Author’s response to reviews

Title: Effects of a partially supervised conditioning programme in cystic fibrosis: an international multi-centre randomised controlled trial (ACTIVATE-CF): Study Protocol

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Author’s response to reviews:

Dear Cecilia Devoto,

Below we respond to your comments, which are included in this letter.

Technical Comments:

1. Please remove the trial registration number from the title.

Done. We have added the acronym (ACTIVATE-CF) in the title as suggested in the SPIRIT Guidelines
2. In the last section of the abstract named Trial Registration please listing the trial registry, the unique identifying number and the date of registration.

Done.

3. Please remove the table with the list of study site investigators from the main ms.

Done.

4. After the Discussion, please add a list of abbreviations.

Done (page 21).

5. After the list of abbreviations, please add the heading "Declarations" followed by the following sub-headings in the order below:

We have added a list of abbreviations, as suggested.

Declarations (please remove the statement "The authors declare no competing interests") from here as this should be under the competing interests sub-heading.

- Ethics approval and consent to participate
- Consent to publish
- Availability of data and materials
- Competing interests
- Funding
- Authors' Contributions
- Acknowledgements - if there is no one to acknowledge, please write "Not applicable".

We have changed the order as requested.

6. In the Declarations section, under the heading "Ethics approval and consent to participate", we notice two discrepancies:

- In the table with the list of study sites, you list the Clinic for Pulmonology, Munich-Pasing, as one of the study sites and you provided proof of ethical approval, yet they are not included in the "Ethics approval and consent to participate" section. Please add them.

Thank you. The missing information has been added: „Ethik-Kommission bei der Ludwig Maximilians Universität München, München, Germany“
- In the table with the list of study sites, you list the Royal Hospital for Sick Children, Edinburgh as one of the study sites and you provided proof of ethical approval, yet under the heading "Ethics approval and consent to participate" you name West of Scotland Research Ethics Service; Glasgow, UK. Please clarify and amend accordingly. If you have ethical proofs form this centre, please send them to BMCSeriesEditorial@biomedcentral.com, as we will need to see them.

Please find the detailed response from our collaborator Don Urquhart (E-mail communication 14.11.2017)

RE: ACTIVATE-CF AND ETHICS APPROVAL

The UK runs a generic UK-wide Ethics submission service

This is known as the Integrated Research Application System (or IRAS)

All research ethics applications are made using IRAS (www.myresearchproject.org.uk)

Once an ethics form has been completed, you are advised of upcoming ethics committees that would consider your submission.

They REC that considers an application can be anywhere in the UK.

I have had Ethics submissions heard in North West England, East Scotland (Dundee), as well as both Edinburgh and Glasgow.

Often RECs will consider an application in absentia but with telephone discussions if needed.

A local REC is clearly beneficial if you intend to attend in person.

I attended the West of Scotland REC (WoSREC)in Glasgow [1 hour by car from Edinburgh] and the ACTIVATE-CF application was heard by and approved by WoSREC.

The application was made with Edinburgh as the only site.

Each study submitted via IRAS also requires local research and development (R+D) approval, with each study site completing a site-specific investigation form (SSI).

Thus IRAS involves REC application (ethical approval for study), R+D approval (institution-specific) , site approval (SSI).

I have attached

1. Ethics approval
- Initial provisional opinion October 2014

-Favourable opinion (Ethics approval) December 2014

[I also have acknowledgement letters for 2 minor amendments that were made and accepted in 2015 and 2016 that can be sent on if required]

2. R+D Approval

- NHS Lothian approval to carry out ACTIVATE-CF study in my institution

I trust that this clarifies the situation satisfactorily.

Best wishes

Don Urquhart

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7. The contributions of Dr Chantal Karila (CK) are not listed in the Authors' contributions section.

Thanks. The contribution of Dr Chantal Karila was added to this section.

8. In accordance with BioMed Central editorial policies (http://www.biomedcentral.com/submissions/editorial-policies#standards+of+reporting), could you please ensure your manuscript reporting adheres to SPIRIT guidelines (http://www.spirit-statement.org/) for reporting study protocols. This is so your methodology can be fully evaluated and utilized.

Can you please include a completed SPIRIT checklist as an additional file when submitting your revised manuscript.

We now provide a SPIRIT checklist with our revised manuscript.

9. On uploading your revisions, please remove any tracked changes or highlighting and include only a single clean copy of the manuscript.
Done.

10. After the References please add a section called "Figures", where you list the following information: * Title of data (e.g. Figure 1) and * Description of data.

Done (p 29).