussion section (page 19): It should be noted that a possible reduction in sitting time, the primary outcome, does not necessarily imply a reduction in CVD risk. However, a possible effect of the intervention on secondary outcomes, CVD biomarkers (cholesterol etc.,) will be simultaneously registered and studied.</td>
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<td>Yes</td>
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<td>The question of whether a sustained (to 18 months) improvement in the CV risk profile results from the 16-week intervention is an interesting one. Patients randomized to counseling and SMS-remainders vs control (usual care). The hypothesis is that the intervention will reduce inactivity and thereby reduce CV risk, consistent with the possibility that the increase in CV risk in RA is, in part at least, due to inactivity. However, to substantiate a clinical value the reduction in inactivity needs not only to be shown but the less inactivity needs to be shown to translate into a reduced CV risk via a CV outcome study or via an improvement in CV risk profile. [This is the classic surrogate scenario: Inactivity associated with increased CV disease risk does NOT, without evidence, imply that a reduction in activity will be associated with a reduction in CV disease outcomes.] The authors have the option to include this in the discussion this or not. It is not essential.</td>
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<td><strong>2. Sufficient detail to allow replication?</strong></td>
<td>Thank you for these comments and questions. First of all, the primary outcome is “Reduction in total daily sitting time in minutes from baseline to 16 weeks” (Page 6 “Objectives”) which has been corrected at page 11 “Primary outcome measure”). The patient-self-reported sitting time has been removed from “Primary outcome measure” to “Secondary outcome measures” (page 11) to avoid the risk of “a win in one, but not the other”.</td>
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<td>Yes, if below is clarified</td>
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<td><strong>3. Statistical analysis appropriate?</strong></td>
<td>Regarding power calculation we have the following comments. The primary end-point is change reduction in total daily sitting time and</td>
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<td>Essential clarifications: Can you clarify which specific primary endpoint was used in the pilot study on which the statistical power of this study is based. The primary outcome is the ACTivPAL@3 TM Activity Monitor (“objectively measured” is called the primary endpoint on page 6). I assume that it was ACTivPAL rather than patient self-reported sitting time that is used in the power calculation. Please provide further information on powering of the trial to clarify in the manuscript. On page 11 both the ACTivPAL and the self-reported sitting time are described as primary. What happens if a win in one but not</td>
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<th>4. Writing acceptable?</th>
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**The power calculation is based on data from ActivPal from the feasibility study measured as “total daily sitting time”. This has been clarified at page 8.**

**Additional (i) Please discuss whether wearing ACTivPAL@3 TM Activity Monitor may be seen as an 'intervention' in itself therefore reduce the size of the between arm difference. Is this something that needs to be factored into the sample size calculation? Please comment and clarify in the manuscript.**

This is an important issue to highlight. We have added following sentence at page 15 (data collection):

*All ActivPAL will be coded to start from midnight on following the first day of application.*

Furthermore, following has been added in the discussion section (page 19):

*We cannot rule out that wearing an ActivPAL may cause reactivity and as such in itself act as a “behavioral intervention”. However, participants in both groups are measured at baseline and follow-up, and the size of the between arm difference is therefore not likely to be affected or considered in the sample size calculation. Also ActivPAL monitors start measuring from midnight following the first day of application in order to minimize reactivity by allowing participants to get used to wearing the device. Finally, the ActivPAL measurements are not shown to participants until after the study is completed.*

**Thank you very much for this point. At page 9 and 15 we have clarified that: Patients will not be blinded to the intervention.**

In addition, we have added following (page 19: discussion-section):

*In behavioral intervention RCT’s patients are difficult to blind completely. We could have offered the control group participants a “sham” counseling intervention with counseling on something else than reduction of sedentary behavior. However, this could...*
Potentially induce an effect in the control group which we wanted to avoid.

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| **1.** Minor essential revisions:  
  • I think it should be described how the independent variable is controlled: will the control group be assessed for MI counseling (or other similar counseling) during the trial? As they have signed up for the study they may well be interested in changing their sitting time.  
  
  We agree that patients from the control may be interested in the intervention since they have shown interest in the trial. Therefore, to avoid contamination we will offer patients from the control group an information session about the principles of the intervention when the trial is completed.  
  
  Because “reduction of sedentary behavior” is relatively new research area and definitely new to the group of RA patients, we consider it unlikely that they will look for specific intervention targeted reduction of sedentary behavior. We have chosen not to ask them whether they look for any intervention aiming to reduce their sedentary time. Therefore we expect the risk of contamination between the groups to be minimal.  |
| **2.** Manipulation check should also be described – how will you check that the counselors delivered what was intended and how much reached the participants in the intervention group?  
  
  Following sentence has been added at page 9: Counselors will simultaneously be trained and supervised by a psychologist to ensure that the intervention will be delivered in a similar way based on the theoretical understanding of MI.  
  
  In addition, we have added following at page 10: After the intervention, all intervention group participants will fill out a questionnaire on process, side effects, quality and impact of intervention. |
| **3.** Discretionary revisions:  
  • To achieve a long-term decrease in sitting time, i.e. maintenance, the intervention should include plans for relapse prevention and booster sessions over longer time. Sixteen  
  
  We agree that relapse prevention and booster sessions are important issues to consider in behavioral change studies. However, as this – to our knowledge - is the first study to investigate reduction of sedentary behavior in a group of RA patients, our primary aims were to test |
weeks may be a short time to achieve sustainable change. Whether it is at all possible to reduce sedentary behavior by motivational counseling in this group of patients (the immediate post-intervention effect) and secondarily whether a possible effect would be sustained in the longer term (maintenance).

4. The self-efficacy measure is not optimal as it does not assess self-efficacy for the specific behaviors targeted in this trial. A measure of generic self-efficacy cannot be expected to be sensitive for change in this context. Development of items according to Bandura’s “Instructions for construction of self-efficacy scales” could be a useful alternative.

We agree that the general self-efficacy measure is not optimal as it does not specifically target sedentary behavior. We choose the general self-efficacy scale over the “self-efficacy to regulate exercise”, because the distinction between reduction of sedentary behavior and promotion of exercise is essential in this study and the intervention specifically targets reduction of sedentary behavior, and does not include promotion of exercise. In addition, the general self-efficacy scale has been translated into Danish.

We thank the reviewer for suggesting Bandura’s “Instructions for construction of self-efficacy scales”.

Additional changes being made after revision of the manuscript

| a) | Page 16: Following sentence “Furthermore, for the purpose of sensitivity analysis and to confirm the robustness of the findings, we will run the analyses where missing data have been imputed by Multiple Imputation. The same rationale applies for the 'as observed' analyses where we will not use any missing data....” has been revised to We will run the analyses where missing data are imputed by Multiple Imputation. For sensitivity we will also perform analyses on 'as observed' analyses where we will not use any missing data. |
| b) | Page 10: Instead of this sentence “The intervention program focuses on 4 key messages or themes, including ideas and suggestions for reduction of sitting time, which are written in booklets that will be handed to the patients at each session” we had made following change: In addition to the motivational counseling 4 key messages or |
themes, including ideas and suggestions for reduction of sitting time (written in booklets), will be handed to the patients at each session.

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<td>c)</td>
<td>Page 20: In the sentence: “The intervention is simple and could relatively easily be implemented in clinical practice along with lifestyle advice and recommendations on …” we have added: “…” physical activity, sports and exercise, diet and smoking habits.</td>
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