

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

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| TITLE (PROVISIONAL) | The effectiveness of a mobile preconception lifestyle programme in couples undergoing in vitro fertilisation (IVF): the protocol for the PreLiFe randomised controlled trial (PreLiFe-RCT) |
| AUTHORS | Boedt, Tessy; Dancet, Eline; Lie Fong, Sharon; Peeraer, Karen; De Neubourg, Diane; Pelckmans, Sofie; van de Vijver, Arne; Seghers, Jan; Van der Gucht, Katleen; Van Calster, Ben; Spiessens, Carl; Matthys, Christophe |

VERSION 1 - REVIEW

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| REVIEWER | Trine Tegdan Moholdt Norwegian University of Science and Technology |
| REVIEW RETURNED | 17-Feb-2019 |

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| GENERAL COMMENTS | <p>I read this manuscript with great interest. The research question is highly interesting and the study design is good. I only have a couple of minor comments to the manuscript:</p> <p>Abstract: I suggest that you include the number of participants in your abstract.</p> <p>Page 7, lines 40-41: I think you should specify that "A deviation of up to two weeks before and after the planned time of measurement is allowed."</p> |
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| REVIEWER | Robert Norman Robinson Research Institute, University of Adelaide FertilitySA Australia |
| REVIEW RETURNED | 25-Feb-2019 |

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| GENERAL COMMENTS | <p>This is a welcome study as lifestyle introduction has failed in almost every non-research study and group so far. The results from RCTs from the Netherlands and Denmark currently provide confusing conclusions for patients and clinicians.</p> <p>1. The authors should look at the AskPCOS app seeking similar outcomes for PCOS subjects. It is far more for patient information but has some similar topics that could be used</p> |
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| | <p>2. How will they sort out the fact that there may be very little time for subjects to change their habits before IVF - should they not have a fixed lead in time free from treatment?</p> <p>3. How will they manage a pregnancy that has not reached 12 weeks but the patient is now 12 months from commencement?</p> <p>4. Why is the general health questionnaire not one that has been validated while all the others have been?</p> |
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VERSION 1 – AUTHOR RESPONSE

Regarding the following comments of reviewer 1 (Trine Tegdan Moholdt):

1. Abstract: I suggest that you include the number of participants in your abstract.
2. Page 7, lines 40-41: I think you should specify that "A deviation of <u>up to</u> two weeks before and after the planned time of measurement is allowed."

We would like to thank the reviewer for pointing this out. We included the number of participants in our abstract and we specified the deviation of time of measurement.

Regarding the following comments of reviewer 2 (Robert Norman):

1. The authors should look at the AskPCOS app seeking similar outcomes for PCOS subjects. It is far more for patient information but has some similar topics that could be used
2. How will they sort out the fact that there may be very little time for subjects to change their habits before IVF - should they not have a fixed lead in time free from treatment?
3. How will they manage a pregnancy that has not reached 12 weeks but the patient is now 12 months from commencement?
4. Why is the general health questionnaire not one that has been validated while all the others have been?

We would like to thank the reviewer for pointing this out. We have tried to clarify these comments in the protocol and in summary below.

1. We want to thank you for referring us to the AskPCOS app. We love the exemplary FODMAP app on diet and the AskPCOS app on PCOS of Monash University. Like the AskPCOS app, we provide evidence-based information organized around frequently asked questions. We do not, however, provide information on the condition of infertility, its impact and medical treatment, since our app will be used in a general infertile population; it was deemed that this information may be too extensive for our app. Like the FODMAP app, we provide dietary advice, including recipes besides information on necessary ingredients. Whereas these two inspiring Monash University apps refer patients to good health care professionals, our PreLiFe app is disseminated by and intertwined with the practice of participating health care professionals which will guarantee the valorization of the app.
2. Regarding the time for subjects to change their habits: It is indeed true that for some subject there is little time to change their habits. It is a nice suggestion to have a fixed time lead in time free from treatment, we also discussed this in the development of our study. However, In Belgium we do not have a waiting list for IVF in which we could offer the PreLiFe-programme. Also, from qualitative interviews with both patients and health care providers we noted that they were not willing to wait. Therefore, the PreLiFe-programme indeed starts right before the start of IVF. To avoid interference with the feasibility of the study and the clinical practice, consequently we decided to have a flexible time lead. However, we will definitely capture the time between start of study (offering PreLiFe-programme) and start of IVF. Furthermore, we integrated this comment as a limitation of our study in our manuscript.

3. Regarding the follow up of pregnancies: All pregnancies occurring within 12 months after randomization will be followed up until 12 weeks of gestational age (12 weeks ultrasound scan). Patients remain in the study and continue using the PreLiFe-programme until they have reached a 12 weeks pregnancy. Patients who have an early miscarriage remain in the study for the remainder of their 12 months study period. Therefore, patients might attempt to achieve another pregnancy within the study period. Thank you for this useful suggestion. We have tried to clarify this in the protocol.
4. Regarding the general health questionnaire and background questions, we used questions from validated scales (smoking), in combination with questions from previous research by our group and new questions; therefore, we noted this as self-developed. Currently there is no Dutch validated version on the combination of questions that we ask. We adapted the name of the questionnaire in the protocol.

VERSION 2 – REVIEW

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| REVIEWER | Robert Norman University of Adelaide Australia |
| REVIEW RETURNED | 11-May-2019 |

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| GENERAL COMMENTS | This is an interesting protocol which should help in determining the better pathways for lifestyle advice dissemination |
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VERSION 2 – AUTHOR RESPONSE

Thank you very much for accepting our manuscript "The effectiveness of a mobile preconception lifestyle programme in couples undergoing in vitro fertilisation (IVF): the protocol for the PreLiFe randomised controlled trial (PreLiFe-RCT)" for publication.

We revised our manuscript a second time according to your recommendations and on behalf of all authors would like to provide you with the following answers, point by point to clarify our decisions on the changes that we have included in the new manuscript. The second revisions are marked in yellow in the word document: "Manuscript_Boedt_et_al_PreLiFe_protocol_BMJ_as submitted_SECONDREVISIONS-MARKED COPY"

1. We revised our manuscript (on page 14 – Availability of data and material) to confirm that data from our trial will be made available on reasonable request once the results are published.
2. We updated the trial registry (clinicaltrials.gov) to include the data sharing plan.
3. We corrected the following typo on page 7 line 42 - "A deviation of two weeks before AND up to two weeks after..."