Resubmission of manuscript to Trials

Dear Editors,

thank you for considering our manuscript “Evaluating a collaborative smoking cessation intervention in primary care (ENTER): study protocol for a cluster-randomized controlled trial” for publication in Trials.

Please find attached the revised manuscript version. We have addressed your editorial requests and the reviewer’s comments as follows:

Editorial requests:

1. Please ensure the title conforms to journal style for study protocol articles. The title should follow the format “_________: study protocol for a randomized controlled trial”. Please note that the title in the submission system should match that of your manuscript.

   We have changed the title as requested and adapted it accordingly in the submission system.

2. Please include a statement in your Methods section explaining that you obtained informed consent from each participant.

   The informed consent procedure is specified under the sub-heading “study procedure” of the method section as follows: “Patients who wish to participate in the study will be asked to provide their contact details on a separate form and complete the first questionnaire (t0) during the waiting time along with the informed consent form and a contact information sheet.”

3. We would appreciate it if you could upload your revised manuscript in a word document, as unfortunately our system no longer supports PDF files.

   We have uploaded the revised manuscript in a word document and formatted it according to the journal style.

Reviewer’s comments:

1. Please provide additional detail on economic analysis, it is clear a cost-utility analysis is being planned. Please provide perspective (patient, health care system, insurer) and what/how costs will be calculated of the intervention but also if appropriate the medical costs savings.

   The analysis adopts the perspective of the German statutory health insurance. Costs will be calculated based on claims data provided by the health insurance. Costs of the intervention will be estimated following a micro-costing approach. We added relevant information to the...
manuscript (p. 11, line 210-20). Whether medical cost savings (i.e., reductions in medical costs covered by the health insurance) can be expected in the short-term is unclear. If the intervention proves effective, the costs of smoking sequelae might be reduced. We added a statement on the the possible economic impact to the discussion section (p.17, l. 355-57).

2. Para 285 – please provide more details on effect size assumptions. The calculations used are based on 30% abstinence rate at 12-months. This appears to be consistent with eval of program (as per discussion) reference this in the sample size justification and/or if it is based on another source then note that. I did not see reference to what we assumed cessation rate would be in control group – this should be added and it was unclear to me if this was considered in the sample size calculation. If I am correctly understanding the assumption is 10% in control 30% intervention with difference of 20%. If this is the case – make this more overt so we are not guessing. 
The estimated effect size has been derived from the meta-analysis by Stead et al., (2008) which concludes that among at-risk patients the relative risk of being abstinent from smoking at follow-up is 1.65 for participants of intensive interventions, compared to participants of minimal interventions (with approximately twelve and seven percent cessation rates in the intervention and control groups, respectively). The figure .30 describes a standardized mean difference (Cohen’s d) that corresponds to this effect. The transformation is necessary, because our primary outcome is measure on a metric rather than a categorical scale. We have clarified the manuscript text accordingly.

3. Para 290 – please provide a source to support the ICC of 0.05.
   We have included two references in support of an ICC of 0.05 in the revised manuscript.

4. Please identify how patients lost to follow-up will be treated in the analysis ie. Assumed to have returned to smoking, replaced with imputation, removed from analysis.
   For the analysis of cessation rates, we will assume that patients lost to follow-up have returned to smoking. We amended the manuscript accordingly and included two supporting references.

Minor Essential Revisions:

5. Title page – add country to institutional affiliations
   The country of the institutional affiliations has been specified on the title page.

6. Para 165 – inclusion criteria, please provide rationale for inclusion of only heavy smokers and/or suffer from COPD or heart disease.
   Heavy smokers are at a high risk of developing smoking-related diseases and benefit most from smoking cessation programs which is why this criterion has been chosen. Moreover, smoking cessation is essential to slow the progression of smoking-related diseases which is why patients suffering from COPD/cardiovascular diseases were also found suitable for inclusion in the study.

7. Para 175 – provide detail on how presence COPD and/or heart disease will be assessed ie. standardized test, physician diagnosis, event etc.
   The presence of COPD and/or heart disease will be diagnosed and documented by the patient’s physician and this has now been detailed in the manuscript version.

8. Para 230 - 1st sentence, repetitive, please remove
   The repetition has been removed.

9. Please add declaration of conflict of interest statements for co-authors.
The declaration of conflict of interest has been adjusted and now refers to all authors.

Please do not hesitate to contact me should you have any questions. I look forward to hearing from you.

Sincerely,

Anna-Lena Bartsch (on behalf of all authors)